



March 20-24, 2026
Boston Marriott
Copley Place



Boston, MA

North American Neuro-Ophthalmology Society

1975-2026





North American Neuro-Ophthalmology Society

52nd Annual Meeting

March 20-24, 2026; On Demand April 20 – December 31, 2026
Boston Marriott Copley Place, Boston, MA

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CME ACTIVITIES FACULTY AND PLANNER DISCLOSURE STATEMENTS



JOINTLY ACCREDITED PROVIDER™
INTERPROFESSIONAL CONTINUING EDUCATION

In support of improving patient care, this activity has been planned and implemented by Medical Education Resources (MER) and North American Neuro-Ophthalmology Society (NANOS). MER is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

STATEMENT OF NEED

The purpose of the North American Neuro-Ophthalmology Society's Continuing Medical Education (CME) program is to present neuro-ophthalmologists with quality lifelong learning opportunities to promote improvement and change in physician practices, performance, and competence needed to provide the best possible neuro-ophthalmic care for their patients.

EDUCATIONAL OBJECTIVES

After completing this activity, the participant should be better able to:

- Identify recent advances in the diagnosis and treatment of neuro-ophthalmic diseases.
- Identify advances in key areas of cutting-edge research and technology in neuro-ophthalmology.
- Apply skills and techniques from the educational sessions into their daily practice.

MISSION STATEMENT

The North American Neuro-Ophthalmology Society (NANOS) is dedicated to achieving inclusive excellence in the care of patients with neuro-ophthalmic diseases by the support and promotion of equitable education, research, and the practice of Neuro-Ophthalmology.

TARGET AUDIENCE

This activity has been designed to meet the educational needs of neuro-ophthalmologists (neurologists and ophthalmologists) involved in the care of patients with neuro-ophthalmic disorders.

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Beau	Bruce	MD, PhD	Speaker, Planner	Bayer, Eli Lilly	Consultant
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Andrew (Drew)	Carey	MD	Speaker, Planner	Bristol Myers Squibb, Springer Publishing	Advisor, Consultant, Royalties or patent beneficiary
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Jointly provided by Medical Education Resources and the North American Neuro-Ophthalmology Society.

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57th Frank B. Walsh Symposium

Host: Harvard Medical School

Lead Host: Gena Heidary, MD, PhD

Host Committee Members:

Joseph Rizzo III, MD; Eric Gaier, MD, PhD; Ryan Gise, MD; Tais Estrela, MD

Expert Panel:

Neuroradiologist: Mary Beth Cunnane, MD

Neuropathologists: Matthew Frosch, MD, PhD; Anna M. Stagner, MD

These sessions will present complex cases that impact the visual pathways and ocular motor systems. The format is a clinicopathologic conference. Clinical cases will be presented by neuro-ophthalmologists with comments by invited experts in neuro-radiology and neuro-pathology. Neuroimaging, laboratory, and surgical pathology data will illustrate clinical points. Cases will be discussed from clinical, anatomic, radiologic, and pathologic aspects with emphasis on diagnosis, pathophysiology, and management.

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Neuroimaging, laboratory, and surgical pathology data will illustrate clinical points. Cases will be discussed from clinical, anatomic, radiologic, and pathologic aspects with emphasis on diagnosis, pathophysiology, and management.

Upon completion of these sessions, participants should be able to:

- (1) Describe the varied clinical presentations of neuro-ophthalmic disease.
- (2) Formulate effective diagnostic testing strategies for complex neuro-ophthalmic cases including the use of new diagnostic tests.
- (3) Explain the value and limitations of neuropathology and neuroimaging.
- (4) Identify newly described neuro-ophthalmic diseases in clinical practice.

Frank B. Walsh I [2.0 CME]

Moderators: Joseph Rizzo III, MD; Nurhan Torun, MD; Bart Chwalisz, MD

8:00 am – 8:15 am	Welcome/Introduction , Heather Moss, MD, PhD; John Chen, MD, PhD; Lindsay DeLott MD, MS; Gena Heidary, MD, PhD & Joseph Rizzo III, MD
8:15 am – 8:35 am	Bright Ain't Right: When Optic Nerve Enhancement Persists , Lauren Colwell, MD
8:35 am – 8:55 am	More than Skin Deep: When the Skin Talks and the Brain Listens , Sannah Vasaya, DO
8:55 am – 9:15 am	A Diagnosis in Plain Sight , Stephanie Syc-Mazurek, MD, PhD
9:15 am – 9:35 am	DNA on Tap , Sydney R. Roston, MD
9:15 am – 9:35 am	Acute Monocular Vision Loss: A Diagnostic Labyrinth , J. Tatiana Hathaway, MD, MPH
9:55 am – 10:00 am	Wrap Up , Joseph Rizzo III, MD; Nurhan Torun, MD; Bart Chwalisz, MD

Frank B. Walsh II [2.0 CME]

Moderators: Tais Estrela, MD; Robert Mallery, MD; Marc Bouffard, MD

10:30 am - 10:35 am	Introduction , Tais Estrela, MD; Robert Mallery, MD; Marc Bouffard, MD
10:35 am – 10:55 am	A Wolf in Sheep's Coating , Sahar Noorani, MD
10:55 am – 11:15 am	Beyond the Usual Suspects: When Painless Progressive Vision Loss and Neuroimaging Don't Align , Neringa Jurkute, MD, PhD, FEBO
11:15 am – 11:35 am	Hummingbird -A Jabbing and Terrifying Monster , Shikha Bassi Talwar, FRCS
11:35 am – 11:55 am	When the Retina Spoke Up , Sumana Naidu, MD
11:55 am – 12:15 pm	If Referred by Retina, it's Retinal...or Not? , Abigail Healy, MD

12:15 pm – 12:20 pm
12:20 pm – 12:30 pm

Wrap-Up, *Tais Estrela, MD; Robert Mallery, MD; Marc Bouffard, MD*
NANOS Award presentations

Frank B. Walsh III [2.0 CME]

Moderators: Gena Heidary, MD, PhD; Eric Gaier, MD, PhD; Ryan Gise, MD

3:30 pm - 3:35 pm

Introduction, *Gena Heidary, MD, PhD; Eric Gaier, MD, PhD; Ryan Gise, MD*

3:35 pm – 3:55 pm

A Diagnosis Bubbles to the Surface, *Madhura Shah, MD*

3:55 pm – 4:15 pm

One gene to explain them all?, *Jorge Cárdenas-Belaunzarán, MD, MSc*

4:15 pm – 4:35 pm

Hidden in Not So Plain Sight, *Steven F. Stasheff, MD, PhD*

4:35 pm – 4:55 pm

Low Visibility & An Air Traffic Control Outage, *Aaron Warning, MD*

4:55 pm – 5:15 pm

In the Garden of the Rare Blooms the Profound, *Zofia Hetman, MD*

5:15 pm – 5:20 pm

Wrap-up *Gena Heidary, MD, PhD; Eric Gaier, MD, PhD; Ryan Gise, MD*

5:20 pm – 5:30 pm

Closing remarks, *John Chen, MD, PhD and Lindsey De Lott, MD, MS*

“Bright Ain’t Right: When Optic Nerve Enhancement Persists”

Lauren Colwell¹, Rebecca Silverman¹, Jurij Bilyk¹, Sarah Thornton¹

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History & Exam: A 78-year-old man with hypertension and hyperlipidemia presented with chronic vision loss in the right eye. Six months prior to presentation, he experienced painless vision loss upon awakening. He was seen at an outside hospital where he underwent MRI of the brain and orbits demonstrating right optic nerve enhancement concerning for optic neuritis. He was treated with high-dose corticosteroids, but his vision did not improve. When he presented to our facility, his vision measured count fingers at 1 foot in the right eye and 20/20 in the left eye. He was unable to identify Ishihara color plates in the right eye, but had normal color vision in the left eye. There was a 2+ relative afferent pupillary defect in the right eye and confrontation visual field testing demonstrated marked constriction in the right eye. External examination revealed mild right upper lid ptosis and limited supraduction (70%) in the right eye. Fundoscopy revealed right optic nerve edema and vitreous cells. Repeat MRI showed progressive enhancement of the right optic nerve. Laboratory evaluation was notable for ESR 59 mm/hr, CRP 1.2 mg/dL (reference < 0.8), and platelet count of 467. An infectious and inflammatory workup was pursued including negative NMO, MOG, ACE, syphilis, tuberculosis, lyme. Lumbar puncture revealed WBC 30/ μ L, glucose 74 mg/dL, and protein 40 mg/dL. No detectable infection on cerebrospinal fluid PCR panel. Flow cytometry showed predominately T lymphocytes with normal morphology. CT scan of the chest, abdomen and pelvis with contrast showed no suspicious lesions. Given the vitreous cells, the patient underwent vitreous biopsy which was unrevealing. Optic nerve biopsy identified an astrocytic neoplasm with pleomorphic, GFAP and OLIG2 positive cells. Mitotic figures were present and the Ki67 index was elevated. Molecular analysis identified a p53 mutation without IDH-1 or IDH-2 mutations.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

“Bright Ain’t Right: When Optic Nerve Enhancement Persists”

Answer

Final Diagnosis: Glioblastoma IDH-Wild type, CNS WHO grade 4 (MOGA)

Summary of Case: A 78-year-old man with hypertension and hyperlipidemia presented with chronic painless vision loss in right eye upon waking. The differential for the patient’s optic neuropathy was broad- initially optic neuritis was suspected, but high dose steroids did not improve the vision. He was found to have progressive optic nerve enhancement on MRI. Ultimately his aggressive disease and unclear diagnosis, an optic nerve biopsy was pursued to diagnose malignant optic nerve glioma (MOGA). MOGA is a rare entity, first recognized in 1973 [1], and it is often considered only after other diagnoses have been excluded and tissue confirmation is obtained [2, 3]. Current treatment options are limited to radiation and chemotherapy, as surgical debulking is generally not feasible. The prognosis remains poor, with most patient dying within months to one year after diagnosis [4]. Various chemotherapy regimens have been trialed [5], but large-scale analyses are challenging due to the rarity of the disease. Our patient received intensity-modulated stereotactic radiotherapy as part of a research trial, designed to reduce radiation toxicity [6]. To date our patient is alive and living independently with functioning vision in his left eye 1.5 years following his biopsy.

Struggle/Dilemma of the Clinical Presentation Description: An extensive evaluation including vitreous biopsy and full-body imaging failed to reveal a diagnosis, and optic nerve biopsy was necessary. The surgical access to the canicular segment of the optic nerve was challenging and required a multidisciplinary skull base team. This case highlights the complex decision-making involved in optic nerve biopsy, as diagnostic necessity must be balanced against the vision loss. The patient’s vision declined from bare light perception to no light perception following biopsy.

Keywords: Optic nerve tumors, Vision loss, Chemotherapy

References: 1. Hoyt, William F., et al. "Malignant optic glioma of adulthood." *Brain* 96.1 (1973): 121-132. 2. Albers, Gregory W., et al. "Treatment response in malignant optic glioma of adulthood." *Neurology* 38.7 (1988): 1071-1071. 3. Wabbels, Bettina, et al. "Unilateral adult malignant optic nerve glioma." *Graefe's Archive for Clinical and Experimental Ophthalmology* 42.9 (2004): 741-748. 4. Albers, Gregory W., et al. "Treatment response in malignant optic glioma of adulthood." *Neurology* 38.7 (1988): 1071-1071. 5. Ashur-Fabian, Osnat, et al. "Long-term response in high-grade optic glioma treated with medically induced hypothyroidism and carboplatin: a case report and review of the literature." *Anti-cancer drugs* 24.3 (2013): 315-323. 6. Narayana, Ashwatha, et al. "Intensity-modulated radiotherapy in high-grade gliomas: clinical and dosimetric results." *International Journal of Radiation Oncology* Biology* Physics* 64.3 (2006): 892-897.

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“More than Skin Deep: When the Skin Talks and the Brain Listens”

Sannah Vasaya¹, Akbar Shakoor², Alexander Varma³, Paul Crane², Alison Crum², Bradley Katz⁴, Judith Warner⁵, Kathleen Digre⁵, Sravanthi Vegunta², Meagan Seay⁶

¹ Moran Eye Center, ² University of Utah, ³ University of Colorado, ⁴ University of Utah Health, ⁵ University of Utah Medical Center, ⁶ University of Utah, Moran Eye Center

History & Exam: A 29-year-old female initially presented to neuro-ophthalmology in 2019 with episodic diplopia, vertigo, and disequilibrium that was invariably followed by a throbbing bi-occipital headache. She had diagnoses of seronegative juvenile idiopathic arthritis, linear scleroderma, and cutaneous polyarteritis nodosa via skin biopsy. Given her history of migraines with visual aura and normal examination, she was diagnosed with basilar migraines. In December of 2020, she had a nearly identical episode, however of acute onset, without subsequent headache, and tetra-paresthesias. Her MRI brain showed punctate bilateral pontomedullary infarcts, but her stroke workup including angiography, vessel wall MR, echocardiogram, lumbar puncture, and extensive serological workup was normal beyond mildly elevated inflammatory markers and did not reveal a clear etiology. She was presumed to have polyarteritis nodosa-associated strokes (PANAS) due to a missed dose of rituximab. She continued to have recurrent sinusitis and urinary tract infections, vasculitic rash, length-dependent peripheral neuropathy attributed to PAN-related compressive neuropathy, hypogammaglobulinemia attributed to rituximab, and had developed Raynaud’s phenomenon. Her rituximab was stopped in December 2022 by her new rheumatologist who favored Sneddon syndrome over PAN. In April of 2024 she presented with acute painless vision loss in her right eye; examination revealed a vision of light perception, minimally reactive pupil, retinal whitening in the macula with a cherry red spot, and arteriolar narrowing around the proximal temporal arcades. MRI brain showed diffusion restriction of the posterior right globe, and subtle enhancement of the right optic nerve. She was treated with hyperbaric oxygen therapy for her central retinal artery occlusion. Her stroke workup was again unrevealing, and the CRAO was attributed to being off rituximab and aspirin while being started on tranexamic acid. Fluorescein angiography done one month later showed nonperfusion in the macula and leakage of the disc and peripheral capillaries. A diagnostic procedure was performed.

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“More than Skin Deep: When the Skin Talks and the Brain Listens”

Answer

Final Diagnosis: This patient has deficiency of adenosine deaminase 2 (DADA2), specifically the inflammatory/vasculitis phenotype with some overlapping features of the immunodeficient phenotype.[4] Deficiency of adenosine deaminase type 2 is an inherited autoinflammatory condition characterized by systemic inflammation, vasculitis, early-age stroke, cytopenias, and mild immunodeficiency. There are four phenotypes - inflammatory/vasculitic, hematologic, immunodeficient, and presymptomatic. The underlying cause of DADA2 is a biallelic loss of function mutation in adenosine deaminase type 2, which is mainly expressed by myeloid cells. Its deficiency causes compromise of endothelial integrity causing perivascular inflammation, presumed to be due to over activation of neutrophils. This can lead to vessel abnormalities including stenosis, aneurysm, and perforation. [4] The theorized pathogenesis is a combination of skewed production of pro-inflammatory versus anti-inflammatory macrophages and excessive production of neutrophils leading to an abundance of tumor necrosis factor (TNF). Most notably, DADA2 can be treated effectively with TNFa inhibitors for stroke prevention.[2][3] The most common neurological manifestation is stroke – typically brainstem or deep gray matter – with additional manifestations including focal neurological deficits, neuropathy, posterior reversible encephalopathy syndrome, seizures, headaches, neurocognitive disorders, and ophthalmologic findings including strabismus and vision loss.[2]

Summary of Case: Since the age of 8, this patient has had various manifestations of her poly-autoimmunity despite treatment with multiple immunosuppressants including tocilizumab and etanercept in childhood, then methotrexate, hydroxychloroquine, azathioprine, cyclophosphamide, rituximab, and mycophenolate. Her earliest skin biopsy was in 1999 confirmatory for linear scleroderma/morphea. She had done well until the birth of her daughter in 2010 when her arthritis and rash flared. In 2015 she developed a rash consistent with livedo vasculitis with skin biopsy in 2016 which showed findings consistent with small to medium vessel vasculitis and IgA deposits on direct immunofluorescence. This prompted a diagnosis of cutaneous PAN which held until late 2022 when the combination of a normal musculoskeletal ultrasound without evidence of inflammation in the presence of symptoms, plus livedo racemosa and early stroke raised suspicion for Sneddon syndrome. There is no treatment for Sneddon syndrome, only recommendations for antithrombotic therapy for stroke prevention and consideration for immunosuppression in severe cases. [1] At this point, her rituximab was stopped but she remained on azathioprine. After her CRAO, due to her diagnostic uncertainty and two ischemic events specifically while off rituximab, her infusions were resumed and she was started on steroids. A new rheumatologist, prompted by her history of PAN, early stroke, and hypogammaglobulinemia, ordered genetic testing for mutation of adenosine deaminase type 2 (ADA2). She tested positive with one pathogenic variant and one likely pathogenic variant and was started on adalimumab.

Struggle/Dilemma of the Clinical Presentation Description: In the course of her disease process, this patient had numerous misdiagnoses, likely due to the limited knowledge of DADA2. DADA2 makes up a large cohort of the patients previously diagnosed with Sneddon syndrome – often a diagnosis given clinically in the setting of livedo racemosa and recurrent strokes. Recent studies have shown that at least 31% of patients diagnosed with PAN test positive for ADA2 mutations.[2]

Keywords: Vasculopathy, Central retinal artery occlusions, Vision loss

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“A Diagnosis in Plain Sight”

Stephanie Syc-Mazurek¹, M. Mateo Paz Soldan¹, Nessa Aghazadeh Mohandesi¹, Jithma Abeykoon¹, Angela Collie¹,
Nneka Comfere¹, John Chen¹, Deena Tajfirouz¹

¹ *Mayo Clinic*

History & Exam: A 48-year-old man presented with new-onset headache and subacute progressive bilateral blurred vision. He had a history of diabetes insipidus five years earlier due to presumed lymphocytic hypophysitis. During initial ophthalmic examination, he had bilateral disc edema with normal visual function. Neurologic evaluation was normal including cranial nerves, strength, sensation, reflexes, and coordination. Skin examination demonstrated bilateral periorbital yellowish papules consistent with xanthelasma-like lesions but no other lesions. MRI brain demonstrated dural enhancement (most prominent around the torcula) and soft tissue involving the sphenoid and cavernous sinuses extending to the clivus. MRV showed concern for cerebral venous sinus thrombosis (CVST) around the torcula. CT chest, abdomen, and pelvis showed no signs of malignancy but showed sclerotic lesions in the femurs and so MRI of the pelvis was obtained which demonstrated heterogeneous mixed T1/T2 signal intensities with enhancement of the bilateral proximal femurs felt to be related to avascular necrosis or osteonecrosis. Serum workup included mildly elevated ANA, ESR, total complement, and C3, but otherwise negative/unremarkable C4, CCP, double-stranded DNA, Smith, Ro, La, MOG, aquaporin-4, and paraneoplastic antibody testing. Cerebral spinal fluid testing demonstrated elevated opening pressure, 27.5cmH2O, with two total nucleated cells with negative cytology, normal/negative protein, glucose, infectious, and paraneoplastic antibody testing. He underwent biopsy of the sphenoid sinus which demonstrated dense fibrosis with chronic predominantly lymphohistiocytic inflammation without a specific etiology. He was treated with rivaroxaban for presumed CVST, acetazolamide for intracranial hypertension, and prednisone and then mycophenolate for an inflammatory condition of unclear etiology without significant change in symptoms. He sought a second opinion. At that time, visual acuity was 20/20 in each eye, and he had bilateral Frisen Grade 1 disc edema. Repeat MRI/MRV was unchanged despite immunomodulatory therapy. FDG-PET scan showed multi-focal uptake in the long bones and testes. Definitive diagnostic testing was completed.

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Grant Support: None.

“A Diagnosis in Plain Sight”

Answer

Final Diagnosis: Erdheim-Chester disease with CNS, pituitary, skin, long bones, and testes involvement

Summary of Case: Our patient was a 48-year-old man with subacute bilateral vision loss with papilledema, intracranial hypertension, pachymeningitis, and facial lesions. Imaging showed enhancement of the dura and around the cavernous sinus as well as question of CVST. The clinical presentation suggested a systemic infectious, inflammatory, or neoplastic etiology of symptoms. He underwent a biopsy of the sphenoid sinus at onset; however, the pathology was nonspecific with dense fibrosis with chronic predominantly lymphohistiocytic inflammation. Empiric treatment with prednisone and mycophenolate did not improve symptoms or alter the pattern of enhancement on MRI. During his subsequent assessment, the longstanding facial lesions, diffuse yellow plaques affecting the bilateral upper and lower eyelids were biopsied. The biopsy of the left eyelid showed a dermal histiocytic neoplasm with numerous Touton giant cells (positive for CD68 and CD163) and immunohistochemical expression of BRAF V600E (strong) and cyclin D1 (partial). The neoplastic cells were negative for S100, CD1a, and langerin. Targeted next-generation sequencing of tumor tissue detected a BRAFV600E alteration with an allele frequency of 5%. These findings supported a diagnosis of multi-system Erdheim-Chester Disease(ECD). A PET scan showed bilateral osteosclerotic lesions of the long bones supportive of this diagnosis. In retrospect, the diabetes insipidus was also felt to be related. ECD is a rare xanthogranulomatous, non-Langerhans cell histiocytic neoplasm which often has multisystem involvement and can also have ocular involvement. Ocular involvement can be present in over two-thirds of patients often with eyelid edema, proptosis, optic nerve sheath involvement, or diffuse orbital involvement. The most common cutaneous manifestations of ECD are xanthelasma-like lesions, which occur in about 25% of patients, as well as patches or papulonodular lesions. Our patient was treated with vemurafenib, a targeted inhibitor for the BRAFV600 mutation, with improvement in the xanthelasma and disc edema. Repeat MRI is planned for December 2025.

Struggle/Dilemma of the Clinical Presentation Description: This patient was initially diagnosed with an unspecific systemic inflammatory condition and treated with immunosuppression. Systemic manifestations of the disease were initially attributed to other etiologies (ie. bone lesions were felt to be avascular necrosis/osteonecrosis; skin lesions thought to be cholesterol; prior diabetes insipidus was thought to be unrelated). Further complicating the diagnosis was that findings of the initial biopsy were nonspecific on hematoxylin and eosin staining.

Keywords: Erdheim-Chester disease, Eyelids, Papilledema, Magnetic resonance imaging (MRI), PET

References: None provided.

Contact Information: None provided.

“DNA on Tap”

Sydney Roston¹, Bryan Neth¹, Deena Tajfirouz¹, Kevin Chodnicki¹, John Chen¹

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History & Exam: A 41-year-old previously healthy man presented with progressive hiccups, nausea/vomiting, gait imbalance, and ophthalmic symptoms of binocular horizontal diplopia. He was initially seen at an outside institution and underwent magnetic resonance imaging (MRI) of the brain with and without IV contrast. This study demonstrated a non-enhancing T2 hyperintense lesion in the posterior medullary region involving the area postrema. He had additional non-specific T2 hyperintense lesions in the subcortical and periventricular white matter. Serum AQP4 and MOG antibodies were negative. Lumbar puncture showed no abnormalities, including no pleocytosis, oligoclonal bands, or malignant cells. A serum and cerebrospinal fluid (CSF) paraneoplastic antibody panel was negative. The patient was felt to have seronegative neuromyelitis optica spectrum disorder (NMOSD) and received treatment with 5 days of IV methylprednisolone followed by two infusions of rituximab without improvement. The patient was referred for a second opinion. Neuro-ophthalmic examination showed a small esotropia, gaze-evoked nystagmus, and saccadic pursuit. The dilated fundus examination was normal without evidence of prior optic neuritis. A repeat MRI showed an interval increase in the size of the brainstem lesion compared to the initial scan done 3 months prior. Neurosurgery was consulted, who did not feel it was safe to biopsy the lesion because of its location in the medulla. A diagnostic procedure was performed.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

“DNA on Tap”

Answer

Final Diagnosis: Diffuse midline glioma, H3 K27-altered (DMG), causing area postrema syndrome

Summary of Case: In summary, this 41-year-old man presented with a clinical picture consistent with area postrema syndrome that was presumed to be seronegative NMOSD. However, there was no abnormal gadolinium enhancement on MRI, and he had clinical and radiographic progression despite corticosteroids and rituximab. The location of the lesion was not amenable to biopsy. This prompted further investigation to facilitate adequate disease-specific treatment. A repeat lumbar puncture including assessment of CSF cell-free DNA (cfDNA) was obtained. CSF cfDNA testing is a less invasive approach that is increasingly utilized to obtain genetic information of CNS lesions, including primary and secondary brain cancers. A liquid sample of CSF can identify circulating genetic material from dead/lysed cancer cells, even if cytology is negative (1). Unlike tissue biopsy, it has less risk for mortality, hemorrhage, infection, or other complications of intracranial or intraspinal instrumentation. Recent expansion in the use of molecular targeted therapies in the treatment of various malignancies renders CSF cfDNA testing a potentially powerful tool. The CSF cfDNA testing in this patient revealed ATM deletion and AKT3 amplification, which were highly suggestive of glioma (2). Cytology and routine CSF studies were otherwise unremarkable. The patient was treated with conventionally fractionated radiotherapy (54 gray across 30 fractions). He reported resolution of the binocular diplopia after radiation. He was also treated with bevacizumab for radiation necrosis. Additional analysis of the cfDNA sample later identified a genetic alteration in a gene encoding a histone protein (H3F3A K28M). This further supported the final diagnosis of diffuse midline glioma, H3 K27-altered (DMG). The patient is continuing treatment with an investigational targeted therapy, ONC201. While his long-term clinical outcome remains guarded given the aggressiveness of DMG, the ability to make a diagnosis based on CSF cfDNA provided an opportunity to understand prognosis and offer other targeted treatments and trial opportunities.

Struggle/Dilemma of the Clinical Presentation Description: Area postrema syndrome is often seen in the setting of neuromyelitis optica spectrum disorder, which can also demonstrate T2 hyperintense lesions on MRI. Therefore, the patient’s presentation was initially attributed to seronegative NMOSD. However, area postrema syndrome can also be seen in other ischemic/inflammatory processes and tumors/malignant processes (as in this case). Definitive diagnosis and adequate treatment traditionally have required a biopsy for diagnosis, which has high morbidity in the case of brainstem lesions.

Keywords: Brain stem syndromes, Lumbar puncture, Neuromyelitis optica spectrum disorder (NMOSD), Diplopia, Intracranial tumors

References: 1. McEwen AE, Leary SES, Lockwood CM. Beyond the Blood: CSF-Derived cfDNA for Diagnosis and Characterization of CNS Tumors. *Front Cell Dev Biol.* 2020;8:45. Published 2020 Feb 18. doi:10.3389/fcell.2020.00045 2. Kim T, Lee A, Ahn S, Park JS, Jeun SS, Lee YS. Comprehensive Molecular Genetic Analysis in Glioma Patients by Next Generation Sequencing. *Brain Tumor Res Treat.* 2024;12(1):23-39. doi:10.14791/btrt.2023.0036 3. Francis JH, Gobin YP, Brannon AR, et al. RB1 Circulating Tumor DNA in the Blood of Patients with Unilateral Retinoblastoma: Before and after Intra-arterial Chemotherapy. *Ophthalmol Sci.* 2021;1(3):100042. Published 2021 Jul 14. doi:10.1016/j.xops.2021.100042 4. Francis JH, Barker CA, Brannon AR, et al. Detectability of Plasma-Derived Circulating Tumor DNA Panel in Patients Undergoing Primary Treatment for Uveal Melanoma. *Invest Ophthalmol Vis Sci.* 2022;63(13):17. doi:10.1167/iovs.63.13.17 5. Francis JH, Arcila ME, Sigler A, Bossert DF, Abramson DH, Diamond EL. Plasma-Derived Cell-Free DNA for the Diagnosis of Ocular-Involving Histiocytosis. *Ophthalmol Sci.* 2024;4(5):100530. Published 2024 Apr 15. doi:10.1016/j.xops.2024.100530

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“Acute Monocular Vision Loss: A diagnostic labyrinth”

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History & Exam: A 78-year-old woman with antiphospholipid antibody syndrome, complicated by prior deep vein thromboses and atrial fibrillation status post ablations, first developed scalp tenderness, jaw discomfort, and elevated inflammatory markers. Based on these findings, she was diagnosed with presumed giant cell arteritis and started on high-dose prednisone. Temporal artery biopsy later returned negative, and prednisone was gradually tapered. During this period, she was also diagnosed with colonic adenocarcinoma and scheduled for hemicolectomy. She was maintained on a prednisone taper and bridging anticoagulation with enoxaparin in preparation for surgery. While on this regimen, she developed fever (102°F) followed by sudden, painful vision loss in the right eye. On presentation, visual acuity was light perception in the right eye and 20/30 in the left. A right relative afferent pupillary defect was present. The right eye demonstrated marked proptosis, diffuse chemosis, and corneal edema, with restricted extraocular motility in all gazes. The contralateral eye showed normal motility and no pain. Intraocular pressure measured 38 mmHg and improved following emergent lateral canthotomy and cantholysis. Anterior segment examination revealed diffuse corneal edema and conjunctival injection. The posterior segment view was limited by media opacity. There were no cutaneous vesicles or cranial neuropathies. The remainder of the cranial nerve, motor, and sensory examinations were unremarkable. The constellation of acute orbital pain, vision loss, ophthalmoplegia, and proptosis in an immunosuppressed patient raised concern for an aggressive orbital process, prompting urgent multidisciplinary evaluation and management.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

“Acute Monocular Vision Loss: A diagnostic labyrinth”

Answer

Final Diagnosis: Fulminant *Clostridium septicum* optic perineuritis and orbital cellulitis in the setting of immunosuppression, colonic adenocarcinoma, and antiphospholipid antibody syndrome.

Summary of Case: Orbital MRI with gadolinium contrast revealed circumferential enhancement of the right optic nerve sheath with surrounding orbital fat stranding (Fig. 1, 2) and reactive enhancement of the right extraocular muscles and lacrimal gland. There was also surface enhancement of the right globe with proptosis (Fig. 3). These findings were consistent with acute optic perineuritis and orbital inflammation. Comprehensive autoimmune and vasculitic testing including ANA, RF, CCP, and IgG4 was negative. Temporal artery ultrasound and CT angiography showed no evidence of large-vessel vasculitis. Given the initial concern for arteritic anterior ischemic optic neuropathy or steroid-refractory orbital pseudotumor, the patient was treated with pulse-dose corticosteroids and broad-spectrum antibiotics. Despite therapy, visual acuity and ocular motility worsened, progressing to corneal melt and eventual globe necrosis. Histopathology from the eviscerated globe showed acute necrotizing keratitis (Fig. 4), with no organism in PAS stain (Fig. 5), with devitalized intraocular tissues (Fig. 6) and an absence of organisms on Brown-Hopps (Fig. 7) and GMS stains (Fig. 8). Orbital wound cultures later grew *Clostridium septicum*, a rare anaerobic organism known for hematogenous spread from gastrointestinal malignancy (Fig. 5). The infectious optic perineuritis and orbital cellulitis were attributed to hematogenous dissemination of *C. septicum* from the patient’s colonic adenocarcinoma in the context of corticosteroid-induced immunosuppression. Management required multidisciplinary coordination among neuro-ophthalmology, oculoplastics, infectious disease, and rheumatology teams. Following evisceration, the patient improved systemically on targeted therapy with amoxicillin–clavulanate and clindamycin.

Struggle/Dilemma of the Clinical Presentation Description: This case presented overlapping features of vasculitic, infectious, and paraneoplastic optic neuropathy. Early steroid treatment for presumed giant cell arteritis obscured the infectious process, delaying definitive diagnosis. The eventual identification of *Clostridium septicum*—a malignancy-associated pathogen—only after enucleation highlights the diagnostic difficulty of differentiating infectious optic perineuritis from autoimmune etiologies in immunosuppressed hosts.

Keywords: Vision loss, Optic neuritis, Orbit

References: None provided.

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“A Wolf in Sheep’s Coating”

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History & Exam: A 25-year-old man presented to an outside hospital in March 2024 with 3 weeks of diplopia, emesis, and headache. His medical history included multiple traumatic brain injuries as a martial arts fighter. His neurologic examination was significant for bilateral sixth nerve palsies. MRI demonstrated meningeal thickening and enhancement without parenchymal involvement. MRV showed bilateral transverse sinus stenosis without thrombosis. Lumbar puncture opening pressure was greater than 55 cm H₂O and CSF analysis demonstrated elevated white blood cells (150, 90% lymphocytes), elevated protein (175), and normal glucose. CSF meningitis/encephalitis panel, autoimmune work up, cytology, and flow cytometry were negative. CT of the chest, abdomen, and pelvis and scrotal ultrasound were negative for malignancy. He received intravenous methylprednisolone and was discharged home on a prednisone taper and acetazolamide. In June 2024 he returned with emesis, headache, imbalance, and intermittent left-sided weakness and numbness. He complained of blurred vision in the left eye. Examination showed bilateral abduction deficits and decreased sensation in the left leg. MRI demonstrated persistent isolated meningeal enhancement. Cerebral angiogram revealed right transverse sinus stenosis but was otherwise unremarkable. Lumbar puncture opening pressure was 42 cm H₂O, and CSF analysis showed 30 white blood cells (96% lymphocytes), elevated protein (196), and normal glucose. There were 5 oligoclonal bands. Infectious studies, serum Mayo Clinic Autoimmune Encephalitis Panel, and CSF cytology and flow cytometry were negative. He was discharged home on acetazolamide. In August 2024 he returned with new-onset confusion and worsening emesis, headache, and blurred vision. He was transferred to our institution. Neuro-ophthalmic examination demonstrated visual acuity of 20/20 OD and 20/25 OS. There was no dyschromatopsia or relative afferent pupillary defect. Visual fields were full to confrontation and extraocular movements were intact. Fundoscopic examination revealed grade 3 papilledema. MRI demonstrated worsening diffuse nodular pachymeningeal enhancement. A diagnostic procedure was performed.

Financial Disclosures: The authors had no disclosures.

Grant Support: None

“A Wolf in Sheep’s Coating”

Answer

Final Diagnosis: Diffuse pediatric-type high-grade glioma, H3-wildtype and IDH-wildtype, CNS WHO grade 4, isolated to the meninges

Summary of Case: The young patient’s diffuse and isolated meningeal thickening and enhancement were initially concerning for an inflammatory or infectious process. However, extensive serum and CSF testing was negative, including cytology and flow cytometry. He underwent a biopsy of the right frontal lobe and dura. Histology and immunohistochemistry were consistent with a high-grade glioma with diffuse leptomeningeal and focal dural involvement without involvement of the underlying parenchyma. The UCSF 500 next-generation sequencing panel demonstrated missense mutations in the TP53 tumor suppressor gene and MED12 with focal high-level amplifications of C19MC, GAB2, PAK1, and IRS2. DNA methylation profiling performed at the NIH was necessary for further classification. This led to a final integrated diagnosis of diffuse pediatric-type high-grade glioma, H3-wildtype and IDH-wildtype, CNS WHO grade 4.[1,2] The patient urgently received whole brain radiation therapy and started temozolomide. Despite persistent elevated intracranial pressure, his visual function remained excellent. He developed urinary retention and bilateral lower extremity weakness and numbness. Neuroimaging revealed diffuse pachy- and leptomeningeal enhancement along the length of the spinal cord. Spinal radiation was performed. Despite therapy, follow-up scans demonstrated disease progression with increased diffuse meningeal enhancement and development of hydrocephalus. He developed worsening pain and somnolence and was transitioned to hospice. The patient died in November 2024. This is the first reported case of a high-grade glioma presenting with isolated pachymeningeal and leptomeningeal involvement completely sparing the underlying parenchyma. Diffuse pediatric-type high-grade gliomas often present with a heterogeneously enhancing mass but have never been described isolated to the meningeal tissues.[2,3] Given isolated meningeal involvement on neuroimaging in this young patient, an autoimmune, infectious, or inflammatory process was deemed most likely, particularly with normal flow cytometry and cytology. This case shows that high-grade gliomas isolated to the meninges should be included in the differential diagnosis in patients with refractory diffuse meningeal disease.

Struggle/Dilemma of the Clinical Presentation Description: This young patient’s neuroimaging demonstrated marked meningeal thickening and enhancement with primary concern for an autoimmune, infectious, or inflammatory condition given his age and otherwise unremarkable medical history. There was little concern for neoplasm given a lack of parenchymal involvement on MRI and unrevealing CSF cytology and flow cytometry on multiple instances. A diagnostic brain biopsy was performed several months after symptom onset, revealing an extremely rare diagnosis of glioma isolated to the meninges.

Keywords: Increased intracranial pressure, Tumor, Magnetic resonance imaging (MRI), Papilledema

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“Beyond the Usual Suspects: When Painless Progressive Vision Loss and Neuroimaging Don’t Align”

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History & Exam: A 67-year-old male presented with a 4-5 month history of gradual, painless bilateral vision deterioration with a short 3-weeks period of stable vision, followed by further gradual decline. He had no prior ocular disease, trauma, or surgery, and denied exposure to toxins or medications associated with optic neuropathy. His medical history included two myocardial infarctions (2009, 2019), hypertension, and hypercholesterolemia. He also reported progressive hearing loss and persistent tinnitus, likely related to occupational noise exposure, and a remote history of childhood head injury. He smoked approximately ten cigarettes daily and consumed moderate alcohol; there was no history of illicit drug use or heavy metal exposure. Family history (Irish ancestry): no other similar visual impairment within the family. Limited history from the paternal side, as father has left when patient was young. Three daughters are healthy with no neurological, nor visual issues reported. He has six grandsons and two granddaughters – all healthy. Over more than 1-year period since onset, ophthalmological examination revealed progressive central visual field loss and sectorial optic atrophy with retinal ganglion cell layer thinning. Anterior segment was unremarkable. Visual electrophysiology testing demonstrated findings consistent with optic nerve /retinal ganglion cell dysfunction. Arranged hearing test indicated mild to moderately severe high frequency sensory-neural hearing loss in both ears. Neurological examination was unremarkable. Neck flexion/extension and limb strength were full (5/5) with brisk reflexes. Terminal tremor was noted on bilateral finger-to-nose testing, likely due to reduced visual acuity. Hoffmann and Babinski signs were negative, and pin-prick and vibration sensations were intact. Neuroimaging studies revealed marked mineralization of the basal ganglia, particularly affecting the globus pallidus and substantia nigra.

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“Beyond the Usual Suspects: When Painless Progressive Vision Loss and Neuroimaging Don’t Align”

Answer

Final Diagnosis: Progressive autosomal dominant optic neuropathy secondary to pathogenic heterozygous variant in MFN2.

Summary of Case: A 67-year-old man presented with progressive painless bilateral central vision loss, raising clinical suspicion for Leber’s Hereditary Optic Neuropathy (LHON). To investigate and rule out alternative causes, a comprehensive series of laboratory and neuroimaging assessments were undertaken. Blood investigations demonstrated a mildly elevated C-reactive protein level and increased methylmalonic acid (while serum vitamin B12 and homocysteine concentrations were within normal limits). Screening for heavy metal toxicity, including mercury, iron, chromium, copper, magnesium, manganese, zinc, cadmium, aluminium, and lead, yielded unremarkable results. Neuroimaging studies revealed marked mineralization of the basal ganglia, predominantly involving the globus pallidus and substantia nigra. These findings suggested the possibility of Neurodegeneration with Brain Iron Accumulation (NBIA), a heterogeneous group of genetic disorders in which specific subtypes—such as those linked to C19orf12, PANK2, PLA2G6, or WDR45 pathogenic variants—may present with progressive visual decline. However, given the patient’s entirely normal neurological examination, NBIA was considered less likely. Genetic testing subsequently identified a heterozygous low-penetrance MFN2 c.707C>T p.(Thr236Met) variant. This variant has previously been described in individuals with autosomal dominant Charcot–Marie–Tooth disease type 2 and, more rarely, in patients exhibiting isolated progressive bilateral optic neuropathy without evidence of peripheral neuropathy. Variant is located within a highly conserved GTPase domain of the MFN2 protein and is predicted to have a deleterious effect on protein function. Based on the clinical presentation and genetic findings, a diagnosis of autosomal dominant progressive optic neuropathy secondary to a pathogenic MFN2 variant was established. MFN2-related disease is thought to arise from disruption of mitochondrial fusion and dynamics, leading to impaired mitochondrial function and progressive retinal ganglion cell degeneration.

Struggle/Dilemma of the Clinical Presentation Description: The patient presented with subacute bilateral painless progressive central vision loss, initially raising suspicion for LHON. However, neuroimaging demonstrated features suggestive of NBIA, a disorder in which some forms can include progressive vision loss. The atypical age of onset, unusually prolonged disease course, and absence of neurological deficits prompted consideration of alternative diagnoses. Ultimately, extended genetic testing led to the final diagnosis.

Keywords: Optic neuropathy, Optic atrophy, Neuro-degenerative disease

References: None provided.

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“Hummingbird -A Jabbing and Terrifying Monster”

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History & Exam: A 52-year-old woman, previously healthy except for hypertension and hypothyroidism on stable treatment, presented with a painful decrease in vision in the right eye. She first noted blurring over 3 weeks, with rapid worsening in the 4 days preceding presentation. She described the eye pain as a mild, intermittent, dull ache in the eye, not particularly associated with eye movements. The vision recorded elsewhere, in the right eye, 14 days before presentation to us, was 20/20. There was no history of headache, fever, trauma, or systemic illness such as weight loss or joint pains. There was a family history of glaucoma in the mother and her brother. On examination, best-corrected visual acuity was perception of light with inaccurate projection in the right eye and 20/20 in the left eye. A grade 3 relative afferent pupillary defect was present. Colour vision as tested with Ishihara's pseudoisochromatic plates, was normal in the left eye. There was a less than 15 prism diopter right exotropia with full, free and painless eye movements in both eyes. Other cranial nerve examination was within normal limits. The anterior segment evaluation revealed early lens changes bilaterally but no inflammation. Intraocular pressure, as checked by applanation tonometry, was 11 mmHg in the right eye and 13 mmHg in the left eye. Fundus showed mild temporal pallor of the optic discs in both eyes, with a cup disc ratio of 0.3 in both eyes. A series of diagnostic tests was performed.

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“Hummingbird -A Jabbing and Terrifying Monster”

Answer

Final Diagnosis: Isolated necrotizing granulomatous inflammation of the anterior skull base, masquerading as a tuberculum sella meningioma.

Summary of Case: This 52-year-old woman presented with a severe decrease in vision over 3 weeks, associated with a dull ocular pain, a relative afferent pupillary defect in the right eye (RE) and a subtle optic disc pallor in both eyes. Humphrey visual field in the RE could not be assessed, and the left eye (LE) revealed peripheral constriction. The visual evoked potential was non-recordable in the RE and revealed delayed latency with reduced amplitudes in the LE. Bilateral optic neuritis was suspected, and a contrast-enhanced magnetic resonance imaging (MRI) of the brain was done, which surprisingly showed a homogeneous enhancing mass lesion (18.2 x 7.4mm) along the tuberculum sella encasing the optic nerves, with an adjacent dural tail sign, suggestive of tuberculum sella meningioma, for which she underwent endoscopic excision. A greyish, soft to firm tumour attached to the dura was excised. The histopathology was suggestive of necrotizing granulomatous inflammation. The Ziehl-Neelsen stain for Mycobacterium tuberculosis (MTB), as well as the Grocott-Gomori Methenamine Silver stain and Periodic Acid-Schiff stain for fungal organisms, were negative. No parasite or polarizable material suggestive of a foreign body was noted. (1) MTB, sarcoidosis, and granulomatosis with polyangiitis were ruled out with a non-contributory interferon gamma release assay, serum angiotensin converting enzyme, lysozyme, calcium, computerised tomography of chest, antinuclear antibody, extractable nuclear antigens anti-neutrophil cytoplasmic antibody assay results. (2, 3). Idiopathic necrotizing granuloma in the brain was considered. (4, 5). She was administered steroid therapy with anti-tubercular treatment, resulting in visual recovery in the LE with no improvement in the RE. There was a worsening of LE vision upon stopping steroids. Mycophenolate Mofetil was added. MRI brain 6 months later revealed a 4.7 x 11 x 10 mm-sized recurrence in the tuberculum sella region, injection rituximab was added. One year post surgery, she was stable.

Struggle/Dilemma of the Clinical Presentation Description: The greatest challenge was the misdiagnosis of a potentially life-threatening intracranial necrotizing granulomatous lesion as a meningioma due to the presence of homogenous post-contrast enhancement and the dural tail sign. Histopathology was suggestive of either granulomatosis with polyangiitis or tuberculosis, but there was no systemic evidence of the disease; hence, an empirical treatment of steroids with antitubercular drugs was given, as tuberculosis is prevalent in our part of the world.

Keywords: Caseating granulomas, Granulomatosis with polyangitis (GPA), Skull base tumors, Magnetic resonance imaging (MRI)

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“When the Retina Spoke Up”

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History & Exam: A 67-year-old man developed headache, scalp sensitivity, jaw pain and anorexia. Four months after symptom onset, his family physician presumptively diagnosed him with giant cell arteritis (GCA) based on elevated CRP(50.6 mg/L). He also had elevated p-ANCA. Treatment with 80 mg of oral prednisone commenced with improvement of headaches. He underwent MRI/A brain 6 months after symptom onset which showed diffuse smooth dural thickening without other signs of intracranial hypotension. CT myelography was normal. Temporal artery biopsy was performed and did not show signs of GCA. Two months later he suddenly lost vision in the left eye. On presentation to neuro-ophthalmology clinic, vision was 20/20 in the right hand motions in the left eye with left RAPD. He had vitritis and bilateral diffuse multifocal subretinal creamy lesions in each eye, which involved the macula in the left eye. The leading diagnosis was now primary intraocular vs CNS lymphoma. He was admitted and MRI brain and orbits revealed new, punctate FLAIR-hyperintense, enhancing lesions in the brain parenchyma. Cerebrospinal fluid was bland and cytology was negative for malignancy. CT chest revealed new mediastinal nodal mass, pulmonary embolus and large pericardial effusion. CT abdomen and pelvis showed retroperitoneal, extraperitoneal and subcutaneous nodules. He rapidly deteriorated systemically requiring urgent admission to the ICU for arrhythmia. This delayed sampling of lymph nodes, now felt to be imperative for diagnostic certainty. Immediately after transferring out of ICU, he attempted suicide, overwhelmed by guilt for previous criminal charges. This further delayed care as he was placed on an involuntary psychiatric hold. His vision worsened to no light perception bilaterally, and he demonstrated enlargement of subretinal lesions now involving the macula in the right eye. Diagnostic vitrectomy was performed. Cytological examination of vitreous fluid was negative for malignancy but vitreous culture grew nocardia arthritis, exalbida and gamkensis.

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“When the Retina Spoke Up”

Answer

Final Diagnosis: Disseminated nocardiosis in the context of prolonged corticosteroid use in a previously immunocompetent host. An initial diagnosis of idiopathic hypertrophic pachymeningitis was deemed the most plausible explanation for his presenting symptoms of severe headache, jaw claudication, scalp tenderness and weight loss.

Summary of Case: It was felt that malignancy rather than infection was the most likely explanation for his multiple findings thus endobronchial ultrasound-guided transbronchial needle aspiration was then performed. Nocardia grew on the cultured sample. Pathological examination of the lymph nodes was negative for malignancy. The diagnosis of disseminated nocardiosis was made. Systemic treatment with linezolid and intravitreal injection of antibiotics commenced, however, vision remained no light perception bilaterally. This patient initially presented with symptoms of GCA and had markedly elevated CRP and slightly elevated p-ANCA titers. However, inflammatory markers remained elevated despite treatment with high doses of corticosteroids and headaches only partially improved. Prolonged immunosuppression with high doses of corticosteroids then undermined cell-mediated immune responses that keep nocardia, a ubiquitous typically commensal organism, from becoming pathogenic and resulted in disseminated nocardiosis. Nocardia are intracellular, partially acid-fast, catalase-positive bacteria that survive inside macrophages and when Th1 signaling and macrophage activation is suppressed by long term corticosteroid therapy, the organism can disseminate. Immunosuppression is the most significant risk factor for nocardia endophthalmitis, and multiple cases have reported re-activation after treatment for presumed GCA. On re-evaluation of this man’s clinical course, his presenting symptoms and only partial response to corticosteroids were not in keeping with GCA. After re-reviewing neuroimaging and obtaining detailed history from patient’s family about early symptomatology, the initial diagnosis of idiopathic hypertrophic pachymeningitis was deemed the most plausible explanation for his presentation. Idiopathic hypertrophic pachymeningitis is a rare disorder with main clinical features including severe headache and anorexia, with normal physical examination. Many patients present with mild to moderate elevation of CRP and p-ANCA and neuroimaging reveals diffuse or localized thickening of the dura. Many patients initially improve with steroids and then relapse, similar to our patient. The prolonged course of steroids eventually led to the final presentation of disseminated nocardiosis.

Struggle/Dilemma of the Clinical Presentation Description: This patient’s journey was complicated by lack of appropriate work-up for presenting symptoms and anchoring bias. While his tissue culture eventually returned positive for nocardia, there was an underlying primary process that was responsible for his presenting symptoms. This primary pathology was presumptively most in keeping with idiopathic hypertrophic pachymeningitis.

Keywords: Endophthalmitis, Giant cell arteritis, Headache and facial pain

References: None provided.

Contact Information: None provided.

“If Referred by Retina, it’s Retinal...or Not?”

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History & Exam: Four days following COVID vaccination, a 60-year-old woman noticed a gray cloud in the vision OS, starting temporally and sparing the center. Medical history included remote treatment of a left paraophthalmic ICA aneurysm with a flow diversion stent. A retina specialist found normal visual acuities, 2+ vitritis OS, and a bull’s eye maculopathy OS. Fluorescein angiography showed no retinal vasculitis or papillitis. Within a week she developed diffuse weakness, balance impairment and was admitted to the hospital for dysautonomia and hypertension requiring several new medications. Contrast-enhanced MRI of the brain and orbits was unrevealing. She developed significant nausea and vomiting after eating, resulting in a 10 lbs weight loss. Her imbalance progressed to a vertiginous sensation, and she developed a binocular oblique diplopia and anosmia. She was seen by another retina specialist and consulted to neuro-ophthalmology, now one month after symptom onset. She entered the examination room in a wheelchair, unable to walk without assistance. Visual acuities were 20/20 OD and 20/25 OS with a trace left relative APD. Confrontation visual fields showed temporal visual field constriction OS, and there was mild dyschromatopsia OS. Ocular ductions were full, but there was direction changing horizontal and rotatory nystagmus with a left hyperdeviation greater in downward gaze. Cerebellar ataxia was present. Vitreous cell was clearing OS. Automated perimetry was normal OD and showed generalized depression OS with deeper areas of defect in the paracentral and inferior arcuate regions (MD -12.31 dB). The fundus OD was normal aside from an inferior chorioretinal scar, but the optic disc OS was mildly hyperemic with peripapillary retinal discoloration. Full field ERG was normal OD and showed reduced cone responses OS, and multifocal ERG was normal OD and flat OS. Additional testing focused the diagnostic workup and led to a diagnosis.

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“If Referred by Retina, it’s Retinal...or Not?”

Answer

Final Diagnosis: Collapsin response-mediator protein-5 (CRMP-5) paraneoplastic syndrome with autoimmune retinopathy, retinal vasculitis, and optic papillitis due to occult small cell lung carcinoma.

Summary of Case: Repeat fluorescein angiography revealed retinal vasculitis and leakage at the optic nerves greater OS than OD. An extensive evaluation for systemic autoimmune or infectious disorders included normal or negative ESR, CRP, Lyme ELISA, RPR, Treponemal antibodies, ANA, ACE level, lysozyme, and ANCA. Lumbar puncture showed 17-26 WBCs (96-99% lymphocytes), no RBCs, protein 44.9 mg/dL, and normal glucose. Cytology showed no malignant cells. Chest CT revealed several lung nodules, the largest being a 9 x 8 mm right upper lobe peribronchial nodule. There was a 25 x 18 mm right subcarinal lymph node. Collapsin response-mediator protein-5 (CRMP-5) IgG Western blot of the serum was positive (titer of 1:30720). PET-CT showed intensely FDG uptake within the lung nodules and subcarinal lymph node. Level 7 (subcarinal) endobronchial ultrasound-guided fine needle aspiration biopsy was consistent with small cell lung carcinoma (SCLC). She received cisplatin and etoposide chemotherapy with concurrent 66 Gy of radiation therapy to the right lung/mediastinum. By one year her CRMP-5 titer decreased to 1:3840, CSF showed resolution of lymphocytic pleocytosis and she was tapered to a low dose of prednisone 5 mg. At 3 years she remains in remission from SCLC, is able to walk unassisted with a wide-based gait, has partial recovery of her visual field OS (MD -6.80 dB), and has no strabismus. Optic disc edema resolved without secondary optic disc pallor, and OCT of the retina shows outer retinal loss around the fovea OS.

Struggle/Dilemma of the Clinical Presentation Description: Unilateral maculopathy is atypical for paraneoplastic retinopathies including CRMP-5, and optic disc edema which is typically prominent, only became evident a month after symptom onset [1,2]. Prominent neurologic signs in our patient included strabismus, dysautonomia (as evident by nausea, vomiting, labile blood pressures) and anosmia which are features associated with CRMP-5 in a small percentage of patients [3]. Testing for CRMP-5 antibodies was delayed and other systemic inflammatory, infectious, and neoplastic disorders were initially pursued.

Keywords: Paraneoplastic syndromes, Autoimmune retinopathy, Optic disc edema, Fluorescein angiography, Neurologic disorders

References: 1. Cohen DA et al. Collapsin Response-Mediator Protein 5-Associated Retinitis, Vitritis, and Optic Disc Edema. *Ophthalmology*. 2020 Feb;127(2):221-229. 2. Cross SA et al. Paraneoplastic autoimmune optic neuritis with retinitis defined by CRMP-5-IgG. *Ann Neurol*. 2003 Jul;54(1):38-50. 3. Yu Z, Kryzer TJ, Griesmann GE, Kim K, Benarroch EE, Lennon VA. CRMP-5 neuronal autoantibody: marker of lung cancer and thymoma-related autoimmunity. *Ann Neurol*. 2001 Feb;49(2):146-54. PMID: 11220734.

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“A Diagnosis Bubbles to the Surface”

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History & Exam: A 13-year-old girl 2 months status post resection of a right high-grade frontal lobe glioma presented with 5 days of low-grade fever, non-positional headaches, and sudden onset left eye vision loss, 2.5 weeks after focal radiation and chemotherapy. On examination, visual acuity was 20/20 OD and 20/350 OS with an afferent pupillary defect OS. Funduscopy revealed Frisen-equivalent grade 3 disc edema OD and grade 4 disc edema OS. Color vision was 8/8 OD and 1/8 OS. MRI Brain and MRV demonstrated patent venous sinuses and expected postoperative changes in the right frontal lobe. Our review revealed subtle bilateral (left more than right) optic nerve and perineural enhancement, prompting MRI Orbits which confirmed right intraorbital and intracanalicular optic nerve enhancement. Lumbar puncture (unsedated) showed an opening pressure of 27 cm H₂O with a lymphocytic pleocytosis (67 cells/ μ L, 90% lymphs) and elevated protein, but cytology and meningoencephalitis panel were negative. Visual field testing revealed bilateral enlarged blindspots with paracentral field defects. Extensive infectious, autoimmune, and paraneoplastic workup was unrevealing, including negative AQP4-IgG, MOG-IgG, CRMP5, ACE, and infectious serologies. The soluble IL-2 receptor was elevated 2489, and CT chest revealed multiple small pulmonary nodules. Intravenous dexamethasone (6 mg q6h) was initiated within hours of presentation by the neurosurgery team for concern of post-surgical vasogenic edema. Around 36 hours after steroid initiation, visual acuity recovered to 20/20 and full color plates OU, with marked reduction in RNFL thickness on OCT. CRMP-5 IgG came back negative. The dramatic response to corticosteroids, perineural enhancement, elevated IL-2 receptor, and compatible chest CT supported a diagnosis of neurosarcoidosis presenting as bilateral optic neuritis following glioma resection and radiation

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

“A Diagnosis Bubbles to the Surface”

Answer

Final Diagnosis: The final diagnosis was bilateral optic neuropathies secondary to neurosarcoidosis associated with multiple pulmonary lesions and elevated IL2, presenting acutely following glioma resection and radiation, with complete visual recovery after corticosteroid therapy.

Summary of Case: This case illustrates bilateral optic neuropathies with papillitis in a child following glioma resection and radiation therapy, ultimately attributed to neurosarcoidosis. The differential diagnosis included radiation optic neuropathy, leptomeningeal spread of glioma, CRMP-5 associated paraneoplastic optic neuropathy, infectious meningitis, and demyelinating disease (MOGAD/NMOSD). Although we attempted to link the presentation to the recent diagnosis of a high grade glioma or the temazolamide therapy, the clinical course and imaging were most consistent with an inflammatory process. Radiation optic neuropathy typically occurs ≥ 6 months post-radiation and is unresponsive to corticosteroids(1). Paraneoplastic optic neuropathy was unlikely given the negative CRMP5-IgG and the lack of association between paraneoplastic optic neuropathy and gliomas. MOG-IgG, oligoclonal bands and AQP4-IgG were negative and there were no white matter changes to suggest multiple sclerosis (2). In contrast, neurosarcoidosis is known for perineural optic nerve enhancement, disc edema with hemorrhages, and dramatic steroid response(3). The elevated soluble IL-2 receptor (specificity ~85%)(4, 5) supported this diagnosis despite a normal ACE level. Finally, while the small pulmonary nodules seen on chest CT are non specific, in this context, they likely represent pulmonary sarcoidosis. This case serves as a reminder that neurosarcoidosis should be considered in the setting of retrobulbar optic neuritis with disc edema, even when systemic involvement is minimal and traditional markers such as ACE are normal.

Struggle/Dilemma of the Clinical Presentation Description: This case was complicated by the lack of evidence to support a diagnosis related to the patient’s existing malignancy or her prior radiation, surgery, or chemotherapy. This left the diagnosis of neurosarcoidosis, which is especially rare in the pediatric population and seemingly improbable in this child with an already uncommon high grade glioma. Her rapid recovery after steroid initiation and lack of tumor progression on imaging ultimately supported an inflammatory etiology.

Keywords: Papilledema, Optic neuritis, Sarcoidosis, Optic perineuritis

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“One gene to explain them all?”

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History & Exam: A 9-year-old female patient presented with a 2-year history of bilateral visual loss in June 2021. One year pre-pandemic, her mother and teacher had noticed that she was having trouble with her school activities, refraction was prescribed, but the visual problems persisted. The patient was not very descriptive about the course of visual loss; however, her mother described increasing difficulty with both near and far vision. She had been diagnosed with neurofibromatosis type 1 (NF1) in 2020 with the following clinical criteria: 2 Lisch nodules, 25 café-au-lait macules, three cutaneous neurofibromas, and axillary and groin freckling. During our initial examination, she presented with best-corrected visual acuity (BCVA) of 20/200 in her right eye (OD) and 20/80 in her left eye (OS). Color vision with Ishihara plates was 2/8 OS, but she was unable to see the control plate with her right eye. She presented with bilateral, slightly sluggish pupillary responses without a relative pupillary afferent defect. Her optic nerves showed symmetrical sectoral temporal atrophy and an increased cup-to-disc ratio (0.7) with neat borders. Confrontation visual fields ruled out heteronymous, homonymous, and altitudinal homonymous visual field defects. She presented one Lisch nodule in each eye, and the rest of her anterior segment and fundus examination was normal. Ocular motility exam, palpebral, and orbital examination were also normal. Diabetes mellitus was also diagnosed in 2021 and was treated with oral hypoglycemic agents. No history of ocular or head trauma, drug exposure, nutritional deficit, or family history of visual loss or NF1 was present. No ataxia, limb sensitive or motor deficits, or other cranial neuropathies were found.

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Grant Support: None.

“One gene to explain them all?”

Answer

Final Diagnosis: Hereditary optic neuropathy as part of Wolfram syndrome. Molecular diagnosis, made by 2 panels of next-generation sequencing, demonstrated the following variants: WFS1 gene presented a compound heterozygous state. One known pathogenic variant, c.2020G>A and one variant of unknown significance, c.1592T>G, recently reclassified as pathogenic. NF1 gene presented a heterozygous pathogenic variant c.1722C>G (pS574R)

Summary of Case: Considering the diagnosis of NF1, we undertook serial assessments of her optic nerves and visual function. Brain and orbit MRI scans were performed in June 2021 and June 2022 (see images 1-6). Neither MRI showed evidence of an optic nerve glioma, nor did it reveal other structural visual pathway lesions, except for atrophy of the optic nerve, chiasm, and optic tracts. She presented with diffuse T2-hyperintense lesions in both the basal ganglia and the left inferior olivary nucleus, classified as focal abnormal signal intensities (FASIs). Initially, OCT and perimetry were difficult to obtain due to poor cooperation. Neuro-ophthalmological follow-up was conducted every four months to clinically detect other signs of chiasmatic syndrome or progressive optic atrophy, and an MRI was performed annually. In June 2022, OCT showed a generalized decrease in both RNFL and GCC layers. Her visual fields showed a generalized depression without a chiasmatic, altitudinal, or homonymous pattern. The clinical setting of apparently progressive bilateral visual loss in a child with NF1 and bilateral optic atrophy strongly suggested an optic pathway glioma. However, its absence led to further testing; in September 2022, VEPs showed decreased amplitude with normal latency. Furthermore, evidence for traumatic, nutritional, or toxic optic neuropathies could not be elicited. Other clinical signs of hereditary optic neuropathies were also absent. Around this time, we also noted she was classified as a hard-to-control insulin-dependent DM by her pediatric endocrinologist, and insulin was started. Through multidisciplinary work-up, diabetes insipidus was ruled out, and genetic testing for Wolfram syndrome was requested, even in the absence of deafness or diabetes insipidus. Her BCVA and color vision have remained stable during a 3-year follow-up.

Struggle/Dilemma of the Clinical Presentation Description: The absence of a visual pathway glioma expanded our differential diagnosis as described: Was there an incipient, small, visual pathway glioma? Did she have an optic nerve glioma at one point? Regression has been documented. Is optic atrophy secondary to a previous inflammatory process? No history of subacute visual loss was found; however, such a presentation may go unnoticed in children. Is a different genetic process, not related to NF1, affecting the optic nerves?

Keywords: Neurofibromatosis, NF-1, Optic atrophy, Mitochondrial disorders, Diabetes mellitus

References: None provided.

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“Hidden in not so plain sight”

Steven Stasheff¹

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History & Exam: A 16-year-old female presented with 3 weeks' progressive blurred and dim vision OS & mild unsteady gait. MRI brain/orbits showed L optic nerve and multifocal dural enhancement, CSF was normal, and she was diagnosed with optic neuritis. Vision improved with 3 days of IV steroids & she was discharged with a 10-day oral steroid taper. She was re-admitted 2 weeks later after vision declined again OS and diminished OD. Repeat MRI and CSF were unchanged, ESR & CRP elevated; NMO & MOG antibodies, multiple infectious and autoimmune markers all were negative, but chest CT revealed a paraspinal mass. Vision continued declining OS > OD despite repeat treatment with IV steroids, IVIG, and rituximab, with modest improvement OD after plasmapheresis x 3 rounds. Biopsy identified the paraspinal mass as a ganglioglioma, which was resected. Her visual field expanded and acuity improved rapidly to 20/30 OD following resection of the ganglioneuroma, but OS remained with only light perception. CSF IL-6 level was elevated and she began tocilizumab, with slow further improvements in vision OD. OCT has revealed only mild thinning of the ganglion cell complex and retinal nerve fiber layer (RNFL) OS, where she retains only light perception vision within a very constricted visual field.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

“Hidden in not so plain sight”

Answer

Final Diagnosis: Paraneoplastic optic neuropathy with basilar meningoencephalitis secondary to mediastinal paraspinal ganglioneuroma.

Summary of Case: A 16-year-old female presented with apparent optic neuritis OS, initially responding to IV steroids but recurring with rapid progression and involvement of the fellow eye, minimally responsive to repeat IV steroids, IVIG, rituximab, and plasmapheresis. Incidental discovery and resection of a mediastinal ganglioneuroma

Struggle/Dilemma of the Clinical Presentation Description: Ganglioneuroma is extremely rarely associated with optic neuropathy, its resection with recover. Multiple laboratory investigations for infectious, autoimmune, or paraneoplastic markers have been negative. Patient's other conditions (hidradenitis suppurativa, folliculitis, intercurrent UTI) may have delayed accurate diagnosis and prompt treatment.

Keywords: Optic neuropathy, Paraneoplastic syndromes, Ganglioglioma

References: COGAN, D. G., et al. "Ganglioneuroma of Chiasm and Optic Nerves." Archives of Ophthalmology 65(4): 481-482 (1961).

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“Low Visibility & An Air Traffic Control Outage”

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History & Exam: A 7-year-old female with alopecia and hypoparathyroidism returned from a three year stay in Ethiopia with two months of recurrent fevers, weight loss, arthralgias, subacute photophobia and profound, bilateral vision loss. Initial examination revealed complete alopecia of eyelashes and eyebrows, severe scalp alopecia, finger clubbing, joint effusions of the knees and ankles, and pigmented lesions of the abdomen which were attributed to an episode of multiple abdominal wall abscesses two years prior. Initial labs showed hypocalcemia, hyperphosphatemia, low magnesium, macrocytic anemia, elevated ESR/CRP, low complement, hypergammaglobulinemia, and low albumin. She was admitted for evaluation of possible autoimmune, infectious, and genetic etiologies. Infectious workup, including malaria, HIV, and TB testing, were all negative. Ophthalmology exam revealed VA Count Fingers in each eye, patchy stromal scarring and irregular epithelium of both cornea, both anterior and posterior cortical/subcapsular cataracts bilaterally. Funduscopy was limited by media, but both optic discs were elevated clinically and B-scan ultrasonography confirmed bilateral optic disc elevation without focal hyperechogenicity. Contrast-enhanced MRI brain and orbits showed approximately 5mm of bilateral retro-bulbar intrinsic enhancement on T1-weighted, fat-suppressed sequences with no other intracranial abnormalities. Lumbar puncture revealed opening pressure 32 cm H₂O with mildly elevated protein, normal glucose and cell count, and positive oligoclonal bands. Genetic testing confirmed biallelic AIRE mutations, establishing diagnosis of Autoimmune Polyendocrine Syndrome Type 1 (APECED) with comorbid bilateral optic neuritis and papilledema. Treatment was started with intravenous corticosteroid therapy, but she quickly developed hypertension and posterior reversible encephalopathy syndrome (PRES), requiring intubation. She later transitioned to an oral taper, and rheumatology initiated ruxolitinib for long-term immunomodulation. Vision improved to 20/200 in each eye. Cataract extraction was deferred until systemic stability improved.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

“Low Visibility & An Air Traffic Control Outage”

Answer

Final Diagnosis: Autoimmune Polyendocrinopathy-Candidiasis-Ectodermal Dystrophy (APECED, formerly known as Autoimmune Polyendocrine Syndrome Type 1) with bilateral optic neuritis, keratopathy, cataracts, and intracranial hypertension secondary to systemic autoimmune and metabolic dysregulation.

Summary of Case: Autoimmune Polyendocrinopathy-Candidiasis-Ectodermal Dystrophy (APECED) is a rare disorder caused by biallelic AIRE mutations that result in loss of immune tolerance and multi-organ autoimmunity. Ocular involvement occurs in roughly 25–30% of patients, most commonly including keratitis, iridocyclitis, and lenticular opacities (Dogru M et al., Br J Ophthalmol, 2002). However, optic neuritis is notably absent from major reviews (Ahonen P et al., N Engl J Med, 1990; Perheentupa J, Endocr Rev, 2006). To our knowledge, bilateral optic neuritis has not been previously reported in a genetically confirmed pediatric APECED patient. This case expands the known neuro-ophthalmic spectrum of APECED and highlights the importance of considering autoimmune optic neuritis when vision loss occurs in this syndrome. Optic neuritis and intracranial hypertension in this child was reflective of her overlapping autoimmune and metabolic derangement. This overlap created diagnostic ambiguity that required close interdisciplinary collaboration.

Struggle/Dilemma of the Clinical Presentation Description: The primary dilemma was distinguishing whether the disc swelling represented optic neuritis, papilledema, or both in the setting of autoimmune and metabolic dysfunction. MRI enhancement favored neuritis, yet elevated intracranial pressure suggested mixed pathology. A secondary dilemma surrounded the consideration of infectious etiologies given multi-system presentation, recurrent fevers, and extended stay in the Horn of Africa.

Keywords: Autoimmune diseases, Optic neuritis, Increased intracranial pressure, Cataracts

References: 1. Ahonen P, Myllarniemi S, Sipila I, Perheentupa J. Clinical variation of autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED) in a series of 68 patients. N Engl J Med. 1990;322(26):1829–1836. 2. Perheentupa J. Autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy. Endocr Rev. 2006;27(4):462–475. 3. Dogru M, et al. Ocular surface changes in autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy. Br J Ophthalmol. 2002;86(12):1343–1348.

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“In the Garden of the Rare Blooms the Profound”

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History & Exam: A 10-year-old girl born to consanguineous parents was referred for neuro-ophthalmologic evaluation of chronic bilateral conjunctivitis (duration > 5 years) and decreased vision in the right eye for two weeks. Her early history included sepsis, pancytopenia, and facial/scalp edema with subcutaneous masses at six months of age. Clinically, she was diagnosed with Hemophagocytic Lymphohistiocytosis (HLH), and symptoms improved with HLH-directed therapy. At age 2, she developed bilateral proptosis, fever, and cervical/inguinal lymphadenopathy. An inguinal biopsy revealed non-Langerhans histiocytic infiltration with Rosai–Dorfman disease (RDD) features. Despite multiple chemotherapy courses, the disease progressed with bilateral sensorineural hearing loss and acute right-eye vision loss, prompting referral for a second opinion at our institution. Neuro-ophthalmic examination showed visual acuity of 20/250 OD and 20/20 OS; Ishihara color vision was 3.5/15 OD and 5/15 OS. Slit-lamp examination demonstrated bilateral proptosis with diffuse conjunctival hyperpigmentation and thickening. Fundus examination revealed pale disc edema OD, mild disc edema OS, and bilateral peripapillary retinal pigment mottling. Fluorescein angiography showed irregular peripapillary staining with hyperfluorescent rims—suggestive of fibrotic scarring and RPE hyperplasia—and bilateral optic disc leakage. MRI of the brain and orbits demonstrated diffuse intraorbital fat enhancement, optic-nerve thickening, enhancing nodules along multiple cranial nerves, and enhancement of the right internal auditory canal and parotid glands. Skin and subcutaneous biopsies showed patchy non-Langerhans histiocytic infiltration with focal RDD-like features. The constellation of multisystem inflammatory manifestations—including cutaneous lesions, lymphadenopathy, cranial nerve involvement, and persistent RDD-like histiocytic infiltration—was consistent with Histiocytosis–Lymphadenopathy Plus Syndrome (H syndrome). Whole-genome sequencing was negative for SLC29A3 mutations, and SLC29A3 expression by qPCR was normal. High-dose corticosteroids led to marked inflammatory improvement, disease regression, and resolution of bilateral optic -disc edema.

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

“In the Garden of the Rare Blooms the Profound”

Answer

Final Diagnosis: Histiocytosis–Lymphadenopathy Plus Syndrome (H syndrome) subtype, genetically negative for SLC29A3.

Summary of Case: A 10-year-old girl with parental consanguinity and prior diagnosis of HLH and RDD presents with disease progression with bilateral chronic conjunctivitis, proptosis, recent sensorineural hearing loss, and acute right eye vision loss. Imaging and biopsy revealed multisystem non-Langerhans histiocytic infiltration with Rosai–Dorfman–like features, consistent with a Histiocytosis–Lymphadenopathy Plus Syndrome (H-syndrome) Histiocytic presentations are challenging, and this case highlights the early differential considerations for HLH and RDD diagnoses, which are characterized by diagnostic ambiguity. HLH is a rare hyperinflammatory syndrome characterized by the infiltration of organs by activated macrophages and lymphocytes, leading to fever, hepatosplenomegaly, cytopenias, and potential CNS involvement (1). Whereas RDD, which is sporadic, typically presents with painless cervical lymphadenopathy with extranodal disease in fewer than half of cases. Orbital involvement occurs in about 11% of cases. Ultimately, multisystem non-Langerhans histiocytic infiltration with Rosai–Dorfman–like features was consistent with H syndrome. H-syndrome is an autosomal recessive histiocytosis that usually begins in childhood, characterized by skin lesions, hearing loss, and hepatosplenomegaly. Pathogenesis involves germ-line loss-of-function mutations in SLC29A3, which encodes a nucleoside transporter found in lysosomes, mitochondria, and endosomes (3). In this patient, whole-genome sequencing was negative for SLC29A3 variants, and qPCR testing of biopsied tissue demonstrated normal gene expression. This case represents a novel subtype of H-syndrome that is SLC29A3-negative. Additional cases of H-syndrome without SLC29A3 mutations have only recently been observed (unpublished). This case highlights that an unidentified molecular pathway likely underlies the clinical phenotype of H-Syndrome, suggesting the presence of multiple parallel or compensatory mechanisms that contribute to disease expression in the absence of SLC29A3 mutation. Given the undefined clinical course of this subtype, the disease progressed despite multiple immunomodulating treatments but was robustly steroid-responsive, with marked improvement in ocular infiltration/inflammation—including the conjunctiva, retina, and optic nerve—following steroid therapy.

Struggle/Dilemma of the Clinical Presentation Description: This represents a novel pediatric case of Histiocytosis–Lymphadenopathy Plus Syndrome (H--Syndrome) presenting without an identifiable SLC29A3 mutation -- a genetic hallmark of this diagnosis. The discordance between phenotype and genotype creates diagnostic uncertainty and underscores the challenge of classifying mixed or overlapping histiocytic presentations. This case highlights the difficulty of recognizing rare diseases amid phenotypic overlap; and the absence of a defined clinical course and optimal treatment approaches for H-Syndrome lacking SLC29A3 mutations in children.

Keywords: Optic disc edema, Optic neuropathy, Hearing loss, Vision loss

References: Chinnici A, Beneforti L, Pegoraro F, Trambusti I, et al; Approaching hemophagocytic lymphohistiocytosis. *Front Immunol.* 14, 1210041, 2023. Henter, J.-I., Horne, A., Aricó, M., Egeler, R.M., et al; HLH-2004: Diagnostic and therapeutic guidelines for hemophagocytic lymphohistiocytosis. *Pediatr. Blood Cancer*, 48: 124-131, 2007. Hamad A, Elwaheidi H, Salameh F, Alyahya M, El Fakih R, et al; H syndrome: A histiocytosis-lymphadenopathy plus syndrome. A comprehensive review of the literature. *Hematol Oncol Stem Cell Ther.* 17(3):159-167, 2024. Elbaz Younes I, Sokol L, Zhang L; Rosai-Dorfman Disease between Proliferation and Neoplasia. *Cancers (Basel).* 14(21), 5271, 2022. Diamond EL, Durham BH, Ulaner GA, Drill E, Buthorn J, et al; Efficacy of MEK inhibition in patients with histiocytic neoplasms. *Nature.* 567(7749), 521-524, 2019. Hamad A, Elwaheidi H, Salameh F, Alyahya M, El Fakih R, et al; H syndrome: A histiocytosis-lymphadenopathy plus syndrome. A comprehensive review of the literature. *Hematol Oncol Stem Cell*

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Descriptive Posters: Meet the Author – March 21, 2026 (Saturday)

Poster #	Submission Title	Author	Category
1	A Narrative Review of AI-Enhanced Multimodal Imaging for Early Neurovascular Compromise in Neurodegenerative Disease	Mohammad Aqil	Cognition, Mood & Neuro-degenerative Disease
2	Spinocerebellar Ataxia Type 7: A Case Series and Review of Pathology	Bobby Goodrich	Cognition, Mood & Neuro-degenerative Disease
3	Glioblastoma Associated with Alice in Wonderland Syndrome	William Sanfelippo	Cognition, Mood & Neuro-degenerative Disease
4	Heidenhain-variant Creutzfeldt-Jakob Disease Without Diffusion Restriction	Erin Finn	Cognition, Mood & Neuro-degenerative Disease
5	Neuronal Intranuclear Inclusion Disease Presenting As Leukoencephalopathy	Fiorella Guido	Cognition, Mood & Neuro-degenerative Disease
6	IgG4-Related Optic Perineuritis Masquerading as Traumatic Optic Neuropathy	Niranjana Kesavamoorthy	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
7	In the Lyme Light: Two Atypical Cases of Giant Cell Arteritis	Rachel Kim	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
8	Bilateral Simultaneous Nonarteritic Anterior Ischemic Optic Neuropathy Following Semaglutide Therapy: A Case Report	Adam Dossey	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
9	Bilateral Compressive Optic Neuropathy Due to Vitamin A Deficiency In An Autistic	Juan Fernandez	Disorders of the Anterior Visual Pathway (Retina,

	Child With Severely Restrictive Diet		Optic Nerve, and Chiasm)
10	Optic Neuropathies Associated With Genetic Variants Of Uncertain Significance: Clinical And Genetic Aspects.	Cedric Lamirel	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
11	Neuro-Ophthalmic Complications Following Surgical Interventions for Craniosynostosis: A Review of the Literature	Nyree Khachikyan	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
12	Ophthalmic Sequela of Combined Vitamin A and B12 Deficiency in a Young Patient	Anna Kaiser	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
13	Optic Nerve Avulsion Presenting as a Nasal Junctional Scotoma	Gabriel Grosswald	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
14	Papilledema as the initial manifestation of anti-phospholipid syndrome	Bo Young Chun	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
15	Bilateral Simultaneous NAION in Early Pregnancy Associated with Buried Optic Disc Drusen and High-Altitude Exposure	Pul Park	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
16	The Critical Role of Early Multidrug Antibiotic Treatment in Preventing Optic Atrophy in Fulminant Cat Scratch Disease Neuroretinitis	Nafiseh Hashemi	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
17	Novel variants in MT-ND4 12027 and MT-CO1 6018 presenting phenotypically as Leber Hereditary Optic Neuropathy	Emily Kang	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)

18	Partial Branch Retinal Artery Occlusion with Concurrent Non-Arteritic Anterior Ischemic Optic Neuropathy Following Regorafenib Therapy for Gastrointestinal Stromal Tumor: A Case Report	Yu-yuan Chung	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
19	A Case of Unilateral Myelin Oligodendrocyte Glycoprotein (MOG) Associated Optic Neuritis	Soon Young Cho	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
20	Retinal Vein Occlusion masquerading as Disc Edema with an unexpected resolution with Anti-Platelet Therapy in a 23-year-old female	Yakira Mishan	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
21	Speaking in Stasis: Ocular Warning Signs of a Clinoid Meningioma	Victoria Cegielski	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
22	Symptomatic Improvement of Congenital Orbital Lymphatic-Venous Malformation With Latanoprost	Miso Ko	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
23	Peaks and Prairies: Stereotypical OCT Finding in 4 Susac Patients Review of 4 cases followed up to 20 years - Retinopathy progression and MRI changes	Norah Lincoff	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
24	Bilateral Optic Papillitis And Anterior Uveitis Following MDMA Ingestion: A Rare Neuro-Ophthalmic Complication	Farial Rahman	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
25	Atypical Ischemic Optic Neuropathy as an Initial Manifestation of Systemic	Daniel Rappoport	Disorders of the Anterior Visual Pathway (Retina,

	Malignancy in Young Patients		Optic Nerve, and Chiasm)
26	Cases Series of Nonarteritic Anterior Ischemic Optic Neuropathy in Patients on Semaglutide Treatment	Yue Li	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
27	Unmasking Disc Edema	Agni Kakouri	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
28	Central and Peripheral Contrast Sensitivity as Markers of Visual Recovery in a Patient with Pituitary Macroadenoma	Uday Parmar	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
29	DOTATATE Unmasking an Atypical Optic Nerve Sheath Meningioma	Zachary Barry	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
30	Hidden in Plain Sight: Case Series of Non-Arteritic Anterior Ischemic Optic Neuropathy Masquerading as Optic Disc Drusen in Young Patients	Oliver Valdivia Camacho	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
31	Asymptomatic Optic Disc Edema Concurrent with Semaglutide Use: A Case Series	Lucie Moore	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
32	The Translaminar Pressure Gradient in Spaceflight Associated Neuro-ocular Syndrome: The Relationship Between Intraocular and Intracranial Pressure and its Role in Pathogenesis	Vivian Paraskevi Douglas	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
33	Leber Hereditary Optic Neuropathy Masquerading As Inflammatory Optic	Daniel Harrast	Disorders of the Anterior Visual Pathway (Retina,

	Neuropathy With Optic Nerve Enhancement		Optic Nerve, and Chiasm)
34	Case of Delayed Onset Right Homonymous Hemianopia after Flow Diversion and Coil Embolization of Left Internal Carotid Artery Saccular Aneurysm	Matthew Debiec	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
35	Visual Recovery Following Decompression of a Petroclival Meningioma with Intra-Orbital Extension	Alyssa Low	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
36	Cilioretinal Artery Occlusion in Cat Scratch Disease: A Rare Complication	Eve Moll	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
37	And Sometimes Things Happen Quickly: Appreciating the OCT as a Time Machine in Afferent Neuro-Ophthalmology	Oded Hauptman	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
38	Eye Spy a Tumor: Anterior segment metastasis and BDUMP in a case with advanced Esophageal Adenocarcinoma	Somya Chowdhary	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
39	Posterior Ischemic Optic Neuropathy Following Semaglutide Use in a Healthy Female Patient	Hyunjin Shin	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
40	Optic Disc Elevation in Inherited Retinal Dystrophies: Diagnostic Pitfalls and Imaging Insights from a Multicenter Case Series	Anat Bachar Zipori	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
41	Spontaneous Visual Improvement In Hemorrhagic Optic Pathway Glioma During Pregnancy	Sarah Allam	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and

			Chiasm)
42	Optic Disc Drusen Mimicking Normotensive Glaucoma In A Young Adult Experiencing Vision Loss: A Diagnostic Challenge	Michael Miltich	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
43	New Onset Optic Nerve Edema After A Resection Of Craniopharyngioma	Anna Beth Harris	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
44	A Case of Traumatic Optic Neuropathy and Partial Medial Rectus Avulsion after an Attempted Self-Enucleation	Karissa Sealey	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
45	Presentation and Outcome of a Primary Papillary Epithelial Tumor of the Sella	Gina Johnson	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
46	Organoid Nevus Syndrome with Optic Pit Associated Maculopathy	Elizabeth Simon	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
47	Anomalous Case of Central Retinal Artery Occlusion: Uncovering Rare Embolic Sources	Aman Kumar	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
48	Sequential, Metachronous Optic Neuropathies From Distinct Optic Pathway Tumors	Manisha Kotay	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
49	The Prognosis of Visual Snow. A Systematic Review	Richard Legge	Disorders of the Posterior Visual Pathway and Visual Processing
50	Hyperglycemia-induced Visual Field Changes	Kevin Yan	Disorders of the Posterior Visual

			Pathway and Visual Processing
51	Acute Leber Hereditary Optic Neuropathy at 86 years	Duncan Fuller	Disorders of the Posterior Visual Pathway and Visual Processing
52	Severe Chronic Dry Eye in Ocular Graft-Versus-Host Disease: Clinical Improvement with Topical Immunoglobulin G as Adjunctive Therapy	Barbara Tylka	Disorders of the Posterior Visual Pathway and Visual Processing
53	The Hidden Culprit: Unmasking a Rare Cause of Uveitis	Rohini Chahal	Disorders of the Posterior Visual Pathway and Visual Processing
54	Visual Snow Syndrome Symptoms With Vision Loss: A Case Series	Isabella Song	Disorders of the Posterior Visual Pathway and Visual Processing
55	Near-Infrared Reflectance Imaging Uncovers Retrograde Degeneration With Minimal Inner Nuclear Layer Changes In Retrochiasmal Visual Pathway Damage	Gabriella Cammarata	Disorders of the Posterior Visual Pathway and Visual Processing
56	Reversible Cortical Blindness Secondary to Carbon Monoxide Poisoning in a Pediatric Patient	Kyra Singh	Disorders of the Posterior Visual Pathway and Visual Processing
57	Optic Tract Syndrome: Clinical and OCT Correlates in a 6-Year Retrospective Case Series	Isabel Torres-Camacho	Disorders of the Posterior Visual Pathway and Visual Processing
58	Familial Neuronal Intranuclear Inclusion Disease with Homonymous Hemianopia: A Case Series	Cory Owens	Disorders of the Posterior Visual Pathway and Visual Processing
59	The Illusion of Sight: Anton's Syndrome Revealing the Late Sequelae of SMART Syndrome.	Farid KalantariTarari	Disorders of the Posterior Visual Pathway and Visual Processing

60	Case Series: Re-Stenting in Idiopathic Intracranial Hypertension	Casandra MacLeod	Idiopathic Intracranial Hypertension (IIH)
61	Bacterial Meningitis Complicating IIH with CSF leak	Susan Recio	Idiopathic Intracranial Hypertension (IIH)
62	Concurrent Idiopathic Intracranial Hypertension and Retinal Degeneration: A Retrospective Case Series	Ashley Hackney	Idiopathic Intracranial Hypertension (IIH)
63	The Myelinated Masquerade: A Case of Misdiagnosed Disc Edema	Alana Bryant	Idiopathic Intracranial Hypertension (IIH)
64	Vascular Etiologies of Secondary Intracranial Hypertension Missed by Noninvasive Imaging: A Case Series	Delia Sanders	Idiopathic Intracranial Hypertension (IIH)
65	Testosterone Use in a Genetically XX Carrier of Leber's Hereditary Optic Neuropathy	Kim Firn	Miscellaneous
66	Homonymous Quadrantanopia Following Odontogenic Brain Abscess In A Patient With Patent Foramen Ovale	Moira Altszul	Miscellaneous
67	Reversible Cecocentral Scotomas Secondary to Vitamin A Deficiency and Posterior Capsular Opacification in a Pseudophakic Patient	Luciana Garcia Dussan	Miscellaneous
68	A Curious Case of Brun's Nystagmus	Florian Guillot	Neuro-Imaging
69	Conventional case of chronic migraine with visual aura takes an atypical turn	Cherie Roberts	Neuro-Imaging
70	Role of DOTATATE PET Imaging in Meningiomas with Neuro-Ophthalmic Implications	Tracy Aoun	Neuro-Imaging
71	Sudden Unilateral Vision Loss in a Healthy Teenager:	Shah Aadil Ali	Neuro-Imaging

	A Rare Intracranial Anomaly Revealed by Neuroimaging		
72	Unique MRI Findings In A Case of Neurosarcoidosis	Grace Xiao	Neuro-Imaging
73	Under Pressure: Intermittent Central Retinal Artery Occlusion From A Glaucoma Drainage Device	Kasey Cooper	Neuro-Imaging
74	Bilateral Optic Neuritis Following Durvalumab Treatment for Recurrent Cholangiocarcinoma	Florence Yan	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
75	Nitrous Oxide Abuse Presenting with Diplopia	Sedona Rosenberg	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
76	A Dilemma of Managing Dueling Diagnoses: Giant Cell Arteritis and Concurrent Myasthenia Gravis	Nikitha Rajendran	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
77	Carotid-Ophthalmic Aneurysm Mimicking Optic Neuritis: Recovery with Conservative Therapy	Cameron Yen	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
78	Giant Cell Arteritis Presenting As Sixth Cranial Nerve Palsy Without Systemic Symptoms	Claire Meyerovitz	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
79	Severe Bilateral Disc Edema with Normal Visual Function as the Initial Manifestation of Neurosyphilis	Jessinta Oseni	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
80	Blind Spot and Droopy Eyelid After Wisdom Tooth Extraction	Celine Dumitrascu	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases

81	A Case of Serous Retinal Detachment Responsive to Plasmapheresis in Neuromyelitis Optica Spectrum Disorder	Forrest Wade	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
82	Blinding Relapse	Mangayarkarasi Thandampallayam	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
83	Neuro-Ophthalmic Manifestations of CACNA1A-Related Disorders	Christian Diaz Curbelo	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
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85	Secondary Central Nervous System Lymphoma Presenting with Bilateral Optic Disc Edema and Optic Nerve Sheath Enhancement	Joanne Li	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
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87	Seronegative, CSF positive MOGAD: Literature review and a case report	Surabhi Beriwal	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
88	Eyelid Myokymia as a Presenting Symptom of Multiple Sclerosis	Kashviya Suri	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
89	Concurrent Optic Perineuritis and Cranial Nerve III Palsy in a Patient	Oluchi Ihionu	Neuro-Ophthalmic Disorders of

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91	Bilateral Optic Neuritis and Transverse Myelitis with Overlapping MOG-IgG and Lyme Seropositivity	João Mendes	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
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96	A Case of Atypical Bilateral Papilledema in a Medically Complex Patient	Rebecca Pan	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
97	Optic Neuritis and Perineuritis Associated with Relapsing Polychondritis	Jessica MacIntyre	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
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100	Head Scratching Cat Scratches: Bartonella Associated Neuroretinitis and Meningitis in an HIV Positive Patient	David Zhao	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
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102	Immunosuppressant Medication Masking Giant Cell Arteritis: A Case Report Of Ischemic Optic Neuropathy	Gloria Pan	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
103	Atypical Structural Orbital Pulsation Following Craniofacial Surgery and Radiation in the Absence of Carotid-Cavernous Fistula	Celine Nguyen	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
104	Refractory Papilledema as an Initial Presentation of Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal Plasma Cell Disorder, Skin Changes (POEMS) Syndrome	Sylvia Villarreal Navarro	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
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106	Diplopia, Papilledema, Meningioma and Dural	Maria Mayorga	Neuro-Ophthalmic

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108	Beyond Diplopia: A Third Nerve Palsy Revealing Multifocal Meningiomas in the Postpartum Period	Aiswarya Raj	Neuro- Ophthalmic Disorders of Neurologic and Systemic Diseases
109	Is Tolosa-Hunt Syndrome a Recurrent Entity? Systematic Review and Relapse Analysis	Paula Boned- Fustel	Neuro- Ophthalmic Disorders of Neurologic and Systemic Diseases
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120	Isolated Optic Neuropathy in Hematologic Malignancies: Diagnostic Challenges and Case Series	Helen Rossmiller	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
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126	A Case Of Severe Panuveitis And Leptomeningeal Inflammation Presenting As A Manifestation of Neuro-Behcet's Disease	Hares Patel	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
127	Adult polyglucosan body disease presenting with progressive visual field loss	Allison Valerius	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
128	Transverse Venous Sinus Compression By Encephalocele As A Rare Cause Of Elevated Intracranial Pressure	Mariam Torres Soto	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
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131	Bilateral Homonymous Superior Quadrantanopia and Cerebral Achromatopsia	Amal Hamed	Neuro-Ophthalmic Disorders of

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183	Lateral Rectus Injuries Following Orbital Decompression	Jennifer Drechsler	Orbital and Eyelid Disorders
184	Efgartigimod Led to Improvement of Myasthenia Gravis Symptoms in Patients Initially Presenting with Ocular Symptoms: A Case Series	Cecelia Johnstone	Orbital and Eyelid Disorders
185	A Case of Double Vision-and Double Takes-at the Core	Malcolm Kates	Orbital and Eyelid Disorders
186	A rare case of Lyme disease presenting as orbital myositis	Cherie Roberts	Orbital and Eyelid Disorders
187	Case Report: A Unique Case of Marin-Amat Syndrome and Crocodile Tears post-Gamma Knife Surgery for Treatment of Vestibular Schwannoma	Andrew Garfield	Orbital and Eyelid Disorders
188	Atypical Presentation of Carotid-Cavernous Fistula Mimicking Idiopathic Orbital Inflammation	Bhakti Panchal	Orbital and Eyelid Disorders
189	Autoimmune-Related Retinopathy and Optic	Stephen Chai	Pediatric Neuro-Ophthalmology

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195	Implementation of a Dedicated Inpatient Pediatric Ophthalmology Exam Room with Advanced Diagnostics	Andrew Fischer	Pediatric Neuro-Ophthalmology
196	Congenital Horner's Syndrome due to Cervical Extension of Thymic Tissue	Andrew Silverman	Pediatric Neuro-Ophthalmology
197	The Pupil Has Become the Master: A Wax on Wax Off Phenomenon	Logan Rademacher	Pupillary Disorders
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A Narrative Review of AI-Enhanced Multimodal Imaging for Early Neurovascular Compromise in Neurodegenerative Disease

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Introduction:

The retina provides a unique, noninvasive window into the central nervous system. With shared embryologic origin and microvascular architecture, retinal imaging offers potential as an early biomarker of neurodegenerative disease. Advances in artificial intelligence (AI) applied to multimodal imaging, including optical coherence tomography (OCT), OCT angiography (OCTA), and fundus photography, enable detection of subtle retinal neurovascular alterations that may precede clinical manifestations in Alzheimer's disease (AD), Parkinson's disease (PD), and multiple sclerosis (MS).

Description of Cases:

This narrative review synthesizes findings from more than 50 published studies examining retinal biomarkers across AD, PD, and MS. In AD, OCT reveals retinal nerve fiber layer and ganglion cell complex thinning, while OCTA demonstrates reduced vessel density correlating with hippocampal atrophy and cognitive decline. In PD, microvascular rarefaction and macular thinning parallel dopaminergic neurodegeneration and motor severity. In MS, peripapillary retinal nerve fiber layer loss and deep capillary plexus alterations mirror axonal degeneration and inflammatory burden. Across all conditions, AI-driven algorithms improve diagnostic sensitivity by integrating multimodal datasets, extracting subtle spatial and vascular patterns imperceptible to clinicians, and stratifying disease severity with high reproducibility. Pilot studies further suggest AI-enhanced retinal analysis may identify at-risk individuals before overt neurological symptoms, raising the possibility of screening and longitudinal monitoring in vulnerable populations.

Conclusions, including unique features of the case:

Retinal imaging is an underutilized yet scalable biomarker for neurodegeneration. Narrative review of AI-enhanced multimodal imaging demonstrates its potential to detect early neurovascular compromise in AD, PD, and MS, supporting earlier intervention and personalized monitoring. Teaching Point: The integration of AI with multimodal retinal imaging positions neuro-ophthalmologists at the forefront of translating ocular biomarkers into neurologic care, strengthening their role in interdisciplinary research and clinical innovation.

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Keywords: Neuroimaging, Retina, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Demyelinating disease

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Spinocerebellar Ataxia Type 7: A Case Series and Review of Pathology

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Introduction:

Spinocerebellar ataxia type 7 (SCA-7) is an autosomal dominant neurodegenerative disorder characterized by progressive cerebellar ataxia and maculopathy with vision loss. Genetic anticipation from CAG trinucleotide repeat expansion in the ATXN7 gene results in earlier onset and greater severity in successive generations. Affected individuals develop profound neurologic disability and blindness, emphasizing the need to correlate clinical findings with underlying pathology.

Description of Cases:

We report a six-generation family with SCA-7, including eleven affected members with detailed clinical records and pathologic findings from one patient. Clinical ocular abnormalities included decreased visual acuity, visual field defects, Flynn phenomenon, color vision loss, and macular pigmentary changes. Ocular histopathologic examination revealed marked retinal degeneration with thinning of the inner and outer nuclear layers, disruption of photoreceptor segments, and intraretinal pigment-laden macrophages. Optic nerve showed axonal loss and widening of the subarachnoid space. Neurologic abnormalities included gait and limb ataxia, dysarthria, dysphagia, and upper motor neuron findings. Neuropathologic analysis demonstrated extensive cerebellar degeneration with loss and malorientation of Purkinje cells, Bergmann gliosis, attenuation of the granule cell layer, and degeneration of the dentate nucleus. Ubiquitin-positive intranuclear inclusions were identified in Purkinje cells, the inferior olivary nucleus, and pontocerebellar tracts, with axonal loss in the spinocerebellar, olivocerebellar, and posterior column tracts.

Conclusions, including unique features of the case:

The combination of cone-rod dystrophy, optic nerve atrophy, and widespread neurodegeneration provides a rare pathologic correlate for the profound visual and neurologic disability characteristic of SCA-7.

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Keywords: Genetic disease, Orbit/ocular pathology, Retina, Ocular motility, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Glioblastoma Associated with Alice in Wonderland Syndrome

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Introduction:

Alice in Wonderland Syndrome (AIWS) is a rare disorder of visual perception, body schema, and distortion in the experience of time first described in 1955. AIWS includes over 40 visual symptoms along with over 15 nonvisual symptoms, but the linking symptomatology is an overall distortion in one's perceptions of sensation rather than new hallucinations. Of the published cases of AIWS, the most common cause is migraine followed by infection and the majority of occurrences have been seen in children less than 18 years old. Based on neuroimaging studies, the convergence of temporooccipital, parietooccipital, and temporoparietal junctions (TPO junction) appears to be the critical neuroanatomical center for developing AIWS.

Description of Cases:

A 63 year old man presented to the emergency department for a subacute nonspecific feeling of dizziness, mild positional headaches, and new micropsia. The patient described this visual disturbance as objects, but especially people and faces, appearing much smaller than normally expected. Brain MRI showed a large, peripherally enhancing, and centrally cystic/necrotic mass centered at the junction of the right temporal, parietal, and occipital lobes measuring 6.2 x 3.7 x 4.4 cm. Patient's exam was significant for left incomplete homonymous hemianopia, left dysmetria, and micropsia. He underwent gross total resection of the mass with Neurosurgery and pathology results showed Glioblastoma. Post-operatively, the patient displayed continued micropsia.

Conclusions, including unique features of the case:

This patient's mass is located precisely at the TPO junction, which may at least anatomically explain his micropsia and correlates to previous studies in which occipital hypoactivation and parietal hyperactivation are associated with micropsia. This case represents only the second reported occurrence of AIWS in the setting of glioblastoma, but further strengthens the claim that this perceptual disorder is centered at the intersection point of the temporal, parietal, and occipital lobes.

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Neuronal Intranuclear Inclusion Disease Presenting As Leukoencephalopathy

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Introduction:

Neuronal intranuclear inclusion disease (NIID) is a rare progressive neurodegenerative disorder with characteristic eosinophilic hyaline intranuclear inclusions within the nervous system and visceral organs. NIID is caused by expansion of GGC repeats in the 5' untranslated region of NOTCH2NLC gene. We present a case of autopsy-proven NIID with unique presentation of a homonymous hemianopia and magnetic resonance imaging (MRI) findings.

Description of Cases:

A 61-year-old white female presented with progressive worsening headaches, cognitive decline, episodes of encephalopathy, and a new homonymous left visual defect. Automated visual field testing was unreliable, but confrontation testing revealed a dense left homonymous hemianopia. OCT showed left retinal nerve fiber layer (RNFL) mild thinning, but was otherwise normal. MRI brain showed diffuse T2 hyperintensity in the right temporal, occipital, and parietal lobes preferentially in the subcortical and deep white matter, extending to periventricular regions and subcortical U fibers with minimal contrast enhancement. CSF was normal including infectious, autoimmune, and cytology studies. Biopsy of the right parietal lesion was nondiagnostic. EEG showed epileptogenic discharges in bioccipital and right posterior temporal regions with generalized background slowing. Skin biopsy demonstrated p62 and ubiquitin positive intranuclear inclusions in fibroblasts, eccrine glands and adipocytes. The patient declined whole-exome sequencing. She continued to decline cognitively and died 5 years after presentation. Autopsy showed neuronal, glial, and ependymal p62 and ubiquitin positive intranuclear inclusions which confirmed the diagnosis of NIID.

Conclusions, including unique features of the case:

NIID involves multisystem degeneration affecting the central, peripheral, and/or autonomic nervous systems. Consequently, it can present with diverse clinical manifestations making diagnosis challenging; however, skin biopsy and genetic testing can help confirm the diagnosis. Our case highlights a unique presentation of autopsy-confirmed NIID leukoencephalopathy presenting with left homonymous hemianopia, episodic encephalopathy with headache, progressive cognitive decline, and imaging findings of extensive white matter involvement of the temporal, parietal, and occipital lobes, including the optic radiations.

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Keywords: Neuroimaging, Genetic disease, Visual fields

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Grant Support: None.

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IgG4-Related Optic Perineuritis Masquerading as Traumatic Optic Neuropathy

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Introduction:

Immunoglobulin G4-related disease (IgG4-RD) is a rare autoimmune fibroinflammatory disorder that can involve multiple organ systems. Optic perineuritis is an exceptionally uncommon manifestation and may be misdiagnosed as other optic nerve pathologies, including traumatic optic neuropathy.

Description of Cases:

An 18-year-old female developed intractable headaches, retro-orbital pressure, left temporal tenderness, and pulsatile tinnitus following a closed head injury. Examination showed left optic disc edema with temporal crescent peripapillary hemorrhage, preserved visual acuity, color vision, visual field, and no relative afferent pupillary defect. She was initially treated for presumed traumatic optic neuropathy with prednisone, but symptoms persisted. MRI brain and CT venography were unremarkable, while orbital MRI revealed left optic nerve sheath distension, perineural hemorrhage, and diffuse sheath enhancement. Lumbar puncture and cytology were normal. Laboratory evaluation demonstrated elevated serum IgG4 (109 mg/dL), elevated immunoglobulin E (IgE), and borderline cytoplasmic anti-neutrophil cytoplasmic antibodies, with other autoimmune markers, including neuromyelitis optica (NMO) and myelin oligodendrocyte glycoprotein (MOG), being negative. Prior urinalysis had shown proteinuria and hematuria. The constellation of findings suggested IgG4-related optic perineuritis. High-dose intravenous methylprednisolone was initiated, followed by a prednisone taper.

Conclusions, including unique features of the case:

This case underscores the importance of maintaining a broad differential diagnosis in optic nerve disorders with atypical clinical and radiological features. IgG4-related optic perineuritis, though rare, should be considered, as early diagnosis and immunosuppressive therapy may prevent irreversible visual impairment.

References: None provided.

Keywords: Optic neuropathy, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Miscellaneous

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In the Lyme Light: Two Atypical Cases of Giant Cell Arteritis

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Introduction:

Lyme neuroborreliosis (LNB)-induced optic neuropathy, though rare, typically presents with bilateral optic nerve head (ONH) swelling and progressive visual loss.¹ When accompanied by headache, disc edema and elevated inflammatory markers, LNB may closely mimic giant cell arteritis (GCA), highlighting the importance of including Lyme disease (LD) in the differential of optic neuropathies.

Description of Cases:

Case 1: A 75-year-old female presented headaches, neck stiffness, scalp tenderness and elevated C-reactive protein (CRP; 61.7 mg/L) and Erythrocyte Sedimentation Rate (ESR; 75 mm/hr). Visual acuity (VA) was 20/20 OU without relative afferent pupillary defect (RAPD). Prednisone (70 mg/day) was started for presumed GCA; bilateral temporal artery biopsies (TABs) were negative. During tapering, symptoms persisted with persistently elevated markers. At 3.5 months, examination revealed right ONH edema; optical coherence tomography (OCT) showed retinal nerve fibre layer (RNFL) thickening. Head magnetic resonance imaging (MRI) excluded a compressive lesion. By 5.5 months, she developed bilateral ONH swelling with hemorrhages prompting repeat MRI which revealed bilateral ONH enhancement. OCT showed progressive RNFL thickening (312 µm OD, 164 µm OS). Two-tiered Lyme serology and cerebrospinal fluid analysis confirmed LNB. Case 2: A 68-year-old man on prednisone (65 mg/day) for presumed GCA presented with scalp tenderness, temporal headaches and elevated CRP (184.6 mg/L) and ESR (36 mm/hr). VA was 20/50 OU without RAPD. Bilateral TABs were negative. Prednisone tapering was halted at 30 mg/day due to recurrent headaches. At 4 months, a cecentral scotoma (OD) and bilateral optic disc edema (OD>OS) developed. Intravenous fluorescein angiography was within normal; head MRI was negative for demyelination. Two-tiered positive Lyme serology confirmed Lyme-related optic neuropathy.

Conclusions, including unique features of the case:

LNB mimicking GCA is rare. Distinguishing features include progressive vision loss, absent ischemic ocular signs and unremarkable vascular or compressive lesions on imaging. In endemic regions, LD should be considered when GCA-like presentations are unresponsive to steroids.

References: 1. Lu, Zand; Characteristics of Lyme optic neuritis: a case report of Lyme associated bilateral optic neuritis and systematic review of the literature, BMC Neurology, 22, 113, 2022.

Keywords: Optic neuropathy, Lyme disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Neuro-ophth & infectious disease (eg, AIDS, prion)

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Contact Information: None provided.

Bilateral Simultaneous Nonarteritic Anterior Ischemic Optic Neuropathy Following Semaglutide Therapy: A Case Report

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Introduction:

Nonarteritic anterior ischemic optic neuropathy (NAION) is the most common acute optic neuropathy in adults over 50 years. Simultaneous, bilateral, NAION is exceptionally rare, occurring in less than 1% of cases. Recent studies identify an association between glucagon-like peptide-1 (GLP-1) receptor agonists and increased NAION risk. We present a case of bilateral simultaneous NAION following semaglutide treatment.

Description of Cases:

A 74-year-old female patient was referred to our outpatient eye clinic with photopsia symptoms in the right eye. Best corrected visual acuity (BCVA) at presentation was 20/30 in each eye. Pupillary reactions were sluggish in both eyes without a relative afferent pupillary reflex. Anterior segment exam and IOP were normal in both eyes. Both optic nerves were elevated and edematous with blurred rim margins. MRI Brain as well as carotid doppler scan was unremarkable. Lumbar puncture revealed an opening pressure of 14 cm H₂O. ESR, CRP, CBC and SPEP were all reported as normal. Initial Humphrey visual field (HVF) testing was initially normal in both eyes. The Semaglutide was discontinued and the optic nerve edema started to improve on OCT. At 3 months, OCT confirmed the improvement of the optic nerve edema and revealed an inferior nerve fiber layer (NFL) defect in the left eye. The 3 month HVF showed a superior arcuate defect in the left eye.

Conclusions, including unique features of the case:

This case represents bilateral simultaneous NAION in temporal association with semaglutide therapy. Bilateral simultaneous NAION is exceptionally rare. The improvement in optic nerve edema following semaglutide discontinuation suggests a potential causal relationship. GLP-1 receptor agonists may precipitate NAION through blood pressure reduction affecting optic nerve head perfusion, particularly in patients with anatomically crowded optic discs. While the absolute risk remains low, the devastating nature of bilateral vision loss warrants careful patient counseling and monitoring.

References: 1. Gundogan FC, Guven S, Yolcu U, et al. Bilateral Simultaneous Nonarteritic Anterior Ischaemic Optic Neuropathy: Case Report. PMC5291059. <https://pmc.ncbi.nlm.nih.gov/articles/PMC5291059/> 2. Hathaway JT, Shah MP, Hathaway DB, et al. Risk of Nonarteritic Anterior Ischemic Optic Neuropathy in Patients Prescribed Semaglutide. JAMA Ophthalmol. 2024;142(8):732-739. <https://jamanetwork.com/journals/jamaophthalmology/fullarticle/2820255> 3. Hakim J, Patel L, Liarakos VS. Utility of Erythrocyte Sedimentation Rate and C-Reactive Protein for the Diagnosis of Giant Cell Arteritis. PMC3307891. <https://pmc.ncbi.nlm.nih.gov/articles/PMC3307891/> 4. Hayreh SS. Visual field abnormalities in nonarteritic anterior ischemic optic neuropathy. Ophthalmology. 2005;112(11):1966-72. <https://pubmed.ncbi.nlm.nih.gov/16286618/>

Keywords: Optic neuropathy, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Bilateral Compressive Optic Neuropathy Due to Vitamin A Deficiency In An Autistic Child With Severely Restrictive Diet

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Introduction:

Autism can be associated with restrictive diets and malnutrition, with Vitamin A deficiency (VAD) being an established problem¹. While commonly associated with xerophthalmia and retinopathy, cases exist of autistic children with VAD developing optic neuropathy ². Herein, we present a case of an autistic child with bilateral compressive optic neuropathy due to sphenoid bone hyperostosis due to VAD.

Description of Cases:

A 9-year-old boy with severe autism (non-verbal) and restrictive diet of chips and juice started exhibiting behaviors concerning for profound bilateral vision loss. On exam, he was LP OD and NLP OS (from a baseline of CSM 4 years earlier). Pupils were minimally reactive OD and non-reactive OS, and optic discs were pale OU. Contrasted MRI brain/orbits was without lesion affecting the visual pathways or optic nerves. Given history of restrictive diet, a metabolic/nutritional optic neuropathy was suspected. Testing for several vitamins and minerals only revealed low vitamin A (5.6 mcg/dL; LLN 18.2 mcg/dL) and negative LHON testing. Patient underwent G-tube placement which led to normalization of vitamin levels. However, on re-evaluation 9 months later, He was LP OU and had profound optic disc pallor OU. Further evaluation of the initial MRI brain revealed bilateral optic canal narrowing due to sphenoid wing hyperostosis.

Conclusions, including unique features of the case:

VAD results in abnormal bone growth due to increased osteoblastic activity, which leads to bilateral compressive optic neuropathy at the optic canals³. Another 11 cases of this rare cause of optic neuropathy have been reported to our knowledge. Vision loss in these cases developed over months, consistent with a compressive etiology¹⁻⁴. Interestingly, our non-verbal patient could not report vision loss until abnormal behaviors became evident. Visual recovery with vitamin replenishment is variable¹⁻⁴, but our patient showed no significant improvement. Routinely screening for vitamin deficiencies in autistic children with restrictive diets may lead to optic neuropathy prevention.

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Keywords: Optic neuropathy, Neuroimaging, Skull base

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Optic Neuropathies Associated With Genetic Variants Of Uncertain Significance: Clinical And Genetic Aspects.

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Introduction:

Current genetic evaluation of unexplained optic neuropathies often identifies genetic variants with variable pathogenicity. The classification of the American College of Medical Genetics and Genomics (ACMG) distinguishes between those variants of uncertain significance (VUS, class 3) that may later be reclassified based on evolving clinical and molecular criteria. We conducted a retrospective single-center study at a tertiary neuro-ophthalmology referral center including all patients with questionable VUS (class « 3+ ») identified during genetic testing between 2010 and 2024. Molecular and bioinformatics analyses were performed at a national hereditary optic neuropathies reference center using a sequencing panel of 87 nuclear genes and complete mitochondrial DNA analysis.

Description of Cases:

Among the 397 patients included, we identified 32 index cases (8%) carrying a questionable VUS. The five most frequently involved genes were WFS1 (39%), OPA1 (18%), ACO2 (11%), SPG7 (11%), and MFN2 (11%). Only one VUS was identified in mitochondrial DNA, in the ND1 gene. On average, patients were 42 years old, with a male-to-female ratio of 0.8. Most presented with bilateral unexplained optic neuropathy. The median visual acuity was 0.46 logMAR, and central scotoma was present in 65% of cases. A family study was conducted in 44% of cases, but segregation analysis yielded no contributory findings. Molecular reclassification led to seven variant updates: two VUS were reclassified as likely benign (class 2), and five were reclassified as likely pathogenic (class 4).

Conclusions, including unique features of the case:

VUS account for nearly 10% of genetic findings in our cases of optic neuropathy of unknown origin. Their pathogenicity status requires both clinical and genetic family investigations, in close collaboration with molecular biologists. Our study found that VUS reclassification occurred at a rate of one case per 20 patient years of follow-up. These results suggest that reanalysis of questionable VUS can be beneficial in cases of unresolved genetic diagnoses.

References: None provided.

Keywords: Optic neuropathy, Genetic disease

Financial Disclosures: Cedric Lamirel; Iulia Tomescu; Samy Zaher; Ines Akopian; Catherine Vignal-Clermont; Manon Philibert; François Audren; Marc Ferré; Christophe Verny; Patizia Amati-Bonneau; Pascal Reynier; Dan Milea: This research was supported by the VISIO Foundation, Bouchemaine, France.

Grant Support: None.

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Neuro-Ophthalmic Complications Following Surgical Interventions for Craniosynostosis: A Review of the Literature

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Introduction:

Craniosynostosis is a birth defect characterized by premature fusion of one or more cranial sutures, affecting approximately 1 in 2,000 to 1 in 2,500 live births. The condition leads to an abnormal head shape, which, left untreated, can cause long-term complications such as intracranial hypertension and ophthalmic conditions; the etiology of these issues lies in the restricted growth of the skull. The standard intervention for craniosynostosis is surgical procedures such as fronto-orbital advancement, calvarial vault remodeling, endoscopic strip craniectomy, or monobloc advancements. These procedures are designed to correct the shape of the skull and alleviate elevated intracranial pressure. While these surgical interventions are generally successful, they are not devoid of risks and can lead to a range of ophthalmic complications.

Description of Cases:

Neuro-ophthalmic complications following craniosynostosis repair include papilledema, optic atrophy, strabismus, and more. These complications are significant as they can have lasting effects on visual function and ocular health, especially if not corrected soon. This poster aims to gather and examine the current body of evidence regarding eye-specific complications following surgical treatment for craniosynostosis. 1,004 patients who received various interventions were compiled from nine articles. Amblyopia, strabismus, and optic nerve complications such as papilledema were notable neuro-ophthalmologic complications. Out of 1,004 patients post-craniosynostosis repair, six developed new optic nerve complications, 27 developed amblyopia, and 83 developed strabismus. Other notable ophthalmic complications included retinal damage, as well as external orbital and corneal changes.

Conclusions, including unique features of the case:

While it's difficult to determine whether post-surgical complications are caused by damage during surgery, inadequate surgical decompression, late surgical intervention, or pre-existing pathology carrying out a natural course, these statistics highlight the need for continued ophthalmic monitoring following intervention. We also hope to contribute to the refinement of surgical techniques and postoperative care protocols, ultimately enhancing the quality of life for individuals affected by craniosynostosis.

References: None provided.

Keywords: Miscellaneous

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Ophthalmic Sequela of Combined Vitamin A and B12 Deficiency in a Young Patient

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Introduction:

Nutritional deficiencies are often overlooked in high income countries such as the United States, but they remain clinically relevant. Recent estimates indicate approximately 3.6% of the US population has B12 deficiency, while fewer than 1% has vitamin A deficiency.^{1,2} Risk factors for developing nutritional deficiencies include poor dietary quality or intake, increased nutrition requirements, increased metabolic losses, or decreased gastrointestinal digestion and absorption.³ Vitamin B12 deficiency is associated with multiple neurologic manifestations including myelopathy, peripheral neuropathy, ataxia, and neuropsychiatric involvement, but it is rarely associated with optic neuropathy. Heaton et al. reviewed 153 patients with B12 deficiency and found only 1 patient (0.5%) with optic neuropathy.⁴ Worldwide, Vitamin A deficiency is the leading cause of childhood blindness, though it is rare in developed countries.⁵ Ophthalmologic manifestations of Vitamin A deficiency, referred to as xerophthalmia, include retinal, conjunctival, and corneal pathology.⁶

Description of Cases:

We describe a case of a 16-year-old female with five months of progressive vision loss with subacute worsening in the left eye. She was found to have asymmetric mild bilateral optic neuropathy with concurrent xerophthalmia with unilateral corneal ulceration. Infectious and inflammatory workup were unremarkable, but serum testing revealed severe Vitamin A and B12 deficiencies in the setting of a severely restricted diet secondary to sequela of eosinophilic esophagitis. The patient was promptly treated with vitamin repletion and antibiotic drops, leading to significant improvement in Bitot spots, visual acuity, optic disc edema, and dyschromatopsia.

Conclusions, including unique features of the case:

This is a case highlighting the ophthalmologic consequences of two vitamin deficiencies rarely encountered in the United States. It emphasizes the importance of early recognition in at-risk patients, as prompt treatment can ultimately be vision saving.

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Keywords: Optic neuropathy, Orbit/ocular pathology, Pediatric neuro-ophthalmology

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Optic Nerve Avulsion Presenting as a Nasal Junctional Scotoma

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Introduction:

Traumatic avulsions of the globe and optic nerve are uncommon, especially those due to high pressure water injuries to the eye. It is important to distinguish the location within the orbit at which the optic nerve is avulsed. Optic nerve avulsions near the chiasm could result in a visual field defect to the contralateral eye, most commonly resulting in a temporal junctional scotoma.

Description of Cases:

We report a case of a 29-year-old male who experienced a traumatic avulsion of the right globe and optic nerve caused by a fireman's water cannon. CT scans revealed fractures of the right orbital medial wall and floor, air in the orbital soft tissues, mild pneumocephalus, sub arachnoid hemorrhage, and blood in the basal cisterns. Left eye visual field testing revealed a significant nasal scotoma. After fifteen years of longitudinal care and compliance to a supplemental combination of supraphysiological doses of neurotrophic vitamins, the scotoma resolved.

Conclusions, including unique features of the case:

The significance of this case is fourfold: 1) We believe this to be the first report of avulsion of the globe due to a water cannon. 2) We believe it to be the longest follow up of a traumatic chiasmal visual field type defect in the literature. 3) Although initially quite severe, a slow but nearly complete recovery of the remaining visual field unfolded by the 15th year. 4) The neurotrophic vitamins methyl B12, L-methyl tetrahydrofolate, vitamin D, and omega-3 fatty acids were used to promote recovery. We are not aware of any other such documented recovery. The literature on traumatic junctional scotomas and their natural history is rare, particularly those concerning contralateral nasal scotomas. Evidence is considered that high doses of omega-3 fatty acids, methyl B12 and L-methyl tetrahydrofolate, and vitamin D may be neuroprotective and support neuro-regeneration. In this patient, the intervention appeared to be successful, albeit slow.

References: None provided.

Keywords: Optic nerve trauma and treatment, Visual fields

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Papilledema as the initial manifestation of anti-phospholipid syndrome

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Introduction:

Antiphospholipid syndrome (APS) is a systemic autoimmune disorder characterized by recurrent thrombotic events and persistently positive antiphospholipid antibodies. While cerebral manifestations are well-recognized complications of APS, papilledema as the initial presenting symptom is rarely reported in the literature.

Description of Cases:

We report a case of a 19-year-old female who presented with a 2-3 week history of headache, nausea, blurred vision, tinnitus, and ocular pain. Ophthalmological examination revealed bilateral papilledema (Frisen grade 2) with concurrent optic nerve hypoplasia. Lumbar puncture demonstrated elevated cerebrospinal fluid opening pressure of 28 mmHg. Laboratory investigations revealed markedly elevated anti-cardiolipin IgG antibodies (>160:1) and anti-beta2-glycoprotein IgG antibodies (>160:1). Lipid profile showed dyslipidemia with total cholesterol 156 mg/dL, triglycerides 355 mg/dL, HDL 26 mg/dL, and LDL 97 mg/dL. The patient had a significant family history of sudden cardiac death in her father during his 40s. One year later, the patient developed corpus callosum infarction, and was formally diagnosed with antiphospholipid syndrome.

Conclusions, including unique features of the case:

This case highlights papilledema as a potential initial manifestation of APS, emphasizing the importance of screening for antiphospholipid antibodies in young patients presenting with unexplained elevated intracranial pressure and papilledema, particularly in the presence of relevant family history. Early recognition and diagnosis are crucial for preventing severe thrombotic complications and optimizing long-term outcomes.

References: None provided.

Keywords: Pseudotumor cerebri, Stroke, Genetic disease

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Bilateral Simultaneous NAION in Early Pregnancy Associated with Buried Optic Disc Drusen and High-Altitude Exposure

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Introduction:

NAION, the most common acute optic neuropathy over 50 years of age, has been associated with various chronic risk factors [1,2]. It can present acutely following physiological stress such as hemorrhage or surgery. A study by Nazarali et al. suggested an increased risk of NAION in patients with optic disc drusen when exposed to hypoxic conditions associated with high altitude [3-11].

Description of Cases:

A 36-year-old female at 15 weeks of gestation presented with sudden, painless inferonasal visual field loss following a 9-hour transatlantic flight four days before symptom recognition. History was notable for nocturnal BP as low as 95/60 during pregnancy compared to daytime readings of 120/80, mild anemia (Hgb 10.9 g/dL), and ulcerative colitis with last flare 18 years prior. An extensive work up revealed lumbar puncture opening pressures of 15 cm H₂O and 16 cm H₂O serially, normal inflammatory markers, and no evidence of infection. Visual acuity was 20/20 bilaterally, and color vision was full. A left RAPD (NDF 0.9 log unit) was present. Fundus exam revealed “discs-at-risk” with grade 4 optic disc edema, and splinter hemorrhages bilaterally. HVF 24-4 demonstrated an inferior arcuate defect in the left eye and a normal right eye. B-scan showed medium-sized optic nerve head drusen bilaterally.

Conclusions, including unique features of the case:

This case highlights an unusually early onset of bilateral simultaneous NAION, with visual field loss in one eye and incipient involvement in the other, in a pregnant patient with multiple predisposing factors. Unlike previous reports of NAION during pregnancy, the patient developed symptoms in the second trimester without acute blood loss [12]. The combination of optic disc drusen, “disc-at-risk” anatomy, anemia and possible hypoxic insult during prolonged air travel may have contributed to ischemic optic neuropathy [13]. Further studies are needed to clarify how the extent and interaction of risk factors influence disease onset, severity, and prognosis.

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Keywords: Optic neuropathy, Visual fields, Optic nerve trauma and treatment

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The Critical Role of Early Multidrug Antibiotic Treatment in Preventing Optic Atrophy in Fulminant Cat Scratch Disease Neuroretinitis

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Introduction:

Bartonella henselae neuroretinitis, the most common infectious cause of neuroretinitis, is typically self-limited that responds well to appropriate antibiotic therapy. We are presenting a case of severe vision loss that did not improve with initial monotherapy. Due to diagnostic uncertainty and the absence of early serologic confirmation, the patient was treated with high-dose corticosteroids which delayed recovery. Visual improvement occurred after several months and the patient ultimately developed optic atrophy.

Description of Cases:

A 49-year-old man with hypertension presented with sudden vision loss in his left eye followed by similar loss in his right eye few day later. Examination showed severe bilateral macular and optic disc edema with a macular star and central visual field defects; visual acuity was finger counting at one foot. Laboratory studies revealed elevated ESR and CRP, and MRI of the brain and orbits and spinal tap were normal. Empiric treatment with trimethoprim-sulfamethoxazole started with no improvement in vision after one week. High-dose intravenous methylprednisolone were given while awaiting serology, and he was discharged on a prednisone taper. A positive *Bartonella henselae* titer and history of a recent kitten scratch established cat-scratch neuroretinitis. Rifampin and doxycycline were started and continued for 6 weeks, but his vision failed to recover to base line and bilateral optic atrophy developed.

Conclusions, including unique features of the case:

Unlike majority of reported cases which are unilateral and present with mild to moderated vision loss, our patient presented with profound visual impairment in count finger range. Given the extent of vision loss and bilateral involvement, initial treatment with combination therapy would have been more appropriate. Furthermore, systemic corticosteroids should be deferred until adequate antibiotic coverage is established and objective improvement in vision is observed to avoid exacerbating the infection and delayed recovery.

References: None provided.

Keywords: Neuro-ophth & infectious disease (eg, AIDS, prion), Optic neuropathy, Visual fields

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Novel variants in MT-ND4 12027 and MT-CO1 6018 presenting phenotypically as Leber Hereditary Optic Neuropathy

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Introduction:

Leber Hereditary Optic Neuropathy (LHON) is an inherited mitochondrial disorder with subacute bilateral sequential vision loss. Pathogenesis typically involves impairment of complex I of the electron transport chain, which leads to retinal ganglion cell death and optic nerve degeneration. Three primary mutations (m.3460G>A, m.11778G>A, and m.14484T>C) account for 90-95% of LHON cases (Carelli et al., 2016). Environmental triggers probably produce oxidative stress as a contributor to the variable penetrance. We present a novel case of two mtDNA variants present in a case of optic neuropathy that is clinically consistent with LHON.

Description of Cases:

A 38-year-old male active-duty service member presented with progressive nyctalopia and central scotoma beginning two years earlier. Family history was noncontributory. He sustained significant wildfire smoke exposure two months prior to symptom onset. Prior uncorrected visual acuity was 20/15 in each eye. Extensive evaluation, including multiple brain/orbit MRIs, revealed only bilateral optic nerve atrophy. Optical Coherence Tomography (OCT) confirmed severe optic atrophy with nasal fiber sparing. Humphrey 30-2 visual field testing demonstrated significant central field loss for both eyes. Lumbar puncture with CSF analysis was unremarkable. Mitochondrial genome sequencing identified homoplasmic (99.9%) m.12027T>C (MT-ND4) and heteroplasmic (22.6%) m.6018G>A (MT-CO1) variants of uncertain significance.

Conclusions, including unique features of the case:

This is the first reported LHON presentation with m.12027T>C and m.6018G>A variants. Synergistic interactions between both mutations are possible. The patient's atypically late onset, as well as the two-month lag period after wildfire smoke exposure, may represent a type II phenotype (Spiegel and Sadun, 2022). This case potentially expands the mutational spectrum of LHON and emphasizes that absence of canonical mutations should not exclude a diagnosis of LHON when clinical presentation is characteristic. Further studies are needed to establish the pathogenicity of these variants and broaden understanding of LHON genetic heterogeneity.

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Keywords: Optic neuropathy, Genetic disease

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Partial Branch Retinal Artery Occlusion with Concurrent Non-Arteritic Anterior Ischemic Optic Neuropathy Following Regorafenib Therapy for Gastrointestinal Stromal Tumor: A Case Report

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Introduction:

We report a rare case of concurrent partial branch retinal artery occlusion (BRAO) and non-arteritic anterior ischemic optic neuropathy (NAION) in a patient receiving oral regorafenib for metastatic gastrointestinal stromal tumor (GIST).

Description of Cases:

A 62-year-old woman with metastatic gastrointestinal stromal tumor (GIST), treated with regorafenib following imatinib resistance, presented with acute, painless visual disturbance in her left eye (OS). Ophthalmic examination revealed best-corrected visual acuity (BCVA) of 0.9 in the right eye (OD) and 0.01 in the central field OS, with preserved lateral acuity of 1.0 OS. A relative afferent pupillary defect, sectoral optic disc pallor, and localized inner retinal whitening were also found in left eye, consistent with partial BRAO. Optical coherence tomography demonstrated inner retinal hyperreflectivity and ganglion cell complex thinning, while fluorescein angiography confirmed focal arterial hypoperfusion. Visual field testing showed a central scotoma, and visual evoked potentials revealed diminished P100 amplitudes. Magnetic resonance imaging excluded optic neuritis or compressive lesions. Based on multimodal findings, a diagnosis of concurrent partial BRAO and NAION was established. The patient declined systemic corticosteroid therapy and was managed conservatively. Despite continued oncologic treatment, her systemic condition deteriorated and she ultimately succumbed to metastatic disease.

Conclusions, including unique features of the case:

This case illustrates a rare but clinically meaningful ocular vascular complication associated with regorafenib therapy. The proposed mechanism involves regorafenib-induced endothelial dysfunction, leading to microvascular compromise within both the posterior ciliary and retinal arterial circulations. Ophthalmologists should maintain a high level of vigilance for retinal or optic nerve ischemia in patients receiving targeted anticancer agents, particularly those with pre-existing vascular risk factors. Early recognition through multimodal imaging, timely communication with oncology teams, and comprehensive systemic evaluation are critical for the appropriate management of such potentially vision-threatening adverse events.

References: None provided.

Keywords: Optic neuropathy, Retina, Vascular disorders, Visual fields

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Contact Information: None provided.

A Case of Unilateral Myelin Oligodendrocyte Glycoprotein (MOG) Associated Optic NeuritisSOON YOUNG CHO¹¹ *Keimyung University School of Medicine***Introduction:**

MOG associated optic neuritis is mostly bilateral disease. We experienced a case of unilateral MOG associated optic neuritis in Korean male patient.

Description of Cases:

A 48-year-old man visited the ophthalmology clinic with a history of left side headache and blurry vision of left eye for 3 days. He was diagnosed with optic neuritis of left eye at the primary eye clinic. Corrected visual acuity was 20/20 on right eye and 20/25 on left eye. Mild optic disc edema was observed on left eye. Orbit MRI showed high signal intensity and thickened left optic nerve intraorbital and intracanalicular segment. Mild restricted diffusion at distal portion and perineural infiltration was noticed in left optic nerve. Under the diagnosis of optic neuritis of the left eye, we started IV steroid pulse therapy 1g/ day for three days. The patient discharged and MOG positivity was reported the day after his discharge.

Conclusions, including unique features of the case:

Although not common, unilateral MOG associated optic neuritis can be present in monocular. We should consider IV steroid pulse treatment 1 g/day for 5 days instead of 3 days to optic neuritis patient in order to avoid insufficient treatment.

References: None provided.

Keywords: Optic neuritis, Neuroimaging

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Retinal Vein Occlusion masquerading as Disc Edema with an unexpected resolution with Anti-Platelet Therapy in a 23-year-old female

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Introduction:

Retinal vein occlusion (RVO) is rare in patients under 50 years of age and is typically associated with hypertension, atherosclerosis, or glaucoma. Emerging data suggest hormonal contraception may increase the risk in younger females. We present an atypical case of branch RVO in a healthy 23-year-old woman with hormonal contraceptive use who was initially suspected of having optic neuritis.

Description of Cases:

A 23-year-old woman on hormonal contraception and with chronic migraines, treated with verapamil and triptans, presented with 10 days of persistent “black dots” and reduced peripheral vision in her left eye after a migraine episode. Examination showed unilateral optic disc edema, focal hemorrhage, and vessel tortuosity. OCT revealed RNFL thickening and visual fields demonstrated superior, temporal, and inferior defects. She was started on high-dose corticosteroids for presumed optic neuritis without improvement. MRI/MRV/MRA and extensive labwork, including CSF, thrombophilia and rheumatological studies were non-contributory. Fluorescein angiography demonstrated delayed filling of the superior branch retinal vein and late optic disc leakage, consistent with branch RVO. Aspirin 81 mg daily was initiated and hormonal contraception discontinued. At two-month follow-up her optic disc and macular edema improved, hemorrhages resolved, and visual field deficits decreased.

Conclusions, including unique features of the case:

Although thrombophilias such as hyperhomocysteinemia and anticardiolipin antibodies are associated with branch RVO in younger patients, the role of oral contraceptives remains debated. (1) UK and Danish studies show increased RVO risk with combined oral contraceptives containing moderate estrogen doses.(2,3) This case supports a possible association between hormonal contraception and RVO in young women without typical vascular risk factors. Treatment data are limited, but some studies have found that antiplatelet agents may improve outcomes .(4) Our case adds to the limited data on patients below age 50 presenting with RVO findings and discusses a potential treatment option worth further exploration both for younger and older patients.

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Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Vascular disorders, Retina, Visual fields

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Speaking in Stasis: Ocular Warning Signs of a Clinoid Meningioma

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Introduction:

Purpose: To report a unique symptomatic and structural presentation of secretory anterior clinoid meningioma with resolution following surgical resection.

Description of Cases:

Case Report: A 41 year-old healthy female presented with episodic peripheral flashing in her right eye over several weeks. Excellent visual acuity was maintained in both eyes. Examination only showed blurred disc margins, mild venous tortuosity, and scattered hemorrhages in her right eye. Broad workup was pursued; imaging showed a small anterior clinoid lesion with surrounding edema that compressed the superior ophthalmic vein. There was initial uncertainty about whether the tumor accounted for her ocular findings until subspecialty evaluations agreed no other cause was more plausible. Microsurgical excision was performed, and histopathology exhibited features consistent with World Health Organization Grade I secretory meningioma. By six weeks after surgery, her symptoms and exam findings were resolved.

Conclusions, including unique features of the case:

Discussion: Meningiomas account for 35% of primary intracranial tumors, commonly with anterior clinoid involvement. Secretory meningiomas are associated with peritumoral edema that can touch neighboring structures. In this case, mass effect likely resulted in impaired venous outflow and subsequent stasis, manifesting as dilated veins, retinal hemorrhages, and low-grade disc edema. Typical orbital meningioma presentation involves vision loss, afferent pupillary defect, proptosis, or motility restrictions. In this patient, absence of such classic signs diluted certainty about the tumor's significance. Given only subtle retinal findings, eventual diagnosis required persistence and cross-specialty evaluation. Venous stasis retinopathy as the primary presentation of a parasellar mass has not been described. This case reinforces the importance of integrating multimodal imaging, partnership, and clinical intuition when presentations do not conform to prototypical patterns. Conclusions: As evidenced, ophthalmologists should maintain clinical suspicion for compressive etiologies in patients with unexplained retinal venous changes, even when classic orbital signs are absent. Multidisciplinary collaboration is essential for achieving accurate diagnosis and treatment.

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Keywords: Tumors, Retina, Optic nerve trauma and treatment

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Symptomatic Improvement of Congenital Orbital Lymphatic-Venous Malformation With Latanoprost

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Introduction:

Surgical resection of orbital lymphatic-venous malformations (LVMs) carry high risks due to potential for bleeding as well as their proximity to critical orbital structures. Intralesional sclerotherapy also carries risks and requires a specialized multidisciplinary team. We report a patient with symptomatic congenital LVM who achieved sustained improvement with conservative therapy using latanoprost.

Description of Cases:

A 24-year-old man with congenital orbital LVM associated with left upper-lid ptosis and amblyopia presented with daily morning left upper eyelid edema and left sided headache, resolving within hours upon waking. First visit intraocular pressure was normal in both eyes and there was no apparent edema. MRI confirmed a 1.8 × 1.2 × 1.4 cm intraconal lesion consistent with a LVM with associated atrophy of the left optic nerve, stable in size compared to recent scans. Given the high risk associated with surgical resection, conservative therapy with nightly latanoprost 0.005%, head elevation, and overnight patching was initiated to mitigate suspected nocturnal venous congestion and elevated eye/orbital pressure-related symptoms. Within four weeks, morning edema and pain improved. At 4 month follow up, the patient had sustained improvement in symptoms despite discontinuation of patching while continuing latanoprost therapy. Sildenafil was also discussed as a medical therapy option, but the patient preferred to continue latanoprost.

Conclusions, including unique features of the case:

The patient's transient morning eyelid edema and headache suggested positional lymphatic or venous outflow obstruction overnight, which may have led to elevated intraocular pressure and direct enlargement of the lesion, as can be seen with orbital varix. Some studies have suggested that lymphatic outflow plays a role in intraocular pressure and that latanoprost may increase lymphatic outflow. This case suggests that topical prostaglandin analogs may enhance venous and lymphatic drainage from orbital LVM as well, providing another potential medical therapy option to help manage this condition.

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Keywords: Vascular disorders, Orbit/ocular pathology, High intracranial pressure/headache, Orbit

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Peaks and Prairies: Stereotypical OCT Finding in 4 Susac Patients Review of 4 cases followed up to 20 years – Retinopathy progression and MRI changes

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Introduction:

Susac Syndrome is a microangiopathic disease of the brain, ear and retina. Immune mediated destruction of the microvascular endothelium of vessels lead to classic branch retinal artery occlusions often visible in the retina. We will present an OCT finding that can help in the diagnosis of Susac Syndrome. This condition is often diagnosed late leading to severe morbidity. We will present 4 cases with this stereotypical finding on OCT and discuss the differential diagnosis. We will discuss the “Peaks and Prairies” found on cross sectional OCT cuts of the retina.

Description of Cases:

Retrospective review of 4 cases of Susac Syndrome followed and treated at one institution from 1997 to present. OCT and MRI findings in these cases will be discussed as will the differential diagnosis. Stereotypical changes on OCT were found in all four cases. They were found to have a sharp inferior temporal demarcation on OCT in at least one eye. Localized retinal thinning temporal to the maculae was found in all 4 patients which we describe as the “Prairie” beyond the “Peak” of the umbo. This was seen as well in other Susac cases presented in the literature. In the differential diagnosis of this retinal finding, Sickle Cell Disease, and large branch retinal occlusions from vascular disease caused similar changes, while the antiphospholipid syndrome and autoimmune states like MS or lupus did not show this finding.

Conclusions, including unique features of the case:

Conclusion: This stereotypical OCT finding is very helpful and should be recognized early if found in patients with or without hearing loss or neuropsychiatric changes who may be suffering from Susac Syndrome. This is especially important for this condition is often diagnosed late in the course of the disease leading to severe morbidity in these patients. The “Peak and Prairie” appearance on OCT will be discussed, as will the differential diagnosis of this finding.

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Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Neuroimaging, Retina

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Bilateral Optic Papillitis And Anterior Uveitis Following MDMA Ingestion: A Rare Neuro-Ophthalmic Complication

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Introduction:

3,4-Methylenedioxymethamphetamine (MDMA, “ecstasy”) is a serotonergic amphetamine derivative known for its sympathomimetic, neurotoxic, and vasospastic effects. While systemic and psychiatric toxicities are well characterized, ocular involvement is exceedingly rare. We describe a case of bilateral optic papillitis with mild anterior uveitis temporally associated with MDMA ingestion.

Description of Cases:

A 41-year-old woman with a history of right oophorectomy for torsion, irritable bowel syndrome, nephrolithiasis, and intermittent hallucinogen use (MDMA, ayahuasca) presented with stated bilateral vision loss within hours of ingesting MDMA. She notes experiencing complete visual loss for approximately 36 hours followed by partial recovery. Examination demonstrated normal visual acuity (20/20 OU), elevated intraocular pressure (35 mm Hg OD → 22 mm Hg after treatment), trace anterior chamber cell, and 360° optic disc elevation OU without hemorrhage. Optical coherence tomography confirmed bilateral disc edema, and Humphrey 24-2 visual fields revealed nonspecific central defects. MRI brain and orbits with and without contrast and MR venography were normal. Lumbar puncture showed normal opening pressure and cerebrospinal fluid indices. Infectious and autoimmune testing, including HIV, Lyme, ANA, ACE, MOG, and AQP4 antibodies, were negative; a reactive treponemal antibody with nonreactive RPR × 2 was noted. The patient was treated with topical corticosteroids, cycloplegic, and intraocular-pressure lowering drops, with gradual improvement.

Conclusions, including unique features of the case:

The temporal association between MDMA ingestion and bilateral optic disc edema with uveitis, in the setting of normal neuroimaging and cerebrospinal studies, supports a diagnosis of MDMA-induced bilateral optic papillitis. Possible mechanisms include microvascular ischemia, serotonergic neurotoxicity, or immune-mediated inflammation. Awareness of this entity is important, as early recognition and corticosteroid therapy may prevent permanent visual loss. This case contributes to the limited literature on MDMA-associated neuro-ophthalmic toxicity and underscores the need to consider recreational drug exposure in acute bilateral optic neuropathies.

References: None provided.

Keywords: Optic neuritis, Optic neuropathy, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Orbit/ocular pathology, Neuroimaging

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Atypical Ischemic Optic Neuropathy as an Initial Manifestation of Systemic Malignancy in Young Patients

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Introduction:

Non-arteritic anterior ischemic optic neuropathy (NAION) is the most common acute optic neuropathy in adults over 50 years of age and is typically associated with vascular risk factors such as diabetes, hypertension, and hyperlipidemia. Although its exact mechanism remains unclear, NAION is thought to result from hypoperfusion of the optic nerve head supplied by the short posterior ciliary arteries. A hypercoagulable state may increase susceptibility to NAION, and malignancy is known to induce such states through tumor-related procoagulant activity and inflammation. However, the relationship between NAION and cancer remains poorly defined, with only limited case reports suggesting a possible link.

Description of Cases:

We describe a case series of four patients who developed NAION in association with a new diagnosis or relapse of malignancy. Two patients presented with NAION before the discovery of new primary tumors—small cell lung carcinoma and ovarian carcinoma—while two others developed NAION in the context of recurrent angiosarcoma and rectal carcinoma. The patients (three females, one male; aged 42–71 years) exhibited typical NAION features of acute painless monocular vision loss, optic disc edema, and corresponding visual field defects. Conventional vascular and inflammatory risk factors were absent or insufficient to explain the presentation in several cases. Notably, in all four patients, NAION preceded or coincided with the detection of active malignancy, suggesting a potential paraneoplastic or hypercoagulable mechanism.

Conclusions, including unique features of the case:

This case series highlights a possible association between NAION and malignancy. NAION may occasionally serve as an early indicator of occult or recurrent cancer, particularly in atypical presentations—such as in younger patients, women, or those without conventional vascular risk factors. While routine malignancy screening is not currently indicated for all NAION cases, clinicians should consider it in such atypical scenarios, especially in individuals with prior or suspected cancer history.

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Cases Series of Nonarteritic Anterior Ischemic Optic Neuropathy in Patients on Semaglutide Treatment

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Introduction:

Recent retrospective cohort studies suggest an increased risk of non-arteritic anterior ischemic optic neuropathy (NAION) among patients receiving semaglutide. Understanding the clinical characteristics of these cases may help to guide management. Here, we present twelve such cases.

Description of Cases:

Chart reviewing of all the patients diagnosed with NAION between January 1, 2018, and October 1, 2025 at Henry Ford Ophthalmology Department. A total of 12 patients (15 eyes) were found to have semaglutide use prior to symptom onset; three patients had bilateral involvement. Most patients (10/12) were white males with a mean age of 62.4 years (95% CI: 57.2–67.6). Associated vascular risk factors include type 2 diabetes (11/12), hypertension (10/12), hyperlipidemia (10/12), and sleep apnea (4/12). All the cases were with discs at risk (Cup to disc ratio < 0.3 in affected eyes or the contralateral eye if no data for the affected eye). The average C/D ratio was 0.18 (95% CI 0.13 - 0.23). The average duration of semaglutide treatment before onset was 15.8 months (95% CI: 5.5–26.2). Presenting vision was better than 20/30 in 12 of 15 eyes (9/12 cases); three eyes had vision below 20/60 and one of which had baseline light perception from prior brain injury. Disc edema lasted an average of 10.3 weeks (95% CI: 5.5–15.0). The majority of patients maintained baseline vision (9/12 cases, 12/15 eyes with VA > 20/30). Only two eyes end up with declined vision after three months (20/30→20/50 and 20/25→20/50). One case (1 eye) was lost to follow-up.

Conclusions, including unique features of the case:

The association between NAION and GLP-1 agonists particularly semaglutide remains unclear. These agents may modestly lower blood pressure through autonomic and vascular effects, while rapid glycemic correction can reduce optic nerve perfusion. Conversely, reported neuroprotective effects of GLP-1 agonists may help explain the generally favorable visual outcomes observed.

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Unmasking Disc Edema

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Introduction:

VZV acute retinal necrosis is a rare, vision-threatening condition presenting with panuveitis, retinal necrosis, and vasculitis. Presentation with isolated optic disc edema prior to retinal findings is uncommon.

Description of Cases:

A 76-year-old female with history of nonfunctioning pituitary macroadenoma s/p resection and ocular history of left eye cataract surgery presented with two months of generalized weakness and four days of painless right-eye blurry vision with inferior field. On exam, visual acuity was 20/30 OD and 20/20 OS with a right RAPD. Ishihara was 10/14 OD and 14/14 OS. Anterior segment was normal, fundus showed 360° optic disc edema OD and normal disc OS. The differential included NAION and GCA. Inflammatory markers were normal, temporal artery ultrasound demonstrated no vasculitis. MRI of the brain/orbits showed residual sellar mass extending into the left cavernous sinus without compression of right optic nerve. The neuro-ophthalmic imaging review showed diffusion restriction of the immediate retrobulbar right optic nerve. She was discharged with presumptive diagnosis of NAION. Twenty days later, vision declined to NLP OD and 20/80 OS. Findings included vitreous hemorrhage OD and disc edema OS with vitreous cells and creamy subretinal lesions. Fluorescein angiography showed patchy peripheral non-perfusion and vascular sheathing. CSF revealed atypical lymphocytic pleocytosis, and vitreous PCR was positive for VZV. She underwent pars plana vitrectomy with silicone oil and was treated with valacyclovir and corticosteroids.

Conclusions, including unique features of the case:

Our patient's presentation with unilateral disc edema initially mimicked NAION or GCA but the absence of pain, normal CRP, and diffusion restriction of the immediate retrobulbar optic nerve supported a non-arteritic etiology. The rapid progression to bilateral involvement, vision loss, vitreous inflammation, and peripheral necrosis redirected the diagnosis toward viral retinitis. This case highlights that optic disc edema may be the only early indicator of viral retinitis, emphasizing the importance of considering infectious etiologies in atypical cases.

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Central and Peripheral Contrast Sensitivity as Markers of Visual Recovery in a Patient with Pituitary Macroadenoma

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Introduction:

Pituitary macroadenomas are among the most frequent sellar masses producing anterior visual pathway compression, yet subtle sensory deficits often precede overt field loss. Contrast sensitivity, particularly in peripheral quadrants, represents a fragile but underexplored marker of early neuronal compromise. While conventional perimetry and visual acuity assess gross function, they frequently underestimate subclinical damage or post-surgical recovery. The Spaeth-Richman Contrast Sensitivity (SPARCS) test provides an objective, reproducible metric of both central and peripheral function, enabling a nuanced view of chiasmal integrity. We report a patient with pituitary macroadenoma in whom dynamic SPARCS mapping revealed early dysfunction and striking postoperative restitution.

Description of Cases:

A 44-year-old woman presented with progressive, painless visual diminution, initially in the right eye and later in the left, accompanied by frontal-temporal headaches and brief memory lapses. Visual acuity measured 20/40 OD and 20/30 OS with defective Ishihara color vision (OD 20/38; OS 2/38). Perimetry revealed bitemporal hemianopia. Central contrast sensitivity by Pelli-Robson was reduced in the left eye, while the Spaeth-Richman Contrast Sensitivity (SPARCS) test demonstrated marked bilateral depression across both central and peripheral quadrants. Optical coherence tomography showed preserved retinal nerve fiber and ganglion-cell complex thickness, suggesting reversible compression. Contrast-enhanced MRI disclosed a 21x16 mm cystic pituitary macroadenoma with suprasellar extension elevating the optic chiasm. Following endoscopic trans-sphenoidal resection, histopathology confirmed pituitary adenoma. Within two weeks, color vision normalized and SPARCS scores nearly doubled, paralleling field improvement and radiologic decompression. Three-month follow-up demonstrated complete recovery of visual acuity, fields, and contrast sensitivity.

Conclusions, including unique features of the case:

This case highlights contrast sensitivity testing as a sensitive, quantifiable adjunct for evaluating optic chiasmal compression. The parallel restoration of central and peripheral sensitivity after decompression revealed rapid neural plasticity and functional reversibility. Utilizing SPARCS testing offers clinicians a low-cost, objective metric for early detection and postoperative monitoring in pituitary tumors.

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DOTATATE Unmasking an Atypical Optic Nerve Sheath Meningioma

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Introduction:

Optic nerve sheath meningiomas (ONSM) are rare, benign tumors classically presenting with painless progressive proptosis, vision loss and optic atrophy(1). MRI and CT may reveal optic nerve enhancement, thickening, “tram-track” appearance, or calcifications; however, both modalities have limitations in distinguishing ONSM from other etiologies(2). Gallium-68 labeled dodecanetetraacetic acid-tyrosine-3-octreotate (Ga-68-DOTATATE) positron emission tomography (PET)/MR may help clarify difficult diagnoses. We describe an atypical presentation of ONSM masquerading as idiopathic orbital inflammation (IOI) and review the current literature on Ga-68-DOTATATE use in primary ONSMs.

Description of Cases:

A 38-year-old, 7-month pregnant female presented with right eye pain, proptosis, and optic nerve edema. Non-contrast MRI Orbits showed focal diffusion restriction of the intraocular/intraorbital right optic nerve (ON), right proptosis and preseptal inflammatory changes. Workup for orbital inflammation was unremarkable, and prednisone controlled her orbital pain. Postpartum contrast-enhanced MRI Brain/Orbit revealed similar enlargement with ill-defined right ON vs perineural enhancement. Attempted steroid taper resulted in peri/retro orbital pain recurrence. Worsening optic disc edema with early visual dysfunction despite steroid use, and MRI appearance suspicious for ONSM triggered further evaluation with PET-MR-DOTATATE. Imaging demonstrated a DOTATATE-avid focus with standardized uptake value (SUV) ratio of 4.3 along the region of right ON sheath enhancement, providing a diagnosis of presumed primary ONSM. Multidisciplinary tumor board recommended intensity-modulated radiotherapy (IMRT) (5040xGy/180's, 28 sessions) given the progression of edema and afferent dysfunction. Mid-treatment evaluation showed improved pain off steroids, stable visual function, and partial reduction of optic disc edema on optical coherence tomography.

Conclusions, including unique features of the case:

An atypical presentation of ONSM masquerading as IOI with retro orbital pain and rapid progression, only partially explained by pregnancy, given the worsening in pain, optic disc edema and visual function five months postpartum, was elucidated by PET/MR-DOTATATE. We share this challenging case and further review the literature on presenting clinical and neuroimaging features of ONSM identified using PET-DOTATATE(3-6).

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Hidden in Plain Sight: Case Series of Non-Arteritic Anterior Ischemic Optic Neuropathy Masquerading as Optic Disc Drusen in Young Patients

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Introduction:

Non-arteritic anterior ischemic optic neuropathy (NAION) is the most common acute optic neuropathy in adults. Despite predilection for older populations, cases are seen under age 50, often from anatomical factors like optic disc drusen.

Description of Cases:

Case 1: A 37-year-old pregnant woman presented with 12 days of progressive, painless blurry vision and peripheral smudging in her left eye. Examination showed 20/20 vision with left relative afferent pupillary defect, decreased red desaturation, and disc edema. MRI imaging revealed FLAIR white matter hyperintensities without frank demyelination. Given concern for optic neuritis, she was treated with steroids. At follow-up, her exam revealed disc drusen corresponding with thinning on OCT and nasal defects on perimetry, more consistent with NAION than optic neuritis. Case 2 A 29-year-old woman presented with one day of painless inferior vision loss in her left eye. She had 20/20 vision with an inferior altitudinal defect, so she was referred urgently to neuro-ophthalmology. Her fundus showed left disc edema, and MRI imaging was unremarkable. She was not treated with steroids. At close follow-up appointments, edema resolved with correspondence to her stable field defect.

Conclusions, including unique features of the case:

Optic disc drusen (ODD) can mimic papilledema. While ODD are often asymptomatic, visual field loss and vascular complications like NAION can occur. Over 50% of younger patients with NAION demonstrate ODD. These cases highlight diagnostic challenges in young patients with vision loss who were ultimately diagnosed with ODD-associated NAION. This series illustrates the need for careful evaluation of presumed optic neuritis in younger patients with optic disc swelling. When inflammatory findings are absent, ODD should be considered. Increased awareness of ODD-related NAION reduces misdiagnosis and limits unnecessary immunosuppressive treatment. Imaging techniques like OCT, FAF, and B-scan ultrasonography also help with establishing correct diagnosis and guiding appropriate management.

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Keywords: Optic neuropathy, Optic neuritis, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Neuroimaging, Vascular disorders

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Asymptomatic Optic Disc Edema Concurrent with Semaglutide Use: A Case Series

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Introduction:

Approximately 6% of US adults take GLP-1RAs as of 2024. As use of these medications has increased, more side effects are being observed such as transient worsening of diabetic retinopathy which is thought to be due to rapid changes in A1c, which triggers increased vascular permeability and neuro-inflammation. There is also emerging evidence that GLP-1RAs are associated with an increased risk of NAION. We describe 5 cases of asymptomatic disc edema associated with GLP-1RA use.

Description of Cases:

Case 1. 59-year-old man developed mild sequential NAION which was an incidental finding on neuro-ophthalmic exam at the follow-up appointment for microvascular cranial nerve 6 palsy. Case 2. 29-year-old woman with incidental finding of mild bilateral optic disc edema on annual eye exam. Optic disc edema improved while off Semaglutide. Patient had opening pressure of 20 cm H₂O. Case 3. 39-year-old woman with IIH suspect, had mild worsening of optic disc edema after starting on Semaglutide. Optic disc edema improved after stopping the medication. Opening pressure was borderline high at 26 cm H₂O. Case 4. 57-year-old man presents with acute NAION in the left eye but also had severe asymptomatic optic disc edema in the right eye while on Semaglutide. Opening pressure was checked twice, 26 and 23 cm H₂O. Case 5. 65-year-old woman with severe right optic atrophy secondary to NMOSD, referred from optometry service for asymptomatic left optic disc edema evaluation while on Semaglutide. There was no clinical or radiological evidence of optic neuritis in the left eye.

Conclusions, including unique features of the case:

Prior studies link GLP-1RA use to increased NAION risk within the first year of use; we suggest that asymptomatic disc edema may be an intermediate step predisposing to ischemic optic nerve injury. These cases also raise the question of the utility of screening eye exam in patients who are taking GLP-1RAs.

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The Translaminar Pressure Gradient in Spaceflight Associated Neuro-ocular Syndrome: The Relationship Between Intraocular and Intracranial Pressure and its Role in Pathogenesis

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Introduction:

Spaceflight associated neuro-ocular syndrome (SANS) refers to the unique clinical and imaging characteristics which can develop during or following long-duration spaceflights. A number of theories about the pathogenesis of SANS have been proposed while there is a continuous interest and research about the effect of these missions on human health. The ocular translaminar pressure gradient, which is generated by the difference of intraocular pressure and retrolaminar intracranial pressure at the level of lamina cribrosa, has been considered a significant factor in the development of glaucoma and papilledema.

Description of Cases:

The objective of this work is to review the changes of IOP and ICP in microgravity conditions and discuss the role of TLPG in the pathogenesis of SANS.

Conclusions, including unique features of the case:

Evidence from in-flight observations and terrestrial analog studies suggests that microgravity induces cephalad fluid shifts, altering intracranial and intraocular pressure dynamics. These shifts lead to vascular and cerebrovascular adaptations, increases in ICP, and fluctuations in IOP and TLPG, all of which may contribute to the development of SANS. Although direct in-flight ICP measurements remain unfeasible, post-flight lumbar punctures have revealed borderline or mildly elevated pressures, while ocular findings such as optic disc edema, globe flattening, and loss of spontaneous venous pulsations support the hypothesis of localized perioptic CSF pressure elevation rather than a global ICP rise. Ground-based simulations, including head-down tilt and parabolic flight studies, have demonstrated transient increases in ICP and IOP, supporting the link between microgravity, cephalad fluid redistribution, and ocular structural changes. Overall, current evidence indicates that SANS results from a complex interplay of cephalad fluid shifts, mild ICP elevation, TLPG imbalance, and metabolic and inflammatory factors rather than a uniform rise in ICP. These findings highlight the need for advanced non-invasive monitoring technologies and countermeasures to protect astronaut visual health during long-duration spaceflight.

References: None provided.

Keywords: Miscellaneous, High intracranial pressure/headache

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Leber Hereditary Optic Neuropathy Masquerading As Inflammatory Optic Neuropathy With Optic Nerve Enhancement

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Introduction:

We report a case of bilateral sequential vision loss with optic nerve enhancement that failed to respond to steroids, eventually diagnosed as Leber hereditary optic neuropathy (LHON). We describe the rare presentation of optic nerve enhancement in LHON.

Description of Cases:

A 42-year-old female presented to the Emergency Department (ED) with acute left eye vision loss. Visual acuity was 20/40 in right eye and counting fingers in left eye. Reduced color vision both eyes, no afferent pupillary defect (APD). Normal optic nerve, prominent retinal blood vessels noted. She denied further work up and discharged against medical advice. She returned after 3 weeks with right eye vision loss. Her visual acuity was counting fingers in both eyes. No APD was noted. Funds exam was unremarkable. Magnetic resonance imaging (MRI) of brain and orbit showed contrast enhancement of left prechiasmatic retroorbital optic nerve. Blood work up unremarkable for demyelinating, infectious, vasculitis. Spinal tap unremarkable. Treated with 3 days of 1 g intravenous methyl prednisone for presumed seronegative inflammatory optic neuritis after which vision did not improve, denied plasmapheresis. In 2 weeks, her son presented to the ED with right eye vision loss to 20/400. There was no APD. Normal fundus. Blood work up unremarkable including heavy metal toxicity screen. MRI brain orbit did not show enhancement. He denied spinal tap. Given bilateral sequential vision loss in mother and new onset vision loss in son, genetic testing ordered; showed positive mitochondrial mutation of MT-ND4 in both mother and son. The atypical clinical presentation with optic nerve enhancement led to delay in diagnosis.

Conclusions, including unique features of the case:

LHON can have optic nerve enhancement mimicking inflammatory optic neuropathy or optic pathway glioma. Leber hereditary optic neuropathy should be considered as a possible cause of unexplained unilateral or bilateral optic neuropathy. It is unknown why enhancement happens in selective individuals.

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Case of Delayed Onset Right Homonymous Hemianopia after Flow Diversion and Coil Embolization of Left Internal Carotid Artery Saccular Aneurysm

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Introduction:

An 86-year-old woman presented with a two-month history of peripheral visual disturbances. Her medical history included endovascular repair of a carotid artery aneurysm. On examination, she was found to have a right homonymous hemianopia. This case illustrates a rare occurrence of delayed visual field loss developing long after aneurysm treatment.

Description of Cases:

This 86-year-old female, with a medical history notable for hypertension, hyperlipidemia, and sleep apnea, presented to her primary care provider with imbalance and dizziness and was found to have an incidental large, lobulated left ophthalmic internal carotid artery saccular aneurysm on magnetic resonance imaging (MRI). She later underwent a cerebral angiogram, which revealed the aneurysm measured 10 × 10.8 × 11.7 mm. Subsequently, the patient underwent an endovascular flow diversion and adjunctive coiling procedure. She was instructed to continue dual antiplatelet therapy for six months following the procedure. Four months after aneurysm repair, she began experiencing peripheral visual changes. A computed tomography angiography (CTA) of the head and neck performed six months after the original procedure showed embolization coils in the area of the aneurysm but no other pathology. MRI of the orbits demonstrated mass effect from the coil on the left optic tract and chiasm. The patient was placed on a short course of oral corticosteroids, with moderate improvement in the visual field defect at her two-month neuro-ophthalmology follow-up visit, eight months after the initial procedure.

Conclusions, including unique features of the case:

To our knowledge, there is limited literature reporting delayed-onset homonymous visual field defects following successful coiling of an aneurysm. Proposed hypotheses for this phenomenon include enlargement of the intra-aneurysmal thrombus, inflammatory changes, or pulsatile effects of the coils against the aneurysm wall, leading to edema. A course of corticosteroids may help ameliorate visual symptoms caused by the compression.

References: None provided.

Keywords: Vascular disorders, Optic neuropathy, Visual fields

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Visual Recovery Following Decompression of a Petroclival Meningioma with Intra-Orbital Extension

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Introduction:

Petroclival and sphenoid wing meningiomas with intra-orbital and cavernous sinus involvement can cause progressive optic neuropathy and cranial nerve palsies from compressive effects. Early recognition and multidisciplinary management are critical for preserving vision.

Description of Cases:

A 30-year-old female with no ocular or neurologic history presented with months of progressive blurred vision and proptosis of the left eye after failing a driving test. She reported having been previously told about a mass near her eye several years earlier, but no intervention had been performed. On initial ophthalmic evaluation, vision was 20/20 in the right eye and count fingers in the left eye with a left afferent pupillary defect. MRI revealed an 8 x 4.5 x 3.8 cm meningioma in the left greater wing of the sphenoid and a suprasellar region with extension to anterior and middle cranial fossa with extension to the pituitary fossa and the bilateral cavernous sinuses, encasement of the left internal carotid artery and abutment of the optic chiasm. She underwent a left pterional craniotomy with resection of the temporal and frontal fossa meningioma and orbitocranial decompression. Pathology confirmed a WHO grade I meningioma with angiomatous and lymphoplasmacytic features. Postoperatively, vision improved to 20/40 in the left eye but was complicated by a new cranial nerve III palsy. Subsequent imaging showed residual tumor with progression of the intraorbital component. She completed radiation therapy and started on pembrolizumab, resulting in tumor stabilization and improvement in vision to 20/80. Partial recovery of cranial nerve III function was noted. She was referred for prism correction and possible strabismus surgery for persistent exotropia.

Conclusions, including unique features of the case:

This case highlights the potential for meaningful visual recovery following decompression even in severe compressive optic neuropathy. Persistent cranial nerve deficits underscore the importance of early intervention, imaging surveillance, and coordinated care among neurosurgery, neuro-oncology, and neuro-ophthalmology teams.

References: None provided.

Keywords: Tumors, Optic neuropathy, Neuroimaging, Ocular motility

Financial Disclosures: The authors had no disclosures.

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Cilioretinal Artery Occlusion in Cat Scratch Disease: A Rare Complication

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Introduction:

Bartonella neuroretinitis is a rare cause of retinal artery occlusion. Prompt diagnosis and treatment is essential to avoid permanent vision loss.

Description of Cases:

A 19 year old female with no past medical history presented with acute painless central right eye vision loss. She denied headache, weakness, tingling, flashes/floaters, dizziness, diplopia, nausea, fever, oral ulcers, or recent illness. Ophthalmological examination showed visual acuity 20/25 OD with large central scotoma, 20/20 OS, normal ocular pressures, right rAPD, normal fundus OS, and grade 2 disc edema OD with whitening around the cilioretinal artery, most consistent with a cilioretinal artery occlusion. The patient was sent to emergency room for stroke workup. Extensive stroke and hypercoagulable workup were unremarkable, including contrasted MRI of brain and orbits. Lumbar puncture was unremarkable. Testing for HIV, Toxoplasma, tuberculosis, Rickettsia, NMO, and MOG were negative except elevated serum IgG Bartonella antibodies 1:640. Upon further history, she was scratched by her cat 3 weeks prior. Repeat fundus examination 2 days after initial presentation demonstrated worsened papillitis and marked edema with the origin of the temporal occluded arteriole buried in the inflammatory lesion. She was treated with IV methylprednisolone 1000mg for 5 days with prednisone taper, rifampin 300mg BID and doxycycline 100mg BID for 6 weeks. Her acuity and scotoma improved over weeks. At follow up visit 6 weeks later, her visual acuity was 20/20 with smaller scotoma. Repeat serum IgG Bartonella titers were 1:2560, confirming prior acute infection.

Conclusions, including unique features of the case:

Cilioretinal artery occlusion in Bartonella neuroretinitis is exceedingly rare and likely results from localized retinal vasculitis and endothelial injury from direct bacterial invasion, causing vessel wall inflammation and secondary thrombosis. In patients without vascular risk factors, this condition should be included in the differential diagnosis, with inquiry about cat exposure. Treatments target the underlying infection and associated inflammation, typically with systemic steroids and antibiotics.

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Keywords: Neuro-ophth & infectious disease (eg, AIDS, prion), Retina, Vascular disorders, Optic neuritis

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And Sometimes Things Happen Quickly: Appreciating the OCT as a Time Machine in Afferent Neuro-Ophthalmology

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Introduction:

Beyond its slow-tracking utility, OCT can instantly differentiate between functional and time-sensitive, reversible pathology. In cases where clinical findings are equivocal, its ability to detect acute GCL dropout with preserved RNFL offers a diagnostic shortcut with therapeutic consequence. In this sense, OCT doesn't just look at structure—it looks back in time

Description of Cases:

A 40-year-old woman presented with bilateral sudden vision loss to counting fingers following abdominal surgery. Fields were unreliable. Fundus and general examination was unremarkable. CT brain was normal. The clinical impression was functional visual loss: "the patient sees nothing, the doctor sees nothing." OCT revealed complete ganglion cell layer (GCL) loss with preserved retinal nerve fiber layer (RNFL), suggestive of toxic or mitochondrial optic neuropathy. National health records confirmed longstanding untreated pernicious anemia, with recent folate-only supplementation. A diagnosis of subacute combined degeneration (SACD)—associated optic neuropathy was made. Following urgent parenteral B12 therapy, her acuity improved to 6/24, with return of partial color vision and a centrocecal scotoma. This case demonstrates a classic injury pattern: massive, synchronous ganglion cell death triggered by excess oxygen free radicals, exceeding a critical threshold. Propagation occurs via gap junctions, initiating a bystander effect. This mechanism is well described in Leber's hereditary optic neuropathy and ethambutol toxicity, and may also underlie nutritional optic neuropathies such as SACD.

Conclusions, including unique features of the case:

In this case, OCT helped distinguish functional visual loss from urgent, reversible pathology when both the history and exam were equivocal. The GCL-RNFL dissociation served as a forensic clue and therapeutic guide. While OCT is a cornerstone for long-term disease monitoring, clinicians should remember that sometimes things happen quickly—and OCT's ability to resolve pattern, timing, and mechanism can rapidly inform treatment in time-critical vision loss.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Non-organic visual disorders, Optic neuropathy

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Eye Spy a Tumor: Anterior segment metastasis and BDUMP in a case with advanced Esophageal Adenocarcinoma

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Introduction:

Bilateral Bdump with anterior segment melanocytic lesions, a rare paraneoplastic syndrome in a 56-year-old male with stage IV esophageal adenocarcinoma on palliative chemotherapy and radiation.

Description of Cases:

A 56-year-old male with stage IV esophageal adenocarcinoma on palliative FOLFOX and nivolumab presented with 1.5 months of progressive right-eye visual loss. He reported blurry vision, right temporal pain, floaters, flashes, and photophobia. Examination revealed best-corrected visual acuity of 20/100 OD and 20/60 OS, bilateral optic disc swelling, subretinal submacular fluid, and pigmentary changes. Optical coherence tomography of retinal nerve fiber layer noted thickening both eyes and OCT macula showed subretinal fluid in both eyes. Two pigmented anterior segment lesions with an associated iris cyst were noted in the right eye. CT brain showed no intracranial metastasis. Based on the clinical findings, bilateral diffuse uveal melanocytic proliferation (BDUMP) and anterior segment metastasis were suspected. The patient received palliative orbital radiotherapy (3000 cGy in 10 fractions). Trans-corneal excisional biopsy and fine-needle aspiration biopsy of the right eye revealed atypical epithelioid melanocytes, consistent with an aggressive form of BDUMP

Conclusions, including unique features of the case:

In this 56-y-o male with stage IV esophageal adenocarcinoma, anterior segment lesions raised concern for metastatic involvement, prompting orbital radiation. However, fine-needle aspiration biopsy (FNAB) revealed that the right eye anterior segment lesions represented an aggressive form of bilateral diffuse uveal melanocytic proliferation (BDUMP). This case highlights BDUMP as a rare paraneoplastic manifestation of metastatic esophageal adenocarcinoma and emphasizes the importance of recognizing ocular involvement in patients with advanced malignancy

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Keywords: Paraneoplastic syndromes, Tumors

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Posterior Ischemic Optic Neuropathy Following Semaglutide Use in a Healthy Female Patient

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Introduction:

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs), such as semaglutide, are increasingly used for diabetes and obesity management due to their metabolic benefits. Recent reports, however, have suggested a possible link between GLP-1 RAs and ischemic optic neuropathy, mostly anterior forms in patients with systemic vascular risks. Posterior ischemic optic neuropathy (PION), characterized by acute visual loss without optic disc swelling, is exceedingly rare. We report a case of unilateral PION in an otherwise healthy woman following semaglutide (Wegovy®) therapy for weight loss.

Description of Cases:

A 41-year-old woman presented with painless, progressive vision loss in the right eye over three days. She initially noticed inferior visual blurring that rapidly progressed to near-total vision loss. She had no history of systemic vascular or autoimmune disease but had been self-injecting semaglutide 0.5 mg weekly for six weeks for weight loss. On examination, best-corrected visual acuity was no light perception in the right eye and 1.0 in the left. Fundus findings were unremarkable, with no optic disc swelling. Fluorescein angiography, MRI with contrast, and neck angiography showed no leakage, enhancement, or vascular obstruction. MOG and AQP4 antibodies were negative. Vision did not improve after three days of high-dose intravenous corticosteroids. Based on the acute, unilateral, and irreversible visual loss without disc edema or neuroimaging abnormalities, posterior ischemic optic neuropathy was diagnosed. Given the close temporal association with semaglutide use and absence of systemic risk factors, semaglutide-associated ischemic optic neuropathy was suspected.

Conclusions, including unique features of the case:

This case highlights a potential association between GLP-1 receptor agonist (semaglutide) use and posterior ischemic optic neuropathy. Although these agents are widely regarded as safe for diabetes and obesity management, clinicians should be aware of possible rare but severe ocular ischemic events. Prompt ophthalmologic assessment and consideration of drug discontinuation are recommended when patients on GLP-1 agonists report visual disturbances.

References: None provided.

Keywords: Graves' disease, Adult strabismus with a focus on diplopia, Ocular motility, Demyelinating disease, Higher visual functions

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Optic Disc Elevation in Inherited Retinal Dystrophies: Diagnostic Pitfalls and Imaging Insights from a Multicenter Case Series

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Introduction:

Inherited retinal dystrophies (IRDs) can cause optic nerve swelling, mimicking papilledema, prompting possibly unnecessary investigations and treatment for raised intracranial pressure. This study described the clinical course and outcomes of children and young adults with IRD presenting with optic disc swelling, to provide practical guidelines to differentiate pseudopapilledema from true papilledema.

Description of Cases:

Methods This multicenter retrospective case series included 13 patients (mean age 14.1 ± 8.8 years; range 4-32 years; eight female) who were referred with a swollen disc. Some were already diagnosed with IRD, others during the workup. Follow-up averaged 24.2 ± 12 months. They underwent multimodal imaging, including optical coherence tomography (OCT) of the macula and optic nerve, fundus autofluorescence, fluorescein angiography, and B-scan ultrasonography, along with neuroimaging and lumbar puncture as clinically indicated. Full-field electroretinography and/or genetic testing confirmed IRD diagnosis. **Results** Papilledema was excluded in 10 of 13 (77%) patients. Six showed structural optic nerve alterations confirmed by multimodal imaging, and four had mild edema that resolved with a borderline increase in opening pressure on lumbar puncture (LP) (25-29 mmHg). Six reported headaches. Three patients (23%) were diagnosed with true papilledema with elevated opening pressure and symptoms; all had headaches. Among them, one had Chiari I malformation with hydrocephalus requiring a ventriculoperitoneal shunt (VPS). Another was suspected of ROSAH syndrome, and one carried biallelic pathogenic variants in TULP1. Disc swelling preceded IRD diagnosis in six (46%). No peripapillary hemorrhages were seen; disc pallor was noted in seven (54%).

Conclusions, including unique features of the case:

Optic nerve swelling may be an early sign of IRD in children and young adults. It is possibly related to an inflammatory response triggered by rapid photoreceptor and RPE breakdown. True papilledema is uncommon, but careful evaluation is essential, especially in symptomatic patients. Accurate differentiation between papilledema and pseudopapilledema relies on multimodal imaging and awareness of IRD phenotypes.

References: None provided.

Keywords: Retina, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Genetic disease

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Spontaneous Visual Improvement In Hemorrhagic Optic Pathway Glioma During Pregnancy

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Introduction:

A hemorrhage in an optic pathway–hypothalamic glioma (OPHG) during pregnancy is an extremely rare event that remains limited in documentation and understanding. Only two cases have been reported, both managed surgically with preterm induction of labour^{1,2}. We describe the first case of spontaneous visual improvement following an OPHG hemorrhage during pregnancy.

Description of Cases:

A previously healthy 34-year-old woman with no stigmata of neurofibromatosis presented at 19 weeks' gestation with a new onset, two-day history of decreased vision OD and mild right-sided headache. Visual acuity (VA) was 20/50–2 with a grade 1 relative afferent pupillary defect (RAPD) and diminished color vision (7/13) OD. Optic discs appeared normal. Humphrey 24-2 visual fields (HVF) revealed superior and inferior arcuate defects (mean deviation –17.18 dB) OD. VA, color vision and HVF were normal OS. Non-contrast magnetic resonance imaging (MRI) of the brain and orbits performed five days after symptom onset demonstrated an expansile lesion involving the right hypothalamus, right optic chiasm and the prechiasmatic right optic nerve. There were intrinsic areas of T1 hyperintensity with blooming to be suggestive of acute hemorrhage within a previously undetected OPHG. Serological investigations including ACE, ANCA, ANA and NMO and anti-MOG antibodies were negative. Ten days later, she reported spontaneous visual recovery. VA improved to 20/25 and color vision to 12/13 OD. HVF demonstrated resolution of the defect OD (mean deviation –0.21 dB). She was observed closely during the pregnancy until she had a normal delivery. Her vision remained stable and mild temporal optic disc pallor OD ensued. Post-delivery contrast-enhanced MRI revealed interval reduction in the size of the OPHG with hemosiderin staining.

Conclusions, including unique features of the case:

This case demonstrates that OPHG hemorrhage in pregnancy may spontaneously resolve with visual recovery. Conservative management and close observation can be an alternative to surgical intervention in visually stable pregnant patients.

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Keywords: Tumors, Visual fields

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Optic Disc Drusen Mimicking Normotensive Glaucoma In A Young Adult Experiencing Vision Loss: A Diagnostic Challenge

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Introduction:

Optic disc drusen (ODD) are acellular deposits presenting as calcified nodules within the optic disc. Studies have reported ODD in 0.2-0.3% of patients. Their presence can be benign or associated with visual field (VF), peripapillary retinal nerve fiber layer (pRNFL), and ganglion cell layer (GCL) defects. VF loss occurs in up to 87% of patients with ODD. These findings can resemble glaucoma. Our case highlights a patient with congenital ODD experiencing vision loss.

Description of Cases:

A 24-year-old female presents with vision loss over the past 2 years, noticing blurred margins of images. Medical history included ODD noted upon birth in both eyes (OU). Right eye (OD) vision was 20/20-2 while left eye (OS) was 20/20. Intraocular pressure (IOP) was 17 OD and 15 OS. Cup to disc (C/D) ratio was 0.05 OU. Fundus photos displayed ODD OU with more OS than OD. VF revealed an inferior nasal quadrant defect OS that repeat testing confirmed. Optical coherence tomography (OCT) indicated normal pRNFL and GCL. ODD was higher on differential than normotensive glaucoma for her VF loss. She is monitored closely for progression, but we have a low threshold to start IOP reducing drops if signs of progression.

Conclusions, including unique features of the case:

Differentiating ODD versus glaucoma poses challenges. ODD forms a “cupless disc” with a near zero C/D ratio that makes the C/D ratio unreliable in diagnosing glaucoma. Their associated VF defects overlap including arcuate field defects, enlarged blind spots, nasal steps and constricted VF. Currently, no accepted therapy exists for ODD. Studies of patients with ODD and IOP within normotensive range have shown greater VF loss at higher IOPs and decreased VF progression on IOP reducing drops. This case underscores the difficulty of diagnosing ODD versus glaucoma, especially in a young patient where preserving vision is imperative.

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Keywords: Optic neuropathy, Visual fields, Pediatric neuro-ophthalmology

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New Onset Optic Nerve Edema After A Resection Of Craniopharyngioma

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Introduction:

The incidence of papilledema in patients with intracranial tumors is reportedly variable, however several factors have a role in likelihood of developing papilledema. Beyond scenarios with direct optic nerve compression by the mass, factors include tumor size, location, and type as well as patient age. We report a case of a 27-year-old patient with papilledema that presented 1 month after craniopharyngioma resection and endoscopic third ventriculostomy.

Description of Cases:

The patient presented with worsening headaches and decreased vision. Her ocular history includes refractive amblyopia in the left eye. Dilated fundus examinations performed 3 weeks and 4 weeks prior to presentation were without any optic nerve abnormalities. At presentation, visual acuity was 20/20 OD and 20/50 OS. Dilated fundus examination revealed bilateral 4+ optic nerve edema. MRI head demonstrated residual mass which was stable compared to post-resection MRI. MRV showed no abnormalities. Lumbar puncture was performed with opening pressure of 51mmHg and unremarkable CSF studies. The challenge in this case is determining the cause of the increased ICP, whether that be idiopathic in nature or as a result of obstructive hydrocephalus in the presence of the craniopharyngioma. A lumbar drain was placed and maintained for 3 days and treatment with acetazolamide was started. Ultimately patient was discharged with instructions to continue oral acetazolamide treatment. After following up with eye clinic, optic nerve edema and her symptoms eventually resolved.

Conclusions, including unique features of the case:

This case emphasizes the importance of frequent monitoring and examination of symptomatic patients with masses near the visual pathway despite history of surgical intervention or resection. Likewise, the presence of a seemingly unchanged MRI and elevated lumbar puncture opening pressure demonstrate the value of optic nerve evaluation in monitoring for change or increase in intracranial pressure.

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Keywords: High intracranial pressure/headache, Tumors

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Contact Information: None provided.

A Case of Traumatic Optic Neuropathy and Partial Medial Rectus Avulsion after an Attempted Self-Enucleation

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Introduction:

Oedipsism, or self-enucleation, is a rare form of self-inflicted ocular trauma, with recent literature suggesting schizophrenia and substance-induced psychosis as the most frequent underlying causes. Traumatic optic neuropathy (TON) is a recognized complication of attempted self-enucleation, with case reports describing irreversible vision loss due to optic nerve traction, avulsion, or compression.

Description of Cases:

A 22-year-old unmedicated male with schizophrenia presented one day after attempting self-enucleation of his left eye using his thumb, stating, "God told me to." Visual acuity was 20/30 with a minimally reactive pupil and relative afferent pupillary defect (RAPD). Motility was severely limited: adduction past midline was absent in all fields and abduction showed significant limitation as well. Posterior segment examination showed disc edema and disc hemorrhage. Operative exploration confirmed a medial conjunctival laceration and partial medial rectus disinsertion, which was successfully reattached. By post-operative month one, the patient's motility had fully recovered. However, traumatic optic neuropathy persisted, evidenced by a persistent RAPD and visual field testing showing dense superior and inferior arcuate deficits.

Conclusions, including unique features of the case:

This case highlights the intersection of untreated psychosis and neuro-ophthalmic trauma and contributes novel insight to a sparsely documented area of neuro-ophthalmology and strabismus surgery. The identification and repair of a partially disinserted medial rectus muscle following attempted self-enucleation adds valuable surgical and diagnostic perspective to a field where traumatic strabismus from psychiatric injury is seldom reviewed. This case underscores the lasting consequences of TON, including irreversible visual field loss, which may persist despite surgical and psychiatric stabilization.

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Keywords: Optic neuropathy, Optic nerve trauma and treatment, Trauma, Ocular motility, Visual fields

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Presentation and Outcome of a Primary Papillary Epithelial Tumor of the Sella

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Introduction:

Pituitary tumors arise from various cell types and often have both systemic and visual effects. A rare, recently described entity is the primary papillary epithelial tumor of the sella (PPETS), a non-neuroendocrine tumor expressing thyroid transcription factor-1 (TTF-1).¹ Limited existing literature focuses on the tumor's histological and molecular characteristics.¹⁻³ Here, we highlight the presentation, management, and visual outcomes of a case of PPETS in comparison to two illustrative cases of common pituitary tumors in similar-aged patients.

Description of Cases:

Patient 1 is a 48-year-old male with increased fatigue and panhypopituitarism (low cortisol, T4, testosterone, FSH and LH, mildly elevated prolactin). MRI showed a 2.4 x 1.9 x 2.5 cm heterogenous suprasellar mass elevating the optic chiasm. Visual acuities were 20/40 OD, 20/20 OS. Humphrey Visual Fields revealed a right hemifield defect OD. Surgical excision was performed with post-operative acuities of 20/20 OU and near-resolution of the right hemifield defect OD. Pathology confirmed a PPETS. Gamma knife radiation was subsequently performed. Patient 2 is a 46-year-old male with progressive vision loss from a prolactinoma, which was treated with cabergoline. Patient 3 is a 43-year-old male with prior pituitary macroadenoma resection who presented with bilateral photopsias from a tumor recurrence, treated with repeat resection. All three patients had ganglion cell layer changes corresponding to the initial optic neuropathy, but demonstrated significant visual field improvement after intervention.

Conclusions, including unique features of the case:

To our knowledge, this is the first report including structural OCT and visual field changes in the setting of a novel pituitary mass. It is prudent to maintain a broad differential with sellar masses, and reassuring to see that PPETS may follow a similar pattern as more classic tumors (Patients 2 and 3) with the potential for visual recovery. Future studies are necessary to further elucidate the systemic and visual manifestations and outcomes of PPETS.

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Keywords: Tumors, Visual fields, Optic neuropathy

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Organoid Nevus Syndrome with Optic Pit Associated Maculopathy

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Introduction:

Organoid Nevus Syndrome (ONS) is an epidermal nevus syndrome characterized by ocular, cutaneous, and neurological abnormalities. Common ocular manifestations include epibulbar choristomas, eyelid coloboma, scleral calcification, and focal hypopigmented fundus lesions. Seizures and neurodevelopmental delays are often reported in conjunction with ocular and cutaneous findings, reinforcing a triad that distinguishes this neurocutaneous syndrome. Genetic mosaicism involving postzygotic mutations is the proposed mechanism of ONS, which supports the wide variation in phenotype.

Description of Cases:

A 39-year-old woman presented with counting fingers vision in her left eye (OS), decreased from 20/100 baseline. She had a prior diagnosis of ONS and a retinal tear treated with laser 20 years earlier. Dilated fundoscopic examination revealed a macula-off retinal detachment with no clear break OS, an anomalous optic nerve OS with a very deep cup, a cup-to-disc asymmetry of 0.3 in the right eye and 0.85 in the left eye, and bullous subretinal fluid emanating from a temporal pit of the optic nerve OS. Optical coherence tomography (OCT) scans of the macula showed subretinal fluid continuous with the nerve, and a B-scan showed posterior calcification of the sclera. MRI of the brain and orbits with and without contrast revealed a presumed arachnoid cyst expanding the left optic canal with possible neurovascular compression of the left optic nerve one centimeter distal to the chiasm. The patient was diagnosed with a mild compressive optic neuropathy OS and optic pit associated maculopathy. She underwent a pars plana vitrectomy with improvement in her vision to 20/60 OS.

Conclusions, including unique features of the case:

This patient's presentation differs from the classic triad of ONS, and the presumed arachnoid cyst on MRI and optic pit associated maculopathy are unique aspects of her disease. These novel manifestations of ONS highlight the genetic mosaicism underlying the pathology and demonstrate the variability of ONS phenotypes.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Neuroimaging, Optic neuropathy

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Anomalous Case of Central Retinal Artery Occlusion: Uncovering Rare Embolic Sources

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Introduction:

Central retinal artery occlusion (CRAO) causes acute, painless monocular vision loss and is most often seen in older patients with cardiovascular risk factors such as hypertension, diabetes, and carotid atherosclerosis. The most common mechanism is embolic obstruction from the internal carotid artery. Because of the retina's exceptionally high metabolic demand, irreversible ischemia develops rapidly, resulting in poor visual outcomes. This report describes a rare case of CRAO in a young patient in whom multimodal evaluation uncovered multiple embolic pathways and an underlying systemic vascular disorder—hereditary hemorrhagic telangiectasia (HHT).

Description of Cases:

A 33-year-old man with a history of sciatica on 80 mg methadone daily presented with sudden, painless, complete vision loss in the left eye. Visual acuity was 20/20 OD and hand motion OS, with diffuse retinal whitening, a cherry-red spot, and a relative afferent pupillary defect. Neurologic examination was normal (NIHSS 0), and no systemic embolic symptoms were reported. CT/CTA and MRI showed no infarction or large-vessel occlusion. During selective intra-arterial thrombolysis (IAT), digital subtraction angiography revealed an anomalous origin of the ophthalmic artery from the middle meningeal artery, prompting further systemic embolic source investigation. Vision improved to 20/800 with eccentric fixation after three days. Additional evaluation identified a patent foramen ovale (PFO) and a large pulmonary arteriovenous malformation (PAVM) as potential embolic sources. Genetic testing subsequently confirmed a diagnosis of HHT.

Conclusions, including unique features of the case:

This case highlights CRAO as the initial manifestation of previously undiagnosed HHT. The occlusion likely resulted from multiple concurrent embolic mechanisms—including paradoxical embolism via a PFO, pulmonary shunting through a PAVM, and altered hemodynamics from an anomalous ophthalmic artery origin. IAT not only served a therapeutic role but also uncovered diagnostic vascular anomalies that directed systemic management and eventual confirmatory genetic testing. This underscores the importance of investigating systemic vascular etiologies when young patients present with retinal arterial occlusion.

References: None provided.

Keywords: Vascular disorders, Retina, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease, Interventional neuroradiology

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Sequential, Metachronous Optic Neuropathies From Distinct Optic Pathway Tumors

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Introduction:

Sequential optic neuropathies separated by years typically raise concern for recurrence, radiation-related change, or a unifying systemic process. Distinguishing these from metachronous, histologically distinct lesions is essential, particularly when a prior benign tumor biases diagnostic reasoning.

Description of Cases:

In 2018, a 75-year-old man developed left periorbital fullness and proptosis with progressive visual decline in 2019. MRI demonstrated a left sphenoid wing lesion consistent with meningioma and enhancement of the right optic nerve. Biopsy confirmed WHO grade 1 meningioma. Resection followed by proton beam therapy (2020) improved left-eye vision to 20/25, with radiographic and clinical stability for several years. In June 2023, he developed progressive right-sided visual loss and periocular headache. MRI showed marked enlargement, T2 hyperintensity, and enhancement of the right optic nerve extending through the canal, while the treated left lesion remained unchanged. Optic canal/nerve decompression did not improve vision, which declined to no light perception. Follow-up MRI showed continued progression, and biopsy demonstrated a low-grade astrocytoma. By January 2024, imbalance emerged. MRI revealed further orbital and intracranial expansion with mass effect, edema, and midline shift. Craniotomy and resection confirmed glioblastoma. Enucleation with chemoradiation (March 2024) followed. The fellow eye remained stable at 20/40–20/50.

Conclusions, including unique features of the case:

This case illustrates sequential, metachronous optic pathway tumors—an initial left sphenoid wing meningioma and a later aggressive right optic nerve glioma. The evolution highlights three plausible mechanisms: transformation of a previously indolent lesion, radiation-induced tumorigenesis or acceleration, and development of an entirely new primary neoplasm. The prolonged interval and divergent histopathology favor independent pathologies, yet prior radiation and reported transformation patterns remain relevant considerations. This case emphasizes the need to avoid anchoring bias, reassess evolving imaging, and pursue repeat histologic confirmation when clinical progression diverges from expectations.

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Keywords: Tumors, Chemotherapy and radiation injury, Optic neuropathy

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The Prognosis of Visual Snow. A Systematic Review

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Introduction:

Visual snow (VS) has been characterized as a disorder separate from migraine aura (1). VS is the bilateral visual perception of static that varies in severity, is commonly associated with other visual symptoms, and results in no change in visual acuity (1). Despite increasing publications on the presentation and pathophysiology of VS, the prognosis of this disorder is poorly understood. Patients are left without a prognosis. The objective of this study is to review the known literature regarding the natural history of VS.

Description of Cases:

Two research questions were formulated: 1. How does VS change over time in age groups 20-39, 40-59 and 60 years of age and older? 2. In the aforementioned age groups, what is the prevalence of migraine, psychiatric disease, neurologic disease and other medical disorders? With the assistance of a medical college research librarian, CINAHL, Cochrane Library, EMBASE, MEDLINE/PUBMED, PsycINFO, SCOPUS, Google Scholar, NOVEL and Clinical Trial Registries were searched. Level of evidence was assigned to each article based on the Oxford Centre for Evidence Based Medicine. The PRISMA flow diagram for meta-analyses was utilized (2). 527 articles were reviewed by 2 independent reviewers and consensus was reached that 6 articles pertained to the 2 research questions. Three articles commented on change in VS symptoms over 30 days, 6 weeks and 6.5-7.3 years. One article identified co-morbidities.

Conclusions, including unique features of the case:

There is insufficient evidence in the literature to understand how VS changes over time, and the prevalence of co-morbid diseases in the 3 age groups studied. A retrospective chart review or patient survey study is needed to know the prognosis of visual snow.

References: 1. Schankin et al. 'Visual Snow' - a disorder distinct from persistent migraine aura. *Brain*. 2014;137(5):1419. 2. Page et al. The PRISMA 2020 Statement: an updated guideline for reporting systematic review. *BMJ*. 2021;372:n71.

Keywords: Miscellaneous

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Hyperglycemia-induced Visual Field Changes

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Introduction:

Hyperglycemia can cause electroclinical seizures in the occipital lobe that manifest as vision changes, but persistent homonymous hemianopic defects from hyperglycemia are rarely reported in the literature. We describe a patient with bilateral homonymous visual field defects associated with episodic positive epileptic visual phenomena, likely both due to hyperglycemia.

Description of Cases:

A 60-year-old woman presented with fluctuating peripheral vision changes described as areas of her vision “going in and out” similar to “tunnel vision” and episodic superimposed fluctuating colored lights in her peripheral field. Past medical history was notable for poorly controlled diabetes mellitus complicated by nonproliferative diabetic retinopathy OU. On presentation, blood pressure was 180/100 and she was intermittently somnolent, with severe hyperglycemia >500mg/dl. Ophthalmologic examination had normal visual acuity and color vision, and fundusoscopic examination showed normal optic discs and mild background diabetic retinopathy. Humphrey visual field 24-2 showed exquisitely homonymous superior left and inferior right quadrantanopias. MRI brain showed subtle cortical enhancement in the right occipital lobe inferior to the calcarine fissure, and subtle cortical diffusion restriction in the left occipital lobe superior to the calcarine fissure. Continuous electroencephalography showed several brief electroclinical seizures in the posterior occipital lobes associated with episodes of flashing colored lights “like looking at a disco ball”. Treatment with levetiracetam improved her mental status and stopped the fluctuating colored lights in her peripheral vision. Her visual field deficits persisted for several days following adequate control of her seizures and treatment of her hyperglycemia, eventually resolving in 1 month.

Conclusions, including unique features of the case:

This patient’s fluctuating mental status and positive visual phenomena were attributable to occipital lobe seizures. While postictal Todd’s paralysis of the visual cortex can cause brief homonymous hemianopic defects and even cortical blindness, the duration of our patient’s persistent visual field defects (1 month) were likely also a direct result of her hyperglycemia.

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Keywords: Visual fields, Neuroimaging, Retina

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Acute Leber Hereditary Optic Neuropathy at 86 years

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Introduction:

This case explores the diagnostic challenges and clinical management of an 86-year-old previously asymptomatic female experiencing acute onset of central visual decline.

Description of Cases:

An 86-year-old woman with sleep apnea, hypertension, autoimmune autonomic neuropathy (improved with IVIG), breast cancer s/p mastectomy, and dry AMD presented with 3 months of rapid visual decline. She denied eye pain. VA was CF at 2' OU, color vision 9/12 OD and 7/12 OS, without RAPD or disc edema. Fundus exam showed macular drusen and moderately cupped, pink optic nerves. HVF-2 revealed bilateral central scotomas. OCT RNFL was normal, but GCC showed nasal thinning OU. OCT-A, mfERG, and MRI orbits/brain were unremarkable aside from mild atrophy. Eleven months later, vision declined to CF 1' OD and HM OS with subtle optic pallor and further GCC/papillomacular bundle thinning. Labs including vitamins B1, B6, B12, folate, and heavy metals were normal. She denied tobacco or alcohol use. Genetic testing confirmed a homoplasmic MT-ND6 m.14484T>C (M64V) pathogenic variant, consistent with Leber Hereditary Optic Neuropathy (LHON).

Conclusions, including unique features of the case:

Identification of a homoplasmic MT-ND6 m.14484T>C (M64V) pathogenic variant in an 86-year-old woman highlights the need to consider hereditary optic neuropathies even in advanced age. Although AMD, ischemic optic neuropathy, and retinal vascular occlusions are more typical in this demographic, OCT, FA, and fundus findings with normal ERG were inconsistent with these diagnoses. LHON from the T14484C mutation typically affects young males and presents with bilateral central vision loss and progressive optic pallor—features seen in this case. Comprehensive nutritional, toxic, metabolic, and imaging evaluations excluded other causes. To our knowledge, this represents the oldest reported onset of LHON, with vision loss beginning at 86 years. While no definitive therapy exists, Idebenone (400 mg TID) may benefit patients with the 14484 mutation lacking spontaneous recovery within one year. Genetic counseling was recommended due to mitochondrial inheritance.

References: Yu-Wai-Man P, et al. LEROS Study Group. Therapeutic benefit of idebenone in patients with Leber hereditary optic neuropathy: The LEROS nonrandomized controlled trial. *Cell Rep Med*, 5(3):101437, 2024 Mar 19.

Keywords: Optic neuropathy, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Genetic disease, Retina, Visual fields

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Severe Chronic Dry Eye in Ocular Graft-Versus-Host Disease: Clinical Improvement with Topical Immunoglobulin G as Adjunctive Therapy

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Introduction:

Ocular graft-versus-host disease (oGVHD) can cause severe keratoconjunctivitis sicca with neurosensory dysfunction and fluctuating vision that is often resistant to standard therapies. Topical immunoglobulin G (IVIG) has been proposed as an anti-inflammatory treatment to restore ocular-surface health and visual function, but evidence in oGVHD remains limited.

Description of Cases:

A 66-year-old man developed chronic oGVHD-associated dry eye following hematopoietic stem-cell transplantation for hematologic malignancy. Symptoms included burning, foreign-body sensation, and blurred vision despite prior therapies (punctal occlusion, scleral and soft bandage lenses, amniotic-membrane placement, steroid drops, topical cyclosporine 0.05–0.09 %, tacrolimus, lifitegrast, and autologous serum tears 20–50 %). Initial best-corrected visual acuity was 20/25-2 OD and 20/40 OS. Examination showed 2+ conjunctival injection, 2–3+ OD and 3–4+ OS diffuse epithelial erosions, and severe meibomian-gland atrophy. Corneal sensitivity was reduced (3 cm OD, 2 cm OS) by Cochet-Bonne esthesiometry, confirming neurosensory concerns. Tear osmolarity was elevated (325 mOsm/L OD, 340 mOsm/L OS); InflammaDry was positive bilaterally; and OSDI score was 82, indicating severe symptoms. A compounded 5 % topical IVIG drop was added twice daily to ongoing surface therapy. After eight weeks, the patient reported symptom improvement and clearer vision. Post-treatment acuity remained 20/20 ± OD and OS, OSDI improved to 42, epithelial erosions decreased to 1+, corneal sensitivity partially recovered (5 cm OD, 4 cm OS), and tear osmolarity normalized (305 mOsm/L OD, 300 mOsm/L OS). No adverse events were noted.

Conclusions, including unique features of the case:

Addition of topical IVIG to a comprehensive dry-eye regimen was associated with objective and subjective improvement in refractory oGVHD-related disease. This case illustrates the novel use of topical IVIG for refractory ocular graft-versus-host disease, supporting its potential as a safe and effective treatment for ocular-surface inflammation with neurosensory and visual involvement.

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Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: Barbara Tylka; Cherie Nau; Brent Christensen; Christine Mun: C (Consultant/Contractor): Selagine, Inc; Sandeep Jain: O (Owner/Co-Owner/Founder/Co-Founder): Advaita, Inc, Selagine, Inc. P (Patent): US9867871B2, PCT/US19/60566 C (Consultant/Contractor): Amgen, GlaxoSmithKline, Neutrolis, Dompe

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The Hidden Culprit: Unmasking a Rare Cause of Uveitis

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Introduction:

Cutaneous melanoma is a malignancy arising from the melanocytes of the skin, accounting for nearly 90% of skin cancer mortality. Less than 5% of metastases to the eye and orbit are due to cutaneous melanoma. This report presents an unusual manifestation of metastatic acral lentiginous melanoma as vitreous seeding masquerading as intermediate uveitis.

Description of Cases:

This is an 86-year-old Caucasian female with Stage III Acral Lentiginous Melanoma of the left ankle with a depth of invasion of 5.8 mm and macular degeneration treated with anti-VEGF. After excision and lymph node biopsy, the patient developed a wound infection, delaying the start of combination immunotherapy. During this delay, she developed multiple in-transit metastases in the left lower leg. She later presented with blurry vision, and a third-party ophthalmologist diagnosed uveitis, leading to discontinuation of immunotherapy and initiation of topical steroids. On presentation to our hospital, slit-lamp examination revealed dense anterior uveitis with vitreous veils and cells in the right eye, with BCVA 20/40. OCT showed AMD in both eyes, for which she continued anti-VEGF therapy. Because of atypical features of unilateral inflammation without pain, redness, or photophobia, and poor steroid response, a diagnostic vitrectomy was performed. Vitreous biopsy revealed malignant melanoma cells, confirming metastatic melanoma. The patient underwent pars plana vitrectomy, intravitreal melphalan injection, and ocular radiotherapy (3500 cGy), with slight visual improvement and resolution of vitreous veils.

Conclusions, including unique features of the case:

To our knowledge, acral lentiginous melanoma has never been reported in the literature to metastasize to the orbit. Several atypical, red flags in this patient may serve as clinical indicators; a unilateral, painless presentation of 'uveitis' with poor steroid response should raise suspicion for a different underlying cause, such as malignancy. This case also underscores the relevance to neuro-ophthalmology in recognizing masquerade syndromes, where metastatic or infiltrative disease can mimic inflammatory ocular conditions.

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Keywords: Orbit/ocular pathology, Tumors

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Visual Snow Syndrome Symptoms With Vision Loss: A Case Series

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Introduction:

Visual snow syndrome (VSS) and Charles Bonnet syndrome (CBS) exhibit “visual snow” and “release” hallucinations, respectively. Conventionally, CBS presents with vision loss, while VSS presents with normal ophthalmic examinations. We present three cases with VSS symptoms and vision loss, challenging current diagnostic criteria.

Description of Cases:

Case 1 A 63-year-old male with optic neuropathy presented with 10 months of “static”, floaters, photopsias, photophobia, and headaches. Vision was 20/40 in the right eye (OD), 20/60 in the left eye (OS). Optical coherence tomography (OCT) demonstrated diffuse thinning of both the retinal nerve fiber layer (RNFL) and ganglion cell layer (GCL) in both eyes (OU). Visual field (VF) testing showed cecocentral scotomas OU. Treatment for VSS-like symptoms with topiramate and gabapentin were ineffective. Case 2 A 72-year-old female with staphyloma posticum and retinal degeneration presented with 2 years of “static”, photopsias, photophobia, and headaches. Vision was 20/30 OD, 20/40 OS. OCT demonstrated macular thinning OS and temporal GCL thinning OU. VF testing showed generalized depression and constriction OU, while full-field ERG showed non-recordable responses OU. While amitriptyline, gabapentin, topiramate, and lamotrigine ineffectively treated VSS-like symptoms, FL-41 lenses improved symptoms. Case 3 A 49-year-old female presented with 1 year of progressive vision loss OS>OD. Neuroimaging revealed a frontal meningioma that was surgically resected. Post-operatively, she presented with “static”, “light forms”, nyctalopia, palinopsia, and headaches. Vision was 20/25 OD, counting fingers (CF) at 1’ OS with afferent pupillary defect (APD). OCT demonstrated optic atrophy OU. VF testing showed generalized depression OU with a central scotoma OD. Topiramate, clonazepam, gabapentin, lamotrigine, and zonisamide unsuccessfully treated VSS-like symptoms.

Conclusions, including unique features of the case:

Our series suggests visual snow-like phenomena can occur with optic nerve or retinal pathology, questioning current guidelines distinguishing VSS and CBS. Additionally, VSS symptoms associated with optic nerve or retinal disease may be more refractory to treatment than isolated VSS.

References: None provided.

Keywords: Miscellaneous

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Near-Infrared Reflectance Imaging Uncovers Retrograde Degeneration With Minimal Inner Nuclear Layer Changes In Retrochiasmal Visual Pathway Damage

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Introduction:

In two previously reported cases of optic tract damage, retinal NIR imaging revealed a semilunar hyporeflective area contralateral to the visual field defect, associated with microcystic changes in the inner nuclear layer (INL) on optical coherence tomography (OCT). These findings have been interpreted as secondary to retrograde retinal degeneration. We aimed to determine whether similar retinal NIR alterations can be observed in retrochiasmal visual pathway damage, even with minimal changes in the INL.

Description of Cases:

We report three patients with retrochiasmal visual pathway damage due to different etiologies and disease durations: one traumatic (12 months after injury), one compressive (5 years after onset), and one vascular with bilateral retrochiasmal lesions (4 years after stroke). In all cases, NIR imaging demonstrated a homonymous hemianopic, semilunar hyporeflective area contralateral to the visual field defect, predominantly localized in the nasal hemiretina. OCT revealed only minimal changes in the INL.

Conclusions, including unique features of the case:

Alterations in retinal NIR may either precede or occur independently to overt microcystic INL changes. They may also represent an early stage of retrograde retinal degeneration probably influenced by the speed and severity of the initial damage. Given its sensitivity to subtle reflectance loss and its non-invasive nature, retinal NIR imaging may serve as an early and adjunctive tool for detecting retrograde retinal degeneration secondary to retrochiasmal visual pathway damage.

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Keywords: Retina, Miscellaneous, Perimetry, Stroke, Trauma

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Reversible Cortical Blindness Secondary to Carbon Monoxide Poisoning in a Pediatric Patient

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Introduction:

Carbon monoxide (CO) poisoning is one the leading causes of accidental exposure to toxins. Though its neurological sequelae are well-documented, acute cortical blindness in pediatric patients is rare. We present a case of seizures and cortical vision loss secondary to CO toxicity that resolved following hyperbaric oxygen treatment.

Description of Cases:

A 10-year-old otherwise healthy female was found unresponsive in a parked car. She presented to the emergency room with altered mental status and seizures. The patients' labs were consistent with acute CO poisoning (COHb = 17%, lactate = 7 mmol/L, pH = 7.17). MRI brain showed diffusion restriction in the putamen, caudate nuclei, parietal cortices, and posterior thalami, consistent with hypoxic-ischemic injury from CO exposure- which was later attributed to wood burning at home. The patient was started on 100% oxygen with a non-rebreather mask which brought her COHb down to 0.9%. Despite the success, the patient reported profound bilateral vision loss. She had count finger visual acuity OU with otherwise normal anterior and posterior segment exam. The patient was treated with hyperbaric therapy and antiepileptic prophylaxis (Keppra then lacosamide). After three treatments, the patient's vision improved (20/30 OD, 20/25 OS), mood and alertness improved, and EEG and ECG were normal. The patient was discharged with complete resolution of vision loss and neurologic dysfunction.

Conclusions, including unique features of the case:

Cortical blindness secondary to CO poisoning in a pediatric patient may be reversible with hyperbaric therapy. Early recognition, neuroimaging, and hyperbaric therapy is of utmost importance, even after COHb levels are normalized. There is potential for reversing CO related cortical injury when managed with hyperbaric oxygen therapy.

References: None provided.

Keywords: Pediatric neuro-ophthalmology

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Optic Tract Syndrome: Clinical and OCT Correlates in a 6-Year Retrospective Case Series

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¹ APEC

Introduction:

Evidence on demographic and clinical optic tract syndrome is limited. Even more on the latinamerican population. We present the data of patients with optic tract syndrome presenting to an ophthalmology referral hospital in Mexico city in the last 6 years. We conducted a retrospective, observational, descriptive study. All patients evaluated between January 1, 2019, and October 21, 2025, who presented with homonymous visual field defects and optic atrophy were included. Patients with other causes of visual field defects or optic atrophy (such as other optic neuropathies or injury to optic radiations) were excluded. Demographic data, visual acuity, color vision, optical coherence tomography (OCT) parameters, and brain MRI findings were reviewed.

Description of Cases:

Sixteen patients were included; 56.2% (n=9) were female, with a mean age of 55.13 years. 68.7% had right optic tract involvement. Color vision data was available for 13 patients, among whom 30.77% had dyschromatopsia. A relative afferent pupillary defect in the contralateral eye was found in only 25% (n=4) patients. The average visual acuity was 0.31 Logmar for the ipsilateral eye and 0.27 for the contralateral one. OCT data were available for 14 patients, showing a mean retinal nerve fiber layer thickness of 64.57µm in the ipsilateral eye and 78.57µm in the contralateral eye. Mean ganglion cell layer thickness was 61.36µm and 64.64µm, respectively. The most frequent etiology was compressive in 50% of patients, followed by trauma in 31.25%; in 12.5% of cases, the cause remained unidentified.

Conclusions, including unique features of the case:

Optic tract lesions produce a characteristic pattern of contralateral homonymous visual field loss and asymmetric optic atrophy. Recognition of this pattern, supported by OCT findings, is crucial for accurate lesion localization and differentiation from primary optic neuropathies, improving diagnostic precision in neuro-ophthalmic practice.

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Keywords: Visual fields, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Miscellaneous, Optic neuropathy, Neuro-opth & systemic disease (eg. MS, MG, thyroid)

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Familial Neuronal Intranuclear Inclusion Disease with Homonymous Hemianopia: A Case Series

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Introduction:

Neuronal intranuclear inclusion disease (NIID) is a rare disease with distinct pathologic and imaging findings and variable clinical manifestations.¹ Homonymous hemianopia has not been commonly reported. We present a case series of three siblings with NIID and who presented with homonymous visual field defects.

Description of Cases:

We present a case series of three siblings who all developed clinical manifestations of NIID in their sixties with homonymous hemianopia being among their first symptoms. Patient 1 was a 63-year-old male who presented with headache, fever, confusion, aphasia, and a right homonymous hemianopia. Patient 2 was a 63-year-old male when he developed a severe headache and a persistent left homonymous hemianopia. Patient 3 was a 61-year-old female when she had new onset headaches, abnormal gait, non-fluent aphasia, and a left homonymous hemianopia. All three had MRI findings significant for high-intensity-T2 signal at the corticomedullary junction along with DWI correlate in some regions, a typical finding for NIID. The diagnosis was confirmed in patients 1 and 3 by skin biopsy revealing p62 and ubiquitin positive intranuclear inclusions and in patients 1 and 2 by genetic testing showing a pathogenic NOTCH2NLC gene along with one FGF14 allele with a trinucleotide repeat expansion with incomplete penetrance.

Conclusions, including unique features of the case:

Each sibling had an episodic neurogenic-event dominant subtype of NIID that included homonymous hemianopia among the earliest symptoms. It is unclear why symptoms vary between patients but mechanisms such as variable numbers of repeats have been suggested.² The most typical NIID-related visual symptoms are related to retinopathy, not homonymous hemianopia.³ In this family, the factors underlying the propensity for posterior cortical involvement leading to homonymous hemianopia are unknown and may include interactions with other genes, such as FGF14, among other factors. NIID should be considered in cases of homonymous hemianopia with episodic neurologic symptoms.

References: None provided.

Keywords: Genetic disease, Visual fields, Higher visual functions, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Miscellaneous

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The Illusion of Sight: Anton's Syndrome Revealing the Late Sequelae of SMART Syndrome.

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Introduction:

Stroke-like migraine attacks after radiation therapy (SMART) syndrome is a rare, delayed complication of cranial radiation, characterized by migraine-like episodes, seizures, and transient or permanent cortical dysfunction. Cortical blindness and Anton's syndrome have only rarely been described in association with SMART syndrome. We report a unique SMART syndrome case with progressive cortical visual impairment and Anton's syndrome occurring more than two decades after childhood cranial radiation.

Description of Cases:

A 28-year-old male presented to the emergency room with acute bilateral vision loss (from 20/20 to NLP) accompanied by a severe migraine headache. His past medical history was significant for medulloblastoma s/p radiation therapy at age 6, right occipital stroke with residual left homonymous hemianopia at age 9, focal unaware seizures, and frequent migraine headaches. MRI showed gyriform enhancement and edema in the right occipital-temporal region, which, along with the clinical constellation of symptoms, SMART syndrome was contemplated. EEG revealed occipital seizures with shifting laterality. His vision improved to 20/250 OD and 20/150 OS after a large dose of steroids and multiple seizure medications treatment. However, over subsequent months, vision deteriorated to hand-motion bilaterally, accompanied by visual anosognosia, consistent with Anton's syndrome. Serial imaging showed chronic bilateral occipital encephalomalacia without evidence of new lesions. Over two years of follow-up, his headaches improved with a combination of anti-seizure therapy and onabotulinumtoxinA injection, and his vision has remained stable.

Conclusions, including unique features of the case:

This case highlights a rare, delayed evolution of SMART syndrome with progression from reversible stroke-like episodes to irreversible cortical blindness and Anton's syndrome long after childhood radiation. Recognition of SMART-related cortical blindness and its behavioral manifestations is crucial for accurate diagnosis, avoidance of unnecessary invasive testing, and optimization of long-term neuro-ophthalmic rehabilitation.

References: None provided.

Keywords: Higher visual functions

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Case Series: Re-Stenting in Idiopathic Intracranial Hypertension

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Introduction:

Venous sinus stenting has become a more frequently employed treatment for idiopathic intracranial hypertension (IIH). Studies including the prospective River trial have shown clinical improvement in most patients, suggesting unilateral stenting as definitive treatment. However, select patients may develop recurrence thereby prompting consideration for re-stenting which is less understood.

Description of Cases:

Patients seen at a tertiary care center between August 2020 and May 2025 who met the Dandy criteria for IIH and underwent venous sinus stenting were included. Five of 119 stented IIH patients required secondary stent placement due to recurrent symptoms and/or worsening neuro-ophthalmic exam. Patients were all female, median age was 25 (interquartile range [IQR], 22.5, 34). Each underwent successful unilateral venous sinus stenting after manometry confirmed increased pressure gradients (median 8 mm Hg, IQR, 7.5, 12). These patients re-presented with tinnitus, headache, and/or progressive vision loss – with recurrence of papilledema found on fundus exam in 2 of 5 patients. Onset of secondary presentations varied among patients, with 3 of 5 never reporting symptom resolution after initial stenting, and 2 with recurrence following initial improvement. None of the patients had in-stent stenosis demonstrated on follow-up MRV nor during cerebral angiograms. All reported compliance with dual antiplatelet therapy (aspirin and clopidogrel [40%] or aspirin and ticagrelor [60%]). Following repeat cerebral angiogram, a second stent was placed in each patient. One patient had a secondary stent placed in the sagittal sinus, another had a proximal stent placed adjacent to the stented transverse sinus, while the remaining (3) patients underwent contralateral transverse sinus stenting. All patients reported symptomatic relief after re-stenting in conjunction with improvement in their neuro-ophthalmic exam.

Conclusions, including unique features of the case:

We report 5 cases of previously stented IIH patients with recurrence who required a second stent prior to prolonged symptom recovery.

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Keywords: High intracranial pressure/headache, Pseudotumor cerebri

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Bacterial Meningitis Complicating IIH with CSF leak

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Introduction:

Idiopathic intracranial hypertension (IIH) may present with spontaneous cerebrospinal fluid (CSF) leak, sometimes as the initial clinical manifestation. Chronically elevated intracranial pressure (ICP) can lead to progressive thinning and erosion of the skull base and adjacent dura, facilitating CSF escape and a direct route for pathogens to access the central nervous system. CSF rhinorrhea appears to be a syndrome associated with an older population with chronic IIH, predisposing meningitis, a risk underrecognized in this patient population.

Description of Cases:

Three female patients aged 53 to 70 presented to neuro-ophthalmology for evaluation of IIH. All had a history of treated bacterial meningitis four to seven months prior to their initial evaluation. All had radiographic findings of anterior skull base thinning and meningoencephaloceles, which were endoscopically repaired. All patients reported a history of clear nasal drainage resolving with surgical repair. Pre-operatively, all patients denied classic symptoms of IIH. Post-operatively, two patients reported new clinical symptoms of elevated ICP (headache and pulsatile tinnitus). One patient had an abnormal neuro-ophthalmic exam concerning for mildly elevated ICP (constricted nasal visual field OD, loss of spontaneous venous pulsations). Only one of the patients had papilledema on fundoscopy. All patients had some radiographic features of IIH such as partially empty sella.

Conclusions, including unique features of the case:

IIH should be considered a risk factor for spontaneous CSF leak and subsequent bacterial meningitis. This may be a syndrome of older patients with bone remodeling secondary to long-standing increased ICP, possibly exacerbated by postmenopausal bone thinning. CSF leak may temporarily alleviate symptoms of elevated ICP, masking classic IIH features on exam and testing, thereby delaying diagnosis. However, worsening symptoms after surgical repair are possible. Early recognition and multidisciplinary management including surgical repair of the CSF leak and postoperative neuro-ophthalmic monitoring are crucial to prevent recurrence and infectious complications.

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Keywords: High intracranial pressure/headache, Skull base, Neuro-ophth & infectious disease (eg, AIDS, prion), Pseudotumor cerebri

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Concurrent Idiopathic Intracranial Hypertension and Retinal Degeneration: A Retrospective Case Series

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Introduction:

Bilateral optic disc edema without papilledema has been reported among patients with retinal degenerations. To our knowledge, idiopathic intracranial hypertension (IIH) in this patient population has not been reported. This retrospective case series highlights the clinical features and treatment course of nine patients with IIH and retinal degenerations. Three patients from this cohort are summarized below.

Description of Cases:

Patient 1: A 19-year-old female with Bardet-Biedl-associated retinitis pigmentosa (RP) and visual acuity light perception OU presented with frequent intermittent pulse-synchronous tinnitus and recurrent headaches. Neuroimaging revealed optic nerve tortuosity, partially empty sella, and low-lying cerebellar tonsils. She was found to have optic disc edema (ODE) grade 2-3 OU and lumbar puncture (LP) demonstrated an opening pressure (OP) of 28.0 cmH₂O. The patient was started on topiramate then acetazolamide, leading to improvement in signs and symptoms. Patient 2: A 26-year-old female with Usher Syndrome Type IIa and associated RP presented with headaches, cystoid macular edema (CME), and ODE grade 3 OU. IIH was diagnosed after neuroimaging demonstrated focal venous sinus stenosis and LP showed OP of 29.5 cmH₂O. Following placement of a venous sinus stent, OP normalized and ODE improved to grade 1-2. Patient 3: A 23-year-old female with cone-rod dystrophy diagnosed in infancy presented with headaches, pulse-synchronous tinnitus, and optic disc edema grade 2-3. Neuroimaging was unremarkable and LP showed OP of 40.0 cmH₂O. Acetazolamide therapy led to improvement of symptoms and disc edema.

Conclusions, including unique features of the case:

IIH and retinal degeneration can manifest simultaneously to produce a complex diagnostic picture with worsened visual outcomes. Further study, including an expanded cohort (n = 9) will be presented at the meeting to explore this association.

References: None provided.

Keywords: Pseudotumor cerebri, High intracranial pressure/headache, Retina

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Grant Support: None.

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The Myelinated Masquerade: A Case of Misdiagnosed Disc Edema

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Introduction:

Papilledema, optic disc swelling secondary to elevated intracranial pressure, is a key diagnostic criterion in idiopathic intracranial hypertension (IIH).¹ An optic nerve myelinated fiber layer may create a whitish, feathery appearance of the disc, mimicking blurred margins and increasing RNFL thickness, raising concern for papilledema.² We aim to describe a case in which a 30-year-old female was referred to neuro-ophthalmology for evaluation of unilateral optic disc edema.

Description of Cases:

Our patient presented to her primary care provider with concern of headaches. Ophthalmic evaluation was requested due to concern for IIH following MRI findings of “ectatic optic nerve sheath complexes with prominence to the subarachnoid spaces and narrowing of the left transverse sinus.” Examination by comprehensive ophthalmology revealed a lack of visual symptoms; unremarkable ophthalmic imaging (OCT RNFL/perimetry testing); and a left optic nerve described as “a little swollen.” Urgent lumbar puncture was subsequently ordered given ophthalmic exam findings and resulted with normal opening pressure (11cm H₂O) and unremarkable CSF analysis. Successive evaluation by neuro-ophthalmology confirmed the presence of an inferior 180-degree myelinated nerve fiber layer of the left optic disc without disc edema, heme or pallor.

Conclusions, including unique features of the case:

Our patient has an uncommon congenital finding: an optic nerve myelinated fiber layer, incorrectly mistaken for papilledema, resulting in lumbar puncture. IIH is a complex diagnosis; all diagnostic criteria should be satisfied to confirm IIH, and our patient failed to meet the well-established guidelines for IIH diagnosis.^{3,4} In addition, unilateral disc abnormalities should raise suspicion for pseudopapilledema, optic disc elevation due to benign structural abnormalities, as true papilledema is rarely unilateral. Her case emphasizes the importance of neuro-ophthalmologic specialist engagement in the ophthalmoscopic examination, assessment and diagnosis of IIH. Accurate distinction between pseudopapilledema and true papilledema is critical, as misinterpretation can lead to unnecessary, costly and invasive procedures in pursuit of diagnosis.⁵

References: 1. Aung AB, Chen BS, Wicks J, Bruce BB, Meyer BI. Presumptive Idiopathic Intracranial Hypertension Based on Neuroimaging Findings: A Referral Pattern Study. *J Neuroophthalmol*. 43(1):55-62. 2023. 2. Chen JJ, Kardon RH. Avoiding Clinical Misinterpretation and Artifacts of Optical Coherence Tomography Analysis of the Optic Nerve, Retinal Nerve Fiber Layer, and Ganglion Cell Layer. *J Neuroophthalmol*. 36(4):417-438. 2016 3. Beier D, Korsbæk JJ, Bsteh G, et al. Magnetic Resonance Imaging Signs of Idiopathic Intracranial Hypertension. *JAMA Netw Open*. 7(7):e2420138. 2024. 4. Friedman DI, Liu GT, Digre KB. Revised Diagnostic Criteria for the Pseudotumor Cerebri Syndrome in Adults and Children. *Neurology*. 81(13):1159-1165. 2013. 5. Fisayo A, Bruce BB, Newman NJ, Biousse V. Overdiagnosis of idiopathic intracranial hypertension. *Neurology*. 86(4):341-50. 2016.

Keywords: Pseudotumor cerebri, Neuroimaging, Miscellaneous

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Vascular Etiologies of Secondary Intracranial Hypertension Missed by Noninvasive Imaging: A Case Series

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Introduction:

While exclusion of secondary causes of intracranial hypertension (SIH) is required to establish a diagnosis of idiopathic intracranial hypertension (IIH), the negative predictive value (NPV) of noninvasive imaging for vascular causes of SIH such as cerebral venous sinus thrombosis (CVST) and dural arteriovenous fistula (dAVF) remains imperfect.¹⁻⁵ We present a case series of patients initially misdiagnosed with IIH based on negative noninvasive neuro-imaging.

Description of Cases:

Five patients were identified who met modified Dandy criteria for IIH based on negative noninvasive imaging prior to recognition of causal vascular SIH. Two required repeat noninvasive imaging to correctly diagnose a CVST, and 3 required conventional angiography to reveal a dAVF or hemodynamically significant sinus stenosis/CVST. Two had a history of remote CVST and were erroneously diagnosed with IIH due to noninvasive imaging's failure to detect a dAVF in one, and to detect the hemodynamic significance of a near-occlusive thrombotic stenosis in the other. Overall, all 5 patients worsened despite moderate-to-high dose acetazolamide; 2 deteriorated despite optic nerve sheath fenestration, and 4 had Frisén grade ≥ 4 papilledema. Two were male, and 4 had BMI ≤ 29 . Among patients who underwent angiography, 2 were male and the female patient was perimenopausal.⁶

Conclusions, including unique features of the case:

The imperfect NPV of noninvasive neuro-imaging to detect vascular causes of SIH occasionally contributes to premature closure and false diagnoses of IIH.⁴⁻⁵ Additional studies were pursued in our patients owing to the presence of demographic features atypical to IIH, but the suboptimal NPV of noninvasive imaging likely leads to under-recognition of vascular SIH in demographics typical to IIH as well. Further, clinicians without neuro-ophthalmology training may fail to recognize features atypical to IIH which should prompt early consideration of conventional angiography, underscoring the need for techniques such as arterial spin labeling which may improve the NPV of noninvasive imaging.⁷

References: None provided.

Keywords: Pseudotumor cerebri, Neuroimaging, High intracranial pressure/headache

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Contact Information: None provided.

Testosterone Use in a Genetically XX Carrier of Leber's Hereditary Optic Neuropathy

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Introduction:

Leber's Hereditary Optic Neuropathy (LHON) is a mitochondrial disease with about a 3:1 male predominance, suggesting an influence of sex hormones in disease development.¹ In vitro studies support the role of estrogen in mitochondrial biogenesis in LHON.²⁻⁴ In addition, testosterone has been shown to increase apoptosis and decrease mitophagy in a cell model of LHON.⁵ However, the link between androgens and LHON conversion may be less than straightforward. For example, two cases of late-onset LHON after initiation of an androgen receptor antagonist have recently been described.⁶ There have been no reports of the effects of exogenous testosterone therapy in LHON carriers with XX chromosomes transitioning from female to male. Here, we report one such case.

Description of Cases:

A 26-year-old LHON 11778 mtDNA mutation carrier with XX chromosomes was started on idebenone after showing early signs of conversion in 2014. At age 16, she developed bilateral mild optic disc pseudo-edema, central scotoma, and decreased visual acuity. This normalized with idebenone 90 mg TID, which was later increased to 200 mg TID. The patient has been taking exogenous testosterone as part of the female-to-male transition process since at least 2023 without evidence of conversion recurring. Visual acuity is 20/20 OU. Peripapillary RNFL has remained stable around 110 μ m OU. There is no GCL loss. HVF 30-2 remains within normal limits.

Conclusions, including unique features of the case:

We present the first case describing the natural history of at least 2 years of exogenous testosterone use in an XX LHON carrier. This example highlights that exogenous testosterone use alone is not sufficient to convert all LHON carriers to LHON disease. More studies are needed to determine whether testosterone therapy is safe for all LHON carriers.

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Keywords: Genetic disease, Optic neuropathy

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Introduction:

Brain abscesses cause morbimortality. (1,2) Incidence in USA is 1:100.000 annually. Prevalence of odontogenic etiology ranges between 3 and 10%. (2) Odontogenic cause is suspected if either oral microorganisms as *Streptococcus* or signs of dental infection are present and by exclusion of other sources of infection. (1) Most odontogenic cerebral abscesses occur after treatment due to bacteremia following dental procedures by hematogenous venous dissemination. (2,3) Congenital heart defects are predisposing factors for brain abscesses. (1,4) Such a rare presentation of undiagnosed patent foramen ovale is believed to occur by shunting of bacteria from right to left circulation bypassing the lung capillary bed filtering capacity. (4) Diagnosis relies on clinical triad (headache, fever and neurological deficit), neuroimaging and identification of dental focus as primary source of infection. (2) Treatment requires neurosurgical drainage and antimicrobial therapy. (5,6)

Description of Cases:

A 57 year-old male with history of myopia and keratoconus presented with a week-long headache, nausea, vomiting, photophobia, blurred vision and elevated neutrophils requiring hospitalization. The previous month he had undergone an uninfected ruptured molar extraction without antibiotic prophylaxis. MRI showed a peripherally enhancing lesion in right occipital lobe with adjacent edema and restricted diffusion centrally. Spectroscopy revealed elevated aminoacids suggesting pyogenic abscess. Empiric antimicrobial agents were administered. Stereotactic pus drainage obtained *Streptococcus Anginosus* growth successfully treated with ceftriaxone. Transesophageal echocardiogram revealed patent foramen ovale without endocarditis. Neuro-ophthalmic examination showed visual acuity of 0.8 OD and 0.5 OS with sequelae left homonymous quadrantanopic defects.

Conclusions, including unique features of the case:

Dental procedures rarely cause brain abscesses. Identification of odontogenic source of infection is essential for both diagnosis and treatment. (1) Predisposing factors such as congenital heart defects should be excluded. This case is unique because it shows an unusual presentation of brain abscess with headache, homonymous quadrantanopia and no fever following uninfected dental extraction in a patient with patent foramen ovale.

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Keywords: Neuro-ophth & infectious disease (eg, AIDS, prion), Visual fields

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Reversible Cecocentral Scotomas Secondary to Vitamin A Deficiency and Posterior Capsular Opacification in a Pseudophakic Patient

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Introduction:

Vitamin A deficiency is a rare but reversible cause of visual dysfunction in developed countries. Its manifestations can mimic optic neuropathies, including cecocentral scotomas, leading to diagnostic uncertainty, particularly in older pseudophakic patients with otherwise normal fundus and imaging studies.

Description of Cases:

A 78-year-old man presented with chronically poor vision, nyctalopia and increasing glare after bilateral cataract extraction with intraocular lens implantation and occasional photopsias. Examination showed best-corrected visual acuity (VA) of 20/50 OD and 20/40 OS, normal intraocular pressures, reactive and symmetric pupils but mild color discrimination loss 10/13 OD and 11/13 OS. Slit-lamp examination revealed trace posterior capsular opacification (PCO) in both eyes; fundus was unremarkable. Humphrey visual fields demonstrated mild, relatively symmetric bilateral cecocentral scotomas with preserved peripheral sensitivity. MRI of the brain and orbits was normal. Laboratory evaluation revealed vitamin A deficiency, and oral supplementation was initiated. At three-month follow-up, the patient experienced transient worsening of VA (20/70 OD, 20/50 OS) attributed to progression of PCO. After YAG capsulotomy, VA improved to 20/25 OD and 20/30 OS, and visual fields showed partial resolution of scotomas. On the third visit 4 months later, serum vitamin A levels had normalized, VA was 20/25 OU with normalization of visual fields, light sensitivity and nyctalopia. OCT of the RNFL and GCC remained within normal limits throughout.

Conclusions, including unique features of the case:

This case highlights the reversible nature of vitamin A deficiency–related visual dysfunction and the potential confounding effect of posterior capsular opacification. Bilateral cecocentral scotomas resolved fully after nutritional repletion and YAG capsulotomy, underscoring the importance of considering reversible systemic and media-related causes before diagnosing optic neuropathy.

References: None provided.

Keywords: Miscellaneous, Visual fields

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A Curious Case of Brun's Nystagmus

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Introduction:

Brun's nystagmus is a distinctive ocular finding typically associated with cerebellopontine angle (CPA) lesions, such as vestibular schwannomas. It presents as a combination of slow, large-amplitude nystagmus when gazing toward the lesion and fine, rapid, small-amplitude nystagmus when gazing away. Although classically linked to CPA tumors, this case highlights a rare pediatric presentation with an alternative underlying finding.

Description of Cases:

A 5-year-old boy with a history of recurrent acute otitis media was referred for abnormal eye movements. Visual acuity was 20/20 in both eyes. Pupils, color vision and visual fields were unremarkable. Eye movements revealed large-amplitude, low-frequency horizontal nystagmus in right gaze and small-amplitude, high-frequency nystagmus in left gaze. This was consistent with Brun's nystagmus, suggesting right CPA involvement. There were no associated symptoms such as headache, diplopia, or tinnitus. Outpatient ENT examination was unremarkable. MRI of the brain, orbits, and internal auditory canals (IAC) under anesthesia showed no mass but identified a small vascular loop within the right IAC contacting the vestibular and facial nerves.

Conclusions, including unique features of the case:

This case illustrates Brun's nystagmus in a child without a CPA mass, but with neurovascular contact as the likely etiology. IAC vascular loops, often branches of the anterior inferior cerebellar artery (AICA), are typically incidental and found in up to one-third of individuals. Certain loop characteristics however, such as direct nerve contact, may contribute to vestibular symptoms in select cases. This case underscores the importance of careful neuro-ophthalmologic localization and highlights that vascular variants, though usually benign, may mimic findings traditionally associated with space-occupying lesions. This case highlights the need to consider vascular causes as potential mimics in the differential diagnosis of pediatric nystagmus and reinforces the teaching point that not all cases with classic localizing signs are due to neoplasms.

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Keywords: Nystagmus, Ocular motility, Pediatric neuro-ophthalmology, Vascular disorders, Vestibular disorders

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Conventional case of chronic migraine with visual aura takes an atypical turn

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Introduction:

In this study, we present a rare case of a patient with chronic, worsening migraines with stable visual auras, but without visual field deficits. The patient had been followed by neurology for ~20 years prior to his presentation in the neuro-ophthalmology office, and had never received brain imaging.

Description of Cases:

Methods: Single case study of a 63-year-old male presenting with a 20-year history of migraine with visual aura. Upon presentation to the neuro-ophthalmology clinic, the patient underwent gonioscopy, a 24-2 and 30-2 Humphrey Visual Field Test, Optical Coherence Tomography, and retinal imaging using fundus photography. MRI of the brain with and without contrast was ordered and performed. **Results:** The 24-2 and 30-2 Humphrey Visual Field Tests, along with OCT measurements, were within normal limits. MRI revealed an avidly-enhancing extra-axial mass lesion along the posterior left occipital convexity measuring 4.8 x 4.2 x 1.7 cm, determined to be a grade II atypical meningioma. Subsequent treatment with gamma knife stereotactic radiosurgical treatment was pursued, but the outcome was complicated by edema and resultant seizures. Full resection of the meningioma was then performed, following which, the patient experienced visual field deficits characteristic of occipital lobe meningioma.

Conclusions, including unique features of the case:

Meningiomas have diverse presentations, which vary based on the size and location of the lesion. Presence of such lesions in the occipital lobe characteristically causes distinct impedances to the visual pathway, resulting in visual field defects. However, as we have seen in this case, not all presentations are typical, and diagnostic caution should be taken when approaching cases that may appear conventional. Clinicians often forgo MRI imaging in patients whose initial presentation is suggestive of classic migraine with visual aura; however, this case highlights the importance of having a low threshold for such imaging techniques, particularly in patients who present with no prior brain imaging.

References: None provided.

Keywords: Neuroimaging, Tumors, Visual fields

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Role of DOTATATE PET Imaging in Meningiomas with Neuro-Ophthalmic Implications

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Introduction:

Meningiomas are the most frequent primary intracranial tumours. Neuroimaging remains a pillar for the diagnosis and the clinical decisions that follow. Magnetic Resonance Imaging (MRI) has been the gold standard tool for evaluating meningiomas, alongside CT scans. However, many obstacles persist, hence the need for new technologies providing functional and molecular information on these tumours. This review examines the current role of ⁶⁸Ga-DOTATATE PET imaging in meningiomas, with a focus on optic nerve sheath and neuro-ophthalmic cases. It discusses the biological rationale, clinical evidence, and emerging applications of this modality in meningioma management.

Description of Cases:

With a sensitivity above 90%, ⁶⁸Ga-DOTATATE was shown to precisely detect meningiomas that had been previously only diagnosed by histopathology. The technology showed better proficiency at detecting osseous involvement, at distinguishing scar tissue from tumour tissue and could detect disease recurrence at a higher sensitivity than MRI imaging. These findings support the use for ⁶⁸Ga-DOTATATE in delimitating radiotherapy treatment volume and resection margins when meningiomas are recurrent or located in challenging areas such as the base of the skull or near the parasagittal sinus. Moreover, the detection of tumour tissue that remains undetected by other imaging modalities can improve radiotherapy planning by radio-oncologists.

Conclusions, including unique features of the case:

The addition of ⁶⁸Ga-DOTATATE PET imaging to clinical management of meningiomas has been shown to provide added benefits for diagnosis, surgical planning as well as post-surgical radiation and surveillance. This modality could be helpful in overcoming certain limitations of CT or MRI imaging alone, such as identifying disease extension in anatomically difficult areas and allowing for smaller and more precise radiation volumes. It is crucial to understand its limitations to interpret results accurately and integrate them into comprehensive meningioma management plans. Larger studies are needed to provide more definitive evidence on its efficacy and to establish standardized protocols for its use in clinical practice.

References: None provided.

Keywords: Neuroimaging, Tumors

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Sudden Unilateral Vision Loss in a Healthy Teenager: A Rare Intracranial Anomaly Revealed by Neuroimaging

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Introduction:

The gyrus rectus is located at the anterior cranial fossa floor superior to the intracranial optic nerves and chiasm. Compression of these structures by the gyrus rectus is often caused by neoplastic growth in the area.¹ Idiopathic spontaneous herniation of the gyrus rectus resulting in compressive optic neuropathy is exceptionally rare. It can be a diagnostic challenge as presentation often mimics optic neuritis. We report a rare case of herniated gyrus rectus impinging on the hemi-chiasm without a clear pathological cause in a young adolescent.

Description of Cases:

A 17-year-old female presented with acute right monocular visual loss (LogMAR 1.24), marked dyschromatopsia, and retro-orbital pain, without a relative afferent pupillary defect or fundoscopic abnormalities. Retro-orbital neuritis was initially suspected. High-resolution MRI showed inferior herniation of the right gyrus rectus compressing the right hemi-chiasm and pre-chiasmatic optic nerve, with no intracranial mass lesion and normal-appearing brain parenchyma and meninges. She later experienced another episode of acute right-eye visual decline (LogMAR 0.7) with colour deficit, prompting further investigation. Visual evoked potentials excluded demyelination. Neurosurgical review was sought, and intravenous corticosteroids were administered. As her visual function improved, surgery was deemed unnecessary, and she was managed conservatively.

Conclusions, including unique features of the case:

We describe an exceptionally rare cause of optic neuropathy from spontaneous, idiopathic herniation of normal gyrus rectus tissue into the optic pathway in an adolescent with no medical or family history—an occurrence scarcely reported in the literature. This case underscores the essential role of advanced neuroimaging of the entire anterior visual pathway when no other cause of optic neuropathy is evident. MRI showed herniation of normal-appearing gyrus rectus causing mild deformity and signal change without compressive lesions or identifiable pathology. Reporting this case increases awareness among neuro-ophthalmologists to support accurate diagnosis and management.

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Keywords: Optic neuropathy, Neuroimaging

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Unique MRI Findings In A Case of Neurosarcoidosis

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Introduction:

Neurosarcoidosis without systemic disease is a diagnostic challenge, and timely diagnosis is essential to prevent significant morbidity. We present a case of recurrent optic neuritis due to pathologically confirmed neurosarcoidosis with unique magnetic resonance imaging (MRI) features.

Description of Cases:

A 49-year-old White male presented with painless right eye vision loss. His history included a prior focal seizure and right optic neuritis one year earlier of unknown etiology with spontaneous resolution. On exam, visual acuity was 20/50 OD and 20/20 OS, with right eye dyschromatopsia and a right relative afferent pupillary defect. Visual fields showed central depression in the right eye and were full in the left. Fundus exam showed right optic disc pallor and left disc edema. OCT revealed right retinal nerve fiber layer (RNFL) thinning and left RNFL elevation with thinning of bilateral ganglion cell layers. Brain and orbit MRI demonstrated increased T2 signal and patchy salt-and-pepper-like enhancement of bilateral optic nerves, optic chiasm, hypothalamus, and right medial temporal lobe. Cerebrospinal fluid analysis showed lymphocytic pleocytosis and elevated protein; extensive infectious studies and cytology were negative. He subsequently developed progressive bilateral visual loss, and repeat imaging showed progressive similar pattern enhancement with extension to the optic tracts and bilateral mesial temporal lobes. Whole-body PET-CT was unrevealing. Biopsy of the left mesial temporal lesion confirmed neurosarcoidosis. He was started on high-dose steroids and transitioned to infliximab monotherapy with marked clinical and radiologic improvement.

Conclusions, including unique features of the case:

Neurosarcoidosis is inherently difficult to diagnose, and optic neuritis as its presenting feature adds to the complexity. When only the optic nerves are affected, biopsy is not typically recommended due to risk of worsening vision loss, making MRI findings diagnostically valuable. Our case highlights unique MRI features of patchy multifocal enhancement of the optic nerves, chiasm, and optic tracts with a salt-and-pepper-like appearance ultimately corresponding to histopathologically confirmed neurosarcoidosis.

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Keywords: Neuroimaging, Optic neuritis, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Under Pressure: Intermittent Central Retinal Artery Occlusion From A Glaucoma Drainage Device

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Introduction:

Transient monocular visual obscurations (TMVOs) may result from vascular, compressive, or positional causes. We report a rare case of intermittent central retinal artery occlusion (CRAO) secondary to mechanical optic nerve compression from a glaucoma drainage device (GDD).

Description of Cases:

A 79-year old woman with atrial fibrillation, hypertension, and primary open angle glaucoma presented to the neuro-ophthalmology clinic with three consecutive days of TMVOs in her right eye while bending forward during gardening, each lasting several hours. Her ocular history included multiple glaucoma surgeries, the most recent being an infranasal Molteno 4 years earlier. Previous surgeries included a supranasal Express shunt with posterior chamber intraocular lens 7 years prior and three bleb revisions. On exam, visual acuity measured 20/20 bilaterally with intraocular pressures of 17 mmHg in the right (OD) eye (above goal) and 6 mmHg in the left (OS) eye. Pupils were without relative afferent pupillary defect. Anterior and posterior segment exam was stable with a well-covered infranasal Molteno plate, a seidel negative supranasal bleb and advanced optic disc cupping (0.9 OD/0.7 OS). Carotid imaging and brain MRI were initially reported as normal; however, subsequent review revealed contact between the inferonasal bleb and the optic nerve. B-scan ultrasonography confirmed bleb enlargement during right sided positioning or bending forward causing an intermittent optic nerve compression and transient CRAO. She was initiated on low-dose aspirin, and surgical revision was considered but deemed high risk. Literature describes a 'safe zone' for GDD placement as ≥ 2 mm from the optic nerve head or ≥ 1 mm of the optic nerve sheath with supranasal then infranasal positioning considered safest.

Conclusions, including unique features of the case:

To our knowledge, this is the first reported case of a GDD causing intermittent CRAO via mechanical optic nerve compression. This case emphasizes the importance of GDD placement and potential for a rare, postoperative positional optic neuropathy.

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Keywords: Optic neuropathy, Neuroimaging, Vascular disorders, Miscellaneous

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Bilateral Optic Neuritis Following Durvalumab Treatment for Recurrent Cholangiocarcinoma

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Introduction:

A patient developed bilateral optic neuritis following treatment with immune-checkpoint inhibitor (Durvalumab) for recurrent cholangiocarcinoma.

Description of Cases:

A 57 year-old man with undifferentiated connective tissue disease (UCTD), lifelong achromatopsia, and recurrent cholangiocarcinoma on cisplatin, gemcitabine, and durvalumab presented with blurry vision in both eyes after six-cycle of therapy. He was found to have nasal field defects and APD in the left eye. Fundoscopy revealed bilateral optic disc edema worse in the left eye. Infectious, inflammatory, and paraneoplastic lab testing (anti-MOG, anti-aquaporin-4, HIV, HSV, VZV, syphilis, West Nile, CRMP5) were negative. Tuberculosis testing was unremarkable. MRI/MRV brain/orbits revealed perineural enhancement of left optic nerve, consistent with optic perineuritis in the left eye. The patient received three days of intravenous methylprednisolone followed by oral prednisone taper. Follow-up exam showed minimal improvement of visual field defects and the disc edema eight days after the treatment. Therefore, the patient underwent five-cycle plasmapheresis over 8 days. He was discharged on a 40 mg daily prednisone taper. Three weeks after receiving plasmapheresis, his visual fields improved and disc edema resolved in both eyes.

Conclusions, including unique features of the case:

Optic neuritis remains uncommon among ocular side effects related to immune checkpoint inhibitors (ICIs). Durvalumab is rarely implicated, with only two published cases describing durvalumab-associated optic neuritis, which were unilateral and corticosteroid-responsive. Our patient had ICIs related bilateral optic neuritis, improving after receiving corticosteroid and plasmapheresis. The patient's autoimmune condition and previous immunosuppressive treatment may have contributed to a more complex immune reconstitution responses. This case emphasizes the importance of early recognition of possible ICIs related ocular side effects and prompt initiation of therapy to avoid permanent visual loss.

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Keywords: Optic neuritis, Chemotherapy and radiation injury, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Nitrous Oxide Abuse Presenting with Diplopia

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Introduction:

A 22 year old male with a medical history of migraines, anxiety, depression, insomnia, and substance abuse is referred to the emergency department by an outside ophthalmologist for bilateral disc edema and diplopia. He has had a headache for three weeks that has not responded to his migraine regimen. He saw his neurologist who tried several new medications and repeated an MRI brain during this time without identified cause or improvement. Two weeks prior, he developed binocular diplopia. On initial exam, visual acuity is 20/40 in the right eye and 20/25 in the left. Pupils are dilated and minimally reactive without an RAPD. There is a large angle, manifest esotropia. Extraocular movements are full. Fundus exam is notable for grade V disc edema bilaterally. CT venogram shows nonocclusive thrombus involving the superior sagittal sinus, confluence, right transverse sinus, right jugular bulb, and left sigmoid sinus. MRI Brain shows diffuse volume loss, particularly affecting the cerebellum and brainstem with some increased FLAIR signal in the cerebellar cortex. Laboratory evaluation identifies homocystinemia, high MMA, low B12, and low folate. The patient was managed with anticoagulation, diamox, and a series of vitamin B12 injections. Visual field testing showed enlarged blind spots which resolved following treatment.

Description of Cases:

This patient developed divergence insufficiency and grade V optic disc edema in the setting of dural venous sinus thrombosis. He was found to be hypercoagulable due to homocystinemia caused by nitrous oxide abuse. Nitrous oxide inactivates vitamin B12, a cofactor in the regulation of homocysteine. His MRI brain results are nonspecific but have been described with medication and recreational drug use.

Conclusions, including unique features of the case:

This case emphasizes the unique presentation of nitrous oxide abuse with homocysteinemia resulting in dural venous sinus thrombosis, presenting with symptoms of diplopia and subacute headache.

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Keywords: Adult strabismus with a focus on diplopia, High intracranial pressure/headache, Vascular disorders

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Contact Information: None provided.

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Introduction:

Giant Cell Arteritis (GCA) and Myasthenia Gravis (MG) are distinct autoimmune disorders that rarely coexist.

Description of Cases:

A 54-year-old man with seizures, neurogenic bladder, and cervical spine myelomalacia following traumatic injury and ACDF was admitted to internal medicine with progressive weakness. He initially developed left arm weakness but MRI head at an outside hospital ruled out stroke. He later developed diffuse left sided weakness, dysphagia, binocular oblique diplopia, right-sided ptosis, and headache. At admission, he had lost 67 pounds and the ability care for himself. Ophthalmology exam showed right upper lid partial ptosis and limited right eye abduction and elevation. Visual acuity was 20/25 OU. Neurological exam showed proximal weakness in bilateral upper extremity and proximal and distal weakness in bilateral lower extremities and left sided hypoesthesia. Further work up showed positive acetylcholine receptor binding antibody. CT chest was negative for thymoma. Non contrast MRI head was unrevealing. A diagnosis of MG was made, and pyridostigmine with IV immunoglobulin were initiated, leading to improvement. While receiving IVIG treatment, he developed severe retro-orbital headaches and right temporal tenderness with elevated ESR and CRP, raising concern for GCA. Temporal artery ultrasound showed bilateral halo sign, and high-dose prednisone (80 mg) was initiated. Within two days, he developed worsening respiratory and extremity weakness consistent with steroid-induced weakness, prompting steroid cessation. Temporal artery biopsy was negative, but persistent inflammatory markers and improvement on low-dose prednisone (10 mg) supported GCA diagnosis. He was transitioned to Efgartigimod alfa infusions for MG and Tocilizumab with PJP prophylaxis for GCA.

Conclusions, including unique features of the case:

MG can be associated with several other autoimmune conditions. This case highlights the rare coexistence of GCA and MG, where treatment of one condition can cause catastrophic effects in another. Corticosteroids can worsen MG in up to 18% of cases. Dual autoimmune disease requires careful management.

References: i. Wendell LC, Levine JM. Myasthenic crisis. *Neurohospitalist*. 2011;1(1):16-22. doi:10.1177/1941875210382918. ii. Schneider-Gold C, Gajdos P, Toyka KV, Hohlfeld RR. Corticosteroids for myasthenia gravis. *Cochrane Database Syst Rev*. 2005;(2):CD002828. doi:10.1002/14651858.CD002828.pub2. iii. 2021 American College of Rheumatology/Vasculitis Foundation Guideline for the Management of Giant Cell Arteritis and Takayasu Arteritis. *Arthritis Care Res*. 2021;73(8):1071–1087. doi:10.1002/acr.24632. iv. Sebastian A, Coath F, Innes S, Jackson J, van der Geest KSM, Dasgupta B. Role of the halo sign in the assessment of giant cell arteritis: a systematic review and meta-analysis. *Rheumatol Adv Pract*. 2021;5(3):rkab059. doi:10.1093/rap/rkab059. v. Pouncey AL, Yeldham G, Magan T, Lucenteforte E, Jaffer U, Virgili G. Halo sign on temporal artery ultrasound versus temporal artery biopsy for giant cell arteritis. *Cochrane Database Syst Rev*. 2024;2:CD013199. doi:10.1002/14651858.CD013199.pub2. vi. Arida A, Kyprianou M, Kanakis M, Sfikakis PP. The diagnostic value of ultrasonography-derived edema of the temporal artery wall in giant cell arteritis: a second meta-analysis. *BMC Musculoskelet Disord*. 2010;11:44. doi:10.1186/1471-2474-11-44. vii. Rubenstein E, Maldini C, Gonzalez-Chiappe S, Chevret S, Mahr A. Sensitivity of temporal artery biopsy in the diagnosis of giant cell arteritis: a systematic literature review and meta-analysis. *Rheumatology (Oxford)*. 2020;59(5):1011-1020. doi:10.1093/rheumatology/kez385.

Keywords: Myasthenia, Neuro-opth & systemic disease (eg. MS, MG, thyroid), Optic neuropathy, Orbit/ocular pathology, Neuroimaging

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Carotid-Ophthalmic Aneurysm Mimicking Optic Neuritis: Recovery with Conservative Therapy

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Introduction:

Unilateral vision loss as the initial sign of an internal carotid artery (ICA) aneurysm is rare, especially in younger patients, where optic neuritis is often the leading diagnosis. Carotid-ophthalmic aneurysms can compress the optic nerve or chiasm, mimicking more common optic neuropathies. We present a case of a 38-year-old woman with subacute monocular vision loss caused by a large carotid-ophthalmic aneurysm, who showed visual improvement with blood pressure control alone.

Description of Cases:

A 38-year-old woman with uncontrolled hypertension presented with 4 weeks of painless, progressive vision loss OD. Initial exam showed visual acuity (VA) 20/30 OD, 20/20 OS, a right RAPD, and an unremarkable fundus and OCT RNFL. She was referred to the hospital for suspected optic neuritis by ophthalmology. Neuroimaging revealed a large, right ICA ophthalmic saccular aneurysm. She was started on anti-platelet therapy, anti-hypertensive agents with plans for outpatient surveillance and possible intervention. Two weeks later, VA declined to 20/50 OD with dense visual field loss, mean deviation (MD) -32.17 dB, though RNFL remained preserved. By 10 weeks, she reported notable improvement in her vision confirmed by improved visual field with MD -15.66 dB. Concurrently, OCT showed thinning of the GLC and RNFL. She continued blood pressure control, lifestyle modifications, and anti-platelet therapy, and deferred aneurysm intervention due to potential risk of permanent vision loss.

Conclusions, including unique features of the case:

Carotid-ophthalmic aneurysms represent a small subset of intracranial aneurysms, comprising approximately 5% of reported cases. This case not only highlights carotid-ophthalmic aneurysm causing monocular vision loss in a young female as an underrecognized mimicker of optic neuritis or neuropathies, but also suggests that in select cases, conservative management targeting underlying vascular risk factors may be a viable option, potentially avoiding the need for invasive procedures. Early recognition is critical, as delay in diagnosis may lead to irreversible visual loss or catastrophic rupture.

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Keywords: Optic neuropathy, Optic neuritis, Optic nerve trauma and treatment, Vascular disorders, Interventional neuroradiology

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Giant Cell Arteritis Presenting As Sixth Cranial Nerve Palsy Without Systemic Symptoms

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Introduction:

Giant cell arteritis (GCA) is an inflammatory vasculitis affecting medium and large arteries that often presents with ocular manifestations and can lead to irreversible vision loss without prompt identification and treatment [1].

Description of Cases:

A 75-year-old male with history of thyroid cancer status post resection, hyperlipidemia, normal tension glaucoma, dry age related macular degeneration and quiescent HLA B27+ anterior uveitis presented with two days of acute onset binocular horizontal diplopia worse on left gaze. He denied headaches, jaw claudication, scalp tenderness, fevers, proximal muscle weakness, or vision changes. Visual acuity was 20/20 in each eye. Motility assessment showed complete left abduction deficit and esotropia larger in left gaze and smaller in right gaze. Dilated exam was notable for symmetric cupping of bilateral optic nerves, drusen, and one cotton wool spot in the right eye. Temporal pulses were palpable without tenderness. Blood work revealed elevated ESR (51), high sensitivity CRP (66) and platelets (541). The patient was started on IV solumedrol. Temporal artery biopsy revealed transmural chronic inflammation with giant cells and multifocal disruptions of elastic tunica intima and externa, consistent with GCA. The patient transitioned to an oral prednisone taper followed by tocilizumab. By day 49 after initial presentation his sixth cranial nerve palsy had completely resolved.

Conclusions, including unique features of the case:

Maintaining a high degree of suspicion for GCA is important, even when presented with a seemingly uncomplicated isolated cranial nerve palsy. Special attention should be paid to other signs of ocular ischemia, such as new cotton wool spots in this case [1]. One in five patients with ocular manifestations of GCA will have no systemic symptoms [2]. Diplopia has been described as a presenting sign of GCA in 6-27% of cases and up to 48% of diplopia in GCA is attributed to sixth cranial nerve palsy [1, 3].

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Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Ocular motility

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Severe Bilateral Disc Edema with Normal Visual Function as the Initial Manifestation of Neurosyphilis

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Introduction:

Syphilis in the US increased from 34,000 (2003) to 209,253 (2023) reported cases with increased incidence of ocular syphilis. Neurosyphilis is rare, may manifest in all stages of syphilis, and may be challenging to diagnose in patients with minimal symptoms. We describe a patient with mild headaches and severe disc edema with normal visual functions who was subsequently found to have CSF-confirmed neurosyphilis.

Description of Cases:

A 35-year-old female (BMI=33.64) was referred for severe optic disc edema. She reported visiting an Optometrist for episodic mild headaches and blurred vision. Examination revealed bilateral normal Snellen (20/20) and Ishihara color (11/11) visions. Anterior and posterior segments were normal except for severe bilateral disc edema (Frisen Grade V) with OCT(RNFL) >421µm (R) and 184µm (L) and normal ganglion cell complexes. Humphrey visual fields were full. She was investigated with a provisional diagnosis of idiopathic intracranial hypertension (IIH). MRI/MRV was unremarkable and LP opening pressure was 16cmH₂O. Lacking evidence for IIH, investigations were expanded and revealed RPR titers=1:256 and CSF with VDRL=1:1. HIV testing was negative. Fundus fluorescein angiography revealed progressively increasing intensity of disc fluorescence with late leakage and without evidence of chorioretinitis. She later volunteered a one-month history of vaginal pruritis. Neurosyphilis in presumed primary syphilis was diagnosed. A CDC-recommended regime of IV penicillin G was administered, with resolution of symptoms and reduction of disc edema. On recent examination, 3-months after presentation, disc edema had decreased substantially with OCT (RNFL) 130µm (R) and 106µm (L). Her visual functions remained intact.

Conclusions, including unique features of the case:

Neurosyphilis can have diverse manifestations and be symptomatic or asymptomatic. Bilateral disc edema with preserved visual function, especially in the appropriate demographic, is suggestive of IIH. Unsupportive investigations should prompt expanded testing. Serologic and confirmatory CSF analysis are key to diagnosis of neurosyphilis with implications for management to prevent neurologic and systemic sequelae.

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Keywords: Neuro-ophth & infectious disease (eg, AIDS, prion), High intracranial pressure/headache, Visual fields

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Blind Spot and Droopy Eyelid After Wisdom Tooth Extraction

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Introduction:

Ocular ischemic complications after dental procedures are rare. We report a case of cilioretinal artery occlusion and Horner's syndrome in a young patient with advanced periodontal disease that underwent tooth scaling, root planning and wisdom tooth extraction. We discuss pathophysiology, targeted investigations, and recommendations to mitigate these neuro-ophthalmic complications.

Description of Cases:

A 39-year-old man with polycystic kidney disease underwent deep oral cleaning for advanced periodontitis and elective left lower wisdom tooth removal, under local anesthesia with 2% lidocaine and epinephrine. The morning after, he woke-up with a left central scotoma. He was diagnosed with left Horner's syndrome and left cilioretinal artery occlusion. Brain MRI was negative for cerebral infarcts. MR angiogram head and neck showed intracranial saccular aneurysms and left cervical carotid dissection with intramural hematoma. Short-term therapeutic oral anticoagulation was initiated, followed by single antithrombotic agent. Genetic testing identified PKD1/PKD2 mutations, and other systemic stigmata due to extracellular matrix dysregulations were found (mitral valve prolapse, aortic root dilatation, colonic diverticulosis). Carotid dissection is a rare complication of dental procedures. Risk factors are periodontitis, dental or systemic infection, prolonged neck hyperextension, hyperhomocysteinemia and connective tissue disease. Retinal arterial occlusions after dental procedures are more common in men than women, due to multiple potential mechanisms: distal embolism from carotid dissection, local anesthesia administration into the inferior or posterior superior alveolar arteries with retrograde transport through the internal maxillary, middle meningeal, and ophthalmic arteries if sufficient injection pressure is applied, embolization of tooth extraction-related debris, or sedation-induced hypotension. Careful history for connective tissue, inflammatory and infectious diseases, and avoidance of prolonged neck extension and epinephrine in high-risk patients are recommended.

Conclusions, including unique features of the case:

Transient or permanent visual loss with anisocoria after prolonged dental procedures should raise concern for carotid dissection, especially when systemic risk factors such as inflammation, infection, or connective tissue disorders are present.

References: None provided.

Keywords: Vascular disorders, Retina, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Genetic disease

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Contact Information: None provided.

A Case of Serous Retinal Detachment Responsive to Plasmapheresis in Neuromyelitis Optica Spectrum Disorder

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Introduction:

Neuromyelitis optica spectrum disorder (NMOSD) is an autoimmune disease targeting the aquaporin-4 protein (AQ4) on central nervous system astrocytes leading to severe relapsing attacks of optic neuritis and transverse myelitis. Management of NMOSD includes treatment with high-dose steroids, plasma exchange, and/or monoclonal antibody therapy. Serous retinal detachment is an unusual recently described feature of NMOSD.

Description of Cases:

A 27-year-old female was referred from the emergency department (ED) for right eye pain and vision loss. The patient claimed a prior episode of vision loss and diagnosis of Vogt-Koyanagi-Harada disease (VKH) treated with prednisone while serving in the military several years prior. Initial fundus, pupillary, color plate and ocular coherence tomography (OCT) examinations were unremarkable. The patient complained of worsening eye pain and subsequent magnetic resonance imaging (MRI) disclosed T2 hyperintensities of the right optic nerve. Visual field testing revealed generalized depression inferiorly in the right eye and arcuate scotoma in the left. The patient was treated with high dose intravenous steroids per Optic Neuritis Treatment Trial (ONTT) protocol and serologies sent for myelin oligodendrocyte glycoprotein (MOG) and AQ4 autoantibodies. Steroid therapy produced incomplete relief of the patient's pain. Upon steroid completion, the patient developed a large serous retinal detachment. The AQ4 level returned as markedly elevated (15.5 U/mL) and MOG autoantibody level was normal. The serous detachment resolved with plasmapheresis. The patient has had no recurrence for over two years on regular Eculizumab infusions.

Conclusions, including unique features of the case:

We present a unique case of NMOSD presenting with optic neuritis followed shortly by serous retinal detachment that resolved with plasmapheresis and stabilized with ongoing eculizumab infusions. Retinal detachment has not formally been established as a typical complication of NMOSD. In patients presenting with retinal detachment who have pre-existing, eye-involving autoimmune disease such as NMOSD and/or VKH, plasma exchange therapies can be an effective modality for acute management.

References: Knaack, Rolfs, Zimmermann, Patel, Reeß, et. al; Central Serous Chorioretinopathy occurs in High Frequency in Myelin Oligodendrocyte Glycoprotein Antibody Disease, Seropositive and Seronegative Neuromyelitis Optica Spectrum Disorders compared to Multiple Sclerosis and Healthy Controls, *Journal of Neuro-Ophthalmology*, 2025, Online ahead of print. Kon, Hikichi, Ueno, Suzuki, Nunomura, et. al; Myelin Oligodendrocyte Glycoprotein-IgG-positive Recurrent Bilateral Optic Papillitis with Serous Retinal Detachment, *J-STAGE*, 57, 22, 2018.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuritis, Optic neuropathy, Demyelinating disease

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Grant Support: None.

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Blinding Relapse

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Introduction:

Here we present an interesting case of vision loss.

Description of Cases:

39-year-old male with past medical history of acute lymphocytic leukemia (ALL) in remission and pulmonary hypertension on Sildenafil presented with sudden onset of vision loss in the right eye associated with eye pain. Pertinent ocular findings include relative afferent pupillary defect, visual acuity 20/100 and grade 4 optic disc edema in the right eye. Left eye was normal. MRI brain and orbits w and wo contrast showed enhancement of the right optic nerve. Lumbar puncture with CSF analysis were unremarkable. He received IV Methylprednisolone 1g daily for 3 days for optic neuritis suspect and was discharged on oral prednisone taper. Vision improved to 20/40 in the right eye at the time of discharge. Four days later, patient woke up with sudden vision loss in the right eye with no light perception. Fundus showed grade 4 optic disc edema in the right eye. Left eye was normal. Repeat MRI imaging was suggestive of optic perineuritis in the right eye. Work up was negative for autoimmune, infection, infiltrative or demyelinating conditions. Differentials considered were leukemic infiltration of optic nerve, seronegative neuromyelitis optica, central retinal artery occlusion, non-arteritic ischemic optic neuropathy from sildenafil use, nilotinib induced optic neuritis. Patient received IV methylprednisolone 1 g daily for 5 days. In the six month follow up, there was pallor of the optic disc in the right eye and was normal in the left eye. MRI imaging was concerning for CNS involvement and leukemic infiltration of the trigeminal nerves, oculomotor nerves and right optic nerve. Repeat lumbar puncture showed blast cells. He was diagnosed with possible leukemic optic nerve infiltration in the right eye.

Conclusions, including unique features of the case:

The optic nerve can be the site of CNS relapse in leukemia even if there is presumed systemic and medullary remission.

References: None provided.

Keywords: Orbit/ocular pathology, Neuro-opth & systemic disease (eg. MS, MG, thyroid), Neuroimaging, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease

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Neuro-Ophthalmic Manifestations of CACNA1A-Related Disorders

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Introduction:

CACNA1A-related disorders are a group of rare channelopathies, caused by mutations in the voltage-gated calcium channel gene. They are associated with heterogeneous neurologic presentations, including ataxia, epilepsy, and intellectual disabilities. Disorders of ocular motility may be appreciated at a young age by families and clinicians. Pediatric ophthalmologists and neuro-ophthalmologists may be the first to encounter affected patients, so awareness of this entity is crucial. A retrospective chart review of four patients with genetically-confirmed CACNA1A mutations at a single institution was done to describe the neuro-ophthalmic manifestations of CACNA1A-related disease and highlight their role as potential presenting signs. Data collected includes disease history, exam findings, diagnostic process, and management history.

Description of Cases:

Average current age is 24 (range 6-43), age at diagnosis was 19 (2-40). All had de-novo heterozygous pathogenic mutations and a primary diagnosis of episodic ataxia 2. Two experienced hemiplegic migraines. Presenting symptoms were non-specific, including early childhood convulsions (3/4), developmental delays (4/4) gait ataxia (2/4). Notable neuro-ophthalmic findings include multiple manifestations of nystagmus (direction changing gaze-evoked, rebound, downbeat), slow/hypometric saccades, saccadic pursuits, and intermittent diplopia from eye misalignment (with associated headaches, blur, and imbalance). Two patients possibly experienced paroxysmal tonic upgaze, a characteristic but often underreported finding. Best corrected visual acuity ranged from 20/25-20/40. No abnormalities were present on fundus, optic nerve, or color vision exam. All but one had intact visual fields, who experienced homonymous superior quadrantanopia after anterior medial temporal lobectomy for medication-refractory seizures. Other shared clinical features include recurrent migraines (3/4), medication-resistant seizures (2/4), intellectual disability (2/4), and cerebellar volume loss on neuroimaging (2/4).

Conclusions, including unique features of the case:

Oculomotor findings may present as early signs of CACNA1A-related disease. With early recognition, neuro-ophthalmologists and pediatric ophthalmologists can improve management by managing associated symptoms and connecting patients to multidisciplinary services and earlier genetic testing. This series is unique for its diversity of presentations.

References: None provided.

Keywords: Genetic disease, Nystagmus, Ocular manifestations of vestibular disorders, Pediatric neuro-ophthalmology

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Clinical–Anatomic Discordance: Bilateral Ophthalmic Manifestations Of A Unilateral Cavernous Sinus Dural Arteriovenous Fistula

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¹ *University of Mississippi Medical Center*

Introduction:

Cavernous sinus dural arteriovenous fistulas (CS-dAVFs) are rare vascular shunts that typically cause ipsilateral ocular findings such as conjunctival arterialization, ophthalmoplegia, elevated intraocular pressure, and vision loss. Bilateral manifestations are uncommon and may obscure localization, particularly when initial neuroimaging is unrevealing. In such cases, diagnosis depends on a high index of suspicion supported by detailed neuro-ophthalmic examination.

Description of Cases:

A 71-year-old woman presented with severe bilateral ocular pain, redness, diplopia, and intraocular pressures exceeding 40 mmHg despite maximal medical therapy. Examination revealed bilateral ophthalmoplegia involving cranial nerves III, IV, and VI, with dilated, tortuous conjunctival vessels and temporal optic disc pallor—findings consistent with venous congestion and chronic optic nerve compression. Initial CT, CTA, and MRI/MRA of the head and neck were nondiagnostic. Cerebral angiography subsequently identified a left-sided CS-dAVF supplied by the sphenopalatine branch of the external carotid artery and cavernous perforators of the internal carotid artery, with bilateral superior ophthalmic vein drainage. The patient underwent staged endovascular embolizations followed by craniotomy and endoscopic transsphenoidal repair, resulting in decreased intraocular pressures, improved ocular congestion, and gradual recovery of motility.

Conclusions, including unique features of the case:

This case underscores the pivotal role of neuro-ophthalmic localization in identifying CS-dAVF when imaging is initially inconclusive. The clinical–anatomic discordance between a unilateral fistula and bilateral ocular findings highlights the complexity of cavernous sinus venous drainage. Maintaining CS-dAVF in the differential diagnosis of refractory bilateral ocular hypertension and ophthalmoplegia is essential for timely, vision-preserving intervention.

References: 1. Benndorf, G.; Classification of cavernous sinus fistulas (CSFs) and dural arteriovenous fistulas (DAVFs), In: Benndorf G. (ed) *Interventional Neuroradiology*, Springer, Berlin, Heidelberg, 51–63, 2010. 2. Fay, L.Y., Luo, C.B., Chen, L.W., Wu, J.C., Wu, C.H., et al.; Bilateral cavernous sinus dural arteriovenous fistulae: the strategies for endovascular treatment, *Clin Neuroradiol*, 31(1), 165–172, 2021. 3. Henderson, A.D., Miller, N.R.; Carotid-cavernous fistula: current concepts in aetiology, investigation, and management, *Eye (Lond)*, 32, 164–172, 2018. 4. Suh, D.C., Lee, J.H., Kim, S.J., Chung, S.J., Choi, C.G.; New concept in cavernous sinus dural arteriovenous fistula: correlation with presenting symptom and venous drainage patterns, *Stroke*, 36, 1134–1139, 2005.

Keywords: Vascular disorders, Neuroimaging, Ocular motility

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Secondary Central Nervous System Lymphoma Presenting with Bilateral Optic Disc Edema and Optic Nerve Sheath Enhancement

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Introduction:

Central nervous system (CNS) lymphoma exists on a spectrum and includes primary CNS lymphoma with the subset intraocular lymphoma, and Secondary CNS Lymphoma (SCNSL) from systemic disease. SCNSL most commonly presents with focal neurological deficits and signs of elevated intracranial pressure. Ocular involvement can be the first presenting sign with bilateral presentation and rapid-onset more common than in primary CNS lymphoma.

Description of Cases:

A 73-year-old woman with history of HTN, HLD presented to the emergency department with painful left eye blurriness with headache and posterior neck pain for two weeks. Patient had no focal neurological deficits and CT of the head and C-spine were negative for acute etiology. Ophthalmology was consulted and exam showed visual acuity 20/20, reduced color vision in the left eye, bilateral disc edema, and CRP was elevated to 5.6 mg/dL. The patient was treated for presumed giant cell arteritis with steroids and had improvement of color vision in the left eye. MRI Brain and Orbits showed contrast enhancement of bilateral optic nerve sheaths and possibly bilateral facial nerves. This prompted a lumbar puncture which showed marked lymphocytic pleocytosis and elevated CSF protein, and CSF flow cytometry showed B cell non-Hodgkin lymphoma. Patient was diagnosed with SCNSL following bone marrow biopsy mature B cell lymphoma. Subsequently, patient was started on rituximab, methotrexate, procarbazine, and vincristine.

Conclusions, including unique features of the case:

SCNSL can initially present with ocular findings. In this patient, reduced color vision with preserved acuity and bilateral disc edema plus bilateral optic-nerve sheath enhancement were the sentinel signs, despite a normal neurological exam and negative CT. Transient steroid responsiveness obscured the diagnosis, which was ultimately made by CSF flow cytometry (B-cell NHL) and bone-marrow biopsy, confirming secondary disease. SCNSL should remain on the differential for bilateral disc edema and optic perineuritis with nonspecific visual symptoms, and early CSF studies are warranted.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Neuroimaging, Paraneoplastic syndromes

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Contact Information: None provided.

Sequential NMDA encephalitis and Inflammatory optic neuritis – A case series

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Introduction:

N-methyl-D-aspartate receptor (NMDAR) encephalitis is a well-recognized autoimmune encephalitis often presenting with neuropsychiatric symptoms and seizures. Myelin oligodendrocyte glycoprotein antibody–associated disease (MOGAD) typically manifests as optic neuritis. Co-occurrence of NMDAR encephalitis and MOGAD is increasingly recognized, but clinical series remain limited.

Description of Cases:

We present 3 patients with concurrent NMDAR encephalitis and MOGAD positive optic neuritis (ON) (two males ages 9 and 26, one woman age 36). The clinical presentation, signs, investigations, and management of each case is discussed. All patients with NMDAR/MOGAD positivity presented initially with headaches and altered mental status. The 26-year-old male presented with simultaneous bilateral blurry vision and the other 2 developed bilateral blurry vision after the initial presentation of encephalitis: 4 months later in the 36-year-old woman and 8 years later in the 9-year-old boy. MRI brain with and without contrast showed abnormal T2/FLAIR lesions in the brain and/or spinal cord and leptomeningeal enhancement. All patients had positive CSF NMDAR receptor titers. All three patients presented with bilateral, asymmetrically reduced visual acuity, and reduced color plates. Examination showed bilateral temporal pallor in 1 patient, and bilateral optic nerve edema in the other 2 patients. Work-up for bilateral optic neuritis revealed positive MOG titers (1:100, 1:1000 and 1:10000 in the 36/F, 26/M and 9/M respectively). The 36-year-old woman was treated with IV steroids, IVIG and rituximab. The 9-year-old boy was treated with IV steroids, PLEX, and tocilizumab. The 26-year-old male was treated with IV steroids, PLEX and IVIG, with radiological improvement. The visual acuity in all patients improved to their prior baseline following treatment.

Conclusions, including unique features of the case:

This series highlights the emerging overlap between NMDAR encephalitis and MOGAD. Optic neuritis may occur months to years after encephalitic presentation, underscoring the need for vigilance in patients with new visual symptoms. Dual autoimmunity may represent a distinct phenotype with implications for long-term immunotherapy.

References: None provided.

Keywords: Demyelinating disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuritis

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Seronegative, CSF positive MOGAD: Literature review and a case report

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Introduction:

Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is an inflammatory demyelination which can be monophasic or relapsing. International consensus diagnostic criteria require a core clinical demyelinating event (optic neuritis, acute disseminated encephalomyelitis (ADEM), transverse myelitis, cerebral monofocal or polyfocal deficit(s), cerebral cortical encephalitis, or brainstem/ cerebellar presentation), a positive serum MOG-IgG (or supporting clinical or MRI feature required if not definitively positive) and exclusion of alternate diagnoses. Positive CSF MOG IgG can support a diagnosis of seronegative MOGAD in setting of consistent clinical and MRI features but this presentation is rare (< 5% MOGAD). We present a case report and review the literature to determine whether there are unique features of seronegative, CSF positive MOGAD.

Description of Cases:

A 28-year-old male presented with count fingers vision due to bilateral retrobulbar optic neuritis. Three weeks prior, he developed decreased vision, gait instability and nystagmus which improved with intravenous steroids. Workup showed longitudinally extensive bilateral optic nerve enhancement and no spine lesions. Serum MOG IgG1, aquaporin-4, and infectious workup were negative. Lumbar puncture revealed pleocytosis, elevated total protein, elevated myelin basic protein, negative oligoclonal bands, and negative meningitis/encephalitis panel. Repeat neuroimaging showed persistent bilateral posterior optic nerve enhancement extending to the chiasm and asymptomatic bilateral cisternal enhancement of cranial nerves III and V. Serum CNS demyelinating panel was again negative. Repeat lumbar puncture showed mild lymphocytosis, positive oligoclonal bands (6) and positive CSF MOG-IgG. Autoimmune/paraneoplastic panel was negative. PET CT was negative. There was excellent visual recovery with intravenous steroids, plasma exchange, and slow steroid taper.

Conclusions, including unique features of the case:

Seronegative, CSF positive MOGAD is a rare presentation. On literature review, seronegative CSF positive MOGAD is not associated with any specific clinical features (reported in association with optic neuritis, transverse myelitis and ADEM) in adults and does not signify a monophasic illness despite seronegativity.

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Keywords: Demyelinating disease, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Optic neuritis

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Eyelid Myokymia as a Presenting Symptom of Multiple Sclerosis

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Introduction:

Eyelid myokymia is often considered benign, representing fatigue, stress, or excess caffeine intake(1). However, facial myokymia might be secondary to an underlying neurological condition- malignancy, infection, or a pontine lesion(2-6). We present a case of facial myokymia initially affecting the eyelid, leading to multiple sclerosis diagnosis.

Description of Cases:

A 27 year old woman with remote history of left sided optic neuritis presented to the Emergency Room with acute onset left lower-lid twitching for four days. She initially presented to an outside hospital, where she was discharged with instructions to improve sleep and diet. She returned to the hospital for persistent symptoms, where she was also observed to have left sided lip twitching and hemisensory loss in V1-V3 distributions. Bloodwork revealed mild anemia but no electrolyte or vitamin abnormalities. She denied associated headache, fever, vision changes, or excessive use of alcohol, cigarettes, or caffeine. Prior left sided optic neuritis, myokymia, and facial hemisensory loss, prompted a brain MRI. Cortical and juxtacortical hyperintensities on T2/FLAIR, punctate subcortical contrast enhancing lesions, and subtle T2 hyperintensity in the right pons were observed. Lumbar puncture also revealed elevated myelin basic protein, IgG, IgG Index, and IgG/Albumin ratio suggestive of multiple sclerosis.

Conclusions, including unique features of the case:

Eyelid myokymia as a chief presentation can be often misdiagnosed as a benign condition. Other associated features should prompt evaluation for serious conditions. Current literature on facial myokymia localizes to the pons(2-6) with multiple etiologies described including demyelination. Our patient had a subtle right pontine hyperintensity, yet literature often reports ipsilateral pontine involvement, if a lesion was present(2-4). While it could be coincidental, our case is unique since it might represent a cross facial ephaptic transmission abnormality resulting in contralateral facial myokymia(7).

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Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Demyelinating disease, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease

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Contact Information: None provided.

Concurrent Optic Perineuritis and Cranial Nerve III Palsy in a Patient with Herpes Zoster Ophthalmicus

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Introduction:

Herpes zoster ophthalmicus (HZO) is a viral disease caused by the reactivation of the varicella-zoster virus (VZV) in the trigeminal ganglion. We report a case of HZO in an immunocompromised patient, presenting with keratitis, optic perineuritis, CN III palsy, suspected retinal involvement, and meningitis in the absence of encephalitis.

Description of Cases:

A 97-year-old female with a past medical history of ANCA vasculitis (in remission, on mycophenolate mofetil) initially presented to an outside hospital with a herpetiform rash in the left V1 distribution with ocular involvement. She was started on oral acyclovir as outpatient. Several days later she developed diplopia and complete ptosis secondary to a pupil-involving CN III palsy. She was then admitted for intravenous acyclovir. Two days later, she was transferred to our hospital for evaluation of retinal whitening. On transfer, vision in the left eye was 20/400. She had a minimally reactive, dilated pupil with no afferent defect. There was complete eyelid ptosis and painless ophthalmoplegia: -4 supraduction, -2 infraduction, and -4 adduction. She had pseudodendrites in the central visual axis associated with edema. Repeat fundus exam by retina specialist noted drusen but no retinal whitening or vitritis. There was enhancement of the left optic nerve sheath on MRI. Lumbar puncture demonstrated a lymphocytic pleocytosis; CSF was positive for VZV. She was treated with 10mg/kg IV acyclovir. At the time of discharge, left eye vision was 20/70 but she still had corneal edema and significant motility deficits.

Conclusions, including unique features of the case:

We report a complex case of HZO secondary to VZV in an immunocompromised patient, notable for keratitis, optic perineuritis, near-complete CN III palsy, and meningitis without encephalitis. While HZO is a well-known complication of VZV reactivation, the simultaneous occurrence of these ophthalmic and neurologic sequelae is uncommon.

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Keywords: Neuro-ophth & infectious disease (eg, AIDS, prion)

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Introduction:

Leber hereditary optic neuropathy (LHON) is a maternally inherited mitochondrial disorder that typically presents with painless central vision loss, predominantly in young males. Although primarily confined to the optic nerve, systemic manifestations such as myopathy, cardiac conduction abnormalities, and cerebellar dysfunction may occur, which is referred to as the LHON-plus phenotype. Chronic progressive external ophthalmoplegia (CPEO)-like presentations are exceptionally rare among these. We report a case of LHON-plus in a 53-year-old man harboring the m.14484T>C mutation.

Description of Cases:

A 53-year-old man presented with progressive bilateral ptosis, ophthalmoplegia, and dysarthria. Fundus examination revealed temporal pallor of both optic discs, and optical coherence tomography showed thinning of the ganglion-cell inner plexiform layer with central scotomas on perimetry. Neurologic findings included a flaccid palate, brisk arm reflexes, and absent leg reflexes. Brain MRI and cerebrospinal fluid studies were unremarkable. Muscle biopsy demonstrated ragged-red and cytochrome-c-oxidase-negative fibers consistent with mitochondrial myopathy. Multiplex ligation-dependent probe amplification excluded large-scale mtDNA deletions, while next-generation sequencing identified a heteroplasmic m.14484T>C mutation in MT-ND6, without additional pathogenic variants. Based on the combination of optic neuropathy, CPEO-like ophthalmoplegia, cardiac conduction abnormality, histologic findings, and molecular confirmation, a diagnosis of LHON-plus was established.

Conclusions, including unique features of the case:

This case broadens the clinical spectrum of the m.14484T>C mutation to include biopsy-confirmed mitochondrial myopathy and CPEO-like ophthalmoplegia in the absence of mtDNA deletions. It emphasizes that LHON can manifest predominantly with efferent deficits, potentially obscuring coexisting optic neuropathy. Mitochondrial diseases should be suspected in adults presenting with progressive external ophthalmoplegia and painless central vision loss, and comprehensive mitochondrial genomic testing is crucial for accurate diagnosis and systemic management.

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Keywords: Optic neuropathy, Genetic disease, Ocular motility, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Bilateral Optic Neuritis and Transverse Myelitis with Overlapping MOG-IgG and Lyme Seropositivity

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Introduction:

Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) can present with optic neuritis and/or transverse myelitis, mimicking infectious or other autoimmune demyelinating conditions. False-positive Lyme serology, particularly isolated IgM reactivity, is a known diagnostic pitfall that may lead to unnecessary antibiotic treatment. We report two cases of central nervous system demyelination with concurrent MOG-IgG and *Borrelia burgdorferi* IgM seropositivity and review CDC criteria for accurate Lyme disease adjudication.

Description of Cases:

A 55-year-old woman developed bilateral optic neuritis with positive serum MOG-IgG and *Borrelia* IgM but no IgG seroconversion or cerebrospinal fluid (CSF) abnormalities. She responded to high-dose corticosteroids, with residual dyschromatopsia. A 28-year-old pregnant woman presented with acute transverse myelitis, CSF pleocytosis, weakly positive *Borrelia* IgM, and high-titer MOG-IgG. She improved following corticosteroid therapy and empiric ceftriaxone. In both cases, clinical and paraclinical features were consistent with MOGAD rather than neuroborreliosis, and the isolated IgM positivity was likely false-reactive.

Conclusions, including unique features of the case:

Dual MOG-IgG and Lyme IgM seropositivity may occur and represents a diagnostic challenge. According to CDC guidelines, IgM reactivity is only valid within 30 days of symptom onset and requires at least 2 of 3 specific Western blot bands; beyond this timeframe, IgM testing is unreliable and prone to cross-reactivity. These cases underscore the importance of strict adherence to CDC Lyme serologic criteria to prevent misdiagnosis and inappropriate antibiotic use in MOGAD. Unique to these cases is the coexistence of MOG-IgG positivity and isolated Lyme IgM reactivity, emphasizing the need for careful interpretation of infectious serologies in autoimmune demyelination.

References: None provided.

Keywords: Neuro-ophth & infectious disease (eg, AIDS, prion), Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Demyelinating disease, Optic neuritis, Lyme disease

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Contact Information: None provided.

Visual Field Constriction Following Carbon Monoxide Poisoning

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Introduction:

If carbon monoxide poisoning does not result in death, it is known to cause permanent neurologic sequelae including cognitive abnormalities, amnesia, seizures, apraxia, agnosia, parkinsonism, incontinence, peripheral neuropathy, and visual dysfunction. Vision loss from carbon monoxide poisoning is rare to clinically encounter. Peripheral and central visual field defects may occur. Cortical blindness and optic neuropathy have been reported. We share a case of constriction of the visual fields with an otherwise normal neuro-ophthalmic examination.

Description of Cases:

A 42-year-old female presented to the clinic with slowly progressive vision loss over 3 months following recurrent exposure to carbon monoxide. She had been repeatedly symptomatic after driving a truck as a post office carrier with complaints of headaches, diplopia, nausea, dizziness, altered mental status, and two episodes of unexplained loss of consciousness. She had coworkers with similar symptoms following use of the same vehicle. She decided to wear a carbon dioxide detector in the truck which confirmed extremely high and toxic levels of carbon monoxide. Her examination revealed 20/30 visual acuity, normal color vision, and normal slit lamp and fundoscopy. Humphrey 24-2 demonstrated prominent constriction of both visual fields. Ocular coherence tomography of the optic nerve and macula were normal. MRI brain with and without contrast was also normal.

Conclusions, including unique features of the case:

Carbon monoxide poses an odorless threat via common sources such as motor vehicles, heaters, appliances, and household fires. It is important to be familiar with the signs and symptoms of carbon monoxide toxicity to facilitate early diagnosis and lower the risk of mortality and morbidity from this lethal condition.

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Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Visual fields, Miscellaneous

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Acute Unilateral Optic Neuritis Caused by Ethmoid Sinusitis and Mucocele as an Uncommon Cause of Vision Loss

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Introduction:

Optic neuritis related to ethmoid sinusitis is an uncommon but a possible cause of vision loss due to the anatomical proximity of the optic nerve to the ethmoid sinus. We present a case report of a woman with acute unilateral optic neuritis associated with ethmoid sinusitis and mucocele.

Description of Cases:

A 73-year-old female presented with a headache at the left frontal area and eyeball followed by sudden visual loss of the left eye. Her symptoms had been gradually progressing spontaneously for a week. Her medical history was unremarkable except for taking statin for dyslipidemia. Neuroophthalmological examination showed left complete ptosis with decreased pupil reactions and slight relative afferent pupillary defect (RAPD) in the left eye. Snellen distance best-corrected visual acuity (DBCVA) of 1.0 in her right eye and finger point in her left eye with increased intraocular pressure in left eye. Brain MRI showed enhancement of the left optic nerve and left posterior ethmoid sinus cystic mass with high protein suggesting mucocele. After the surgery, her headache, vision loss and other neurological symptoms resolved.

Conclusions, including unique features of the case:

The optic nerve is most vulnerable to injury where it runs adjacent to bone or in a confined space like the orbital apex or optic canal. A delay in diagnosis is not uncommon since the vision loss is insidious and the clinical findings may be missed. Sinusitis is a rare but treatable cause of optic nerve injury and vision loss. One must consider optic neuropathy due to sinusitis in patients who have clinical evidence of optic neuritis with atypical features such as a history, any symptoms of sinus disease, and vision loss progression within a few weeks. In the context of such a vision loss with paranasal sinusitis symptoms, a relationship between the two entities should always be considered and never dismissed as coincidental.

References: None provided.

Keywords: Optic neuritis, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

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One Year, Two Eyes, One Diagnosis: B-Cell Non-Hodgkin Lymphoma

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Introduction:

Optic neuropathy in adults is most commonly attributed to glaucoma, ischemic optic neuropathy, compressive lesions, optic neuritis, or hereditary optic neuropathies. We present a rare case of sequential bilateral optic neuropathy, separated by nearly one year, ultimately attributed to B-cell non-Hodgkin lymphoma.

Description of Cases:

A 76-year-old vasculopathic man presented with rapidly progressive, painless vision loss OD. Examination revealed right optic disc edema and visual field constriction. A trial of high-dose corticosteroids failed to improve vision. Neuroimaging demonstrated a dural arteriovenous fistula arising from the left superior cerebellar artery, which was embolized. The patient was subsequently lost to follow-up. Nearly one year later, he returned with rapidly progressive vision loss OS. Examination now showed optic disc pallor OD and optic disc edema OS, with generalized field constriction OU. Neuroimaging revealed left cervical ICA stenosis, for which he underwent carotid endarterectomy. Extensive serologic evaluation was unrevealing except for the presence of an M-spike on serum protein electrophoresis. Hematologic evaluation ensued, and bone marrow biopsy confirmed CD5-/CD10- B-cell non-Hodgkin lymphoma. The patient was initiated on chemotherapy with partial visual improvement thus far.

Conclusions, including unique features of the case:

This case highlights an uncommon neuro-ophthalmic presentation of B-cell non-Hodgkin lymphoma manifesting as sequential bilateral optic neuropathy separated by one year, in the absence of radiographic or serologic evidence of inflammation or compression. The course was confounded by incidental findings, including a dural AV fistula and carotid stenosis, which initially obscured the underlying diagnosis. Clinicians should maintain a high index of suspicion for systemic malignancy in cases of progressive, idiopathic optic neuropathy. Early systemic evaluation is critical to prevent irreversible vision loss.

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Keywords: Optic neuropathy, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Paraneoplastic syndromes

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A Case of a Ruptured Subarachnoid Cyst Requiring Fenestration in the Setting of Worsening Papilledema

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Introduction:

Arachnoid cysts are rare developmental cerebrospinal fluid (CSF) collections that, when ruptured, may lead to signs and symptoms of increased intracranial pressure. There is currently no widely agreed upon management of ruptured arachnoid cysts, with recommendations ranging from conservative observation with temporizing acetazolamide to surgical fenestration or a CSF diverting procedure. In this report, we present a case where a ruptured arachnoid cyst initially was managed with observation; however, despite improvement in symptoms, the patient's papilledema worsened, leading to neurosurgical intervention.

Description of Cases:

A 13-year-old female presented to the ophthalmology clinic with severe headaches, right cranial nerve 6 palsy, and grade 3 disc edema in both eyes. She reported head trauma 3 weeks prior to symptom onset. Emergent MRI brain without contrast demonstrated a ruptured middle cranial fossa arachnoid cyst with bilateral subdural hygromas and signs of increased intracranial pressure. She initially was managed with observation and acetazolamide, during which time her headaches and 6th nerve palsy improved but not resolve and despite maximum acetazolamide dosage, her papilledema worsened, and she developed new visual field defects. Accordingly, she was taken to the operating room 10 days after presentation for temporal craniotomy and arachnoid cyst fenestration. Postoperatively, her headaches, papilledema and 6th nerve palsy completely resolved.

Conclusions, including unique features of the case:

This case highlights the importance of interdisciplinary care in the management of a ruptured arachnoid cyst, as repeat optic nerve evaluation was ultimately the deciding factor on pursuing surgical management.

References: None provided.

Keywords: High intracranial pressure/headache

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A Case of Atypical Bilateral Papilledema in a Medically Complex Patient

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Introduction:

Papilledema is optic disc swelling from elevated intracranial pressure (ICP), typically presenting with headache, nausea, vomiting, and transient visual changes. Management includes targeting the underlying condition. Aseptic meningitis, defined as meningeal inflammation with cerebrospinal fluid (CSF) pleocytosis and negative bacterial cultures, may have viral causes as well as noninfectious causes. Papilledema as a complication of viral meningitis is uncommon, although rare cases have been documented.

Description of Cases:

A 64-year-old female with a history of end stage renal disease, hypertension, dyslipidemia, and chronic headaches presented to the emergency department with bilateral blurry vision and headache. Lumbar puncture (LP) revealed elevated CSF protein of 57.3 mg/dL, white blood cell (WBC) count of 13/ μ L, normal glucose, and elevated lymphocytes at 86%, consistent with aseptic/viral meningitis. She was discharged with aspirin and acetazolamide. On follow-up, her visual acuities (VA) were 20/50 OD and 20/250-1 OS with partial outer inferior nasal deficiencies, 1+ nuclear sclerosis, and a C/D ratio of 0.0 OU. There was marked edema of both optic nerves on exam and optical coherence tomography (OCT) scan. Subsequent LPs (at one and four week follow-ups) showed persistently abnormal CSF and worsening VA despite acetazolamide treatment, which was poorly tolerated. A viral meningitis panel at this point was negative. 4 week follow-up showed spontaneous VA improvement to 20/80-1 OD and 20/80 OS, resolved disc edema, and decreased RNFL thickness OU despite the patient reporting persistent blurry vision and dry eyes.

Conclusions, including unique features of the case:

We report a medically complex patient who presented to the emergency department with bilateral blurry vision and headache. LP showed elevated protein, WBC count, and lymphocytes suspicious for secondary intracranial hypertension (SIH) and papilledema associated with aseptic meningitis. The course underscores meningitic/inflammatory causes of SIH and the need for close ophthalmic monitoring, as disc edema may resolve despite functional deficits persistence.

References: None provided.

Keywords: High intracranial pressure/headache, Neuro-ophth & infectious disease (eg, AIDS, prion), Visual fields, Retina

Financial Disclosures: The authors had no disclosures.

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Optic Neuritis and Perineuritis Associated with Relapsing Polychondritis

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Introduction:

Relapsing polychondritis is a rare immune-mediated disorder that causes episodic inflammation of cartilaginous and proteoglycan-rich tissues. Ocular manifestations commonly include episcleritis, scleritis, and uveitis. Cases with optic nerve involvement have been reported, but are rare without consistent presentations.

Description of Cases:

A 58-year-old man presented to the emergency department with painful left eye movements, conjunctival injection, and bilateral ear swelling. Two months prior, after Influenza A, he noticed ear swelling and tenderness. He was treated for otitis externa with antibiotics and a prednisone taper. One month later, he had left eye injection, pain, and photophobia. Initial evaluation raised concern for corneal abrasion. Progressive symptoms prompted emergency evaluation. Inpatient ophthalmic examination revealed VA 20/20 OD 20/30 OS, no RAPD, left conjunctival injection with chemosis, and left optic disc edema without hemorrhage. MRI orbit revealed asymmetric enhancement of the distal left optic nerve and nerve sheath, suggestive of optic neuritis and perineuritis. He was treated with 3 days of IVMP with symptom improvement. He presented weeks later with worsening left eye pain, photophobia, blurred vision, and recurrence of bilateral ear tenderness, redness, and swelling. Ophthalmic examination revealed nasal conjunctival injection, chemosis, and diffuse optic disc edema with flame hemorrhages. Extensive laboratory studies including autoimmune panels, demyelinating, and infectious studies were completed. Lumbar puncture and brain and cervical spine neuroimaging were unrevealing. With bilateral erythematous and tender pinna, scleritis, optic neuritis, he was diagnosed with relapsing polychondritis. He was admitted for repeat 3 days of IVMP with prednisone taper and plan to transition to steroid sparing agent.

Conclusions, including unique features of the case:

This is a rare case of relapsing polychondritis with optic nerve involvement. While auricular chondritis is the most common manifestation, ocular manifestations occur in about 65% of cases. Early diagnosis and treatment is critical to avoid irreversible damage.

References: None provided.

Keywords: Optic neuritis, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Sellar metastases: unusual causes of “pituitary mass”

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Introduction:

Metastasis to the sella is a rare finding accounting for only 1% of all pituitary tumor surgical resections and for less than 1% of intracranial metastatic lesions(1,2). The most common primary cancers that metastasize to the sella are breast in women and lung in men(1), but gastrointestinal, prostate and renal cancers have been reported(3,4). Although they typically grow faster and produce more severe chiasmal syndromes than classic pituitary adenomas, the diagnosis remains difficult, often only made after surgical resection.

Description of Cases:

We present four cases of sellar metastases from three different primary tumors: a 56- and 70-year-old male with renal cell carcinoma, a 69-year-old male with prostate cancer and a 65-year-old female with breast cancer. Their clinical presentation, investigations and management are discussed. One case presented with panhypopituitarism and no visual symptoms initially. MRI showed an enhancing well-circumscribed mass lesion along the suprasellar cistern obscuring the infundibulum, potentially representing lymphoma or a glioma. The other three presented with a classic chiasmal syndrome. In one the MRI showed an enhancing infiltrative dural-based mass centered at the left planum sphenoidale encasing both bilateral optic canals, most concerning for dural based metastasis. MRI in the other two patients showed a large sellar mass felt to most likely represent a pituitary macroadenoma; there were no other intracranial or calvarial lesions to suggest intracranial metastatic disease. All 4 patients underwent transsphenoidal resection of their mass, which were diagnosed as metastasis by pathology. They all received adjuvant radiotherapy/chemotherapy.

Conclusions, including unique features of the case:

The sella should not be overlooked as a possible site for metastasis from different primary cancers. Although sellar metastases are usually associated with a poor visual prognosis, one of our three patients had no visual symptoms at presentation and one patient with a chiasmal syndrome had marked improvement of visual function with complete resolution of the chiasmal syndrome after treatment.

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Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Skull base, Optic neuropathy, Neuroimaging

Financial Disclosures: Nashwa Abdelhafiz; Valérie Biousse: Consultant for Topcon medical; Michael Dattilo

Grant Support: None.

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Neurosyphilis Presenting as Bilateral Uveitis with Optic Disc Edema

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Introduction:

Neurosyphilis is caused by the spirochete bacteria *Treponema pallidum*, which can have destructive effects on both the body and life. This infection is often termed the “great imitator” as its manifestations are often heterogeneous and vary from focal to systemic involvement.

Description of Cases:

A 69-year-old male with history of multiple sclerosis presented with one month history of bilateral blurred vision. He also endorsed increased fatigue, weight loss, and alopecia. He was previously evaluated at another hospital where all these symptoms were attributed to medications’ side effects. Examination showed VA of CF at 3’ in both eyes, with features of bilateral anterior and intermediate uveitis and bilateral mild optic disc edema. The patient was admitted for expedited workup. MRI brain and orbit showed chronic lesions from multiple sclerosis without enhancement of optic nerves. CT chest, abdomen, pelvis was negative. Systemic lab workup was positive for syphilis with RPR titer of 1:512 and positive ANA 1:320. He was treated for suspected neurosyphilis with penicillin G IV 4 million units every four hours for two weeks. Topical prednisolone was also started in both eyes, which improved his vision while inpatient. LP was considered but deferred due to the patient’s anticoagulation and absence of other neurologic symptoms. One month after completion of IV penicillin, the vision improved to 20/25 right eye and 20/40 left eye with resolution of uveitis and optic disc edema.

Conclusions, including unique features of the case:

- Neurosyphilis is a potentially vision and life-threatening condition that should be promptly evaluated and treated.
- The manifestations of neurosyphilis are broad and must be considered for unusual ocular presentations, especially if uveitis or optic disc edema is present.
- While cerebrospinal fluid testing can aid in diagnosis, it may not be necessary for patients with isolated ocular symptoms with positive serum serology.

References: None provided.

Keywords: Neuro-ophth & infectious disease (eg, AIDS, prion)

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Head Scratching Cat Scratches: Bartonella Associated Neuroretinitis and Meningitis in an HIV Positive Patient

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Introduction:

Infection with *Bartonella henselae* may present as unilateral vision loss from neuroretinitis. The presentation in immunosuppressed individuals is often more severe and warrants prompt treatment.

Description of Cases:

A 27-year-old male with history of childhood meningitis and polysubstance use presented with 1 week of progressive right-sided headache and right eye vision loss. Two weeks prior to presentation, he developed a sore throat without fever or other constitutional symptoms, found to have a right facial abscess treated with amoxicillin. One week later, the patient caught a falling heavy window and subsequently developed progressive right-sided headache and right monocular vision loss. Presenting visual acuity was 20/250 in the right eye. Examination revealed grade 5 Frisen-like right optic disc edema with peripapillary subretinal fluid extending to the macula. MRI showed right maxillary odontogenic sinusitis and non-specific white matter foci of T2 prolongation. Lumbar puncture demonstrated a lymphocytic pleocytosis, elevated protein, and low glucose, but no organism was identified. Serologic testing revealed newly diagnosed HIV (CD4 315, viral load 41,900) and elevated *Bartonella henselae* IgG (1:4096) with negative IgM. Relevant social history includes 2 cats at home and recent unprotected intercourse with 2 partners. Repeat ophthalmic exam 1 week later showed visual acuity progressed to counting fingers with new trace anterior chamber cell, 2+ vitreous cell, and a macular star in the right eye. He was diagnosed with atypical *Bartonella*-associated neuroretinitis and meningitis in the setting of a new HIV infection. The patient was treated with doxycycline and rifampin, corticosteroids for optic nerve edema, and empiric antibiotics for odontogenic disease. Antiretroviral therapy was initiated.

Conclusions, including unique features of the case:

This case highlights an atypical presentation of *Bartonella* neuroretinitis with associated meningitis in the setting of new HIV infection, emphasizing the importance of broad infectious evaluation in neuroretinitis despite possible confounders (Valsava, odontogenic and sinus infection, no febrile illness), particularly in immunocompromised hosts.

References: None provided.

Keywords: Neuro-ophth & infectious disease (eg, AIDS, prion), Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

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VKH presenting as a Cranial Nerve Palsy

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Introduction:

Vogt-Koyanagi-Harada disease is a rare condition that affects melanocytes in the meninges, eyes, skin, hair, and ears. Clinical manifestations involve bilateral granulomatous uveitis, vitiligo, tinnitus, and neurologic symptoms. We present a case of a cranial nerve palsy as the initial presentation, which created a diagnostic dilemma.

Description of Cases:

A 60-year-old female with a medical history of hypertension, ischemic heart disease, and prediabetes presented with sudden onset diplopia. Examination revealed left abducens nerve palsy, which was initially considered microvascular. However, a follow-up exam showed worsening, with new onset of headaches. MRI brain showed diffuse pachymeningeal enhancement with focal asymmetric dural thickening and enhancement marginating the left cavernous sinus. In addition, MRI features were suggestive of intracranial hypotension. Autoimmune workup was positive for ANA (1:160) and positive dsDNA (1:80). A few weeks later, she developed bilateral anterior and intermediate uveitis with bilateral optic disc edema and resolution of the left 6th nerve palsy. Lumbar Puncture showed opening pressure of 27cm H₂O, and cerebrospinal fluid was positive for elevated IgG and oligoclonal bands. Serum IgG subclass was negative. CT chest, abdomen, pelvis and paraneoplastic panel was negative. She was evaluated by Rheumatology, Neurology, Uveitis specialist, and Neuro-ophthalmology. She endorsed a history of vitiligo/psoriasis and Cherokee Native American ancestry. HLADRW52 was positive. She was treated with oral methotrexate, topical steroid eye drops, oral steroids, and acetazolamide, which improved the uveitis and optic disc swelling without significant vision loss. Repeat MRI is awaited

Conclusions, including unique features of the case:

1. VKH can rarely present with cranial nerve palsy, and pachymeningitis can be a diagnostic dilemma if it presents as the initial isolated symptom/presentation. 2. Asymmetric dural thickening and enhancement marginating the left cavernous sinus has a broad differential - malignancy or autoimmune etiologies. 3. In any patient with neurologic symptoms and bilateral uveitis, VKH should always be considered in the differential diagnosis.

References: None provided.

Keywords: Ocular motility, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Neuroimaging

Financial Disclosures: The authors had no disclosures.

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Immunosuppressant Medication Masking Giant Cell Arteritis: A Case Report Of Ischemic Optic Neuropathy

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Introduction:

Ischemic optic neuropathy (ION) is characterized by vision loss precipitated by acute ischemic damage to the optic nerve. Anterior arteritic ION (A-AION) is associated with vascular risk factors, such as giant cell arteritis (GCA), but other risk factors include hypertension, diabetes mellitus, and obstructive sleep apnea, among others. However, few cases have reported ION arising from suspension of immunosuppressant therapy.

Description of Cases:

A 71-year-old female with a history of ankylosing spondylitis was instructed to stop golimumab one week before her knee arthroscopy. She restarted 8 weeks post-surgery but had symptoms of headache and vision loss in the left eye within two weeks of the first infusion. She presented to the emergency department with headache and black spots in the left upper visual field, decreased visual acuity at 20/80, and 2+ optic nerve edema. Due to suspected GCA, she was started on prednisone 80 mg. Bilateral temporal artery biopsies were negative. Initial ophthalmology exam showed left visual acuity at count fingers 1' and 2+ edema with average retinal nerve fiber layer thickness of 141 on optical coherence tomography. Optic nerve edema eventually improved 1 month after diagnosis without improvement in vision.

Conclusions, including unique features of the case:

Restimulation of the immune system following golimumab discontinuation may have contributed to the subsequent flare of GCA. Despite restarting golimumab 2 weeks before presentation, it was not yet at a therapeutic level to prevent the A-AION and vision loss. While reports of inflammation-induced optic neuropathy after withdrawal of immunosuppressive therapy are scarce, this phenomenon is a rare but recognized adverse event linked to agents that enhance immune activation, such as immune checkpoint inhibitors. These findings suggest that medication-associated optic neuropathy may play a greater role in vision loss than currently appreciated in the literature.

References: None provided.

Keywords: Optic neuropathy, Higher visual functions, Optic neuritis

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Atypical Structural Orbital Pulsation Following Craniofacial Surgery and Radiation in the Absence of Carotid-Cavernous Fistula

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Introduction:

Orbital pulsation is rare neuro-ophthalmic finding most often associated with vascular lesions such as carotid-cavernous fistula or arteriovenous malformations. However, similar pulsatile globe movements may also result from secondary structural defects that allow intracranial pulsations to transmit into the orbit. Recognition of these mechanisms is important to avoid unnecessary invasive vascular evaluation. We present an unusual case of unilateral orbital pulsation from post-surgical and post radiation orbital wall loss, a sequela of post oncologic treatment.

Description of Cases:

A 71-year-old woman reported progressive visual disturbance and rhythmic motion of the left eye. Her history included sinonasal carcinoma treated 22 years earlier with craniotomy and external-beam radiation, later complicated by recurrence requiring re-irradiation. A left sphenoid wing meningioma had also been managed with gamma knife therapy, and subsequent radiation necrosis was treated with bevacizumab. External examination revealed enophthalmos, deep superior sulcus, reduced palpebral aperture, and rhythmic retrobulbar pulsation synchronous with the cardiac pulse in the left eye. Visual acuity measured 20/40 OU with a 0.6 log unit relative afferent pupillary defect OS. Fundus examination showed normal optic discs without edema. Automated perimetry demonstrated nonspecific defects. Orbital MRI and CT revealed absence of the left medial orbital wall, temporal lobe deformity, and extension of meningioma into the orbit without optic nerve compression. CT angiography demonstrated no vascular abnormality, excluding a carotid-cavernous fistula. Observation was recommended, and findings remained stable over three months of follow-up.

Conclusions, including unique features of the case:

Orbital pulsation may arise from structural rather than vascular causes, particularly in patients with prior craniofacial surgery or radiation. Loss of orbital wall integrity reduces resistance to intracranial pressure fluctuations, resulting in transmitted pulsations that mimic vascular pathology. Careful clinical evaluation and multimodal imaging are essential to distinguish structural from vascular etiologies and to guide management without unnecessary intervention.

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Keywords: Orbit, Skull base, Vascular disorders, Trauma

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Refractory Papilledema as an Initial Presentation of Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal Plasma Cell Disorder, Skin Changes (POEMS) Syndrome

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Introduction:

POEMS syndrome is a rare paraneoplastic plasma cell disorder with multisystem involvement. Ocular manifestations include papilledema and macular edema. Although papilledema occurs in 29–55% of patients, it is rarely the presenting symptom. Its pathophysiology remains unclear but may result from vascular permeability changes driven by imbalanced pro-inflammatory and angiogenic cytokines, and it carries a poor prognosis.

Description of Cases:

A 29-year-old female presented with four weeks of headache and transient visual obscurations. Ophthalmologic examination demonstrated bilateral papilledema. Lumbar puncture revealed an opening pressure of 26 cm H₂O, WBC count of 2/cmm, and elevated protein at 138 mg/dL. MRI of the brain and orbits showed segmental T2 hyperintensity along the left optic nerve and indirect signs of intracranial hypertension. MRI of the spine revealed diffuse sclerotic bone changes and enhancement of cauda equina nerve roots. CT demonstrated splenomegaly and lymphadenopathy. Serum studies showed elevated kappa and lambda light chains, thrombocytosis (406,000/μL), and VEGF of 297 pg/mL (ref. 9–86). An IgA lambda monoclonal band was identified on serum electrophoresis. Acetazolamide 1500 mg daily led to improvement in symptoms and papilledema. One year later, she developed recurrent transient visual obscurations. Optical coherence tomography demonstrated thickening of the peripapillary retinal nerve fiber layer (185 μm OD, 349 μm OS). Bone marrow biopsy showed clonal plasma cells with mixed B and T lymphoid aggregates. Electrodiagnostic testing revealed moderate sensorimotor demyelinating polyneuropathy. With these findings, she met criteria for POEMS syndrome. Dexamethasone, lenalidomide, and daratumumab were initiated, with stem cell transplantation under consideration. At one-month follow-up, papilledema improved (83 μm OD, 141 μm OS).

Conclusions, including unique features of the case:

Refractory papilledema led to the diagnosis of POEMS syndrome. Prompt recognition and immunotherapy resulted in marked visual improvement. Only one prior case has reported papilledema as the initial symptom of POEMS. This case emphasizes including POEMS in the differential diagnosis of papilledema, preventing delayed diagnosis.

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Keywords: Paraneoplastic syndromes, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)

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Introduction:

Autoimmune Glial Fibrillary Acidic Protein (GFAP) Astrocytopathy is an inflammatory central nervous system (CNS) disorder that may affect any anatomic region from optic nerve to spinal cord. While meningoencephalitis is the predominant clinical phenotype, isolated GFAP papillitis can be the initial presentation of GFAP astrocytopathy. We report a case of GFAP papillitis with isolated MS like lesion on brain MRI and positive cerebral spinal fluid(CSF) oligoclonal band (OCB).

Description of Cases:

A 48-year-old woman with medical history of type I diabetes presented with bilateral blurred vision. Best corrected visual acuity (BCVA) was 20/30 both eyes without relative afferent pupil defect (RAPD). She had mild superior optic disc swelling left eye. Automated perimetry showed non-specific threshold loss right eye and inferior arcuate visual field defect left eye. Optical coherence tomography (OCT) showed mild retinal nerve fiber layer (RNFL) thickening worse on left eye. MRI orbit reported subtle intraocular protrusion of the left optic nerve head without retrobulbar abnormality. MRI brain reported oval non-enhancing periventricular lesion oriented perpendicularly to the lateral ventricles. Spinal cord MRI unremarkable. Extensive serum workup for infectious and systemic autoimmune conditions was unremarkable. Lumbar puncture with normal intracranial pressure and mildly elevated protein at 50mg/dl, normal cell count and 9 CSF unmatched oligoclonal band (OCB). Patient was treated with intravenous solumedrol 1gram daily for 5 days with significant vision improvement. Autoimmune encephalopathy panel resulted positive glial fibrillary acidic protein antibody (GFAP-ab) at titer 1:8.

Conclusions, including unique features of the case:

GFAP papillitis with isolated MS-like brain lesion and positive CSF unique OCB is a rare and clinical challenging condition especially for consideration of preventive immunotherapy. The underlying mechanism is uncertain but likely related to co-existing autoimmune conditions and shared pathophysiology between GFAP astrocytopathy, MS and other systemic autoimmune disorders. Astrocytic activation might play a role in the shared pathology between GFAP astrocytopathy and MS.

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Keywords: Optic neuritis, Demyelinating disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Neuroimaging, Optic neuropathy

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Diplopia, Papilledema, Meningioma and Dural Venous Sinus Compression: A Case Report.

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Introduction:

Meningiomas are the most common intracranial neoplasms. They can arise close to the dural venous sinuses (DVS), compressing them, and leading to secondary intracranial hypertension (IH) and papilledema, mimicking idiopathic intracranial hypertension.

Description of Cases:

An 80-year-old man was referred for cataract surgery due to difficulty while driving. He reported a 2-month history of mild headaches, tinnitus, and double vision. His past medical history included controlled hypertension and glaucoma, treated with topical medication and selective laser trabeculoplasty. His best-corrected visual acuity was 20/20 in both eyes, and biomicroscopy revealed a nuclear sclerotic cataract, grade 2. He had a left fourth cranial nerve palsy, and fundoscopic examination revealed bilateral papilledema, predominant in the right eye. Confirmation was obtained by optical coherence tomography. Neuroimaging, including magnetic resonance imaging (MRI), showed an extra-axial expansive lesion measuring 37×36mm in the right parasagittal parietal region. Lumbar puncture showed an opening pressure of 30cmH₂O. Posterior magnetic resonance venography (MRV) demonstrated the lesion was in contact with and partially compressing the superior sagittal sinus. Surgical resection was performed by the neurosurgery department. The pathological diagnosis was chordoid meningioma, World Health Organization grade 2. One-month follow-up revealed improvement of diplopia and tinnitus, as well as a reduction in bilateral papilledema.

Conclusions, including unique features of the case:

Meningiomas compressing the DVS represent a challenging diagnosis. In this case, the patient was referred for cataract surgery, being his visual acuity unremarkable, but presented diplopia from left fourth nerve palsy, further complicating the diagnosis. Diagnosis is usually delayed because the tumor is often thought to be too small to cause IH and papilledema. The role of MRV, along with a multidisciplinary approach, is crucial for the correct diagnosis and treatment.

References: None provided.

Keywords: Tumors, High intracranial pressure/headache, Ocular motility, Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Optic Neuropathy in IgG4-Related Ophthalmic Disease: A Case Series from a Latin American Tertiary Center

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Introduction:

Immunoglobulin G4-related disease (IgG4-RD) is a systemic fibroinflammatory condition characterized by lymphoplasmacytic infiltrates rich in IgG4-positive plasma cells, storiform fibrosis, and obliterative phlebitis. Its orbital manifestation, IgG4-related ophthalmic disease (IgG4-ROD), may involve the lacrimal glands, extraocular muscles, and optic nerve, often mimicking idiopathic orbital inflammation. Early recognition is critical to prevent irreversible visual loss.

Description of Cases:

Methods: A retrospective, descriptive case-series study was conducted at the Neuro-Ophthalmology Section of a Latin American Tertiary Center care (2014–2024). Medical records of patients fulfilling the 2014, 2019, and revised 2023 diagnostic criteria for IgG4-ROD were reviewed. Demographic, serologic, imaging (OCT, visual field), and clinical data were analyzed. **Results:** Of 60 institutional IgG4-RD cases, 13 met criteria for IgG4-ROD. The mean age was 46.9 ± 18.4 years; 53.8% were male. Ocular involvement preceded systemic diagnosis in 61.5% of cases. Most patients (76.9%) presented the “head and neck” phenotype. More than half (53.8%) had normal serum IgG4 levels. Eyelid edema (38.5%) and diplopia (30.8%) were the most frequent symptoms. Four patients (30.8%) developed optic neuropathy with structural variability on OCT, ranging from severe peripapillary RNFL thinning (34 μ m) to near-normal values in subclinical stages. One case showed steroid-induced central serous chorioretinopathy.

Conclusions, including unique features of the case:

IgG4-ROD remains a diagnostic challenge due to its clinical heterogeneity and frequent normal IgG4 serology. Optic nerve involvement, although uncommon, may cause irreversible axonal loss if not detected early. The combined use of OCT, visual field testing, and neuro-ophthalmologic evaluation is essential for timely diagnosis and management. This study represents the first Latin American case series describing optic neuropathy in IgG4-ROD, providing region-specific evidence to enhance early recognition and multidisciplinary care. **Keywords:** IgG4-related ophthalmic disease, optic neuropathy, IgG4-RD, neuro-ophthalmology, case series.

References: None provided.

Keywords: Optic neuropathy, Orbit/ocular pathology, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Orbit/ocular pathology

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Beyond Diplopia: A Third Nerve Palsy Revealing Multifocal Meningiomas in the Postpartum Period

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Introduction:

Cavernous sinus meningiomas are rare causes of isolated oculomotor palsy and can be challenging to recognize, particularly in the postpartum period. Hormonal and hemodynamic changes surrounding pregnancy may accelerate growth of previously indolent meningiomas. We present a postpartum woman with acute third cranial nerve palsy due to cavernous sinus meningioma in the setting of multifocal meningiomas including bilateral optic nerve sheath involvement.

Description of Cases:

A 40-year-old woman with no prior medical history presented one week after cesarean section for acute diplopia and right-sided headache. Two weeks before delivery, she had developed retro-orbital pain and dizziness that worsened postpartum with new ptosis and vertical binocular diplopia at distance. Examination showed bilateral optic nerve head pallor, and a partial right third nerve palsy (–1 limitation of adduction and supraduction, 2 mm ptosis) with otherwise full motility. Visual fields demonstrated an inferior field defect in the left eye, and OCT revealed diffuse ganglion cell attrition in both eyes. MRI and CT imaging showed multiple enhancing extra-axial masses consistent with meningiomas: a dominant lesion in the left cavernous sinus extending into Meckel's cave and sphenoid wing, a smaller lesion within the right cavernous sinus, parafalcine foci, and linear calcified thickening along the optic nerve sheaths (L > R). Catheter angiography excluded aneurysm or fistula. The right partial oculomotor palsy was attributed to subtle compression or infiltration of the right cavernous sinus by meningioma, whereas optic disc pallor and field defect reflected optic neuropathy likely due to longstanding bilateral optic nerve sheath meningiomas. Due to multifocal distribution, she was counselled to follow up for neurofibromatosis 2 testing and consider radiation therapy.

Conclusions, including unique features of the case:

This case underscores the diagnostic challenge of multifocal meningiomas presenting peripartum as pupil-sparing third nerve palsy, often mistaken for microvascular ischemia. Recognizing hormonal effects on meningioma growth is vital for timely diagnosis, counseling, and coordinated management

References: None provided.

Keywords: Optic neuropathy, Pupil, Neuroimaging, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

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Is Tolosa–Hunt Syndrome a Recurrent Entity? Systematic Review and Relapse Analysis

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Introduction:

ICHD-3 defines THS as unilateral orbital pain, cranial nerves paresis, granulomatous inflammation of the cavernous sinus, superior orbital fissure, or orbit, and response to steroids. THS remains a diagnosis of exclusion, and recurrence complicates diagnosis.

Description of Cases:

The aim was to identify differences among recurrent and non-recurrent THS. Cases mimicking THS were excluded: 8 infectious, 27 oncologic, 18 autoimmune /inflammatory, 7 vascular, 3 endocrine and metabolic, 1 post-surgical. A systematic PubMed search identified all THS case reports and series, including only those with follow-up. Variables included demographics, clinical presentation, diagnostic workup, management, outcomes and time to relapse. Fisher's exact and Man Whitney U were used, calculating P values, 95% confidence intervals, and statistical power. False discovery rate using Benjamini–Hochberg was applied. We identified 114 studies (134 patients, 45% recurrent). Follow-up ranged from 1 to 27 months. There were no significant demographic and comorbidities differences. Orbital pain was significantly more frequent in recurrent cases ($p=0.0072$; OR 0.49, 95% CI 0.29–0.83; Power=0.77). Likewise, diplopia ($p=0.0081$; OR 0.48, 95% CI 0.28–0.83; Power=0.78), proptosis ($p=0.0168$; OR 0.52, 95% CI 0.31–0.89; Power=0.65) and ptosis ($p=0.0134$; OR 0.51, 95% CI 0.30–0.87; Power=0.72). In recurrent cases, CT ($p=0.0126$; OR 0.51, 95% CI 0.30–0.87; Power=0.69) and MRI ($p<0.001$; OR 0.30, 95% CI 0.18–0.52; Power=1.00) were used more often. No significant CSF or blood test differences were found. Treatment characteristics did not differ. Recurrent patients showed shorter recovery for pain ($p=0.0051$; Δ median=–4.0 days; Power=0.79) and cranial nerve function ($p=0.0050$; Δ median=–16.0 days; Power=0.80).

Conclusions, including unique features of the case:

This review underscores the wide range of alternative diagnoses. Recurrence was significantly associated with orbital pain, diplopia, ptosis, and proptosis. Recurrent cases needed more imaging, reflecting evaluation during relapse. Management was similar, suggesting recurrency was not treatment-related. Shorter recovery times in recurrent cases, could be attributed to reporting bias.

References: None provided.

Keywords: Neuroimaging, Ocular motility, Orbit, Miscellaneous, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Presumed Optic Nerve Granulomas: Diagnostic Challenge with Potential Benefit of Long-Term Corticosteroid Therapy

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Introduction:

Sarcoidosis can present with a variety of neuro-ophthalmological findings, including cranial nerve palsies, optic neuropathy, perineuritis and less commonly optic nerve head granulomas. Neuro-sarcoidosis can present a diagnostic dilemma, with limited confirmatory diagnostic tests aside from biopsy. This dilemma can be more problematic when patients present with normal systemic history but extensive optic nerve head swelling, raising a question of optic nerve head granuloma.

Description of Cases:

Three patients presented with extensive and persistent monocular optic nerve head edema with significant peripapillary subretinal fluid, with a presumed diagnosis of optic nerve head granuloma. Neuro-imaging did not identify a structural etiology. Each patient presented with unilateral painless episodes of transient, then progressive vision loss. Our first patient had lymphadenopathy with biopsy confirming non-caseating granulomas; she was treated with high dose of steroids and methotrexate, with gradual improvement in optic nerve head appearance but minimal improvement in vision. Our second patient had lymphadenopathy with an inconclusive biopsy; he was treated with high dose steroids with gradual resolution of optic nerve head edema, improved visual acuity and visual field. Our third patient had a negative diagnostic evaluation without lymphadenopathy; she was treated with steroids with improvement of visual acuity, only to have recurrence of visual loss with steroid taper. She is being evaluated for a steroid sparing agent.

Conclusions, including unique features of the case:

Our cases had nearly identical ophthalmic presentations. One case was confirmed to have sarcoidosis by biopsy. The other two were presumed to have sarcoidosis given the similarity in the optic nerve head appearance and the lack of an alternative diagnosis even after a detailed investigation. Two of the three improved with prolonged corticosteroid therapy. Cases of this type can be challenging to diagnose but the presumption of sarcoidosis is reasonable and supports the use of long-term corticosteroids. Longer-term management decisions are pending.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Sequential 3rd, 4th, 5th, 6th and 7th Cranial Neuropathies and Ataxia as Initial Manifestations of Nodular Lymphocyte Predominant Hodgkin Lymphoma

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Introduction:

Neuro-ophthalmological presentation in the form of sequential ocular motor and other cranial neuropathies is a rare initial manifestation of Hodgkin lymphoma. Recognition of this association is important when considering the diagnostic approach in such patients.

Description of Cases:

A 72-year-old man developed sequential, transient cranial neuropathies beginning in early 2022. Initial symptoms included vertical diplopia and gait instability, followed by a right pupil-sparing third cranial nerve palsy with complete ptosis and right-sided trigeminal paresthesia that resolved. He then developed a left fourth cranial nerve palsy, left-sided trigeminal paresthesia and left-sided cerebellar ataxia. Serial brain MRIs showed fluctuating enhancement of the right third and left seventh cranial nerves, without facial nerve palsy or associated parenchymal or meningeal abnormality. Extensive laboratory testing for inflammatory and infectious processes was unrevealing. Cerebrospinal fluid on two occasions was acellular and showed modestly elevated total protein. Serum and CSF paraneoplastic antibody testing was negative. In late 2022, he developed a partial right sixth cranial nerve palsy and recurrent imbalance. Contrasted thoracic spine MRI revealed a right paratracheal mass. NM/CT parathyroid SPECT showed mild asymmetry in the right thyroid lobe. Fine-needle aspiration was nondiagnostic. In 2023, PET/CT showed hypermetabolic activity in the right paratracheal region. Surgical biopsy of a paratracheal lymph node in 2024 demonstrated pathology consistent with nodular lymphocyte predominant Hodgkin lymphoma.

Conclusions, including unique features of the case:

Ocular motor and other cranial nerve palsies, with fluctuating radiographic nerve enhancement, and cerebellar ataxia may represent the initial clinical manifestations of lymphoma. This neuro-ophthalmological presentation, due to neurolymphomatosis or paraneoplastic process, highlights the diagnostic challenge in such patients.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Neuroimaging, Paraneoplastic syndromes, Miscellaneous

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The Impact of a Multimodal Patient Educational Intervention for Ocular Manifestations of Giant Cell Arteritis

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Introduction:

Vision loss is the most serious complication of giant cell arteritis (GCA), requiring prompt recognition and evaluation. Despite this, few patient educational resources adequately address visual manifestations of GCA or provide guidance on appropriate actions. The purpose of this study was to develop and assess the impact of a multimodal educational intervention on patients' knowledge and self-efficacy in managing ocular disease in GCA.

Methods:

This pre-post intervention study included patients diagnosed with GCA. Educational materials included a low-literacy illustrated flyer and a 3-minute video developed collaboratively with patients, health communication experts, and clinicians. Pre- and post-intervention knowledge and self-efficacy were assessed using a 10-item multiple choice test and 5-point Likert scale, respectively. Pre- vs. post-intervention scores were compared using the Wilcoxon signed rank test. Factors associated with knowledge gain and low pre-intervention scores were analyzed using linear regression.

Results:

A total of 61 patients participated in the study (31% male; mean age, 73 years). Knowledge scores improved significantly from pre-intervention (mean 73% correct, SD 19) to post-intervention (mean 92% correct, SD 11; $P < 0.01$). Self-efficacy also improved significantly, with the proportion of patients who reported feeling uncomfortable or unsure about managing GCA-related eye symptoms decreasing from 44% pre-intervention to 13% post-intervention ($P < 0.01$). Female sex was associated with greater knowledge gain ($P = 0.01$). Patients who had never received a GCA-related eye exam or had longer disease duration demonstrated lower baseline knowledge.

References: None provided.

Keywords: Vascular disorders, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Miscellaneous

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Tumoral Calcinosis: Case Report And Comprehensive Review Of The Literature

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Introduction:

Tumoral calcinosis (TC) is a rare condition of ectopic calcium-phosphate deposition, often presenting with periarticular masses, and can include ocular findings such as conjunctival calcifications, angioid streaks, and rarely optic disc drusen (ODD). Ocular manifestations of TC are minimal in the current literature with only a few case reports. TC can often present as a diagnostic challenge due to its overlapping features with more common diseases and variable expressivity.

Description of Cases:

A 70-year-old woman with a history of progressive visual loss and multiple orthopedic injuries presented to neuro-ophthalmology for evaluation of an optic neuropathy in both eyes (OU). She previously had an extensive autoimmune and systemic workup that was normal. Genetic testing for primary forms of TC (GALNT3, FGF23, KLOTHO, SAMD9) was negative, and her calcium and phosphate levels were normal. She had a sciatic nerve biopsy which revealed classic calcific deposits for TC on pathology examination, and was diagnosed with secondary tumoral calcinosis (STC). Dilated fundoscopic exam revealed bilateral optic disc pallor, and bilateral ODD. Optical coherence tomography (OCT) scans showed thinning of the RNFL OU with a preserved ganglion cell layer, which was stable over a two year period. Fundus autofluorescence revealed superficial ODD OU. Humphrey visual field testing showed relative stability of a superonasal step in the right eye, and a generalized peripheral depression in the left eye over two years.

Conclusions, including unique features of the case:

This case presents the diagnostic difficulty of STC in the absence of abnormal serum markers or positive genetic tests, emphasizing the need for clinical vigilance and multidisciplinary evaluation; its novelty lies in the combination of optic nerve head drusen without angioid streaks, normal phosphate levels, and negative genetics, pointing to an atypical ocular manifestation of TC.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Bilateral Central Retinal Vein Occlusion as a Sentinel Ophthalmic Manifestation of Acute Myeloid Leukemia: A Case Series

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Introduction:

Central retinal vein occlusion (CRVO) is a vision-threatening event, is an uncommon yet striking complication in hematologic malignancies. Acute myeloid leukemia (AML) related ocular vascular occlusions can be triggered by leukostasis, anemia-related hypoxia, thrombocytopenia, and disseminated coagulopathy. The occurrence of bilateral CRVO is rare, often signaling severe systemic disease or compromised vascular integrity. This is the largest case series describing bilateral CRVO in patients with AML, as previous reports in the medical literature have been limited to single cases. We describe two cases of bilateral CRVO associated with AML, each unfolding within distinct hematologic contexts, underscoring the urgent need for of early ophthalmic evaluation.

Description of Cases:

Case 1: A 59-year-old woman with refractory AML (M0 subtype, FLT3-wildtype) presented with progressive, painless bilateral vision loss. She was profoundly pancytopenic and developed multifocal intracerebral hemorrhages. Brain MRI excluded CNS infiltration. Fundus examination revealed four-quadrant retinal hemorrhages, venous tortuosity, and cystoid macular edema in both eyes. Fluorescein angiography showed blocked fluorescence without neovascularization. She received transfusion support and intravitreal bevacizumab. Visual acuity remained count-fingers bilaterally. Case 2: A 30-year-old man with newly diagnosed core binding factor AML with inv(16) presented with progressive bilateral visual decline. Fundus examination showed optic disc edema, venous engorgement, and diffuse intraretinal and preretinal hemorrhages. He was treated with FLAG-GO induction chemotherapy and transfusions to maintain platelets above $50 \times 10^3/\mu\text{L}$. Ocular findings showed improved with systemic stabilization, and anti-VEGF therapy was deferred.

Conclusions, including unique features of the case:

Bilateral CRVO represents a rare yet devastating manifestation of AML-related vascular injury. The concurrent concurrence of retinal and cerebral vascular events underscores the shared microvascular vulnerability between retina and brain in leukemia. These cases highlight the importance of prompt recognition, platelet counts optimization, and multidisciplinary coordination between hematology and ophthalmology are essential for preserving vision and addressing the underlying systemic pathology.

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Keywords: Neuroimaging, Vascular disorders, Retina

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Sellar mass – Dual pathology with metastasis from renal cell carcinoma and pituitary adenoma

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Introduction:

Although uncommon, renal cell carcinoma is known to metastasize to the sella. The authors present a patient with a symptomatic sellar mass, initially thought to be a pituitary adenoma, that was biopsy-proven to be both pituitary adenoma and metastatic carcinoma.

Description of Cases:

81-year-old male with medical history significant for prostate cancer and clear cell renal carcinoma presented with two months of headache and occasional horizontal diplopia. Of note, pupils were without relative afferent pupillary defects. On examination, the patient was found to have left upper lid ptosis and mild left abducens deficit. Initial CT head/orbits was completed and demonstrated a heterogeneously enhancing mass abutting the optic chiasm and extending eccentrically to the left. Patient was referred to Neuro-surgery with outpatient MRI sella. In the interim, he presented 5 weeks later with worsening left eye ptosis and limitations in all duction movements in left eye. Overall, these findings were consistent with left cranial nerve III and VI palsies. MRI was completed and redemonstrated the sellar mass with minimal suprasellar extension and invasion into the left cavernous sinus, report being consistent with pituitary adenoma. Corresponding laboratory investigations were consistent with panhypopituitarism. The patient underwent tumor resection. The pathology demonstrated metastatic carcinoma, consistent with the patient's known renal cell primary as well as corticotrophin pituitary adenoma. Following tumor resection and radiation, there was improvement in patient's ptosis and extra-ocular movements, although not full resolution.

Conclusions, including unique features of the case:

Although uncommon, renal cell carcinoma can metastasize to the sella without parenchymal or dural involvement. While imaging and laboratory studies may be suggestive of a pituitary adenoma which is a slow growing benign tumor, the rapid progression of related sellar neurological deficits should raise suspicion for alternative and additional pathologies, especially inflammatory or neoplastic.

References: None provided.

Keywords: Tumors, Ocular motility

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Complex Syphilis History Masking Optic Neuritis from Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease

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Introduction:

Syphilis is the great disease mimicker. This infection can affect any visual pathway structure, with optic nerve involvement in at least 75% of ocular syphilis patients. However, optic nerve pathology is common in demyelinating disorders like multiple sclerosis (MS) and myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD). These etiologies can have accompanied CSF abnormalities to varying degrees. These overlaps can complicate medical decision-making. This case highlights the aforementioned diagnostic challenge.

Description of Cases:

A 33-year-old male, with PMHx of seizures and doxycycline-treated syphilis, presented for acute-onset central vision loss and eye pain OS. Family history was notable for MS. Initial workup revealed a positive syphilis screen and RPR ratio 2:1. Visual acuity was 20/20 OD, 20/HM OS. Fundoscopy revealed bilateral optic neuritis. Ceftriaxone was started for possible ocular syphilis, and a lumbar puncture (LP) was completed. MRI brain without contrast showed a small T2-hyperintense right medial pontine lesion. Methylprednisolone was added. LP showed WBC 53/uL, lymphocytes 86%. VDRL-CSF was negative; therefore, ceftriaxone was discontinued. Oligoclonal bands were positive, and the anti-MOG Ab ratio was 1:160. Over time, his vision quickly improved to 20/40 OS and was discharged with an oral steroid course.

Conclusions, including unique features of the case:

MOGAD is a rare inflammatory demyelinating disease that has a clinical presentation that overlaps with other diseases such as MS, transverse myelitis, and neurosyphilis. The patient's background and presentation led the team to believe ocular syphilis was the primary etiology. LP fluid studies showed CSF pleocytosis, a finding in up to 70% of neurosyphilis and in more than 50% of demyelinating disorders.²⁻⁴ However, upon further review of imaging and labs including CSF studies, the patient had MOGAD and responded well to steroids. This case represents the importance of not anchoring to one diagnosis, but instead further evaluating other etiologies of optic neuritis including MOG antibody testing.

References: 1) Klein, Ainat, et al. "The Great Imitator on the Rise: Ocular and Optic Nerve Manifestations in Patients with Newly Diagnosed Syphilis." *Acta Ophthalmologica*, vol. 97, no. 4, pp. e641–e647, 17 Oct. 2018. (<https://doi.org/10.1111/aos.13963>) 2) Ghanem, Khalil G., et al. "The Modern Epidemic of Syphilis." *New England Journal of Medicine*, vol. 382, no. 9, pp. 845–854, 26 Feb. 2020. (<https://doi.org/10.1056/nejmra1901593>) 3) Berek, Klaus, et al. "Cerebrospinal Fluid Findings in 541 Patients with Clinically Isolated Syndrome and Multiple Sclerosis: A Monocentric Study." *Frontiers in Immunology*, vol. 12, 17 June 2021. (<https://doi.org/10.3389/fimmu.2021.675307>) 4) Jarius, Sven, et al. "Cerebrospinal Fluid Findings in Patients with Myelin Oligodendrocyte Glycoprotein (MOG) Antibodies. Part 1: Results from 163 Lumbar Punctures in 100 Adult Patients." *Journal of Neuroinflammation*, vol. 17, no. 1, 3 Sept. 2020. (<https://doi.org/10.1186/s12974-020-01824-2>)

Keywords: Optic neuritis, Demyelinating disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Altered Mental Status After Teprotumumab Infusion: A Diagnostic Clue To Small Cell Lung Carcinoma

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Introduction:

Thyroid eye disease (TED) is an autoimmune orbital disorder commonly managed with systemic corticosteroids, orbital decompression, or targeted therapy such as teprotumumab, a monoclonal antibody against the insulin-like growth factor-1 receptor. While teprotumumab has been associated with fatigue, headache, hearing changes, and metabolic effects such as hyperglycemia, severe electrolyte or neuropsychiatric complications have not been reported. We present a patient who developed confusion and hyponatremia following a teprotumumab infusion, ultimately leading to the discovery of small cell lung carcinoma.

Description of Cases:

A 62-year-old male with thyroid eye disease initiated teprotumumab therapy. After his second infusion, he experienced tinnitus with normal audiometric testing. Following the third infusion, he developed dizziness, nausea, and fatigue progressing to altered mental status characterized by vomiting, confusion and lethargy. Teprotumumab was discontinued with no improvement in symptoms. He was admitted in the emergency department and laboratory testing revealed marked hyponatremia. Chest CT was ordered and demonstrated a mass confirmed as small cell carcinoma of the lung. The patient began chemoradiation therapy, resulting in normalization of serum sodium and gradual improvement in mental status.

Conclusions, including unique features of the case:

This case emphasizes the importance of looking beyond medication side effects when evaluating new neurologic or systemic symptoms. While teprotumumab is associated with fatigue and hearing changes, anchoring on a single presumed cause can delay recognition of coexisting or alternative pathologies. Clinicians should maintain a broad differential and consider paraneoplastic processes such as SIADH secondary to small cell lung carcinoma when unexplained hyponatremia and encephalopathy occur. A comprehensive, systems-based approach can prevent diagnostic oversight and enable earlier cancer detection and management.

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Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Graves' disease, Paraneoplastic syndromes, Tumors

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COG5-Congenital Disorder of Glycosylation Diagnosed by Whole Genome Sequencing in Siblings with Unexplained Optic Atrophy and Developmental Delay

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Introduction:

Congenital disorders of glycosylation (CDG) are rare inherited metabolic diseases affecting protein and lipid glycosylation. CDG type Ili (COG5-CDG) is an autosomal recessive disorder characterized by developmental delay, hypotonia, and structural brain abnormalities, with variable ophthalmologic involvement. While strabismus has been commonly reported, detailed characterization of combined optic atrophy and retinal dystrophy in COG5-CDG is limited. We report two siblings with progressive visual impairment who were diagnosed with COG5-CDG through whole genome sequencing (WGS) after a negative focused ocular exome panel.

Description of Cases:

A 17-year-old female and her 7-year-old brother presented with developmental delay and progressive visual impairment. The female was diagnosed with bilateral nystagmus, optic atrophy, polymicrogyria, scoliosis, and bilateral macular atrophy. Visual acuity was 20/1600 OD and 20/2000 OS. Autofluorescence demonstrated central macular hypo-autofluorescence with a hyper-autofluorescent ring. The male presented with microcephaly and bilateral optic atrophy at 6 months, and later autism spectrum disorder, central retinal atrophy, sensory nystagmus, and sensory esotropia. Visual acuity in the brother was qualitatively assessed as good fix and follow to a 3-inch toy at 1 foot in either eye. Family history was otherwise negative for retinal, neuro-ophthalmologic, and neurodevelopmental disorders. Prior focused ocular exome panels (309 genes) were negative for both siblings. However, quad whole genome sequencing including both parents identified COG5 variants: a paternally inherited c.1415dup (p.G474Wfs*3) known pathogenic frameshift mutation and a maternally inherited c.417+4779A>G deep intronic variant of unknown significance, predicted to affect splicing (SpliceAI score 0.98). Given that the phenotype of both siblings was consistent with COG-related CDG, they were given a preliminary diagnosis pending RNA sequencing to assess pathogenicity of the intronic variant.

Conclusions, including unique features of the case:

This report illustrates the ophthalmologic manifestations of COG-related CDG, a rare genetic condition, and demonstrates the diagnostic advantage of WGS in patients with unexplained neuro-ophthalmologic disorders.

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Keywords: Genetic disease, Pediatric neuro-ophthalmology

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Demyelinating Disease Following TNF-Alpha Inhibitor Treatment for Vogt-Koyanagi-Harada Syndrome

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Introduction:

Studies have reported associations between TNF- α inhibitors and CNS demyelinating disease, although the underlying mechanism remains poorly understood. The association of multiple sclerosis (MS) and Vogt-Koyanagi-Harada (VKH) syndrome is rare, with T-cell-mediated autoimmunity implicated in the pathogenesis for both conditions. We present a case of a patient developing MS while on adalimumab for VKH.

Description of Cases:

58-year-old female with history of VKH characterized by bilateral panuveitis and serous retinal detachments presented with worsening vision loss despite improvement of ocular inflammation on IV methylprednisolone while on adalimumab. Visual acuity was LP bilaterally decreased from HM right eye and CF left eye. Pupils were minimally reactive to light. IOP was normal. Anterior chamber and vitreous cell improved to 1+ from 3+. Optic discs were not edematous. OCT of the retina showed improved choroiditis and serous detachment bilaterally. Oculomotor exam revealed a new left internuclear ophthalmoplegia. Laboratory workup was unremarkable. Lumbar puncture revealed normal opening pressure, CSF pleocytosis, 5 oligoclonal bands, and melanin-laden macrophages by cytology. MRI showed bilateral optic nerve T2/FLAIR hyperintensity and T2/FLAIR hyperintensities of the supratentorial and infratentorial white matter. The patient was diagnosed with MS, treated with IV methylprednisolone, and transitioned from adalimumab to rituximab. Visual acuity improved to 20/60 OD and 20/200 OS.

Conclusions, including unique features of the case:

Only one previous case of concurrent VKH and MS has been reported, and that patient was not treated with a TNF- α inhibitor. Adalimumab, a TNF- α inhibitor approved for uveitis, modulates cytokine-driven inflammation but has been linked to demyelinating events. Earlier studies, including a 1999 trial of lenercept, demonstrated exacerbation of MS with TNF- α blockade. Whether demyelination represents a de novo process or immune dysregulation in predisposed individuals remains uncertain. Clinicians should exercise caution when prescribing TNF- α inhibitors and consider baseline brain MRI prior to initiation.

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Keywords: Demyelinating disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Retina, Neuroimaging, Miscellaneous

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Contact Information: None provided.

Isolated Optic Neuropathy in Hematologic Malignancies: Diagnostic Challenges and Case Series

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Introduction:

Chronic lymphocytic leukemia (CLL) and other low-grade B-cell lymphomas are typically diagnosed by persistent lymphocytosis and characteristic immunophenotypes on flow cytometry (CD5+, CD19+, CD23+, low intensity CD20/surface Ig). Central nervous system (CNS) involvement, particularly isolated optic nerve infiltration, is rare and may present as the initial or sole manifestation of systemic disease. We describe three patients with a history of CLL or marginal zone lymphoma who presented with isolated optic neuropathy, emphasizing diagnostic and clinical considerations.

Description of Cases:

Patient 1, a 75-year-old female with marginal zone lymphoma, presented with unilateral optic disc edema as her initial sign of CNS infiltration. MRI revealed left intraorbital optic nerve enlargement and enhancement, and flow cytometry confirmed low-grade B-cell lymphoma despite negative cytology and zero CSF nucleated cells. Patient 2, an 89-year-old male with marginal zone lymphoma in leukemic phase, developed visual loss and optic disc edema despite unremarkable orbital MRI findings. CSF demonstrated zero nucleated cells and negative cytology, but flow cytometry detected clonal B cells, confirming CNS involvement despite normal cell counts. Patient 3, a 72-year-old male with long-standing CLL on Venetoclax, presented with right central scotoma. MRI showed no optic nerve enhancement, but CSF analysis demonstrated pleocytosis and cytology revealed atypical small lymphocytes. Flow cytometry confirmed lymphoma excluding giant cell arteritis.

Conclusions, including unique features of the case:

These cases demonstrate that isolated optic neuropathy can be the initial or only presentation of CNS infiltration in systemic lymphoma or leukemia, even in patients with stable disease. MRI may be inconclusive, emphasizing the critical role of lumbar puncture, particularly with cytology and flow cytometry—even when CSF cell counts are normal. Recognizing this atypical presentation is vital to avoid misdiagnosis and allow timely initiation of appropriate oncologic management. Clinicians should maintain a high index of suspicion for infiltrative optic neuropathy in patients with hematologic malignancies presenting with unexplained visual changes.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuropathy, Neuroimaging

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Grant Support: None.

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Somya Chowdhary¹¹ West Virginia University**Introduction:**

Cryptococcal meningoencephalitis is usually seen as an opportunistic infection in immunocompromised adults, can be fatal if untreated.

Description of Cases:

A 54-year-old Caucasian female presented to ER in December 2024 with headaches and dizziness. Initial brain imaging was unremarkable. On February 12, 2025, a diagnostic lumbar puncture confirmed cryptococcal meningitis. She was treated with IV ceftriaxone, followed by oral antifungal therapy with fluconazole. Brain MRI with and without contrast revealed multiple areas of meningeal enhancement. In March 2025, she underwent a neuro-ophthalmic examination due to pounding headaches and whooshing sounds when bending forward. Best-corrected visual acuity (BCVA) was 20/30 in the right eye (OD) and 20/25 in the left eye (OS), Color vision 14/14 OD and 12/14 OS. Visual fields were constricted, and grade 3 papilledema was noted. An urgent MRI demonstrated multiple ring-enhancing lesions and embolic infarcts consistent with cryptococcomas. She was admitted and underwent ventriculoperitoneal (VP) shunting for hydrocephalus secondary to ventriculitis from cryptococcal meningitis. Fluconazole therapy was continued under infectious disease (ID) supervision. In June 2025, she re-presented with altered mental status and a left third nerve palsy was noted. The VP shunt was tapped and tested positive for cryptococcal antigen. She received intrathecal amphotericin B. A brain MRI on June 2 showed decreased size of the previously noted cryptococcal lesions. Her cognition gradually improved, and on follow-up neuro-ophthalmology evaluation, the left third nerve palsy persisted but was managed with prism glasses. She continues to improve clinically; her VP shunt is tapped every six weeks, looking for cryptococcal antigen. Notably, she still owns the chicken coop

Conclusions, including unique features of the case:

We report an unusual case of recurrent cryptococcal meningitis in a 54-year-old female, complicated by secondary hydrocephalus and a left third cranial nerve palsy. The patient received intrathecal amphotericin B, which was associated with notable clinical improvement, including resolution of some neurological symptoms.

References: None provided.

Keywords: Neuro-ophth & infectious disease (eg, AIDS, prion), Neuroimaging

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What's All The Hype(rtension) About? Is It Really Idiopathic?

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Introduction:

There are various, potentially life-threatening, etiologies of papilledema, necessitating a comprehensive evaluation for the cause of the intracranial hypertension (IH). When no cause is found, a diagnosis of idiopathic intracranial hypertension (IIH) is made. However, when there is no clinical improvement despite appropriate therapy, it can be extremely challenging to avoid internal biases (anchoring and availability biases), and to repeat the work-up looking for alternate diagnoses.

Description of Cases:

A 56-year-old non-obese male with headaches, transient visual obscurations, blurry vision, and pulsatile tinnitus presented to the emergency department after being found to have bilateral disc edema. Neuroimaging found sequelae of IH. Lumbar puncture showed an opening pressure of 43 mmHg with bland CSF. He was diagnosed with IIH, based on negative work-up and a recent 20-pound weight gain (BMI 27.4). He was started on acetazolamide (1000 mg BID) with resolution of his papilledema. Due to recurrent papilledema with attempted discontinuation of acetazolamide and worsening papilledema with re-initiation of acetazolamide, he underwent a repeat work-up, which revealed a posteriorly draining right transverse sinus dural arteriovenous fistula (dAVF) and stenosis of the left transverse sinus. He underwent left transverse sinus stenting and gamma knife radiosurgery for his dAVF. His symptoms and papilledema resolved. His acetazolamide was discontinued, and his papilledema did not re-occur.

Conclusions, including unique features of the case:

Although he was an atypical demographic for IIH, work-up for typical and atypical causes of IH was initially unremarkable, and he was diagnosed with IIH. However, due to an unusual course, his work-up was repeated and the underlying etiology of his IH, a dAVF, was identified. He then received definitive treatment. It can be challenging to avoid anchoring and availability bias in IIH, especially when a previous comprehensive workup was unremarkable, however we must be vigilant in our search for alternate causes for IH when the clinical course deviates from the expected.

References: None provided.

Keywords: High intracranial pressure/headache, Neuroimaging, Pseudotumor cerebri

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The Eye Reveals ALL: Optic Perineuritis with concurrent Central Retinal artery and Vein occlusion as a manifestation of Acute Lymphoblastic Leukemia Relapse

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Introduction:

Ocular involvement in B-cell acute lymphoblastic leukemia (B-ALL) with acute painful vision loss secondary to leukemic infiltration or secondary vascular complications is very uncommon. The co-occurrence of optic nerve involvement with simultaneous central retinal artery occlusion (CRAO) and central retinal vein occlusion (CRVO) is exceedingly rare overlap of neuro-ophthalmic and retinal manifestations in ALL. This case highlights a unique manifestation of ALL relapse with vision loss secondary to infiltrative optic perineuritis with concurrent CRAO and CRVO despite persistently negative minimal residual disease (MRD) studies.

Description of Cases:

A 71-year-old woman with history of intraductal breast carcinoma and Philadelphia chromosome-positive B-ALL on intrathecal and oral chemotherapy presented 15 months into treatment with right eye pain and floaters progressing to complete vision loss over 24-hours. Examination revealed severe optic disc edema bilaterally, foveal cherry red spot and diffuse dot and blot hemorrhages in the right eye. Imaging studies demonstrated bilateral perineural enhancement greater on the right, outer retinal edema and arterial filling defect in the right eye. Initial cerebrospinal fluid analysis (CSF) was negative; however, repeat large-volume analysis six weeks later showed B-lymphoblasts, confirming intracranial relapse. Prior to the presentation, Bone marrow and CSF MRD studies have remained negative and fluorescence in situ hybridization (FISH) analysis for BCR/ABL1 revealed a single dual-fusion cell, which is below the diagnostic threshold.

Conclusions, including unique features of the case:

This case illustrates an uncommon presentation of leukemic ocular relapse manifesting as optic perineuritis with concurrent retinal vascular occlusions. Neuro-ophthalmic findings preceded systemic confirmation of relapse and underscored the importance of high clinical suspicion for leukemic relapse in patients with new ocular symptoms despite frequent nonrevealing systemic MRD studies. This case also highlights the potential diagnostic significance of low-level FISH positivity, which may herald occult disease activity.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Orbit/ocular pathology, Tumors, Retina, Vascular disorders

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Bilateral Eyelid Swelling And Leg Rash In An 86-Year-Old Man

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Introduction:

VEXAS (Vacuoles, E1 enzyme, X-linked, Autoinflammatory, Somatic) syndrome is a newly recognized, multi-system inflammatory disorder typically affecting older men, caused by somatic ubiquitin-activating enzyme 1 (UBA1) mutations. Ocular involvement occurs in ~48% of cases (1), including periorbital edema, conjunctivitis, orbital inflammation, uveitis, episcleritis, scleritis, optic neuritis, and giant cell arteritis-like symptoms (2-5).

Description of Cases:

An 86-year-old man presented with right followed by left eyelid swelling and blurry vision for 2 days. He had a history of fevers and right leg cellulitis on day 7 of oral cefadroxil. On examination he was febrile and had petechia coalescing into purpuric patches on bilateral lower extremities in a background of pitting edema. Visual acuity was 20/40 OD and 20/20 OS with normal pupil response. Exam showed bilateral periorbital edema, erythema, conjunctival injection and chemosis, right worse than left. There was limitation to eye movement in all directions in the right eye. Fundus exam was normal bilaterally. He was initially diagnosed with preseptal cellulitis, with differentials including orbital inflammation, carotid-cavernous fistula, and allergic ocular disease. He was admitted for IV antibiotics and investigations. CT orbits was unremarkable. Inflammatory markers were elevated (ESR 140 mm/min, CRP 180 mg/dL); ANCA, IgG4, ACE, and ANA were negative. MRI brain and orbits with contrast showed mild optic nerve sheath enhancement (right>left). Skin biopsy revealed leukocytoclastic vasculitis. PCR testing confirmed a UBA1c.121A>G; p.Met41Val mutation. Additional findings included macrocytic anemia, subsegmental pulmonary embolism, possible Raynaud's phenomenon, and chondritis of the nose bridge. He was diagnosed with VEXAS syndrome and treated with prednisone, later transitioned to tocilizumab, with improvement of orbital and skin symptoms.

Conclusions, including unique features of the case:

The initial ocular presentation of VEXAS syndrome can be puzzling, mimicking other eye conditions including orbital cellulitis or cavernous sinus disease. Multidisciplinary collaboration is key to establishing the diagnosis.

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Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Genetic disease, Orbit/ocular pathology

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Introduction:

Isolated sphenoid sinus inflammatory disease (ISSID) is a rare entity that includes sphenoid sinusitis, sphenoid mucocoele and fungal infection. The sphenoid sinus proximity to the cavernous sinus, optic nerve, internal carotid artery and cranial nerves III-VI, makes neuro-ophthalmic manifestations an important key to early diagnosis. The following cases represent some of the neuro-ophthalmic manifestations of ISSID.

Description of Cases:

Case number 1 73 years old female, complained of new deep seated headache and blurred vision. Ophthalmic examination revealed intact optic nerves function and a mild right abduction deficit, also demonstrated on Hess screen test. Imaging was performed; an isolated right sphenoid sinusitis was diagnosed. The patient was treated with intravenous antibiotics and endoscopic sinus surgery. Symptoms completely resolved and repeated Hess screen was normal. Case number 2 10 years old female, complained of right eye blurred vision and pain exacerbated with eye movements. Ophthalmic examination demonstrated only very mild decreased right visual acuity and red desaturation, and mild right optic nerve elevation, also noted on OCT-RNFL analysis. Computer Tomography illustrated right sphenoid sinus mucosal thickening, but diagnosis was delayed because of clinical suspicion of demyelinating disease. A Magnetic Resonance Imaging was performed; no demyelination plaques were illustrated. Afterwards, intravenous antibiotic treatment was initiated, and the patient completely recovered. Case number 3 65 years old female, complained of new binocular horizontal diplopia. Anamnesis revealed 6 years history of headaches and a known right sphenoid opacity. Repeated imaging illustrated a sphenoid lesion that expanded and caused bone loss. Sphenoid Mucocoele was removed by endoscopic neurosurgery and diplopia resolved.

Conclusions, including unique features of the case:

ISSID are relatively uncommon and as in our cases, are often not considered as the first “working diagnosis”. The keys to diagnosis and prevention of serious complications are familiarity with presentation of sphenoid sinus disease, high index of suspicion, and multidisciplinary approach.

References: 1. Chen L, Jiang L, Yang B, Subramanian PS: Clinical features of visual disturbances secondary to isolated sphenoid sinus inflammatory diseases. *BMC Ophthalmol* 17(1): 237, 2017. DOI: 10.1186/s12886-017-0634-9 2. Wang ZM, Kanoh N, Dai CF, Kutler DI, Xu R, Chi FL, Tian X. Isolated sphenoid sinus disease: an analysis of 122 cases. *Ann Otol Rhinol Laryngol.* 2002;111:323–7 3. El Mograbi, A. and Soudry, E. (2017), Ocular cranial nerve palsies secondary to sphenoid sinusitis. *World Journal of Otorhinolaryngology - Head and Neck Surgery*, 3: 49-53. <https://doi.org/10.1016/j.wjorl.2017.02.001> 4. Coexistent Optic Neuritis and Isolated Acute Sphenoid Sinusitis. MG Rajiniganth, Usha R Kim, Mahesh Kumar *Clinical Rhinology: An International Journal*, September-December 2009;2(3):47-50 5. Moorman CM, Anslow P, Elston JS: Is sphenoid sinus opacity significant in patients with optic neuritis? *Eye (Lond)* 13(1): 76-82, 1999. DOI: 10.1038/eye.1999.15 6. Hejazi N, Witzmann A, Hassler W. Ocular manifestations of sphenoid mucocoeles: clinical features and neurosurgical management of three cases and review of the literature. *SurgNeurol* 2001;56:338–343

Keywords: Ocular motility

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A Case Of Severe Panuveitis And Leptomeningeal Inflammation Presenting As A Manifestation of Neuro-Behcet's Disease

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Introduction:

Behçet's Disease (BD) is a multisystem vasculitis characterized by mucocutaneous, ocular, vascular, and neurological involvement. Ocular manifestations, particularly uveitis, are common and can lead to significant visual impairment. Neuro-Behçet's Disease (NBD), a rare but severe neurological complication of BD, may co-occur with or follow ocular symptoms. We present a case highlighting a presentation of severe panuveitis and optic perineuritis as the initial symptoms leading to a diagnosis of NBD.

Description of Cases:

A 44-year-old caucasian male with history of oral and genital ulcers and recurrent red eye presented with unilateral panuveitis and scleritis. Ophthalmic exam was 20/50 in the right eye and 20/70 in the left eye, positive for severe bilateral panuveitis. There was no hypopyon. The patient was admitted, and MRI revealed bilateral scleritis and optic perineuritis, and multi-lobe leptomeningeal enhancement. Meningeal biopsy revealed nonspecific focal inflammation without granulomas. Cerebrospinal fluid analysis showed elevated protein and lymphocytic pleocytosis. HLA-B51 testing was positive. Fluorescein angiogram was negative for occlusive vasculitis. Given the clinical history and inpatient work-up, a diagnosis of Neuro-Behçet's Disease was made using the International Criteria for Behçet's Disease. The patient was treated with high-dose IV methylprednisolone followed by infliximab, leading to clinical stabilization and complete visual and neurological recovery.

Conclusions, including unique features of the case:

This case highlights the unique aspects of Neuro-Behçet's Disease in a patient initially presenting with scleritis, panuveitis, optic perineuritis, and leptomeningeal inflammation. Histology of brain lesions showed predominantly necrotic tissue with focal inflammation. Clinical history and labs were consistent with Neuro-Behçet's disease. Early diagnosis and aggressive immunosuppressive therapy are crucial in preventing permanent visual and neurological deficits.

References: None provided.

Keywords: Vascular disorders, Retina, Orbit/ocular pathology

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Contact Information: None provided.

Adult polyglucosan body disease presenting with progressive visual field loss

Allison Valerius¹, Deena Tajfirouz¹, Kevin Chodnicki¹, Stephanie Syc-Mazurek¹, Eoin P. Flanagan¹, Lisa Schimmenti¹, Ryan Walsh², John Chen¹

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Introduction:

Adult polyglucosan body disease (APBD) is a rare glycogen metabolism disorder due to pathogenic variants in the GBE1 gene. Presenting symptoms include peripheral neuropathy, autonomic dysfunction and spastic paraparesis. We report a patient with APBD with an atypical presentation of isolated visual field loss.

Description of Cases:

A 45-year-old female patient presented for progressive visual field loss. At age 35, she underwent myopic LASIK surgery with post-surgical testing notable for asymptomatic visual field loss resulting in a diagnosis of normal tension glaucoma. RNFL thickness was decreased with a CTD ratio of 0.65. Repeat ophthalmologic exams in the following years noted progressive field loss. At age 43, she underwent an ExPress shunt in the left eye for presumed normal tension glaucoma. She also reported lower extremity tingling/weakness. She was referred to neuro-ophthalmology for progressing visual field loss despite glaucoma management. Visual fields showed severe constriction OU. The optic nerves were cupped and pale. She had diffuse hyperreflexia. MRI brain showed multiple nonenhancing T2 hyperintensities in the brain and dorsal column of the cervical spine. Broad CSF, autoimmune and nutritional studies were unrevealing. Given optic nerve pallor, constellation of other neurologic symptoms and MRI abnormalities, whole genome sequencing was pursued. Two pathogenic variants in the GBE1 gene were identified, consistent with a diagnosis of APBD. Reported neuro-ophthalmologic complications of APBD include optic neuropathy, gaze palsies, and disorders of higher cortical visual function, but this was atypical given the vision loss started in isolation. While she later developed symptoms typical of APBD, this did not occur until 8 years after the onset of vision loss. Rather than central vision loss characteristic of genetic conditions affecting the optic nerves, the patient's visual field loss was peripheral and mimicked glaucoma.

Conclusions, including unique features of the case:

Our case demonstrates that progressive peripheral visual field loss may be the initial presenting symptom of APBD.

References: None provided.

Keywords: Genetic disease, Neuroimaging, Optic neuropathy, Visual fields

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Contact Information: None provided.

Transverse Venous Sinus Compression By Encephalocele As A Rare Cause Of Elevated Intracranial Pressure

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Introduction:

Primary causes of intracranial hypertension may vary and can present with symptoms similar to idiopathic intracranial hypertension. In patients of a certain demographic, this overlap can lead to diagnostic confusion. Structural causes of intracranial hypertension have been described including space occupying lesions, hydrocephalus, and various venous pathologies. These include cerebral venous sinus thromboses, intrinsic arachnoid granulations, and extrinsic compression of the venous sinus.

Description of Cases:

We present a case of elevated intracranial pressure due to compromised venous return from compression caused by encephalocele, as well as a review of the relevant literature. An 18 year old female with no significant past medical history and a BMI of 23 experienced 3 weeks of severe headache and transient visual obscurations. She was examined by an optometrist and found to have severely swollen optic nerves with peripapillary nerve fiber layer hemorrhages. Automated perimetry revealed enlarged blind spots and mild, diffuse depression. Brain MRI revealed no space occupying lesions or hydrocephalus, but did show a right dominant transverse sigmoid sinus with focal compression from an encephalocele. A lumbar puncture was done and showed a pressure of 43 cmH₂O with a normal CSF profile. She underwent urgent venous sinus manometry and stenting across the encephalocele-induced stenosis, which provided significant improvement in headaches and visual symptoms. Papilledema rapidly improved and completely resolved over a period of two months.

Conclusions, including unique features of the case:

IIH is the most common cause of elevated intracranial pressure and papilledema in women of childbearing age. However, in cases with atypical features, other structural causes of elevated ICP need to be considered. Compromise of intracranial venous return can result in elevated intracranial pressure. Extrinsic compression of the transverse sigmoid sinus by encephalocele has been only rarely reported in the literature, and venous sinus stenting can be an effective treatment to normalize intracranial pressure and limit risk of vision loss.

References: None provided.

Keywords: High intracranial pressure/headache, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Contact Information: None provided.

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Introduction:

Although uncommon, perioperative visual loss after intracranial tumor surgery can occur, particularly in patients with preexisting compressive optic neuropathy. When the optic nerve and retina are already compromised by chronic ischemic or compressive injury, even minimal perioperative vascular disturbances may precipitate irreversible visual loss. We report two patients who developed postoperative retinal and optic nerve ischemia. This report highlights the importance of comprehensive preoperative ophthalmic assessment, awareness of potential visual risks during neurosurgical procedures, and recognition of predisposing factors associated with postoperative vision decline.

Description of Cases:

Case 1: A 42-year-old man presented with bilateral optic disc swelling and peripheral visual field constriction associated with a right frontal mass. Preoperative visual acuity (VA) was 0.4/0.9 (OD/OS) and optical coherence tomography (OCT) demonstrated marked bilateral optic disc edema. The day after neurosurgical resection, his right-eye VA declined to light perception with a fixed, dilated pupil. Fundus examination revealed retinal whitening and a cherry-red spot, consistent with central retinal artery occlusion. The right eye showed optic disc pallor and complete visual field loss. Case 2: A 43-year-old man presented with bilateral proptosis, left-eye ophthalmoplegia, and decreased visual acuity due to an orbital-apex meningioma. Preoperative VA was 1.0/0.3 (OD/OS), with near-complete visual field loss and temporal optic disc pallor in the left eye. Postoperatively, his left eye exhibited further visual decline to light perception, with a fixed, dilated pupil and total ophthalmoplegia. Fundus examination and OCT demonstrated diffuse optic disc pallor and generalized thinning of the retinal nerve fiber and ganglion cell layers in the left eye.

Conclusions, including unique features of the case:

These observations emphasize the importance of thorough preoperative neuro-ophthalmic evaluation for baseline documentation and patient counseling regarding the likelihood of visual recovery. The unexpected postoperative visual deterioration underscores the need for heightened vigilance for perioperative vascular or ischemic insults, especially among patients with preexisting optic nerve compromise.

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Keywords: Tumors, Optic neuropathy

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Cavernous Sinus Thrombosis-Related Central Retinal Vein Occlusion: A Case Report With Favorable Outcomes

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Introduction:

The most common ocular complications of cavernous sinus thrombosis (CST) include ophthalmoplegia, proptosis, chemosis, periorbital edema, and vision loss. Vision loss may result from ischemic or compressive optic neuropathy, elevated intraocular pressure, or retinal vessel occlusion related to venous stasis (1,2). Persistent ophthalmoplegia or irreversible vision loss occur in one-third of cases (2). Early recognition and multidisciplinary management are essential to reduce morbidity (3).

Description of Cases:

A 75-year-old man with a history of obesity was referred to our clinic following hospitalization for acute left-eye pain, proptosis, and decreased vision. Eight months earlier, he had a transient episode of diplopia that resolved spontaneously, and in the preceding two months, he developed headaches. Three weeks before the presentation he was diagnosed with CST and started appropriate management. He also had ocular hypertension in the left eye, controlled with topical brinzolamide. At his first ophthalmic evaluation, best-corrected visual acuity was 20/20 OD and 20/50 OS, with a 3+ relative afferent pupillary defect, marked episcleral vessel tortuosity, macular hemorrhages, cotton-wool spots, and 360° venous congestion, consistent with central retinal vein occlusion (CRVO) secondary to CST. During follow-up, vision progressively improved, reaching 20/25 OS by two months and 20/20 by five months, with normal OCT and visual field findings and minimal residual retinal and episcleral vessel tortuosity that improved with low-dose brimonidine.

Conclusions, including unique features of the case:

Impaired orbital venous drainage from CST leads to venous stasis, elevated orbital pressure, and retinal congestion that may cause secondary CRVO. Prompt recognition of CST-related CRVO, an exceedingly rare condition, is crucial as timely management can yield excellent visual and structural recovery (1,4,5). Early multidisciplinary care and vigilant follow-up are key to favorable outcomes even after severe onset.

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Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Vascular disorders, Retina

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Bilateral Homonymous Superior Quadrantanopia and Cerebral Achromatopsia Following Occipitotemporal Hemorrhages Secondary to Traumatic Brain Injury: A Case Report

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Introduction:

Homonymous visual field defects and acquired color vision loss are uncommon but diagnostic outcomes of occipitotemporal brain injury. These cortical disorders can mimic optic neuropathies, leading to misdirected workups if the lesion localization is not carefully assessed. Bilateral congruent superior quadrantanopias (pie-in-the-sky defects) localize to the inferior optic radiations within the temporal lobes. Injury to the ventral occipitotemporal cortex can produce cerebral achromatopsia. This is an acquired loss of color perception. The occurrence of bilateral superior quadrantanopia and cerebral achromatopsia is rare and often reflects bilateral involvement of the posterior cerebral artery. Such findings can arise after trauma or hemorrhage but are easily overlooked in patients initially presenting with retinal or optic nerve findings.

Description of Cases:

A 60-year-old man with HTN, diabetes, and a recent head injury presented with dimming of vision and difficulty distinguishing colors. He described needing to tilt his head upward to view objects directly ahead. Ocular examination revealed visual acuity of 20/40 OD and 20/200 OS, normal pupils without a relative afferent defect, and intact optic discs. Color vision testing showed 1/11 Ishihara plates correct in each eye. Visual field testing demonstrated bilateral superior homonymous quadrantanopia, consistent with lesions involving the inferior optic radiations. Optical coherence tomography of the retinal nerve fiber layer was normal. Brain MRI revealed bilateral occipitotemporal intraparenchymal hemorrhages consistent with cortical visual pathway injury. He required a decompressive craniotomy and middle meningeal artery embolization. Visual acuity improved, though his superior field loss and profound color vision impairment persisted, consistent with residual cortical damage.

Conclusions, including unique features of the case:

This case illustrates how bilateral occipitotemporal hemorrhages from TBI can produce both homonymous superior quadrantanopia and cerebral achromatopsia without optic neuropathy. Recognizing cortical causes of bilateral visual loss is essential to prevent misdiagnosis. Early identification and multidisciplinary management can optimize neurological outcomes and functional adaptation for patients with cortical visual disorders.

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Keywords: Visual fields, Trauma, Non-organic visual disorders

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Blindness By Backflow: Progressive Visual Loss From Metastatic Prostate Cancer Via Batson's Plexus Causing Elevated Intracranial Pressure

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Introduction:

Progressive visual loss is an uncommon but serious complication in patients with advanced malignancies, often signaling metastatic spread to the central nervous system or orbit. In the context of metastatic prostate cancer, visual impairment can rarely be due to venous outflow obstruction via spread from Batson's plexus, a series of valveless large veins between the skull base to the coccyx. Typically, visual loss secondary to prostate results from direct invasion of the optic canal and nerve rather than venous outflow obstruction (resulting in raised intracranial pressure (ICP) and papilledema). This case study highlights the unique entity of metastatic disease to the intracranial venous system, leading to irreversible vision loss.

Description of Cases:

A 67-year-old male with metastatic prostate adenocarcinoma presented with progressive painless bilateral vision loss over 5 months. Vision decline began gradually OD and intermittently OS, before rapidly causing complete vision loss OS upon awakening. Visual loss OD continued over the subsequent months. MRI Brain revealed dural and calvaria thickening along the right temporal and occipital bones with narrowing of the superior sagittal sinus and a right posterior fossa mass. Lumbar puncture revealed an opening pressure (46 cm H₂O) with normal CSF indices and no malignant cells. Biopsy of the right parietal mass confirmed metastatic prostate adenocarcinoma. Exam was significant for APD OS and papilledema OD. Treatment included IV methylprednisolone (IVMP), Diamox, and a ventriculoperitoneal (VP) shunt to preserve vision (20/200 OD). Optic neuropathy occurred secondary to venous outflow compromise with significant papilledema rather than direct optic nerve infiltration.

Conclusions, including unique features of the case:

This case demonstrates the unusual occurrence of optic neuropathy due to venous sinus compression and elevated ICP with severe papilledema from metastatic prostate cancer rather than optic nerve canal involvement. The likely route of spread was via Batson's plexus. Understanding these alternative mechanisms is critical, as prompt management may help preserve remaining vision.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuropathy, Neuroimaging

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A Peripheral H.I.N.T.S.-Plus Exam From a Central Vascular Cause: A Unique Case of Acute Vestibular Syndrome

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Introduction:

The Head Impulse, Nystagmus, Test of Skew, and Hearing (HINTS+) examination is highly sensitive and specific for differentiating peripheral vs. central causes of Acute Vestibular Syndrome. However, in rare circumstances a peripheral-appearing examination may still have a central cause.

Description of Cases:

A 39 year-old man presented to the emergency department with sudden-onset headache and spontaneous continuous vertigo after exercise. Examination revealed left-beating nystagmus in all directions of gaze, catch-up saccades with head-impulses to the right, no skew deviation, and no hearing loss. The remaining examination was normal. Despite the peripheral-appearing exam, a central source was suspected given the severe headache and onset after exercise. MRI and MR-angiogram showed no diffusion restriction, but did reveal nonopacification and narrowing of the right cervical vertebral artery with corresponding intramural hematoma on dissection protocol images. Aspirin 81mg daily was administered. His symptoms significantly improved overnight, and he was discharged the following day. Days later he reported his symptoms had nearly resolved. He had no spontaneous nystagmus with fixation and left-beating nystagmus with fixation removed. Caloric testing showed an 87% unilateral weakness in the right ear, and video head-impulse testing showed scattered catch-up saccades on head thrust to the right. There were no central findings on the remainder of his video-oculography or examination, and his hearing was symmetrically normal.

Conclusions, including unique features of the case:

This case is a rare example of Acute Vestibular Syndrome with HINTS+ exam indicating a peripheral vestibular impairment, but originating from a central vascular source. Labyrinthine infarction is a possible cause of acute vestibular syndrome, but is classically associated with ipsilateral hearing loss. In this case, we propose an embolus traversed through the labyrinthine artery and occluded the anterior vestibular artery, infarcting the superior and lateral semicircular canals and utricle while sparing the cochlea. This case highlights the importance of a careful history despite an otherwise reassuring examination.

References: None provided.

Keywords: Vestibular disorders, Stroke, Vascular disorders

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HTLV-1–Associated Adult T-Cell Leukemia/Lymphoma Presenting with Predominant CNS Involvement and Bilateral Sixth Nerve Palsies: A Case and Literature Review

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Introduction:

Human T-lymphotropic virus type I (HTLV-1) is an oncogenic retrovirus associated with adult T-cell leukemia/lymphoma (ATL) and HTLV-associated myelopathy. Neurological involvement in ATL is uncommon and typically occurs in advanced, disseminated disease. CNS-predominant presentations without overt systemic manifestations are exceedingly rare and diagnostically challenging. We present a case of HTLV-1–associated ATL initially manifesting with isolated cranial neuropathies and leptomeningeal involvement.

Description of Cases:

A 56-year-old Caribbean man with hypertension and hyperlipidemia presented with one month of progressive binocular diplopia. The diplopia was initially intermittent and horizontal, later becoming constant with new positional headaches. Neurological examination revealed bilateral sixth nerve palsies without other focal deficits or systemic findings. Brain MRI demonstrated diffuse leptomeningeal FLAIR hyperintensity over the cerebral hemispheres (left greater than right), and lateral midbrain, with mild enhancement of the distal optic nerves. MRI of the spine revealed leptomeningeal enhancement along left lumbar nerve roots (L1–L3). Cerebrospinal fluid analysis showed glucose 23 mg/dL, protein 126 mg/dL, and 183 nucleated cells (mononuclear predominant). Cytology revealed atypical lymphoid elements, and flow cytometry identified an aberrant CD4⁺CD8⁺ T-cell population consistent with post-thymic T-cell neoplasia. IL-2 receptor was elevated, and both ELISA and Western blot confirmed HTLV-I/II antibody. Although initial peripheral studies were normal, repeat testing showed circulating abnormal T cells, and bone marrow biopsy confirmed a clonal T-cell lymphoproliferative disorder consistent with ATL. The patient remained without lymphadenopathy, cytopenias, or constitutional symptoms.

Conclusions, including unique features of the case:

CNS-predominant presentations of HTLV-1–associated ATL are exceedingly rare, as most cases present with systemic disease. This case demonstrates that neurological signs, such as diplopia from cranial neuropathies, can be the initial and most prominent manifestation. Recognizing this atypical pattern can prompt earlier cerebrospinal fluid analysis, targeted imaging, and HTLV testing, enabling timely diagnosis and hematologic evaluation before systemic progression. Awareness of such presentations may help clinicians identify and manage these uncommon cases more effectively.

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Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Neuro-ophth & infectious disease (eg, AIDS, prion), Neuroimaging, Ocular motility

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Contact Information: None provided.

Unmasking the Migraine Genome: Insights from a patient with intermittent hemifield loss and severe migraine headache.

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Introduction:

Hemiplegic migraine (HM) is a rare and genetically heterogeneous condition that usually starts in early life. In neuro-ophthalmology, it represents a diagnostic challenge because its visual and neurological manifestations can resemble other acute disorders. It may occur as familial or sporadic form, with mutations in the CACNA1A gene being the most frequently implicated in familial HM type 1 (FHM1). To date, over 476 pathogenic and likely pathogenic variants have been reported in the ClinVAR database, but due to the genetic complexity of this disorder a clear genotype–phenotype association has not yet been established.

Description of Cases:

A 36-year-old woman presented with recurrent episodes of severe headache associated with hemifield vision loss. Neuro-ophthalmic examination during the attack revealed a right homonymous hemianopia or monocular hemifield loss with normal optic discs and visual acuity. Brain MRI showed no mass lesion or demyelination. Her medical history included complicated migraines since adolescence and transient episodes of quadriparesis and right hemibody dysesthesia. Family history was notable for migraines, speech delay, and seizure disorders in first-degree relatives. Given the atypical course and negative neuroimaging, a genetic etiology was considered. Whole exome sequencing identified an autosomal dominant heterozygous CACNA1A variant, c.6616C>T (p.Arg2206Trp), classified as a variant of uncertain significance (VUS). However, pathogenicity analyses using the HumDiv and HumVar prediction models both suggested a deleterious effect, reporting scores of 0.997 (sensitivity=0.41; specificity=0.98) and 0.927 (sensitivity=0.67; specificity=0.91), respectively. These findings support the likely pathogenic role of the CACNA1A variant and provide genetic confirmation consistent with FHM1.

Conclusions, including unique features of the case:

This case underscores the importance of comprehensive clinical and molecular evaluation in patients with recurrent neurological deficits and complex migraine phenotypes. When routine imaging and laboratory studies are inconclusive, genetic testing can reveal underlying genetic disorder where the phenotype-genotype correlation analysis is crucial to identify novel variants and a better understanding of difficult cases.

References: None provided.

Keywords: Genetic disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Visual fields

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Ischemic Painless Optic Neuritis as the Presenting Symptom of Neuromyelitis Optica Spectrum Disorder

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Introduction:

We will describe a case of atypical optic neuritis with secondary posterior ischemic optic neuropathy (PION) leading to the diagnosis of neuromyelitis optica spectrum disorder (NMOSD). PION describes a vascular insult to the optic nerve posterior to the optic nerve head. Typically, non-arteritic PION is secondary to arterial thrombotic or watershed ischemic injury particularly in perioperative patients. We describe an atypical case of PION secondary to severe edema associated with optic neuritis later confirmed to be aquaporin-4-positive NMOSD.

Description of Cases:

A 73-year-old woman presented with sudden-onset painless central vision loss in the left eye upon awakening. She denied scalp tenderness, jaw claudication, pain with eye movements, or dyschromatopsia. Given concern for giant cell arteritis, she was started on 1000 mg IV methylprednisolone. Neuro-ophthalmologic examination showed left relative afferent pupillary defect, decreased visual acuity (20/200 OS), and dyschromatopsia. Funduscopic examination was unrevealing for disc edema or evidence of retinal ischemia. MRI of the brain and orbits demonstrated restricted diffusion in the posterior half of the intraconal optic nerve with longitudinally extensive enhancement extending further posteriorly to the optic chiasm. MRI of the cervical spine did not show any lesions. Bilateral temporal artery biopsy was negative. Inflammatory markers, MOG-IgG, Lyme, ANA, and paraneoplastic antibodies were negative. Lumbar puncture showed elevated protein and normal WBC. Serum aquaporin-4 antibodies were positive (titer 1:1000). She was diagnosed with NMOSD. Mycophenolate mofetil was initiated, as the patient refused infusion treatment. Visual acuity improved to 20/40 at follow-up. Nine months later, she presented with optic neuritis of right eye consistent with and was started on intravenous therapy with inebilizumab.

Conclusions, including unique features of the case:

Painless monocular vision loss without optic disc edema is concerning for PION in older patients. Evidence of ischemia/restricted diffusion on neuroimaging should not mislead the clinicians from completing the work-up for causes of atypical optic neuritis such as NMOSD.

References: None provided.

Keywords: Demyelinating disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuritis, Optic neuropathy

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Introduction:

Follicular lymphoma (FL) is a low-grade malignancy that rarely spreads to the nervous system. We present a case of polycranial neuropathy secondary to spread of FL to the CSF.

Description of Cases:

An 85-year-old woman with a history of Follicular lymphoma (FL), thought in remission following treatment, developed diplopia one year after her diagnosis. Workup during an outside hospitalization included MRI brain, MRA head, and MRV head, which were reportedly normal. Following discharge, she lost sense of taste and touch on the right side of her tongue. An outside neurologist prescribed an oral prednisone taper for presumed inflammatory polycranial neuropathy. Symptoms improved, then worsened following the taper, prompting admission to our hospital. Neurologic exam revealed complete right ophthalmoplegia and ptosis, anisocoria, a right pupil that constricted poorly to light, right tongue deviation, and hypesthesia to pinprick over the right anterior tongue. The exam was otherwise normal. Repeat MRI brain showed enhancement of the right third cranial nerve, while spine MRI showed cauda equina enhancement suggestive of leptomeningeal disease. MRA head, MRV head, CRP, and ESR were unremarkable. Lumbar puncture was performed. CSF studies showed elevated protein (78 mg/dL) and abnormal flow cytometry (a CD10+ kappa-restricted B-cell population, consistent with clonal proliferation of FL). PET imaging showed hypermetabolic, enlarged axillary and right inguinal lymph nodes (SUV max 4.4), consistent with FL. Axillary lymph node biopsy showed FL without evidence of transformation to diffuse large B-cell lymphoma (DLBCL), matching the flow cytometry in the CSF and peripheral blood. Blood cytology revealed small lymphoma cells consistent with FL.

Conclusions, including unique features of the case:

Our case demonstrates that polycranial neuropathy secondary to spread of FL to the CSF can occur. In such cases, a discrepancy exists between clinical findings suggestive of more aggressive pathology and features of low-grade malignancy on cytometry, histology, and PET.

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Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Ocular motility

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Seronegative Myasthenia Gravis Characteristics in a Neuro Ophthalmology Clinic

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Introduction:

Myasthenia gravis (MG) is an autoimmune disorder of the neuromuscular junction, typically associated with acetylcholine receptor (AChR) or MuSK antibodies. A subset of patients lack detectable antibodies and are classified as seronegative MG (SnMG). Ocular presentations, ptosis and diplopia, are common and frequently seronegative, posing diagnostic challenges. Recognition of this subgroup in neuron-ophthalmology practice is essential for timely management.^{1,2}

Description of Cases:

We retrospectively reviewed 77 patients with SnMG presenting to a neuro-ophthalmology clinic from January 1, 2014 to January 1, 2023 (59 female, 18 male; mean age 57 years). Racial/ethnic distribution: 58 White, 13 Black, 4 Other, 1 Multiracial; 74 non-Hispanic, 3 Hispanic. Mean AChR-blocking value 14, modulating 3.64, binding 0.0446. Sixty-seven (87%) presented with ocular-only findings; ten were generalized at onset. Diagnosis was confirmed by single-fiber EMG in 41, Tensilon testing in 7, and clinical evaluation alone in 19.

Conclusions, including unique features of the case:

In this cohort of patients presenting to neuro-ophthalmology, SnMG predominantly affected middle-aged women and presented with isolated ocular findings. Despite negative antibody panels, SFEMG confirmed neuromuscular transmission defects in more than half of cases. These findings underscore that seronegativity does not exclude MG and that ocular SnMG may rely heavily on electrophysiologic or clinical confirmation.^{3,4}

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Keywords: Myasthenia

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Introduction:

Inherited mitochondrial optic neuropathies, such as Leber Hereditary Optic Neuropathy and Dominant Optic Atrophy, present with painless, progressive vision loss earlier in life. Nuclear gene mutations that affect mitochondrial function including FARS2 are typically associated with a spectrum of neurological syndromes. Isolated adult-onset optic neuropathy linked to dual nuclear and mitochondrial variants has not been previously reported.

Description of Cases:

A 27-year-old male presented with painless, progressive bilateral vision decline, and dyschromatopsia. Visual acuity declined to 20/60 OD and 20/80 OS, with severe loss of color vision (1/14 OD and 0/14 OS), on color plate testing. Humphrey visual fields 10-2 revealed bilateral cecocentral scotomas, and funduscopy revealed subtle bilateral temporal pallor. OCT demonstrated mild temporal RNFL thickening and significant GCL thinning, more pronounced OS. Extensive laboratory evaluation, including nutritional, autoimmune, infectious, and metabolic testing, and MRI of brain and orbits, were unremarkable. Genetic testing revealed a heterozygous pathogenic FARS2 variant (c.407 C>A), and a mitochondrial MT-CYB variant (m.14983 C>A) with ~58% heteroplasmy, with absent LHON mutations. The heteroplasmy level suggests sufficient mutant mtDNA to impair optic nerve mitochondrial function.

Conclusions, including unique features of the case:

This case represents adult-onset bilateral optic neuropathy associated with FARS2 mutation and MT-CYB second hit, with progressive cecocentral visual loss, severe dyschromatopsia, and GCL thinning. To our knowledge, it is the first reported instance of these variants presenting as isolated adult optic neuropathy. The findings highlight the importance of combined nuclear and mitochondrial genetic testing in unexplained progressive optic neuropathies and suggest a potential second hit effect from dual genetic variants on optic nerve vulnerability.

References: None provided.

Keywords: Genetic disease

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Contact Information: None provided.

EyeSpy Consults: A Neuro-Ophthalmology Survival App to Guide Trainee Approach to Common Consults

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Introduction:

Neuro-ophthalmology uniquely requires structured diagnostic reasoning and precision at the chiasmic intersection of neurology and ophthalmology. Qualities of well-rounded neurologists or ophthalmologists are partly demonstrated by a solid foundation in this subspecialty, emphasizing the importance of incorporating core neuro-ophthalmology competencies into both neurology and ophthalmology residency training. Currently, neuro-ophthalmology exposure is highly variable nationally for both ophthalmology and neurology residencies, contributing to lack of trainee confidence in approaching common neuro-ophthalmic consults. Readily accessible digital educational apps can strengthen foundational knowledge and help develop a structured approach. EyeSpy Consults is a mobile app in its development phase to guide both neurology and ophthalmology trainees in this matter, improving the timeliness and quality of patient care.

Description of Cases:

EyeSpy Consults is an interactive, app-based educational tool that focuses on how trainees should think through common neuro-ophthalmic consults. The app will be organized around three main entry points: by symptom, suspected diagnosis, or exam finding. Under “symptoms,” users can start with common presentations. For example, selecting vision loss will branch into transient versus persistent, then unilateral versus bilateral. It will then walk the trainee through key questions and explain why those questions matter, highlighting details that separate urgent from non-urgent cases. If trainees have a suspected diagnosis, they can navigate directly to conditions like migraine or optic neuritis. Each section will include brief summaries, recommended testing, and management pearls. The exam findings section will cover ocular signs such as anisocoria, providing structured guidance on how to interpret and manage these findings. The app will include the most common presentations, with emphasis on critical diagnoses not to miss. The tool will be piloted through both neurology and ophthalmology residents. Trainees will complete pre- and post-use surveys assessing their confidence level with these consults.

Conclusions, including unique features of the case:

EyeSpy Consults introduces an innovative framework, empowering trainees and improving neuro-ophthalmic care.

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Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Neuro-Ophthalmic Sequelae of Sports-Related Injuries: Mechanisms, Manifestations and Management

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Introduction:

Sports-related trauma remains a significant cause of neurologic and ophthalmologic morbidity worldwide. While the systemic consequences of athletic injuries are well-documented, the neuro-ophthalmic manifestations are often under-recognized and under-reported. Early identification and management are critical to preventing permanent visual and neurological deficits.

Description of Cases:

This descriptive review synthesizes existing literature on the epidemiology, mechanisms, clinical presentations, diagnostic approaches, and management strategies of neuro-ophthalmic injuries in sports. We analyzed peer-reviewed studies, clinical guidelines, and expert consensus on traumatic optic neuropathy, concussion-related visual symptoms, oculomotor nerve palsies, orbital fractures, and vascular events associated with sports participation.

Conclusions, including unique features of the case:

Neuro-ophthalmic injuries result from both direct head trauma and indirect forces such as whiplash and rotational acceleration. Common conditions include visual disturbances post-concussion, traumatic optic neuropathy, ocular motor dysfunction, and retinal/choroidal injuries. Imaging (MRI/CT), visual field testing, OCT, and electrophysiology are critical for diagnosis. Management requires a multidisciplinary approach, including acute care, vision rehabilitation, surgical intervention when necessary, and adherence to return-to-play protocols. Despite the use of protective equipment, limitations exist in fully preventing these injuries. Preventative strategies, including improved gear, athlete education, and conditioning, show promise in mitigating risk. Neuro-ophthalmic complications of sports injuries span a wide clinical spectrum with potentially lasting consequences. Increased awareness, prompt diagnosis, and comprehensive care are essential. Future research should focus on long-term outcomes, enhanced diagnostic tools, and rehabilitation innovations to optimize care for affected athletes.

References: None provided.

Keywords: Trauma

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Bilateral Ophthalmic Artery Occlusions Following Bilateral Middle Meningeal Artery Embolization for Subdural Hematomas

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Introduction:

Middle meningeal artery (MMA) embolization is increasingly prevalent for high-risk subdural hematomas (SDH).[1] Collaterals to major arteries must be avoided to prevent periprocedural stroke and vision loss.[2]

Description of Cases:

A 71-year-old female presented with left lower extremity weakness and speech difficulty. She had bilateral subacute SDHs with mass effect and underwent burr holes. CT demonstrated reduction in SDHs with residual fluid, and Neurosurgery recommended bilateral MMA embolization. Pre-embolization microcatheter angiograms demonstrated bilateral normal variant meningo-orbital arteries. Post-operatively, the patient awoke completely blind, right gaze deviation, and left facial droop. MRI brain showed numerous small foci of acute infarction throughout both hemispheres (R>L) suggestive of embolic phenomenon, and hyperintense right optic nerve. She had no light perception OU. Pupils were 5mm OD and 3mm OS, nonreactive. IOP was 15 mmHg OU, extraocular movements were full. Anterior examination was unremarkable. The right fundus exam revealed extreme optic disc pallor and ischemic peripheral retina, no cherry red spot, with complete lack of patency of all arterioles—demonstrating complete ophthalmic artery occlusion. The left optic disc was pink with sharp margins, and superior macular fovea-sparing whitening was thought to be BRAO, although with impaired vision out of proportion. Neuro-Ophthalmology and Retina confirmed NLP and no neovascularization.

Conclusions, including unique features of the case:

This patient had acute neurologic change with neuroimaging findings of an embolic shower and found to have small patent foramen ovale on TTE. Possible etiologies include retrograde travel of embolic particles from bilateral MMA embolization, or elsewhere traveling across the PFO. Notably, her aorta and carotids had no atherosclerosis. Cases of sudden vision loss after inadvertent ophthalmic artery embolization have been reported, particularly when embolization particles flow through anastomoses.[3] Review of her arteriograms revealed bilateral MMA blush, suggestive of the meningo-ophthalmic artery anatomical variant.[4] Neuro-interventionalists should avoid MMA embolization in patients with meningo-orbital branch anatomy visualized on microcatheter angiography.

References: 1. Liu, Ni, Zuo, et al. Middle meningeal artery embolization for nonacute subdural hematoma. *New England Journal of Medicine*. 2024;391(20):1901-1912. doi:<https://doi.org/10.1056/nejmoa2401201> 2. Rudy, Catapano, Jadhav, Albuquerque, Ducruet. Middle meningeal artery embolization to treat chronic subdural hematoma. *Stroke: Vascular and Interventional Neurology*. 2023;3(1). doi:<https://doi.org/10.1161/svin.122.000490> 3. Jauregui, Galetta. Ophthalmic artery occlusion: a rare, vision-threatening complication from middle meningeal artery embolization for subdural hematomas. *Journal of the Neurological Sciences*. 2025;471:123428. doi:<https://doi.org/10.1016/j.jns.2025.123428> 4. Bonasia, Smajda, Ciccio, Robert. Middle meningeal artery: anatomy and variations. 2020;41(10):1777-1785. doi:<https://doi.org/10.3174/ajnr.A6739>

Keywords: Stroke, Interventional neuroradiology, Neuroimaging

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Delayed Recanalization of A Coiled Ophthalmic Artery Aneurysm Presenting With Visual Pathway Compromise

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Introduction:

Ophthalmic artery aneurysms can present with visual loss due to direct compression of the optic apparatus, ischemia, or both. Endovascular coil embolization is often used to treat these aneurysms, particularly when dual antiplatelet therapy is contraindicated (1). However, recurrence remains a recognized risk, even years later (2). We present a rare case of late aneurysm recanalization with optic chiasm and lateral geniculate nucleus (LGN) compression, manifesting as profound vision loss.

Description of Cases:

A 77-year-old woman underwent coiled embolization of a 1.4 x 1.4 cm unruptured left ophthalmic artery aneurysm in September 2019 and was lost to follow-up. In 2025 she presented to Neuro-Ophthalmology with progressive bilateral visual. Visual acuity measured count fingers OD and 20/40 OS. Humphrey Visual Field (Standard 30-2) testing revealed a dense left homonymous hemianopsia OS, while OD testing was precluded due to poor visual acuity. OCT demonstrated severe temporal RNFL and ganglion cell layer (GCL) thinning OD and thinning at the inferior and superior poles OS, correlating with visual field findings. OCT demonstrated severe temporal RNFL and ganglion cell layer thinning OD and thinning at the poles OS, correlating with the field defect. Magnetic resonance imaging (MRI) of the orbits with and without contrast demonstrated recanalization of the previously treated left ophthalmic artery aneurysm with mass effect on both the optic chiasm and right LGN.

Conclusions, including unique features of the case:

This case highlights some important and unique aspects of delayed vision loss after coiled embolization. Late aneurysm recanalization can produce complex patterns of vision loss when both anterior and posterior visual pathways are compressed. Long-term imaging surveillance is essential, particularly for large or irregular aneurysms, and neuro-ophthalmic evaluation plays a key role in detecting clinically significant recurrence (3-5).

References: 1. Ospel JM, Brouwer P, Dorn F, Arthur A, Jensen ME et al. Antiplatelet Management for Stent-Assisted Coiling and Flow Diversion of Ruptured Intracranial Aneurysms: A DELPHI Consensus Statement. *AJNR Am J Neuroradiol*, 41, 1856-1862, 2020. 2. Ferns SP, Sprengers ME, van Rooij WJ, Rinkel GJ, van Rijn JC et al. Coiling of intracranial aneurysms: a systematic review on initial occlusion and reopening and retreatment rates. *Stroke*, 40, e523-e529, 2009. 3. Ahmad SS, Blair K, Kanukollu VM. Optic Atrophy. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing, 2025 Jan-. 4. Ahn JH, Cho YD, Kang HS, Kim JE, Cho WS et al. Endovascular treatment of ophthalmic artery aneurysms: assessing balloon test occlusion and preservation of vision in coil embolization. *AJNR Am J Neuroradiol*, 35, 2146-2152, 2014. 5. Chalouhi N, Daou B, Kung D, Zanaty M, Phillips JL et al. Fate of the Ophthalmic Artery After Treatment With the Pipeline Embolization Device. *Neurosurgery*, 77, 581-584, 2015.

Keywords: Vascular disorders, Neuroimaging, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Perimetry

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Bilateral Optic Disc Edema, Ophthalmoplegia, and Venous Congestion: A Case of Spontaneous Indirect Bilateral Carotid-Cavernous Fistula with Cavernous Sinus Thrombosis.

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Introduction:

Carotid-cavernous fistulas (CCFs) are abnormal arteriovenous shunts between the branches of the carotid and the cavernous sinus. Indirect (dural) CCFs may be insidious and initially resemble thyroid eye disease or orbital inflammation. Early recognition is imperative to avoid vision loss and neurological problems.

Description of Cases:

A 65-year-old woman with a history of breast cancer, recently diagnosed hypertension, and suspected obstructive sleep apnea presented to our institution with progressive bilateral vision loss, conjunctival injection, proptosis, ophthalmoplegia and tortuous episcleral vessels. Fundus examination revealed bilateral Optic disc edema. CT orbits revealed Extraocular Muscle Hypertrophy and moderate Proptosis. Brain MRI/MRA (9/15) were unremarkable, CTA (10/9) showed subtle left cavernous sinus venous enhancement without definite fistula. Digital subtraction angiography established the diagnosis of bilateral indirect CCFs (type D right, type C left) with bilateral cavernous sinus thrombosis, which precluded the opportunity to perform endovascular embolization. The patient was initiated on therapeutic anticoagulation and oculoplastic assessment was planned for possible superior orbital vein access.

Conclusions, including unique features of the case:

This rare case of spontaneous, indirect fistulas on both sides of the carotid-cavernous region, combined with a clot in the cavernous sinus, highlights how hard it is to make the diagnosis when non-invasive imaging doesn't give a clear answer. Key exam findings are bilateral conjunctival vascular congestion, proptosis, ophthalmoplegia, and optic disc edema. Awareness of these signs of bilateral involvement can guide in prompt angiographic evaluation. When thrombosis is limiting endovascular access medical management and other venous access routes may be considered. Neuro-ophthalmologists should retain high suspicion of CCF with similar presentations. Though noninvasive neuroimaging modalities dominate modern neuro ophthalmology, dedicated angiography may be necessary to achieve a diagnosis in such complex cases.

References: None provided.

Keywords: Interventional neuroradiology

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Grant Support: None.

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Stargardt's Disease Associates with Demyelization of the Central Nervous System: a Case ReportLepsa Zoric¹¹ UKCS, Eye Clinic, Belgrade; Faculty of Medicine, UPKM.**Introduction:**

Stargardt's disease is an inherited retinal disease that causes progressive loss of central vision. Stargardt disease is linked to loss of gray matter, but it is not described with demyelination of white matter.

Description of Cases:

An 18-year-old female patient was hospitalized at the UKCS Eye Diseases Clinic due to acute vision loss in the right eye, as an optic neuritis and retinal dominant drusen. Visual acuity in the right eye was 0.2, and in the left 0.8. Clinically, we revealed Stargardt's disease on the eye posterior pole, but signs of optic nerve were obvious, as well. Magnetic resonance imaging of the endocranium indicated the presence of multiple punctiform and focal lesions of the white matter of the brain. Whole-exome sequencing was performed, which showed the presence of two heterozygous pathogenic variants of the ABCA4 gene (c.5312+1G>A and c.5714+5G>A), which are associated with Stargardt macular degeneration type A heterozygous missense variant in the CLCN7 gene (c.718G>A, p.Gly240Arg) was also detected, which is associated with various entities such as autosomal dominant osteopetrosis, hypopigmentation with organomegaly, and delay in myelination and development. The presence of a pathogenic variant in the RBM8A gene (c.-21G>A) is associated with TAR syndrome. We describe clinical manifestations and course during two years of follow-up our patient

Conclusions, including unique features of the case:

This case might be interesting due to the association/simultaneous existence of Stargardt disease with demyelination disease, and predisposition and signs of some other disease which requires further genetic evaluation and continued follow-up by a neurologist.

References: None provided.

Keywords: Demyelinating disease, Retina, Neuroimaging

Financial Disclosures: The authors had no disclosures.

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Contact Information: None provided.

New Insights on AAV2-ND4 transfer Between Eyes: Post-Mortem Analyses in Leber Hereditary Optic Neuropathy Following Gene Therapy

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Introduction:

Lenadogene nolpharvec is an AAV2-based gene therapy (LNGT) for Leber hereditary optic neuropathy (LHON) patients carrying the m.11778G>A ND4 variant. All LNGT trials have demonstrated a bilateral effect after unilateral intravitreal injection. We report post-mortem ocular analyses in two patients who received LNGT in one eye and a sham injection in the other.

Description of Cases:

Post-mortem histopathological and molecular (ddPCR) analyses were performed on laser-captured retinal and optic nerve (ON) samples. Within 2 months of LNGT, both participants developed intraocular inflammation in the treated eye, which resolved within months. Both patients died for reasons unrelated to the clinical trial. Patient 1 had severe optic atrophy and loss of retinal ganglion cells (RGCs), while patient 2 was a milder case of LHON, with consistent preservation of RGCs and ON axons, with only the temporal fibers lost. In patient 1, an angiocentric lymphocytic chronic inflammation was noted in the ON head and temporal retina. No persistent inflammation was seen in patient 2. ND4 transgene copies were detected in RGCs and retinal pigment epithelium/photoreceptors, but also in vessels, choroid, meninges and ON in both eyes. A much lower level of ND4 was detected in the retina and ON of the untreated eye in both cases. AAV2-ND4 distribution in the treated eye was asymmetric in both patients, more prevalent in the macular/temporal hemiretina. In patient 2, a parallel gradient of ND4 was observed from the retina, in the anterograde direction, along both visual pathways (injected and sham), which decreased in the distal direction. Finally, ND4 was also detected in occipital and entorhinal cortex.

Conclusions, including unique features of the case:

The AAV2-packaged ND4 transgene diffuses to a small extent, from the injected retina to the contralateral uninjected eye. Results suggest alternative routes besides axonal and trans-synaptic, such as vascular and/or cerebrospinal fluid diffusion. The contralateral diffusion may partially explain bilateral effect of LNGT.

References: None provided.

Keywords: Optic neuropathy, Retina, Genetic disease

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Clinical Practice Guidelines for Managing Thyroid Eye Disease: A Systematic Review

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Introduction:

With growing understanding of pathophysiology and increasing treatment options for thyroid eye disease (TED), updated and consistent clinical practice guidelines (CPGs) are needed. This systematic literature review evaluated global CPGs for management of TED to inform development of future guidelines.

Description of Cases:

Embase, Medline, PubMed, Google Scholar, Guideline Central, and Turning Research into Practice databases were systematically searched (January 2020–March 2025) to identify global CPGs/consensus statements on management and treatment of TED. CPGs were assessed for quality using the Appraisal of Guidelines for Research and Evaluation (AGREE) II instrument, consisting of 6 domains; higher scores reflect higher quality. Data were extracted on how each guideline defined disease severity/activity, and whether other factors were considered in the classification. Among 281 records identified, 5 global TED CPGs or consensus statements were included [1-5]. Experts developing CPGs included endocrinologists, ophthalmologists, oculoplastic surgeons, and others. Overall, AGREE II scores ranged from 66.7 to 100% (mean [SD] score: 83.3 [11.8]%). Mean (SD) scores were highest for domains of Editorial Independence (92.5 [8.5]%) and Scope and Purpose (88.3 [12.3]%) and lowest for Rigor of Development (65.4 [21.6]%) and Stakeholder Involvement (67.2 [23.1]%). Three CPGs were “recommended” and two were “recommended with modifications.” Recommended CPGs had higher total AGREE II scores (Bartalena 2021, 73.55; Burch 2022, 86.23; and NICE 2024, 94.62). Disease severity was defined more consistently than disease activity across guidelines. There were inconsistencies on use of orbital imaging and diagnosing active TED independently of clinical activity scores. The role of disease phenotype, antibody levels, and disease duration to direct management was not addressed in any guideline.

Conclusions, including unique features of the case:

All global CPGs identified were recommended by the reviewers, suggesting high quality. However, among CPGs, recommendations for classifying disease activity and severity varied, highlighting the need for a new, rigorously developed CPG for TED to ensure greater consistency in clinical practice.

References: References: 1. National Institute for Health and Care Excellence (NICE). Thyroid disease: assessment and management. Accessed October 16, 2025. <https://www.nice.org.uk/guidance/ng145/resources/thyroid-disease-assessment-and-management-pdf-66141781496773> 2. Lee V et al. Eye (Lond). 2020;34(9):1662-1671. 3. Bartalena L et al. Eur J Endocrinol. 2021;185(4):G43-G67. 4. Douglas RS et al. J Neuroophthalmol. 2022;42(3):334-339. 5. Burch HB et al. Thyroid. 2022;32(12):1439-1470.

Keywords: Graves' disease, Ocular motility, Orbit, Orbit/ocular pathology

Financial Disclosures: Gaurav Seth: Employment and Stocks or Stock Options: Genentech, Inc.; Lilly Wagner: Consulting fees: Genentech, Inc.; Stella Ko: Employment and Stocks or Stock Options: Genentech, Inc.; Oluwatobi Idowu: Employment and Stocks or Stock Options: Genentech, Inc.; Naz Jehangir: Employment and Stocks or Stock Options: Genentech, Inc.; Abena Otu-Adum: Employee: Medicus Economics, LLC; Consulting fees: Medicus Economics, LLC received consulting fees for research from Genentech, Inc.; Marjorie Crowell: Employee: Medicus Economics, LLC; Consulting fees: Medicus Economics, LLC received consulting fees for research from Genentech, Inc.; H       Paris  : Employee: Medicus Economics, LLC; Consulting fees: Medicus Economics, LLC received consulting fees for research from Genentech, Inc.; Shih-Wen Lin: Employment and Stocks or Stock Options: Genentech, Inc.

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Integration of Genetic Evaluation Into Patient Care Leads To Wolfram Syndrome Diagnosis

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¹ *Metis Genetics*

Introduction:

Approximately 30% of optic neuropathies have a detectable genetic cause with 10 genes accounting for 96% of diagnoses.¹ Despite the high yield, many patients don't receive a genetic evaluation due to time and process constraints within the clinic. Positive results establish a diagnosis and potential treatment while negative results can exclude suspected conditions, reduce uncertainty, and guide health decisions. This case demonstrates a collaborative approach between a neuro-ophthalmology clinic and telehealth genetic counseling provider to integrate genetic evaluation into patient care.

Description of Cases:

Patient is a 47 year-old female with optic atrophy, a central visual field defect, and progressive color vision abnormalities, with a family history of vision loss in a sibling. Her neuro-ophthalmologist recommended a telehealth consultation with an ABGC-certified Genetic Counselor (GC) to discuss the patient's personal and family medical history, relevant ocular conditions, and genetic testing. The patient proceeded with the recommended 189 mitochondrial and nuclear gene-focused Next-generation sequencing panel performed by an external laboratory. Sample submission and test ordering was coordinated by the GC. The patient completed a second telehealth visit with the GC to review the test results before follow-up with the neuro-ophthalmologist.

Conclusions, including unique features of the case:

Two likely pathogenic variants in the WFS1 gene were found confirming a diagnosis of autosomal recessive Wolfram syndrome, a rare condition characterized by optic atrophy, diabetes, and progressive hearing loss. A Variant of Unknown Significance (VUS) in the SPG7 gene (c. 1939 G>T, p.Ala647Ser) was detected. SPG7 is associated with autosomal recessive spastic paraplegia 7. A second VUS was detected in the FBXL4 gene (c. 737 T>C). FBXL4 is associated with increased risk for autosomal recessive FBXL4-related encephalomyopathic mitochondrial DNA depletion syndrome. These VUSs were interpreted as not relevant to the patient's diagnosis. Genetic counseling provided integrated genetic expertise that assisted the patient's diagnosis while reducing time constraints of a neuro-ophthalmology clinic.

References: 1. Aude Rocatcher, et al. "The Top 10 Most Frequently Involved Genes in Hereditary Optic Neuropathies in 2186 Probands." *Brain*, vol. 146, no. 2, February 2023, pp. 455–460. *Brain*, doi:10.1093/brain/awac395.

Keywords: Genetic disease, Optic neuropathy, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Miscellaneous

Financial Disclosures: Amanda Elms: Amanda Elms has ownership in the telehealth genetic counseling service provider.; Amber Peterson: Amber Peterson is a genetic counselor for Metis Genetics and receives a consulting fee for cases.; Maranda Lunning: Maranda Lunning is an employee of Metis Genetics.; William Craigen, MD PhD: Dr. William Craigen is a consultant for Metis Genetics and receives fees for serving as Medical Director.

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Vision Loss Following Initiation of Sotorasib: A Rare Ocular Complication of Targeted KRAS Inhibition

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Introduction:

One of the most frequently reported side effects of targeted anticancer drugs is ocular changes. Most often these include conjunctivitis and vague visual disturbances. More severe ocular side effects include retinal vascular occlusion, corneal ulceration, and blindness. We highlight a case of a patient starting sotorasib, a new KRAS inhibitor, who developed vision changes simultaneously.

Description of Cases:

An 88-year-old female reported a “veil” covering her left eye (OS) over the past 2 weeks with 2 months of flashing lights. Medical history included lung cancer treated with radiation, chemotherapy, and daily sotorasib, which she started approximately when the flashing lights appeared. Vision of the right eye (OD) was 20/30-2 and 20/400-2 OS. Optic disc edema OS was appreciated on fundoscopy. Visual field (VF) showed inferior loss OS. Optical coherence tomography showed retinal nerve fiber layer (RNFL) thickness of 106um OD and 202um OS, presumably from the disc edema, with sectorial atrophy of ganglion cell complex OS. Findings were highly suspicious of non-arteritic anterior ischemic optic neuropathy (NAION). After methylprednisolone 500 mg for 3 days followed by 40 mg prednisone taper, her vision improved to 20/80 OS with reduced disc edema. RNFL improved to 133um OS. A multidisciplinary team discussed her sotorasib given the overlap in its initiation and her ocular symptoms. For now, she continues sotorasib and is monitored closely.

Conclusions, including unique features of the case:

This case underscores the importance of recognizing potential ocular complications associated with targeted anticancer therapies such as sotorasib. Although significant ocular side effects are uncommon, prompt identification and management are necessary. The timing overlap of this patient’s sotorasib initiation and NAION onset highlights the need for a high index of clinical suspicion when new visual symptoms occur during cancer treatment. Early intervention, interdisciplinary communication, and close monitoring are essential for optimizing visual outcomes in patients receiving emerging cancer therapeutics.

References: None provided.

Keywords: Optic neuropathy

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Diplopia To Diagnosis: Unmasking A Multifocal Germinoma

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Introduction:

Germinomas are a class of tumors composed of germ cells that are often complex in terms of presentation, diagnosis, and management. We present a case of a WHO Grade 4 germinoma with severe clinical findings without ophthalmic imaging changes.

Description of Cases:

An 18-year-old male presented with diplopia and blurry vision. The patient was recently diagnosed with a 5 mm pineal gland mass extending anteriorly, involving the midbrain, the splenium of the corpus callosum, and the left thalamus, and a 9 mm pituitary mass with enhancement of the pituitary stalk. Enhancement of the margin of the third ventricle and a 5 mm right midline shift of the ventricles were concerning for hydrocephalus. On ocular examination, visual acuity was 20/50 in the right eye (OD) and 20/40 in the left eye (OS). Ishihara color plates were 13/14 in both eyes (OU). Pupils were chemically dilated by an outside provider, and a relative afferent pupillary defect could not be assessed but was not present on following exams. Retinal nerve fiber layer (RNFL) imaging had slight elevation OU and ganglion cell layer (GCL) analysis was full OU. 30-2 Humphrey visual field (HVF) testing showed no deficits. Slit lamp examination was significant for Grade 1 disc edema in both eyes, concerning for elevated intracranial pressure. Given the severe clinical changes, the patient was subsequently seen by neurosurgery, where a biopsy was positive for a WHO Grade 4 Germinoma. The patient underwent ventriculoperitoneal shunt placement with spontaneous resolution of all visual symptoms.

Conclusions, including unique features of the case:

This case highlights the clinical findings of a complex germinoma involving both the pituitary and pineal glands, with subsequent hydrocephalus, decreased visual acuity, and grade 1 disc edema. The lack of HVF defects and full GCL, despite significant clinical findings, highlights the importance of a thorough clinical assessment rather than reliance on diagnostic imaging.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), High intracranial pressure/headache, Tumors

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

A Biopsy Avoided, Better DOTATATE Than NeverMichael Carper¹¹ Wilmer Eye Institute - Johns Hopkins Hospital**Introduction:**

MRI is the common relied upon method for working up optic nerve disease, including space occupying lesions. In atypical scenarios, biopsy is employed but is not without risk, resulting in reasonable hesitancy at the cost of diagnostic efficiency. Recent comparative studies demonstrate the high sensitivity and specificity of Ga-68 DOTATATE PET/CT for accurately delineating optic nerve sheath meningioma (ONSM) from normal tissue. This case details a challenging clinical scenario aided by this imaging modality for diagnosis and avoidance of biopsy.

Description of Cases:

A 16 year old female presented reporting sudden painless blurring in her left eye. MRI revealed enhancement of the left optic nerve raising concern for optic neuritis. She had no improvement following steroid treatment, and vision worsened. She had no subsequent improvement following PLEX. Serial MRIs revealed continued enhancement, reading as optic neuritis, and broad workup including CSF and genetic analysis was negative. Multidisciplinary discussion was held, and optic nerve biopsy was recommended. Before formally pursuing, Ga-68 DOTATATE scan was considered for its utility in screening for optic nerve sheath meningiomas.

Conclusions, including unique features of the case:

The Ga-68 DOTATATE scan revealed "radiotracer uptake along the left optic nerve, raising concern for left optic nerve sheath meningioma." Several variables contributed to the diagnostic uncertainty: 1. Report of sudden blurring of vision, where it's possible this was newly perceived 2. Persistent radiographic reporting of "optic neuritis" on serial MRI 3. Enhancement of the entire nerve would be atypical for ONSM 4. Atypical course for other considered diagnoses (eg. optic neuritis, lymphoma, glioma) with broad negative workup. This case ultimately benefited from the unique use of an imaging modality commonly used for neuro-endocrine tumors in the gut, and avoided the patient undergoing an optic nerve sheath biopsy. It remains hopeful this modality can be employed more regularly in the future to help offset the need for ON biopsy.

References: Al Feghali KA, et al. The Use of 68Ga-DOTATATE PET/CT in the Non-invasive Diagnosis of Optic Nerve Sheath Meningioma: A Case Report. *Front Oncol.* 8:454. 2018 Oct 16 Rachinger W, Stoecklein VM, Terpolilli NA, Haug AR, Ertl L, Poschl J, et al. Increased 68Ga-DOTATATE uptake in PET imaging discriminates meningioma and tumor-free tissue. *J Nucl Med.* 56:347–53 (2015)

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Tumors, Neuroimaging, Optic neuropathy, Orbit/ocular pathology

Financial Disclosures: The authors had no disclosures.

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Diagnostic Value of the GCL/INL Ratio in NF1-Associated Optic Pathway Gliomas

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Introduction:

Previous studies have demonstrated a correlation between ganglion cell layer(GCL) and prognosis of visual outcome and tumor progression. As young children often cannot cooperate with traditional OCT scans, a single macular scan measuring the GCL to inner nuclear layer(GCL/INL) ratio can be obtained. This ratio has been proposed as a surrogate biomarker of optic neuropathy. This study evaluated the GCL/INL ratio in NF1-associated optic pathway gliomas(OPGs) and correlation with OCT-derived mean GCL thickness.

Description of Cases:

The cohort included 121 NF1 pediatric patients who underwent OCT images scanned between 2015 and 2025. We included 66 eyes of 40 patients, with MRI-confirmed OPGs (mean age 4.6 ± 3.2 years; equal gender distribution). The data includes 112 OCT scans. Nasal and temporal GCL/INL ratios were manually measured at the thickest parafoveal points and averaged. Correlation with OCT-derived mean GCL thickness was assessed using Spearman analysis. Logistic regression was performed with GCL/INL ratio as predictor and GCL classification as outcome, with abnormality defined as mean GCL thickness $< 42\mu\text{m}$. ROC analysis evaluated discrimination, and the optimal cutoff was determined with the Youden index. Mean GCL/INL ratio was 0.94 ± 0.34 nasally, 0.99 ± 0.29 temporally, and 0.96 ± 0.27 overall. OCT-derived GCL thickness was $42.9 \pm 9.2\mu\text{m}$. The GCL/INL ratio correlated strongly with mean GCL thickness ($p=0.70$; 95% CI, $0.59-0.79$; $p < 0.001$). Logistic regression identified a GCL/INL ratio cutoff of 0.80 (sensitivity 91%, specificity 75%, accuracy 86%), allowing reliable detection of eyes with reduced GCL thickness but with lower specificity. The Youden index yielded an optimized cutoff of 0.88 (sensitivity 90%, specificity 82%, accuracy 88%), providing improved diagnostic accuracy. ROC analysis yielded an AUC of 0.93, indicating excellent discriminatory power for distinguishing eyes with reduced versus normal GCL thickness.

Conclusions, including unique features of the case:

In this cohort, the GCL/INL ratio correlated substantially with OCT-derived GCL thickness and demonstrated strong diagnostic value, supporting its use as a practical and sensitive tool for assessing optic neuropathy in NF1-associated OPG.

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Keywords: Optic neuropathy, Pediatric neuro-ophthalmology, Genetic disease

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Yoga Causing Vertebrobasilar Ischemia with Neuro-ophthalmic Presentation

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Introduction:

We present a case of a woman experiencing blurry vision and dizziness consistent with vertebrobasilar insufficiency during yoga confirmed with dynamic transcranial Doppler ultrasound. This is the first case identifying yoga as a cause of vertebrobasilar ischemia leading to neuro-ophthalmic findings and documenting the use of dynamic imaging to confirm vertebrobasilar ischemia during symptomatic positioning.

Description of Cases:

A 56-year-old female with a past medical history of ADHD, dysthymia, allergic rhinitis, vertigo, and abnormal uterine bleeding presented to neuro-ophthalmology clinic for evaluation of transient painless bilateral “shadowing” of vision over the past year. The patient’s symptoms began two years prior with vertigo. She was treated with Epley maneuvers which resolved the vertigo. A year later, she had an acute vision change described as a shadow or blurriness in the center of her vision which lasted ten minutes. At the time, she was unable to identify a trigger. She was referred to neuro-ophthalmology clinic for further evaluation of her visual episodes, which tended to occur during yoga and were accompanied by dizziness, especially in the “upward-facing dog” pose. She subsequently underwent a dynamic transcranial Doppler ultrasound during head-turning maneuvers and yoga poses, which showed posterior cerebral artery reduction in velocity indicating vertebral artery compression. She was counseled on starting aspirin and avoiding triggers for VBI including yoga and chiropractic manipulations.

Conclusions, including unique features of the case:

In conclusion, neck hyperextension or rotation may lead to vertebrobasilar ischemia. Physicians should consider yoga as a potential cause of neck hyperextension leading to vertebrobasilar ischemia. This case represents the first report of yoga with a neuro-ophthalmic presentation of vertebrobasilar insufficiency confirmed by dynamic imaging.

References: 1. Lima Neto AC, Bittar R, Gattas GS, Bor-Seng-Shu E, Oliveira ML, Monsanto RDC, Bittar LF. Pathophysiology and Diagnosis of Vertebrobasilar Insufficiency: A Review of the Literature. *Int Arch Otorhinolaryngol*. 2017 Jul;21(3):302-307. 2. Go JA, Al Othman B, Kini A, Beaver HA, Lee AG. Vertebrobasilar ischemia (VBI) related neuro-ophthalmic syndromes after routine activities involving hyperextension or rotation of the neck (hairdresser syndrome). *Eye (Lond)*. 2020 May;34(5):901-905. 3. Jasien JV, Jonas JB, de Moraes CG, Ritch R. Intraocular Pressure Rise in Subjects with and without Glaucoma during Four Common Yoga Positions. *PLoS One*. 2015 Dec 23;10(12):e0144505. 4. Nayar G, Desai A, Agarwal N, Alan N, Moossy JJ. Cervical arterial dissection and traumatic myelopathy following yoga: surgical case report. *Spinal Cord Ser Cases*. 2022 Apr 27;8(1):46. 5. Kesav P, Manesh Raj D, John S. Cerebrovascular Fibromuscular Dysplasia - A Practical Review. *Vasc Health Risk Manag*. 2023 Aug 28;19:543-556.

Keywords: Stroke, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)

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Feasibility of Chromatic Visual Evoked Potentials in Healthy Adults

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Introduction:

Standard visual evoked potentials rely on black/white contrast to assess visual pathway function, but only assess a limited component of the afferent visual pathway. Different visual stimuli activate distinct retinal ganglion cell populations and pathway components. Chromatic visual evoked potentials (cVEPs) have been described (1-4) to evaluate parvocellular and koniocellular pathways. They may detect color specific alterations but are not part of routine assessment. With the recent McDonald criteria revision highlighting optic nerve involvement in multiple sclerosis, more sensitive visual tests are needed to evaluate demyelinating injury. We describe early experience evaluating the feasibility of cVEPs in healthy adults.

Description of Cases:

We assessed the feasibility of recording cVEPs in five healthy adults using standard equipment. Chromatic pattern reversal stimuli were used to engage the parvocellular (red/green) and koniocellular (blue/yellow) visual pathways, and black/white VEPs were recorded as baseline. VEPs were recorded monocularly with a standard occipital montage. Latencies from both eyes (10 total) were pooled for descriptive analysis. Recordings showed identifiable P100-like components for both red/green and blue/yellow stimuli. Mean $\pm$ SD P100 latencies were 102 ± 2 ms (range 99-106) for black/white, 102 ± 5 ms (range 95-107) for red/green, and 103 ± 3 ms (range 97-108) for blue/yellow stimuli. Interocular latency differences were small (≤ 4 ms), indicating internal consistency. We plan to further refine key parameters such as check size, visual angle, contrast and room luminance to optimize chromatic responses and establish normative data. Enrollment of at least 20 participants is planned to establish normal ranges. Future plans include exploring the implementation of this approach in demyelinating disease and to assess their potential added value.

Conclusions, including unique features of the case:

cVEPs can be recorded in healthy adults using standard recording methods. These preliminary findings support feasibility and reproducibility, and will help guide ongoing work and future applications, particularly in demyelinating disease.

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Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Demyelinating disease

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Resolution of Post-Concussion Horner's Syndrome and Oculomotor Dysfunction Documented by Virtual Reality Diagnostics

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Introduction:

Concussion frequently disrupts visual pathways, making neuro-ophthalmic assessment critical for both diagnosis and monitoring recovery. The purpose of this case study is to describe what appears to be, after literature searches on PubMed and Google Scholar, one of the first reported cases of post-concussive Horner's syndrome, as well as oculomotor dysfunction, and to illustrate its resolution using a virtual-reality (VR) neuro-ophthalmic diagnostic platform.

Description of Cases:

A 44-year-old man developed frontal-temporal headaches provoked by near-vision tasks—scrolling on phone, reading, and gaming—after a ball struck his face several months earlier. While the patient demonstrated normal best-corrected visual acuity, his initial examination revealed left-eye Horner's syndrome (upper-lid ptosis, lower-lid "reverse" ptosis, anisocoria with dilation lag) and saccadic intrusions on near-point-of-convergence testing. Ocular health was otherwise unremarkable. VR-based neuro-ophthalmic testing showed a comitant eso deviation, left-eye dilation lag without relative afferent pupillary defect, saccadic inaccuracies and corrections, reduced saccadic velocity in down going saccades > up going saccades, saccadic intrusions and endgaze nystagmus during smooth pursuit, mildly inaccurate convergence beyond 5°, and limited divergence ($\approx 1.5^\circ$). Six months later the clinical signs of Horner's syndrome had completely resolved, along with some signs of oculomotor dysfunction. Repeat VR testing demonstrated normal pupillary function, more accurate saccades, fewer saccadic intrusions and less endgaze nystagmus on pursuits, improved convergence, and absent divergence fusion; vertical-saccade velocities were unchanged.

Conclusions, including unique features of the case:

This case demonstrates that Horner's syndrome can occur as a transient sequela of concussion and may resolve within months. Serial assessment with a VR neuro-ophthalmic platform objectively captured both the presence and the resolution of sympathetic dysfunction as well as broader oculomotor recovery. This helps underscore the technology's value in the diagnosis and monitoring of concussion and, by extension, more severe traumatic brain injury.

References: None provided.

Keywords: Retina, Stroke, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease, Pediatric neuro-ophthalmology

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Grant Support: None.

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Revealing aberrant choroid and optic nerve blood flow in carotid cavernous fistula using Laser Speckle Flowgraphy

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Introduction:

Carotid cavernous fistulas shunt high-pressure blood into venous system, causing a variety of neuro-ophthalmic symptoms from upstream venous congestion in the orbit and the eye. Laser speckle flowgraphy (LSFG) measures blood velocity in the eye dynamically throughout the cardiac cycle, and can demonstrate delayed venous outflow from the retinal veins during systole. Choroid vessels can remodel, rerouting outflow. We evaluated for differences in blood flow velocity in the optic nerve and choroid that are attributable to a CCF.

Description of Cases:

Consecutive patients with unilateral or bilateral indirect and direct CCF underwent LSFG imaging at baseline and at follow up after resolution, where possible. Average Mean Blur Rate, a measure correlated with blood flow velocity, was measured in the optic nerve head, and over tortuous collateralized choroid veins. 2 patients with direct and 12 patients with indirect CCF were imaged with LSFG. Blood flow in the optic nerve head trended lower in affected eyes (5.57 ± 2.1 vs 6.46 ± 1.17 AU, $p=0.069$), and increased following treatment or spontaneous improvement (increase of 0.59 AU, $p=0.016$). Visual acuity was reduced (LogMAR 0.21 ± 1.6 in affected eyes vs 0.03 ± 0.1 in unaffected eyes, $p=0.014$). Abnormal collateral choroidal veins with delayed outflow were identified in three affected eyes and zero unaffected eyes.

Conclusions, including unique features of the case:

LSFG reveals abnormal blood flow beyond the major retinal vessels. Mild vision loss and reduced blood flow in the optic nerve were observed in the affected eyes, and fistula closure increased blood flow. Abnormal, remodeled choroidal veins were found to have delayed flow during systole suggesting dynamic outflow resistance.

References: Linton EF, Tedeschi TR, Ahmad NU, Wang JK, Kardon RH. Retinal arterial-venous pulse delay: a new specific marker for a carotid-cavernous fistula. *Front Ophthalmol* (Lausanne). 2023 Dec 11;3:1301410. doi: 10.3389/fopht.2023.1301410. PMID: 38983038; PMCID: PMC11182162.

Keywords: Vascular disorders, Orbit/ocular pathology

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Painful Pupil-Sparing Ophthalmoplegia in a Diabetic Patient: Simultaneous Cranial Nerve III and VI Palsies with Normal Neuroimaging

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Introduction:

Diabetes mellitus is a common cause of cranial mononeuropathies, typically affecting CN III in a pupil-sparing pattern. However, simultaneous CN III and VI palsies are rare and often mimic compressive or inflammatory cavernous sinus disease, requiring careful evaluation to exclude alternative etiologies.

Description of Cases:

A 41-year-old woman with poorly controlled type 2 diabetes (A1c 8.8%) presented with three weeks of progressive left periorbital pain, ptosis, and binocular diplopia. Examination revealed complete external ophthalmoplegia OS, sparing the pupil, without sensory loss or optic disc edema. MRI/MRA/MRV of brain and orbits were normal. Lumbar puncture showed elevated protein (93 mg/dL) and mild pleocytosis. Broad infectious and autoimmune testing was negative. The patient was empirically treated with intravenous methylprednisolone followed by an oral prednisone taper. Pain improved within days, and ocular motility progressively recovered: partial abduction at one week, significant ptosis/duction improvement at two weeks, and full resolution by three months. At five months, BCVA was 20/20 OU, motility was normal, and repeat MRI remained unremarkable.

Conclusions, including unique features of the case:

This case illustrates that diabetic microvascular disease can cause simultaneous, painful CN III and VI palsies despite normal imaging, mimicking Tolosa-Hunt or cavernous sinus pathology. Recognition of this presentation prevents unnecessary invasive testing and underscores the importance of glycemic control and close follow-up in atypical diabetic cranial neuropathies.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Ocular motility, Vascular disorders, Neuroimaging

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Downbeat Nystagmus in Association with the Dorsal Midbrain Syndrome

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Introduction:

Downbeat nystagmus (DBN) is frequently attributed to cerebellar pathology. Far less often, DBN arises from brainstem disease with midbrain etiologies being exceptionally rare and poorly characterized. In particular, DBN occurring with the dorsal midbrain syndrome has been reported only sporadically and has never been systematically examined.

Description of Cases:

We present three patients with DBN in central gaze and other manifestations of a dorsal midbrain syndrome. Each patient had aqueductal pathology: obstructive hydrocephalus from aqueductal stenosis, tectal glioma compressing the aqueduct, and infectious meningoencephalitis with secondary aqueductal narrowing. Upgaze paresis was evident in all three, skew deviation was present in two, and parkinsonism developed in two after shunt-related complications. To place these findings in context, we reviewed the literature using strict criteria requiring DBN in central gaze and at least two definitive features of the dorsal midbrain syndrome. The search identified two additional patients. Across all five patients, aqueductal stenosis or compression was observed, and upgaze paresis was a consistently associated clinical finding.

Conclusions, including unique features of the case:

Involvement of the interstitial nucleus of Cajal, disruption of descending midbrain projections to paramedian tracts, or unstable cerebellar outflow could conceivably produce DBN at the level of the midbrain, but clinical and experimental evidence make these explanations less compelling. Converging evidence from our series, prior reports, and animal models, instead, points to posterior commissural dysfunction related to aqueductal pathology as the most plausible mechanism for DBN in association with the dorsal midbrain syndrome. Lesions of the posterior commissure may disrupt fibers responsible for vertical gaze holding and input from the vertical vestibular system, creating a rare imbalance that drives slow upward eye movement to create downbeat nystagmus, even with impaired upward range of eye movement.

References: None provided.

Keywords: Nystagmus, Vascular disorders, Ocular motility

Financial Disclosures: The authors had no disclosures.

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Delayed Intracranial Perineural Spread Of Cutaneous Squamous Cell Carcinoma Presenting As Ophthalmoplegia

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Introduction:

Perineural spread of cutaneous squamous cell carcinoma (SCC) is a known but uncommon cause of multiple cranial neuropathies. Neuro-ophthalmologists most often encounter perineural invasion along the ophthalmic division of the trigeminal nerve. Spread via the maxillary division with intracranial extension is rare and diagnostically challenging due to subtle early radiologic findings and delayed presentation relative to the primary tumor.

Description of Cases:

An 83-year-old woman presented with a six-month history of progressive left ptosis, diplopia, facial pain, and numbness. Her medical history was notable for longstanding rheumatoid arthritis and a recent diverting colectomy for abdominal abscess. Examination revealed complete left ophthalmoplegia involving cranial nerves III, IV, and VI, decreased facial sensations in the V1-V2 distributions, and neurotrophic keratitis. MRI showed subtle enhancement in the left Meckel's cave extending through the foramen ovale into the cavernous sinus. Systemic workup for inflammatory or metastatic disease was negative. Skull base biopsies revealed poorly differentiated SCC with perineural invasion, positive for high-molecular-weight cytokeratin and negative for CD45 and melanocytic markers. On further history, the patient recalled a cutaneous SCC resected from the left malar cheek three years earlier with involvement of the deep margin. Repeat MRI showed significant progression along the pterygopalatine fossa, and maxillary and Vidian nerves. The multidisciplinary tumor board recommended proton therapy.

Conclusions, including unique features of the case:

This case illustrates delayed perineural spread of remote cutaneous SCC along the maxillary nerve, presenting with multiple cranial neuropathies. Neuro-ophthalmologists should recognize that perineural spread of SCC can also occur via the V2 branches. Key teaching points include (1) perineural spread can occur years after initial cancer treatment, even without cutaneous recurrence; (2) early radiologic findings are often subtle, requiring detailed anatomic knowledge and strong clinical suspicion; and (3) a targeted history about skin cancer is crucial, since patients may not volunteer this information unless specifically asked.

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Keywords: Tumors, Skull base, Orbit/ocular pathology, Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Fundus Video Recording to Diagnose Superior Oblique Myokymia

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Introduction:

Superior oblique myokymia is a rare ocular motor disorder characterized by brief, rhythmic, unilateral contractions of the superior oblique muscle, leading to intermittent episodes of oscillopsia and more rarely episodes of vertical diplopia. These episodes are typically triggered in downgaze and often described by patients as a fluttering or shimmering sensation in one eye. Clinical diagnosis is challenging, as these movements are subtle, fleeting, and frequently missed during standard examination.

Description of Cases:

A 64-year-old man presented with a one-year history of daily, debilitating intermittent episodes of vertical binocular diplopia. Initial eye exam including ocular motility was normal. Magnetic resonance imaging brain and orbits with contrast was normal. Tests for myasthenia gravis including antibody testing (AChR, MuSK, and LRP4) and single-fiber EMG were unremarkable. Therapeutic trials were pursued including pyridostigmine 90 mg three times daily and oral prednisone 30 mg daily for three weeks, targeting presumed ocular myasthenia gravis, and carbamazepine 200 mg twice a day, targeting presumed ocular neuromyotonia. There was no symptom improvement. Superior oblique myokymia was considered in the differential, however episodes were not observed on several clinic visits. At a subsequent visit, Heidelberg Spectralis infrared video imaging successfully captured fine, high-frequency, low-amplitude torsional and vertical fundus movements in real time during a symptomatic episode confirming the diagnosis of superior oblique myokymia. This represents a novel clinical application of Spectralis for documenting ocular motor abnormalities. The patient improved on oral gabapentin medication ramped up to 400 mg twice a day.

Conclusions, including unique features of the case:

This case illustrates the diagnostic challenge in patients with superior oblique myokymia and the utility of Spectralis infrared video recording as a documentation tool of the abnormal torsional and vertical eye movements.

References: None provided.

Keywords: Ocular motility, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)

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Eye Movement and Lid Disorders in Patients with Alternating Hemiplegia of Childhood due to ATP1A3 Gene Variants

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Introduction:

ATP1A3 gene variants cause heterogeneous neurological phenotypes of alternating hemiplegia of childhood (AHC), rapid-onset dystonia-parkinsonism (RDP), and cerebellar ataxia, areflexia, pes cavus, optic atrophy, and sensorineural hearing loss (CAPOS) syndrome [1]. Paroxysmal neurological episodes—such as hemiplegia, dystonia, ataxia, and seizure-like events—are common; progressive findings include developmental delay and cognitive impairment [1]. Hours-long ocular motor episodes are reported; however, they have not been systematically characterized [1,2].

Description of Cases:

Home videos of 29 abnormal eye movement episodes from 11 AHC patients with ATP1A3 gene variants were analyzed and categorized. Monocular deviation/strabismus (MD/S) occurred in 34% of episodes (n=7 exo, 2 eso, 1 hyper), conjugate tonic gaze deviation in 31%, and nystagmus in 17% (n=3 downbeat, 1 upbeat, 1 rightbeat). Lid findings (all co-existing with abnormal eye movements) included ptosis in 31% of episodes and dynamic lid movements (e.g., excess blinking, lid twitches/flutterers) in 31%. In the 7 patients with MD/S and exotropia, all exhibited a unique eye movement, consisting of sudden large abduction of one eye accompanied by dissociated nystagmus/saccadic pulses in the abducting eye. Four additional patients had unidirectional horizontal saccadic pulses without prominent ocular misalignment.

Conclusions, including unique features of the case:

This study provides detailed analysis of episodic ocular motor and lid abnormalities in ATP1A3-related AHC. The diversity of findings highlights the phenotypic complexity of paroxysms, though most eye movements could be categorized into monocular gaze deviations, conjugate tonic gaze deviations, or classic nystagmus patterns. Several other disorders can also cause paroxysmal conjugate gaze deviations or nystagmus; however, the abrupt onset of monocular abduction accompanied by abducting saccadic pulses is unique, and possibly pathognomonic for AHC. Hypothetical mechanisms for this type of event may include third nerve or medial longitudinal fasciculus hypofunction, sixth nerve activation, or aberrant innervation between the two.

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Keywords: Genetic disease, Pediatric neuro-ophthalmology, Ocular motility

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Lid Nystagmus as Initial Manifestation of CLIPPERS

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Introduction:

Chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS) is an inflammatory disorder characterized by a “salt-and-pepper” enhancement pattern. Upbeat nystagmus (UBN) and gaze-evoked nystagmus (GEN) have both been described with CLIPPERS. We describe a patient whose initial manifestation was vertigo and prominent eyelid (lid) nystagmus. Lid nystagmus is a rare phenomenon in isolation, and is typically associated with midbrain pathology. It can be seen with UBN (especially in upgaze), horizontal GEN, or with convergence. The M-group of neurons resides in the midbrain and coordinates firing of the superior rectus (SR) muscles via rostral interstitial medial longitudinal fasciculus (riMLF) and the levator palpebrae (LP) via the central caudal nucleus (CCN). The M-group is necessary to coordinate LP and SR activation for upward eye movements. Lid nystagmus may result from decoupling of LP and SR perhaps at the level of the M-group (or its efferent projections).

Description of Cases:

A 76-year-old female presented with dizziness, and examination showed prominent lid nystagmus, especially with convergence and upgaze (where there was clear UBN). With video-oculography, a very mild spontaneous UBN was seen. She had horizontal GEN and mild abduction deficits bilaterally with a comitant esotropia, thought to represent cerebellar divergence insufficiency vs symmetric bilateral sixth nerve palsies. Contrasted MRI showed curvilinear and nodular enhancement throughout the entire posterior fossa, characteristic of CLIPPERS. She had near resolution of MRI findings, vertigo and lid nystagmus with steroids.

Conclusions, including unique features of the case:

Lid nystagmus is rarely seen in isolation, and when it is seen with UBN, the lid and upward eye movements are usually proportional. Our patient had lid nystagmus that was much more prominent than UBN, suggesting relative overaction of the LP or underaction of the SR, perhaps resulting from disrupted M-group outflow. Lid nystagmus has not been described in CLIPPERS previously.

References: 1. Dudesek A, Rimmele F, Tesar S, et al. CLIPPERS: chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids. Review of an increasingly recognized entity within the spectrum of inflammatory central nervous system disorders. Clin Exp Immunol. 75(3):385-396. 2014 2. Anderson T. Eyelid Nystagmus and Other Involuntary Movements of the Upper Lids; What’s in a Name? Mov Disord Clin Pract;10(9):1419-1422; 2023

Keywords: Nystagmus, Ocular motility, Ocular manifestations of vestibular disorders

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An Ominous Sign: Transient Cranial Nerve VI Palsy From A Giant Basilar Tip Aneurysm

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Introduction:

CN VI palsy is a well-recognized non-localizing sign of increased intracranial pressure due to its long intracranial course. Transient CN VI palsies have rarely been reported in the literature. We report a case of an initially transient CN VI palsy due to a giant acutely thrombosing basilar tip aneurysm with intraluminal thrombus, emboli, and paradoxical mass effect on the brainstem, third ventricle, and cerebral aqueduct, eventually leading to obstructive hydrocephalus.

Description of Cases:

A 61-year-old woman with hypertension and tobacco use presented with new-onset headaches, vision loss, and weakness. On initial examination, she was awake and alert, and was found to have right hemiparesis, right homonymous hemianopsia, complete left pupil-involving CN III palsy with bilateral ptosis, and right CN VI palsy. Imaging revealed a partially thrombosed giant basilar tip aneurysm with infarcts in the left thalamus and left occipital lobe, without hydrocephalus. During her initial hospitalization, her left CN III palsy improved, and her headaches and right CN VI palsy had fully resolved. Given the high procedural risk, neurosurgery and interventional radiology deferred embolization, and she was started on therapeutic antithrombotics. She was discharged to acute rehabilitation in stable condition. Two weeks later, she was readmitted with acute encephalopathy and recurrent ocular dysmotility and was found to have obstructive hydrocephalus. An external ventricular drain improved her status, followed by ventriculoperitoneal shunt placement. She returned to rehabilitation, where she remains clinically stable.

Conclusions, including unique features of the case:

Transient CN VI palsy may serve as the first sign of impending obstructive hydrocephalus. Although basilar tip aneurysms have been linked to ophthalmoplegia and hydrocephalus, outcomes remain poor despite intervention. This case underscores the need for hypervigilance in patients with symptomatic giant aneurysms and transient CN VI palsy, as early recognition may help mitigate morbidity and mortality.

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Keywords: Ocular motility, Vascular disorders, Neuroimaging, Stroke

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Macro-Square Wave Jerks Following Mild Traumatic Brain Injury: A Quantitative Case Perspective

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Introduction:

Common eye movement disorders following mild traumatic brain injury (mTBI) include convergence insufficiency, impaired pursuit, and saccadic dysmetria. Saccadic intrusions (SI), such as ocular flutter,¹ are reported but have received little attention. We report a patient with post-mTBI macro-square wave jerks (mSWJ).

Description of Cases:

A 28-year-old professional dancer presented with persistent 'shifting' vision 8 months after mTBI. Initial photophobia, dizziness, cognitive impairment, and dysautonomia had improved. Brain MRI was normal. Examination revealed moderate-amplitude saccadic intrusions. Video oculography (VOG, EyeLink) confirmed frequent mSWJ with brief intersaccadic intervals (ISI). Based on reports of SI dampening with memantine, an NMDA-receptor antagonist, she was started on 5 mg daily.² On treatment, she reported 80% symptom reduction, with return to dancing. Repeat VOG included three trials: morning memantine dose held and 30 and 60 minutes after 5 mg. New baseline traces were improved compared with original recordings. At 30 minutes, mSWJ were reduced and at 60 min, nearly resolved. To investigate the possibility of functional mSWJ, we recorded a healthy individual attempting to simulate mSWJ. Average amplitude (7.5 deg patient, 7 deg control) and ISI duration (171.7 msec patient, 219.0 msec control) were similar; however, ISI variance (ISI standard deviation: 62.4 msec patient, 114.1 msec control), velocity, and qualitative waveform inspection showed distinct patterns between the two. Additionally, our patient's mSWJ were not suppressed during pursuit, as they were in our control individual.

Conclusions, including unique features of the case:

Functional SI are reported as distinguishable by lack of physiologic ISI and resolution with distraction.³ Notably, our patient's mSWJ did not dissipate with pursuit, which could require sufficient cognitive load to qualify as distraction. While we cannot exclude the possibility of functional SI in our patient, we propose, based on quantitative analysis, that pathologic mSWJ may occur with mTBI, suggesting focal disruption of descending superior colliculus signals for fixation maintenance.

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Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Ocular motility, Trauma, Non-organic visual disorders

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Introduction:

Understanding efferent neuro-ophthalmic pathways can be challenging for trainees due to their three-dimensional complexity and limited exposure during formal teaching. To engage the new generation of learners (“Zoomers”) accustomed to digital interactivity, iMovements was developed as an educational app combining animation, simulation, and self-assessment to visualize efferent visual system function in real time.

Description of Cases:

Description: iMovements presents animated models of ocular motility, cranial nerve innervation, and efferent disorders through interactive modules that respond dynamically to user input. Each lesson integrates labeled pathways, muscle activation overlays, and clinical correlations (e.g., sixth-nerve palsy, internuclear ophthalmoplegia). Educators can project modules during teaching rounds or allow learners to explore them independently using “learn → test → review” cycles with immediate feedback. Early classroom use among ophthalmology residents and neuro-ophthalmology fellows demonstrated increased engagement and improved recall of efferent anatomy and lesion localization. Feedback emphasized clarity of visualization, spatial understanding, and the motivational effect of interactivity.

Conclusions, including unique features of the case:

Conclusions: iMovements offers a modern, mobile-based approach to teaching efferent neuro-ophthalmology, translating complex ocular motor pathways into accessible, visually intuitive lessons. By aligning with the learning preferences of digital-native clinicians, the app provides a scalable adjunct to traditional teaching and may help sustain interest in the efferent side of neuro-ophthalmology.

References: None provided.

Keywords: Ocular motility, Ocular manifestations of vestibular disorders, Adult strabismus with a focus on diplopia, Pupil, Miscellaneous

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Introduction:

Anti-Kelch-like protein 11 (KLHL11) encephalitis is a rare paraneoplastic neurologic syndrome linked to germ cell tumors in young men. Although cerebellar and brainstem findings are common at onset, some patients initially present with isolated cochleovestibular symptoms that mimic peripheral ear disease. This early phenotype can delay recognition, particularly when MRI is nondiagnostic. Importantly, progressive or bilateral sensorineural hearing loss (SNHL) that later evolves into cerebellar ocular motor abnormalities represents an underrecognized presentation of KLHL11 disease. We report a case exemplifying this trajectory.

Description of Cases:

A previously healthy 27-year-old man presented with acute right-sided SNHL. Infectious and autoimmune serologies were unremarkable. MRI showed an enhancing lesion along the right eighth cranial nerve, initially interpreted as possible vestibular schwannoma. He received intratympanic steroids and was monitored. Over the following year, he developed profound right-sided loss, new left-sided SNHL, oscillopsia, intermittent diplopia, and episodic vertigo, with stable MRI findings. Audiometry confirmed bilateral cochlear involvement. Neurologic examination revealed downbeat and left-beating nystagmus, saccadic pursuit, and bilateral catch-up saccades, consistent with combined peripheral and central vestibulocerebellar dysfunction. CSF showed mild lymphocytic pleocytosis. A paraneoplastic antibody panel returned positive for anti-KLHL11 (1:960). Testicular ultrasound was normal, but chest CT revealed an anterior mediastinal mass. Surgical resection confirmed a primary thymic seminoma.

Conclusions, including unique features of the case:

This case illustrates how KLHL11-associated disease may initially resemble a peripheral cochlear disorder before progressing to a mixed peripheral–central syndrome. The evolution from isolated SNHL to bilateral cochleovestibular dysfunction with cerebellar ocular motor signs—despite stable MRI—was the key diagnostic clue prompting paraneoplastic evaluation. KLHL11 antibody positivity provided diagnostic specificity and guided tumor detection. Clinicians should consider KLHL11 encephalitis in young men with progressive or bilateral SNHL and emerging central ocular motor abnormalities. Broad tumor screening, including the mediastinum, is essential, as thymic seminoma is a possible underlying malignancy. Early recognition enables timely oncologic and immunologic treatment.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Nystagmus, Ocular manifestations of vestibular disorders, Paraneoplastic syndromes, Vestibular disorders

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Ocular Neuromyotonia After Gamma Knife Stereotactic Radiation Therapy

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Introduction:

Ocular neuromyotonia, a phenomenon attributed to radiation damage to the ocular cranial motor nerves. It is a paroxysmal misalignment of the eyes due to spontaneous repetitive firing of the third, sixth, or, less commonly, fourth cranial nerve. The characteristic clinical finding is an intermittent, incomitant misalignment lasting seconds to minutes that is often evoked by eccentric gaze.

Description of Cases:

We present two patients who underwent transsphenoidal operations for non-secretory pituitary adenoma and secretory tumor causing endogenous Cushing's syndrome, followed by stereotactic Gamma Knife radiosurgery. Both patients developed intermittent diplopia and strabismus at 19 months and at the second year after treatment. Eye examination revealed features of ocular neuromyotonia. In first case, the neuromyotonia affected the third and sixth nerves of the left eye, and the second case affected the third bilateral nerve with marked palpebral contracture.

Conclusions, including unique features of the case:

Several cases of ocular neuromyotonia secondary to external beam radiation therapy have been reported, but very few cases of neuromyotonia have been reported after Gamma Knife radiosurgery in one motor nerve. In this report both patients received Gamma Knife radiosurgery, previously and one of them have a third and sixth nerves affected in one side, and the second has a bilateral palpebral contracture. Both patients improved their clinical symptoms after receiving treatment with oral carbamazepine.

References: None provided.

Keywords: Adult strabismus with a focus on diplopia, Chemotherapy and radiation injury, Ocular motility

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IgG4 Hypertrophic Pachymeningitis With Multiple Cranial Nerve Palsies

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Introduction:

IgG4-related disease is an uncommon (though increasingly well-known) fibroinflammatory disorder that has been implicated in a variety of organs, including the orbit and pachymeninges. If the pachymeninges become hypertrophic, it can result in cranial neuropathies.

Description of Cases:

A 22-year-old African American male presented with four days of blurry vision and occasional double vision while watching television. Sensory eye examination was normal. Examination of extraocular movements showed limitation of abduction of the right eye, with alignment measurements consistent with right 6th cranial nerve palsy. MRI acoustic protocol was positive for asymmetric thickening over right aspect of the clivus at Dorello's canal, suspicious for inflammatory process or lymphoma. Lumbar puncture was positive for increased IgG index in serum and CSF, with 4 oligoclonal bands in CSF only. Serum IgG3 and IgG4 were elevated, and workup for other infectious, inflammatory, and neoplastic conditions was negative. The patient declined biopsy and was discharged with outpatient plan for biopsy, but was lost to follow-up. The patient presented 6 weeks later with debilitating retro-orbital eye pain, and examination revealed both CN6 and CN3 palsies, though orthophoric in primary position. Repeat MRI showed progressive thickening of dura which extended into the right cavernous sinus. Biopsy was deferred given the high-risk location. He was treated with two days of intravenous steroids with a slow oral steroid taper. His EOMs, eye pain, and headaches all improved completely.

Conclusions, including unique features of the case:

Hypertrophic pachymeningitis is a characteristic feature of CNS IgG4- disease, but the differential diagnosis is broad. Headache and cranial nerve dysfunction are the most common neurologic manifestations of the disease. If untreated, the inflammatory process may continue to spread along the dura, causing further neurological deficits. Steroids with slow taper are usually effective in treating IgG4-related hypertrophic pachymeningitis in most patients.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Opsoclonus Myoclonus Syndrome in Early Pregnancy with Rapid Response to Treatment

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Introduction:

Opsoclonus Myoclonus Syndrome (OMS), classically associated with childhood neuroblastoma, is rarely reported in association with pregnancy. Historically, OMS in pregnancy has shown favorable clinical outcomes, generally without consequence to the fetus.

Description of Cases:

A 38-year-old G1P0 at 16 weeks gestation presented with two weeks of dizziness and progressive gait instability. She was initially diagnosed with vestibular neuronitis by otolaryngology, but she experienced rapid symptom progression within a 48-hour period, developing severe ataxia, sleep disturbance, tremor, diplopia, and oscillopsia. Best-corrected visual acuity was 20/25 in both eyes. Sensorimotor exam demonstrated opsoclonus with small-angle left hypertropia. Neurologic exam demonstrated myoclonic jerks of the head and extremities. Given low index of suspicion for paraneoplastic etiology and risk/benefit discussion with the patient, the decision was made to forgo whole-body imaging and lumbar puncture in favor of empiric therapy. The patient started prednisone 1 mg/kg/day for four weeks, followed by weekly taper to be completed by the time of her glucose tolerance test. Non-contrasted magnetic resonance imaging of the brain was unremarkable. Within 10 days of corticosteroid initiation, the patient noted significant improvement in ambulation and visual symptoms. Oral clonazepam was offered to treat residual tremor, but she declined treatment. By the third trimester, gait and sleep normalized, tremor resolved, and oscillopsia was minimal. In the 35th week of pregnancy, she delivered a healthy infant. By 5 months post-partum, residual opsoclonus and oscillopsia completely resolved.

Conclusions, including unique features of the case:

To the authors' knowledge, this is the fifth reported case of OMS associated with pregnancy and the second case presenting in early gestation with near-complete symptom resolution prior to delivery. The pathophysiology of OMS remains unclear, but it is postulated that pregnancy-related immune modulation may contribute to OMS onset and remission. Recognition of this rare presentation is important to guide timely, pregnancy-safe management and avoid unnecessary diagnostic delays.

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Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Ocular motility, Nystagmus

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A Case of Oculogyric Crisis Improved by Intramuscular Botulinum Toxin InjectionHyuna Kim¹¹ Soonchunhyang University Seoul Hospital**Introduction:**

Oculogyric crisis (OGC) is a rare, acute dystonic reaction characterized by involuntary upward deviation of both eyes due to spasms and increased tone of extraocular muscles. Typically, last minutes and may occur in conjunction with other dystonic symptoms. It can be triggered by various medications, including neuroleptics, or may result from underlying brain lesions or metabolic abnormalities. However, there is currently no established treatment that produces consistent improvement other than discontinuation of the causative drug. We report a case of OGC successfully managed with botulinum toxin injection into the bilateral superior rectus muscles.

Description of Cases:

A 47-year-old woman presented with a one-year history of episodic upward eye deviation and headache. The episodes were characterized by involuntary sustained upward gaze lasting for several seconds, which resolved with blinking, and were often accompanied by periocular pain, headache, and blepharospasm during examination. Fundus examination revealed branch retinal vein occlusion in the right eye, which was monitored without intervention. Brain magnetic resonance imaging showed a probable right frontal meningioma and a 3-mm aneurysm of the right posterior communicating artery, but cerebrospinal fluid analysis was unremarkable. A thorough review of the patient's medication history revealed no identifiable drug that could be implicated as the cause. Over a four-year follow-up period, the patient showed no improvement despite trials of multiple medications, including alprazolam (0.125 mg BID), gabapentin (100 mg BID), baclofen (5 mg BID), carbamazepine (100 mg BID), and trihexyphenidyl (1 mg TID). Finally, botulinum toxin (15 IU) was injected into both superior rectus muscles, leading to significant improvement in the paroxysmal upward gaze. Transient right ptosis occurred after the injection but resolved within one month.

Conclusions, including unique features of the case:

This case suggests that extraocular muscle botulinum toxin injection may be an effective therapeutic option for refractory oculogyric crisis.

References: None provided.

Keywords: Ocular motility

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Delayed Sixth Nerve Palsies More Than One Year After Durable Transvenous Embolizations Of Indirect Carotid Cavernous Sinus Fistulas

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Introduction:

Indirect carotid cavernous sinus fistulas (CCFs) are acquired arteriovenous shunts between dural branches of the internal or external carotid artery and the cavernous sinus. Congestion from increased arterial pressure and mass effect at the cavernous sinus apex leads to proptosis, chemosis, pulsatile tinnitus, and cranial nerve palsies with diplopia. Standard treatment of indirect CCFs via transvenous embolization (TVE) is meant to reverse these signs and symptoms. There are rare cases of new or recurrent sixth palsy occurring months or even years following definitive CCF treatment.

Description of Cases:

We report three cases of recurrent isolated sixth nerve palsy following durable TVE of indirect CCFs. In each, treatment resulted in complete or near-complete resolution of initial symptoms. Patients then developed progressive partial sixth nerve palsies in delayed fashion 1, 3, and 15, years later despite stable MRA/CTA and conventional angiography, without coil migration or CCF recurrence. Each patient ultimately underwent strabismus surgery to address persistent esotropia. One patient, whose CCF had initially been treated with stereotactic radiosurgery, developed concurrent ocular neuromyotonia requiring medical management.

Conclusions, including unique features of the case:

Treatment of indirect CCFs occasionally leads to worsening cranial nerve palsies soon after intervention. Rarely, sixth nerve palsy can manifest years after TVE. Cranial nerve six is susceptible to mechanical damage given its course through the narrow lateral and posterior portion of the cavernous sinus via chronic mass effect from dense coils. Delayed-onset diplopia is therefore a long-term risk even after successful TVE.

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Keywords: Ocular motility, Vascular disorders, Orbit/ocular pathology, Adult strabismus with a focus on diplopia, Neuroimaging

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Real Time Measurement of Subthalamic Nucleus Activity During Saccades In Parkinson's Disease: A Synchronization Study With Eye-Tracking And Deep Brain Stimulation

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Introduction:

Saccadic impairment in Parkinson's disease (PD) reflects a defective control of the ocular motor behaviour by the basal ganglia. Deep brain stimulation (DBS) seems to improve motor function in PD by decreasing beta band potency (BBP), which is pathologically increased. The subcortical network responsible for the generation of saccades has not been investigated in vivo, using IPG-PerceptTMPC DBS. This study aimed to synchronize DBS and eye-tracking signals to measure the activity of the ocular motor network in the subthalamic nucleus (STN).

Description of Cases:

A 69-year-old PD patient with predominantly right bradykinesia and implanted IPG-PerceptTMPC underwent horizontal and vertical prosaccades. Saccadic behavior, BBP and local field potential (LFP) amplitude were analyzed during DBS on and off. With DBS off, the velocity/gain of vertical saccades was lower than that of horizontal saccades. With DBS on, the gain of leftward saccades was increased ($p=0.018$) and the latency of vertical saccades was shortened ($p<0.035$). With DBS off, the right hemisphere BBP was lower during leftward (contralateral) saccades ($p=0.044$), while in the left hemisphere, rightward and leftward saccades-related BBP was similar. Importantly, with DBS on, left hemisphere BBP during rightward (contralateral) saccades could be significantly decreased when compared to DBS off ($p=0.034$). Left hemisphere BBP positively correlated with the gain of rightward saccades ($R=0.67$; $p=0.016$) with DBS on. There were no significant BBP differences between upward and downward saccades in either hemisphere during DBS on or off. LFP results roughly matched BBP results.

Conclusions, including unique features of the case:

This work shows real-time changes in the right STN activity predominantly during contralateral saccades with DBS off, and the restoring of a similar pattern in the left STN with DBS on, providing important insights into the probable normal (lateralized) ocular motor-related STN activity, and the effect of DBS on restoring such activity in the presumably more affected STN.

References: None provided.

Keywords: Ocular motility, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Two Cases Of Cyclic Vertical Deviation Following Eye Surgery

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Introduction:

Cyclic strabismus, typically characterized by a 24-hour on-off cycle, is a rare condition, particularly when it manifests as a vertical deviation in adults. Cyclic deviations involve alternating periods of significant strabismus and orthotropia or little heterotropia. Here we report two cases of cyclic vertical deviation after eye surgery in adults.

Description of Cases:

Case 1: A 37-year-old male with goniodysgenesis related glaucoma developed alternate-day right hypertropia with bothersome diplopia after Ahmed glaucoma valve implantation in the right eye. On diplopia days the 45 prism diopter (PD) hypertropia was associated with -2 duction of the right superior oblique muscle. On asymptomatic days only a vertical phoria of 3 PD with binocular single vision and normal eye motility was present. As negative for other causes, a revision of the valve was performed, resulting in improved IOP control but without resolving the cyclic strabismus. Case 2: A 44-year-old myopic female underwent scleral buckling and vitrectomy for retinal detachment of the left eye, following which a diplopia of alternate day character with underfunction of the left superior rectus muscle emerged. On bad days the patient presented with moderate right hyperesotropia (18 PD RHT, 14 PD ET) diminishing to 2PD RHT and 5 PD ET on good days. The buckle was explanted leading only to a slight change in the rythm of the cycles.

Conclusions, including unique features of the case:

Cyclic deviations are rare in adults, with most cases involving horizontal deviations. While commonly associated with visual loss, some cases have been linked to motor injuries such as fibrous dysplasia, myositis, thyroid eye disease and trauma. Both glaucoma valve implantation and scleral buckling could impact the extraocular muscles. To our knowledge, this is the first report of cyclic vertical deviation following glaucoma or retinal surgery.

References: None provided.

Keywords: Adult strabismus with a focus on diplopia, Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Reversible Bilateral Vision Loss and Abducens Palsies from Nutritional Deficiency Following Gastrointestinal Illness

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Introduction:

Thiamine deficiency remains an important but underrecognized cause of acute, reversible bilateral vision loss. Although Wernicke's encephalopathy classically presents with confusion, ataxia, and ophthalmoplegia, optic nerve dysfunction may occur even in the absence of characteristic MRI findings. With the increasing use of GLP-1 receptor agonists and appetite-suppressing medications, new patterns of nutritional deficiency are emerging in non-alcoholic patients.

Description of Cases:

A 41-year-old woman with hypertension and migraine developed several weeks of nausea, vomiting, and poor oral intake following *Clostridioides difficile* colitis and recent use of a GLP-1 receptor agonist. She reported a 20-pound weight loss and progressive painless bilateral vision loss over four days. Examination revealed counting-fingers visual acuity in both eyes, mild esotropia, bilateral abduction limitation, and large-amplitude horizontal nystagmus. The optic discs showed mild elevation without edema or pallor. Neurologic evaluation noted areflexia and mild confusion. MRI of the brain and orbits demonstrated no optic nerve enhancement or brainstem abnormality. OCT of the optic nerves and macula were normal. Cerebrospinal fluid was acellular with normal protein and glucose. Laboratory studies showed hypokalemia, hypophosphatemia, and hypomagnesemia, with normal B12 and folate levels. Given profound malnutrition, empiric intravenous thiamine (500 mg three times daily) was initiated along with vitamin repletion. Within 72 hours, visual acuity improved to 20/30 bilaterally, and ocular motility deficits partially resolved.

Conclusions, including unique features of the case:

This case illustrates a reversible nutritional optic neuropathy within the Wernicke spectrum presenting with acute bilateral vision loss and abducens palsies despite normal neuroimaging and OCT findings. Early recognition and empiric thiamine treatment can be vision-saving. Neuro-ophthalmologists should maintain high suspicion for nutritional etiologies of visual loss, particularly in patients with recent gastrointestinal illness, rapid weight loss, or appetite-suppressing therapy.

References: None provided.

Keywords: Adult strabismus with a focus on diplopia, Ocular motility, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

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Evolution of PAMM Lesions following Improvement of SLE Related Retinal Artery Occlusion after Systemic Steroid Therapy

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Introduction:

Retinal artery occlusion (RAO) is a serious condition that almost invariably results in vision loss of various degrees that are often severe. Although the most common mechanism is thrombo-embolic, inflammatory conditions can also cause RAO. Systemic lupus erythematosus (SLE) is an autoimmune disorder of various clinical implications, including occlusive vasculitis that can, though rarely, involve retinal vessels and cause RAO.

Description of Cases:

A 45 year old female re-presented with acute painless vision loss OS. 1 week prior, she presented with a similar complaint OD that was found to be the result of a combined cilio-retinal artery occlusion and optic disc edema. Following which, she was admitted at the rheumatology department for work-up and pulse steroid therapy. The patient fulfilled the diagnostic criteria of SLE and because of the lack of improvement OD, cyclophosphamide was initiated and steroid therapy was shifted to a reduced oral dose. One day later, she endorsed the previously mentioned acute vision loss OS. Examination revealed counting fingers vision and abnormal macular appearance OS that OCT revealed to be the result of middle retinal layer opacification, suggesting an ongoing RAO, presumably vasculitis related. Therefore, rescue systemic steroids were resumed. One week later, visual acuity improved to 6/36 and OCT showed recovery of retinal lamination, along with evolution of paracentral acute middle maculopathy (PAMM) lesions

Conclusions, including unique features of the case:

We present a rare case of SLE in which OCT established the diagnosis of RAO findings and the subsequent dramatic response to steroid therapy was associated with the evolution of PAMM lesions. The case highlights the value of OCT in identifying subtle RAO, the potential reversibility of vasculitic RAO following proper anti-inflammatory treatment, and PAMM lesions as sequelae of RAO.

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Keywords: Retina, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)

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Optical Coherence Tomography (OCT) Evaluation of Peripapillary Hyperreflective Ovoid Masses (PHOMS) in Patients with Glaucomatous Optic Neuropathy

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Introduction:

The incidence of PHOMS has been reported at 9% in the pediatric (1), up to 33% in the adolescent (2) and 1.6% in the adult population (3). To our knowledge, there have not been any studies investigating the presence or morphology of PHOMS in patients with glaucomatous optic neuropathies. Given the still nebulous pathogenesis of glaucoma and the proposed nature of PHOMS as markers of axoplasmic stasis, we investigate if there may be any association between the two entities. Purpose: To determine the incidence and associated factors for PHOMS in glaucomatous optic neuropathy compared to the reported adult incidence.

Methods:

A retrospective review of patients with primary open angle glaucoma (POAG) in an academic glaucoma clinic. Patients had 360-degree OCT optic nerve head and retinal nerve fiber layer (RNFL) thickness measurements, and a glaucomatous appearing visual field defects performed within 1 year of OCT. Peripapillary OCT nerve fiber layer 3-ring scans were reviewed for the presence of PHOMS using a standardized training set (4,5).

Results:

115 eyes of 79 POAG patients were evaluated. Mean age 72.7 years (range: 44-102, SD: 12.1) with 41 males (51.9%). There were 35 White (44.3%), 20 Black (25.3%), 11 Hispanic (13.9%), 4 Asian (5.1%), 3 Other (3.8%), and 6 Unknown (7.6%). Mean RNFL thickness was 60.6, 53.8, 49.6 μ m for the inner, middle and outer RNFL rings, respectively. Humphrey visual field mean deviation -11.25 dB (range: 31.19 to -3.02, SD: 7.54). Bruch's membrane opening mean average was 2.07 mm³. No PHOMS were detected in any eyes of the OCT scans evaluated.

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Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Miscellaneous, Demyelinating disease, High intracranial pressure/headache

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Fool me twice: Diplopia and motility restriction secondary to cutaneous squamous cell carcinoma with perineural invasion of the supraorbital nerve

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Introduction:

Squamous cell carcinoma (SCC) is the second most common skin cancer in the periorbital region. Perineural invasion (PNI) is estimated to occur in 2.5-14% of SCCs and is associated with a poor prognosis. Most cases of SCC with PNI are initially asymptomatic; PNI often may not be considered until patients present with visual disturbances or cranial nerve palsies due to tumor extension into the orbit or cavernous sinus.

Description of Cases:

A 78-year-old female with medical history notable for basal cell carcinoma treated with Mohs micrographic surgery on the left forehead presented with 2 years of persistent facial numbness in the left V1 dermatome, followed by 5 months of orbital pain and diplopia. Physical exam revealed a large abduction deficit of the left eye and more minor elevation and depression deficits of the left eye. Magnetic resonance imaging (MRI) of the orbits was obtained, which revealed asymmetric signal changes in the left cavernous sinus. A trial of oral steroids was initiated to treat possible idiopathic orbital inflammatory syndrome. The patient failed to respond to steroids and left eye motility worsened; she also had more prominent proptosis on follow-up. A cerebral angiogram was subsequently obtained which did not show any cavernous carotid fistula. Repeat MRI of the orbits revealed worsening cavernous sinus enhancement and more prominent enhancement of the left supraorbital nerve. Biopsy of the left forehead and orbital lesion confirmed the diagnosis: poorly differentiated invasive SCC with perineural and intraneural invasion. The patient was subsequently referred to dermatology, medical oncology, and radiation oncology for additional workup and treatment.

Conclusions, including unique features of the case:

In patients with orbital disease that is steroid non-responsive without a clear etiology, a history of previous skin malignancy can be helpful in determining the final diagnosis. Early recognition and treatment of PNI in periorbital SCC is crucial to prevent disease progression and ophthalmic complications.

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Keywords: Orbit, Orbit/ocular pathology, Ocular motility, Tumors

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Contact Information: None provided.

Orbital Apex Syndrome From Middle Meningeal Artery Embolization

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Introduction:

Middle meningeal artery embolization (MMAE) is an increasingly utilized treatment for chronic subdural hematomas due to lower retreatment/recurrence rates, and comparable complication rates compared to surgical intervention[1]. MMAE complications are rare and include vision loss due to MMA and ophthalmic artery (OA) anastomosis[2], and diplopia from inadvertent lacrimal artery embolization; however, no cases of both in the same patient have been reported[3,4]. We present two patients with orbital apex syndrome related to MMAE.

Description of Cases:

A 75-year-old male presented with upper extremity weakness from a right-sided subdural hematoma with midline shift. Following surgical evacuation and MMAE, he developed vertical diplopia. Examination showed normal visual acuity OU, a left relevant afferent pupillary defect (RAPD), a 6PD right hypertropia, and limited supraduction and adduction OS, concerning for a left orbital apex syndrome. MRI showed high density foci in the posterior and superior orbit, likely representing embolization material. Ocular motility improved after treatment with IV methylprednisolone. A 44-year-old male developed horizontal and vertical diplopia due to an acute subdural hemorrhage. Following surgical evacuation and MMAE, his diplopia resolved. One year later, he developed a right abduction deficit; afferent visual function was normal OU. The following year, examination showed visual acuity of 20/125 OD and 20/20 OS, a right RAPD, right optic atrophy, a right hypotropia and adduction deficit, and a small nasal island of vision OD on visual fields, concerning for a right orbital apex syndrome. MRI showed soft tissue enhancement at the right orbital apex consistent with a granulomatous reaction to embolization material.

Conclusions, including unique features of the case:

While vision loss or diplopia following MMAE has been reported, no previous reports of orbital apex syndrome from MMAE exist. As MMAE becomes more common, it is important to recognize that embolic material can reach the orbit, sometimes years after MMAE, causing diplopia, vision loss, or an orbital apex syndrome.

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Keywords: Orbit/ocular pathology, Neuroimaging, Interventional neuroradiology, Ocular motility, Optic neuropathy

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Primary Extraocular Muscle Lymphoma

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Introduction:

This case explores isolated extraocular muscle enlargement in a patient with Hashimoto's thyroiditis, ultimately diagnosed with primary extraocular muscle lymphoma (PEML).

Description of Cases:

A 71-year-old man with Hashimoto's thyroiditis presented with one month of binocular horizontal diplopia, left eye proptosis, and chemosis. Exam showed left proptosis with resistance to retropulsion, chemosis, esotropia in left gaze, hypotropia, and mild limitation of abduction, adduction, and supraduction. MRI demonstrated a homogeneously enhancing lesion confined to the left medial rectus belly. Thyroid peroxidase and thyroglobulin antibodies were elevated (47.7 IU/mL and 241 IU/mL); T3 was slightly low (67 ng/dL), TSH mildly elevated (4.71 μ IU/mL), T4 normal, and TSH receptor antibodies negative. IgG4, ANA, ANCA, QuantiFERON-TB, ACE, lysozyme, CSF, and chest CT were unremarkable. Initial medial rectus biopsy showed scant normal muscle. Repeat biopsy after prednisone taper (60 mg to 10 mg) revealed nonspecific inflammation. PET/CT demonstrated focal uptake in the medial rectus without other lesions. A third biopsy confirmed atypical B-cell lymphoid proliferation with IgH/IgK rearrangement. The patient responded well to focal radiation with minimal residual diplopia in extreme left gaze and remains under imaging surveillance.

Conclusions, including unique features of the case:

This case underscores the need for a broad differential when evaluating extraocular muscle enlargement, even in patients with autoimmune thyroid disease. The differential included thyroid ophthalmopathy, IgG4-related disease, lymphoma, and orbital pseudotumor. Thyroid ophthalmopathy was unlikely given rapid progression, isolated muscle involvement, and absent TSH receptor antibodies [1]. Adequate muscle biopsy sampling is essential for diagnostic yield. Although no consensus exists on optimal steroid washout duration, withholding steroids may prevent histologic obscuration. In primary CNS lymphoma, corticosteroid use before biopsy increases non-diagnostic sample risk [2]. Our patient's first two biopsies—one with scant tissue and another while on corticosteroids—were non-diagnostic, with lymphoma identified only on the third, supporting the potential negative impact of steroids on biopsy accuracy.

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Keywords: Orbit/ocular pathology, Neuroimaging, Neuro-opth & systemic disease (eg. MS, MG, thyroid)

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Teprotumumab Associated with Retinal Detachment in a Young Patient with Thyroid Eye Disease: A Cautionary Case Report

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Introduction:

The current standard of care for Thyroid Eye Disease (TED) is teprotumumab, a human monoclonal antibody targeting insulin-like growth factor 1 receptor (IGF-1R). Despite its high efficacy, the full scope of its side effects is yet to be determined, and retinal detachment (RD) has not been reported.

Description of Cases:

A 19-year-old female with severe active TED and pre-existing severe bilateral myopia who completed a full course of teprotumumab with successful TED remission. Four months post-treatment, she presented with a Rhegmatogenous Retinal Detachment (RRD) in the right eye, requiring surgical repair.

Conclusions, including unique features of the case:

We provide supportive imaging data that the RRD was influenced by teprotumumab's action, either through the rapid decompression and globe repositioning in an already thinned, myopic retina, and/or by IGF-1R pathway blockage, which is hypothesized to accelerate vitreous liquefaction and increase traction. (Toth et al., 2022) This is also supported by new biomechanical studies linking globe proptosis to increased traction forces and retinal axonal thinning (Chiang et al., 2025). With this imaging data, we also present a new methodology for clinically identifying proptosis using MRI neuroimaging, allowing for a clearer and more consistent diagnosis that can be standardized across providers. RRD may be a rare but serious complication, particularly in young, highly myopic patients, and this risk factor should be carefully considered when prescribing teprotumumab.

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Thyroid eye disease (TED) impact, treatment goals, and treatment experience from the patient perspective: Results from the ElevaTED survey

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¹ Brady Neuroscience Clinic, ² TED Community Organization, ³ Outcomes Insights, ⁴ Viridian Therapeutics, Inc., ⁵ Sarasota Retina Institute

Introduction:

TED is a chronic, debilitating autoimmune disease with diverse symptoms and clinical subtypes. Here we present a subset of results from the ElevaTED survey to better understand patient-reported TED impact, treatment goals, and treatment experience.

Description of Cases:

ElevaTED, a 30-minute online survey, was designed to improve understanding of key issues affecting adults diagnosed with TED. It was distributed to members of multiple patient advocacy organizations and a national panel of patients. Questions focused on QoL, activities of daily living, pain, sleep, depression, anxiety, work productivity, and treatment experience and goals. 204 respondents qualified and completed the survey. Mean age was 50 years; 74% were female. Broad ranges of race/ethnicity (53% White) and geographical location (42% suburban, 43 states in U.S.) were represented. Time since start of TED symptoms was ≤15 months for 40%, 16-35 months for 35%, and ≥36 months for 25% of respondents. Regardless of time since first symptoms, ~75% had reported severity of symptoms to be moderate-to-severe in the past month, with eye pain and diplopia the most bothersome. The most frequently reported treatment goals were to improve the following: how eyes feel (86%), sleep (74%), sensitivity to light (65%), vision (63%), ability to do daily activities (62%), and appearance (62%). When asked about satisfaction with medications tried, respondents were “very/extremely” satisfied most often with teprotumumab (85% [54% extremely satisfied]) and IV steroids (77% [15% extremely satisfied]) and least often with tocilizumab, rituximab, and subconjunctival steroids (all < 15%). Over 80% of respondents were worried about symptoms returning/worsening regardless of prior treatments and want to discuss the impact of TED more with their physicians.

Conclusions, including unique features of the case:

TED is a chronic condition that affects QoL and mental health for years. Better understanding of its long-term impacts and individual patient treatment goals will improve physician-patient dialogue, multidisciplinary care, and new treatment development.

References: None provided.

Keywords: Graves' disease, Orbit, Orbit/ocular pathology, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Contact Information: None provided.

Lateral Rectus Injuries Following Orbital Decompression

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Introduction:

Lateral rectus injuries are a rare complication of orbital decompression surgery. Adhesions of the lateral rectus to the temporalis muscle have been associated with deep lateral and medial wall decompression surgeries.¹ Studies also show that following orbital decompression surgery, the extraocular muscles have been found to enlarge, the lateral rectus increasing in width more significantly than the medial rectus.² This presentation presents two cases of abduction deficits from lateral rectus injury following orbital decompression surgery.

Description of Cases:

The first case is a 59-year-old woman with thyroid eye disease and exophthalmos who underwent a bilateral orbitotomy with bone decompression of the lateral orbital wall and a bilateral endoscopic medial wall orbital decompression. During her postoperative phase, the patient was found to have new abduction deficits, worse left than right, which showed some improvement on oral steroids. The patient underwent MRI, which showed myositis of the left lateral rectus muscle, and was offered a longer oral steroid course, but declined and preferred strabismus evaluation. The second case is a 60-year-old woman with a history of thyroid eye disease who underwent orbital decompression surgery, who was referred for strabismus evaluation due to diplopia following the decompression surgery. On exam, the patient was found to have bilateral abduction deficits. On MRI, the bilateral lateral rectus muscles appeared to be damaged or slipped. The patient underwent bilateral medial rectus recession and bilateral superior rectus Hummelsheim transposition with foster modification to correct the diplopia.

Conclusions, including unique features of the case:

Lateral rectus injury following orbital decompression is a rare complication, especially as most cases report motility disturbances in the setting of muscle enlargement or scarring. True lateral rectus injury is rare, but can be seen in cases of orbital decompression.

References: 1.) Burch, H. B., Perros, P., Bednarczuk, T., Cooper, D. S., Dolman, P. J., Leung, A. M., Mombaerts, I., Salvi, M., & Stan, M. N. Management of thyroid eye disease: a Consensus Statement by the American Thyroid Association and the European Thyroid Association. *European thyroid journal*, 11(6), e220189. (2022). <https://doi.org/10.1530/ETJ-22-0189> 2.) Gupta, A., Nobori, A., Wang, Y., Rootman, D., & Goldberg, R. Lateral Rectus Muscle Expands More Than Medial Rectus Following Maximal Deep Balanced Orbital Decompression. *Ophthalmic plastic and reconstructive surgery*, 34(2), 140–142. (2018). <https://doi.org/10.1097/IOP.0000000000000894>

Keywords: Ocular motility, Orbit, Neuroimaging

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Efgartigimod Led to Improvement of Myasthenia Gravis Symptoms in Patients Initially Presenting with Ocular Symptoms: A Case Series

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Introduction:

Myasthenia gravis (MG) is a neuromuscular autoimmune disease mediated by pathogenic immunoglobulin G (IgG) autoantibodies that target components of the neuromuscular junction. A common initial manifestation of MG is focal ocular weakness, and many patients who present with ocular symptoms subsequently develop generalized weakness. Efgartigimod is a human IgG1 antibody Fc fragment that selectively reduces IgG levels by blocking neonatal Fc receptor–mediated IgG recycling. Here, we describe the response to efgartigimod treatment in 2 patients who were diagnosed with acetylcholine receptor autoantibody positive (AChR-Ab+) MG after initial presentation of ocular symptoms.

Description of Cases:

Patient 1, an 81-year-old male, was diagnosed with MG in 2021 after sudden onset of binocular diplopia. The patient's symptoms were initially controlled with 1 month of prednisone and ongoing treatment with pyridostigmine. In 2024, efgartigimod IV treatment was initiated after the patient began to experience generalized weakness and fatigue. After multiple treatment cycles, the patient's symptoms improved, including resolution of diplopia and regaining the ability to do most of their daily activities without issue. Patient 2, a 78-year-old male, was diagnosed with MG in 2024 after developing ptosis. Initial treatment with pyridostigmine led to insufficient symptom improvement, and treatment with subcutaneous (SC) efgartigimod PH20 (coformulated with recombinant human hyaluronidase PH20) was initiated approximately 2 months after diagnosis. After several treatment cycles, the patient had improvements in ptosis and reported an overall increase in energy. In both patients, efgartigimod was well tolerated and there were no notable adverse events.

Conclusions, including unique features of the case:

Two patients who initially presented to the clinic with new ocular symptoms due to MG achieved improvement of both ocular and generalized MG symptoms after efgartigimod treatment. Efgartigimod was well tolerated.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Myasthenia, Ocular motility

Financial Disclosures: Jody Abrams: JA has served as a speaker for Amgen and ANI and has been involved in clinical studies with Amgen, Veridian, and argenx.

Grant Support: None.

Contact Information: None provided.

A Case of Double Vision—and Double Takes—at the Core

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Introduction:

An 88-year-old woman presented with three weeks of horizontal diplopia in lateral gaze, beginning one week after noticing a ruptured blood vessel in the right eye. Her oncologic history includes prior lung, breast, bladder, skin, and kidney cancers. Visual acuity was 20/20-3 OD and 20/20 OS. Pupils were equal without afferent defect; fields were full. Color vision was reduced (3/10 OD, 6/10 OS). Motility showed -2 abduction, -3 adduction, and mild supraduction/infraduction deficits OD with incomitant horizontal deviations. Exophthalmometry showed 1 mm proptosis OD with mild resistance to retropulsion. MRD1 was 5 mm OD and 4 mm OS. Anterior exam revealed dilated, tortuous conjunctival vessels extending superomedially to a dark purple mass beneath the superior semilunar fold.

Description of Cases:

Orbital MRI showed a well-circumscribed 2.9 × 1.6 × 2.0 cm enhancing mass centered on the medial rectus with intraconal and anterior peribulbar extension. The lesion was predominantly T1- and T2-hyperintense. Transconjunctival biopsy demonstrated a tumor positive for S-100, MyoD1, and desmin, initially suggesting adult rhabdomyoma. Outside review identified a BCOR c.1118C>A (p.S373*) mutation, seen in 1–2% of sarcomas and associated with aggressive behavior, raising concern for a BCOR-mutated rhabdomyosarcoma—rare in adults. Given presumed malignancy and the patient's age, management options included observation, exenteration, globe-sparing resection, chemotherapy, or radiation. Limited chemotherapy tolerance and expected toxicity of radiation were concerns. The patient elected orbital exenteration. Final pathology showed negative margins and loss of desmin, MyoD1, and myogenin expression. Cytology suggested a possible TFE3-rearranged tumor, but FISH and sequencing were negative. The relevance of the BCOR mutation remained uncertain.

Conclusions, including unique features of the case:

The patient was diagnosed with a low-grade orbital sarcoma harboring a BCOR c.1118C>A mutation. Complete excision was achieved, and metastatic risk is felt to be minimal. This represents a rare orbital sarcoma with atypical morphology in which radiologic and pathologic findings were incongruent, highlighting diagnostic challenges.

References: 1.COSMIC, cBioPortal for Cancer Genomics 2.Lewis N, Soslow RA, Delair DF, et al. ZC3H7B-BCOR high-grade endometrial stromal sarcomas: a report of 17 cases of a newly defined entity. *Mod Pathol*. 2018;31(4):674-684. 3.Jaru-Ampornpan P, Tansirisithikul C, Prukajorn M, Sampattavanich S, Pithukpakorn M. Germline ATM mutation and somatic PIK3CA and BCOR mutations found in an infant with aggressive orbital embryonal rhabdomyosarcoma. *Am J Ophthalmol Case Rep*. 2021;23:101189. Published 2021 Aug 4. 4.Salman SS, Kakkar A, Kashyap S, Rastogi S, Meel R. Orbital Sarcoma with BCOR Genetic Alterations in the Pediatric Age Group. *Fetal Pediatr Pathol*. 2024;43(6):492-499. 5.Vempuluru VS, Mishra DK, Kaliki S. Primary orbital BCOR-positive sarcoma. *J Fr Ophtalmol*. Published online July 25, 2025.

Keywords: Orbit, Tumors, Ocular motility, Neuroimaging

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A rare case of Lyme disease presenting as orbital myositis

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Introduction:

In this discussion, we present a rare case of a patient with headache, periorbital edema, diplopia, and eye redness, who was initially diagnosed and treated for Bell's Palsy, but was later found to have Lyme-associated orbital myositis.

Description of Cases:

Single case study of a 66-year-old female with a PMHx of HTN, RA, and Adie's pupil OD, presenting with two weeks of gradually worsening eye pain, redness, diplopia, and peri-orbital edema. One month prior, she had presented to an OSH for similar symptoms and was diagnosed with Bell's Palsy and treated with one week of PO Valtrex and Prednisone. Her exam at the time of this second presentation showed left proptosis, left ptosis, conjunctival injection, and limited motility in all gazes. MRI brain and orbits revealed mild left proptosis with subtle infiltration of the left retrobulbar fat and enlargement of the left extra-ocular muscles with left mesial, pre-septal soft tissue swelling of unclear etiology. Workup for orbital inflammatory disease revealed positive serum Lyme titers, and the patient was started on Ceftriaxone. Lumbar puncture also revealed positive CSF Lyme titers. The patient's symptoms and exam improved with antibiotic therapy alone, with subsequent resolution of MRI findings.

Conclusions, including unique features of the case:

Lyme disease is a multi-system infection with a wide range of clinical presentations, including fatigue, joint pain, numbness, tingling, and classic "bull's-eye" rash. Neuro-ophthalmologic manifestations typically include cranial nerve palsy, optic neuritis, and papilledema. Orbital myositis is a rare complication of Lyme disease that is not well described. It results from direct spirochetal invasion of the extra-ocular muscles or immune-mediated, post-infectious inflammation. While intravenous steroids are often the treatment of choice in orbital myositis, this patient recovered with antibiotic therapy alone. It is important to note that the lack of classic "Lyme" symptoms or skin rash exam findings should not delay diagnosis and treatment.

References: None provided.

Keywords: Orbit/ocular pathology, Lyme disease, Ocular motility, Neuro-ophth & infectious disease (eg, AIDS, prion)

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Case Report: A Unique Case of Marin-Amat Syndrome and Crocodile Tears post-Gamma Knife Surgery for Treatment of Vestibular Schwannoma

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Introduction:

Marin Amat syndrome (MAS) is a rare, acquired phenomenon of aberrant facial nerve re-innervation. We report a patient with co-existent MAS and Crocodile Tears Syndrome (CTS), two co-existent phenomenon not previously reported together in the literature.

Description of Cases:

A 40-year-old female presented with dizziness, left hearing loss, and subsequent left facial droop with weakness that emerged during pregnancy. On MRI there was a 1.7 x 1.6 x 1.1 cm left cerebellopontine angle (CPA) mass, consistent with vestibular schwannoma. The mass invaded the left internal auditory canal, obstructing the trigeminal nerve and the middle cerebellar peduncle. Two months following diagnosis, the patient underwent gamma knife stereotactic radiosurgery. Immediate post-operative course was uncomplicated, with resolution of facial weakness. Nine months after surgery, the patient reported new onset of twitching of the left lower eyelid. Twelve months after surgery, involuntary tearing of the left eye with left upper eyelid closure while eating or making facial movements occurred. A follow-up MRI showed reduction of the mass to a stable 0.5 cm lesion. The patient was found to have left trigeminal-facial synkinesis, indicative of MAS. Findings also suggested potential gustatory lacrimation with crocodile tears.

Conclusions, including unique features of the case:

We present a unique case of CTS occurring with MAS. Current literature has not described the location of nerve damage leading to MAS, but studies have shown that CTS occurs secondary to damage outside of the superior salivatory nucleus in the CPA. Our case suggests that aberrant nerve re-innervation leading to MAS may occur in the CPA.

References: None provided.

Keywords: Tumors, Skull base, Neuroimaging, Ocular manifestations of vestibular disorders, Miscellaneous

Financial Disclosures: The authors had no disclosures.

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Contact Information: None provided.

Atypical Presentation of Carotid-Cavernous Fistula Mimicking Idiopathic Orbital Inflammation

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Introduction:

Carotid-cavernous fistula (CCF) typically presents with acute onset of conjunctival injection, chemosis, proptosis, and diplopia due to cranial nerve involvement. However, indolent or atypical cases may resemble idiopathic orbital inflammation (IOI), leading to diagnostic delay. We present a case initially presumed to represent IOI, later confirmed to be a CCF.

Description of Cases:

A 49-year-old woman with no prior ocular history presented with two months of progressive left upper-lid swelling and periocular pain with no diplopia. She reported headaches radiating to the forehead and nasal bridge which began six months ago. She was treated empirically for presumed trigeminal neuralgia without improvement. Her examination revealed visual acuity of 20/20 OU and intraocular pressures were 18 mmHg OD and 31 mmHg OS. Extraocular movements were full, but painful on supraduction OS. Confrontational visual fields were full and no APD was present. The patient had left-sided lid edema causing mechanical ptosis, 2 mm of proptosis OS, and mild conjunctival injection OS. ESR and CRP were elevated at 66 mm/hr and 15.7 mg/L. CT orbits demonstrated preseptal swelling without orbital mass. Infectious and autoimmune work-up was negative; however, IgG studies were mildly elevated, raising consideration of IgG4-related orbital disease. Based on the unilateral inflammation, pain, and elevated inflammatory markers, IOI was suspected, and a lacrimal gland biopsy was considered. Subsequent MRI orbits and MR angiography revealed an underlying CCF. Patient underwent fistula embolization and on examination 2 days later, patient had resolved ptosis, proptosis, and chemosis. After being treated with IOP lowering drops, IOP OS was 16 on post-operative evaluation.

Conclusions, including unique features of the case:

This case highlights an unusual presentation of CCF without diplopia or classic conjunctival arterialization, mimicking IOI. Elevated inflammatory markers and preseptal edema further obscured the vascular etiology. Recognition of this atypical presentation is critical since prompt vascular imaging can avoid unnecessary biopsies and facilitate definitive endovascular treatment.

References: None provided.

Keywords: Orbit/ocular pathology, Vascular disorders, Orbit, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: N/A

Contact Information: Bhakti Panchal, MD, Bhakti.K.Panchal@medstar.net

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Autoimmune-Related Retinopathy and Optic Neuropathy in a Child Complicated by Dragged Fovea Diplopia Syndrome

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Introduction:

Autoimmune-related retinopathy and optic neuropathy (ARRON) is a rare autoimmune condition defined by antibodies against retinal and/or optic nerve antigens in the absence of malignancy. We describe a pediatric case of ARRON with anti-enolase and anti-PKM3 antibodies, complicated by dragged fovea diplopia syndrome.

Description of Cases:

A 13-year-old girl presented with progressive vision loss over one week, affecting primarily the left eye. She denied pain and neurological symptoms. Examination revealed visual acuity of 20/25 OD and 2/800 OS, 2+ RAPD OS, and sensory left exotropia. OCT RNFL showed superior thinning OD and thickening OS. There was a concern for an intracranial lesion causing Foster Kennedy syndrome, and brain/orbit MRI was obtained, which was unremarkable. Repeat OCT was performed on both the optic nerve and macula; the macular OCT demonstrated paracentral and subfoveal ellipsoid zone (EZ) loss OS and vitreous cells OU. Infectious workup was negative and an autoimmune etiology was suspected. An oral steroid course was initiated, leading to improved vision (20/20 OD, 20/40–2 OS) and reconstitution of the EZ OS. Further testing identified both anti-enolase and anti-PKM3 antibodies. Paraneoplastic screening was negative, and the patient was diagnosed with ARRON. Monthly IVIg was initiated. Three months after diagnosis, new cystoid macular edema (CME) OS developed, and the patient reported diplopia. Examination demonstrated sensory exotropia measuring 40 PD and inability to fuse with prisms in free space. The lights on-off test revealed that the patient had dragged fovea-diplopia syndrome. Because of this, the patient was advised to defer strabismus surgery until CME improved.

Conclusions, including unique features of the case:

This case illustrates a rare complication of ARRON with CME, dragged fovea diplopia syndrome. Clinicians should be aware of the possibility of dragged fovea diplopia syndrome in patients with CME, which may influence the decision to pursue strabismus surgery.

References: 1. De Pool ME, Campbell JP, Broome SO, Guyton DL; The dragged-fovea diplopia syndrome: clinical characteristics, diagnosis, and treatment, *Ophthalmology*, 112:1455-1462, 2005. 2. Grewal DS, Fishman GA, Jampol LM; Autoimmune retinopathy and antiretinal antibodies: a review, *Retina*, 34:827-845, 2014. 3. Grange L, Dalal M, Nussenblatt RB, Sen HN; Autoimmune retinopathy, *American Journal of Ophthalmology*, 157:266-272, 2014. 4. Almarzouqi SJ, Morgan ML, Carvounis PE, Lee AG; Autoimmune-Related Retinopathy and Optic Neuropathy Accompanied by Anti-GAD Antibodies, *Neuroophthalmology*, 39:195-200, 2015. 5. Oyama Y, Burt RK, Thirkill C, Hanna E, Merrill K; A case of autoimmune-related retinopathy and optic neuropathy syndrome treated by autologous nonmyeloablative hematopoietic stem cell transplantation, *Journal of Neuroophthalmology*, 29:43-49, 2009.

Keywords: Pediatric neuro-ophthalmology, Retina, Optic neuropathy, Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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FOXC1-Related Morning Glory-like Papillopathy and Cerebral Vasculopathy

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Introduction:

Axenfeld-Rieger Syndrome (ARS) is characterized by anterior segment dysgenesis and is associated with FOXC1 or PITX2 mutations [1]. While glaucomatous optic neuropathy is well-documented in ARS, non-glaucomatous optic nerve anomalies such as Morning Glory Disc Anomaly (MGDA) are rare [2, 3]. We report a unique case of ARS associated with unilateral MGDA-like optic nerve excavation, persistent fetal vasculature, and cerebrovascular dysplasia.

Description of Cases:

A 2-year-old girl with strabismus and autism spectrum disorder was referred for evaluation of a left optic nerve anomaly, initially diagnosed as MGDA with atypical features. On examination, her visual acuity by preferential looking (Teller) was 20/130 with both eyes and strong objection to right eye occlusion. There was a left relative afferent pupillary defect. Extraocular movements were full with no nystagmus. Anterior segment exam was unremarkable on examination by penlight. Examination under anesthesia to thoroughly evaluate for retinal pathology revealed excavation of the left optic nerve head with persistent fetal vascular stalk emerging centrally. MRI/MRA revealed abnormal tortuosity of the internal carotid arteries and superior cerebellar arteries with left ICA dilation, consistent with cerebral arterial dysplasia, but not moyamoya disease. Whole exome sequencing identified a novel heterozygous de novo FOXC1 variant at c.401A>T p.(E134V), predicted to be deleterious. At 8-years-old, a more detailed slit-lamp exam revealed subtle posterior embryotoxon for several clock hours temporally in both eyes. In light of the genetic results and anterior segment findings, the unifying diagnosis of Axenfeld-Rieger Syndrome (ARS) was established.

Conclusions, including unique features of the case:

This case expands the phenotypic spectrum of FOXC1-related ARS to include MGDA-like optic nerve excavation and persistent fetal vasculature. It reinforces the role of FOXC1 in ocular and cerebrovascular development. Genetic testing has an important role in atypical optic nerve anomalies, since recognition of such presentations is critical for early diagnosis and surveillance for glaucoma, neurovascular abnormalities, and other syndromic sequelae.

References: 1) Tripathy K, Salini B. Axenfeld-Rieger Syndrome. [Updated 2024 Feb 12]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK538504/> 2) Jacobson, A. and B.L. Bohnsack, Posterior segment findings in Axenfeld-Rieger syndrome. J aapos, 2022. 26(6): p. 320-322. 3) Muzyka L, Winterhalter E, LoPresti MA, Scoville J, Bohnsack BL, Lam SK. Axenfeld-Rieger syndrome: A systematic review examining genetic, neurological, and neurovascular associations to inform screening. Heliyon. 2023 Jul 13;9(7):e18225. doi: 10.1016/j.heliyon.2023.e18225. PMID: 37539177; PMCID: PMC10395477.

Keywords: Pediatric neuro-ophthalmology, Genetic disease, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Cause Of Visual Loss In Two Overweight Adolescents with Idiopathic Intracranial Hypertension (IIH) and Micronutrient Deficiency – Papilledema and/or Folate Deficiency?

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Introduction:

Obesity is associated with post pubertal IIH as well as micronutrient deficiencies. The pathophysiology in IIH is not clear but micronutrient deficiency is due to diets which are calorie-dense but nutrient poor. Both conditions can result in optic neuropathy and visual loss.

Description of Cases:

We describe 2 adolescents who presented with progressive blurring of vision. Both had a body mass index of greater than 24. One patient was autistic (case1) and both were picky eaters. Both did not eat any fruits or vegetables. Case 1: Acuity in the right eye was 6/30 and no light perception on the left. Optic discs were pale bilaterally. He had no headache, but magnetic resonance imaging (MRI) raised concerns for increased intracranial pressure. Lumbar puncture opening pressure was 40 cm water. He had folate deficiency. There was no improvement in vision despite folate replacement and diamox Case 2: Acuity in the right and left eye was 6/75 and 6/12 respectively. The right disc was pale but the left was swollen. Lumbar puncture opening pressure was >40 cm water. She was deficient in folate and vitamin A. Her vision improved to 6/12 and 6/6 respectively in the right and left eye after folic acid replacement and diamox.

Conclusions, including unique features of the case:

With both parents working, adolescents are left to eat on their own. The most accessible foods is ultra- processed foods/fast food, which are calorie rich but nutrient poor. This results in obesity as well as micronutrient deficiency. Visual loss in these children can be due to chronic papilledema secondary to IIH or from micronutrient deficiency, in particular folate. A thorough diet history as well as work-up for IIH is essential.

References: None provided.

Keywords: Pseudotumor cerebri, Pediatric neuro-ophthalmology, Optic neuropathy, Visual fields, High intracranial pressure/headache

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Vision Loss With Self-Selective Diet: A Case of Vitamin A Deficiency

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Introduction:

Vision loss due to vitamin A deficiency (VAD) is a rare occurrence in developed countries. Many foods in developed countries are fortified with vitamins, making it unlikely to have a deficiency. In these rare cases, vitamin deficiency often occurs due to an underlying medical history of malabsorption or behavioral problems restricting diet.

Description of Cases:

Our case describes a nine-year-old boy with a history of refractive amblyopia, myopia, and astigmatism but with preserved vision of 20/20 who presented with three months of blurry vision and light sensitivity. On exam, the patient could only see hand motion and light perception. Fundus examination showed mild optic disc pallor in both eyes. MRI of the head and orbit showed no abnormalities. Labs revealed essentially absent vitamin A of less than 0.06 mg/L with likely depleted stores in the liver as well as IL2R elevated at 1404.3, ANA nucleolar at 1:160, Vitamin D low at 11.7, and vitamins E and K at normal levels. NMO and MOG antibodies were negative. Work-up was negative for infection, demyelinating condition, infiltration or autoimmune causes. He was diagnosed with nutritional optic neuropathy secondary to VAD. In this case, VAD could have occurred from a chronic self-selective diet of peanut butter sandwiches on white bread, strawberries, French fries, and strawberry lemonade. Supplementation of vitamin A was started, but the patient has shown minimal improvement in vision.

Conclusions, including unique features of the case:

Due to low prevalence of vision loss due to VAD in developed countries, cases are identified late or missed, leading to permanent ocular sequelae, as in our case. This is a preventable problem with fortified foods and vitamin supplementation. Our case highlights the importance of obtaining a thorough history early in presentation of patients with unexplained ocular symptoms to promptly initiate treatment. Additionally, our case highlights the importance of adequate vitamin intake in children.

References: Patil S, Zamwar UM, Mudey A. Etiology, epidemiology, pathophysiology, signs and symptoms, evaluation, and treatment of vitamin A (retinol) deficiency. *Cureus*. 2023;15(11):e49011. doi:10.7759/cureus.49011

Keywords: Pediatric neuro-ophthalmology, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Exercise Induced Esotropia

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Introduction:

Childhood esotropia is characterized by inward eye deviation and can be either congenital or acquired. Acquired forms include refractive esotropia, sensory esotropia, consecutive esotropia, and non-refractive acute acquired comitant esotropia (AACE). AACE is typically seen in older children and is often associated with late onset comitant esotropia and diplopia, it can result from various causes such as neurological conditions, neuromuscular imbalances, or idiopathic. (1,2,7) While the diagnosis of esotropia remains essentially clinical, it is important to identify unusual cases that can reflect more serious underlying pathologies. (3) This case report will describe a rare case of AACE, presenting as exercise induced esotropia with an unremarkable neurological and neuro-ophthalmic evaluation.

Description of Cases:

Exercise induced esotropia is a very rare entity that to our knowledge was documented in two previous case reports and in a case series that involved three patients. (4,5,6) In this case report, we present a case of a 14-year-old male patient, who developed esotropia and diplopia during exercise, specifically Boxing and occasionally jogging with episodes lasting 15 minutes and resolving spontaneously within a minute of exercise cessation. Patient is otherwise healthy, with no significant family history and has a normal ophthalmic exam, neurological evaluation and neuroimaging. In a previous report, a similar case was managed by recession of a single medial rectus muscle, with resolution of symptoms afterwards. (8)

Conclusions, including unique features of the case:

Exercise induced esotropia is an unusual presentation that needs to be further discussed and explored to understand the etiology and guide the diagnosis and management.

References: None provided.

Keywords: Ocular motility, Adult strabismus with a focus on diplopia

Financial Disclosures: Acil Alasheh; Milena Stosic; Lawrence Kaufman; Nikolas Mata-Machado

Grant Support: None.

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Ocular manifestations of MED27 variation and a case of post-operative myopic shift: A case series

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Introduction:

A pathogenic MED27 variant causes an autosomal recessive neurodevelopmental disorder marked by spasticity, cataracts, and cerebellar hypoplasia. Although cataracts occur in 89% of cases, the ocular features remain poorly characterized.^{1,2} This case series reports ophthalmic findings in two pediatric siblings with MED27-associated disease.

Description of Cases:

Patient A: An 11-month-old male with unknown MED27 diagnosis was referred to pediatric ophthalmology for difficulty tracking and intermittent eye crossing. Examination revealed poor fixation with roving eye movements. Cycloplegic refraction demonstrated high myopia with significant astigmatism. No cataract formation was present at that time. At 23 months of age, he was noted to have developed a total white cataract in the left eye and a central nuclear cataract in the right eye. Patient B: A 7-month-old female with a known MED27 diagnosis was referred for similar concerns. Examination revealed difficulty with fixation and following, and nystagmus. Sensorimotor evaluation demonstrated a variable alignment with alternating esotropia and dissociated vertical deviation. Cycloplegic refraction revealed high hyperopia with significant astigmatism. No cataracts were present at the initial visit. The patient returned for follow-up at 34 months of age with bilateral cortical cataracts. Both patients underwent uncomplicated bilateral cataract extraction with intraocular lens implantation, pars plana vitrectomy, and posterior capsulotomy. Immediate postoperative outcomes were favorable, with both meeting targeted refraction goals. Two years postoperatively, Patient A exhibited a marked myopic shift of -6.50 D in the right eye and -9.00 D in the left eye. Based on this, a more hyperopic target of approximately +2.00 D was selected for Patient B's IOL implantation.

Conclusions, including unique features of the case:

This is the first case series presenting the rapid onset of bilateral cataracts and an unexpected postoperative myopic shift in a child with MED27 variation, emphasizing the need for continued reporting to identify refractive outcome patterns.

References: 1. Maroofian R, Kaiyrzhanov R, Cali E, et al. Biallelic MED27 variants lead to variable ponto-cerebello-lental degeneration with movement disorders. *Brain*. 2023;146(12):5031-5043. doi:10.1093/brain/awad257 2. Meng L, Isohanni P, Shao Y, et al. MED27 Variants Cause Developmental Delay, Dystonia, and Cerebellar Hypoplasia. *Ann Neurol*. 2021;89(4):828-833. doi:10.1002/ana.26019

Keywords: Pediatric neuro-ophthalmology, Genetic disease

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Grant Support: None.

Contact Information: None provided.

Implementation of a Dedicated Inpatient Pediatric Ophthalmology Exam Room with Advanced Diagnostics

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Introduction:

Pediatric ophthalmology consultations occur frequently in the inpatient setting and often involve complex pathology. While portable instruments are useful for bedside examinations, they may lack the precision or technical capabilities to make certain diagnoses or track disease progression. Neuro-ophthalmic concerns have previously been described as some of the most frequent indications for pediatric ophthalmology consultation and often benefit from advanced imaging/testing. In this study we describe the implementation and utilization of a dedicated inpatient ophthalmology exam room with specialized diagnostic instruments in a children's hospital.

Description of Cases:

The usage of a dedicated ophthalmology exam room for inpatient pediatric ophthalmology consultations at a pediatric tertiary care hospital was tracked from October 1, 2024 to August 31, 2025. The clinical space was equipped with distance visual acuity testing, a slit-lamp, non-mydratic fundus photography, optical coherence tomography, automated visual field testing, a handheld autorefractor, and B-scan ultrasound. A total of 204 patients were examined with an average age of 12 years old (range: 0 - 23 years old). The slit-lamp was used in 144 instances (70%). Fundus photography and OCT imaging were used in 119 (58%) and 108 (52%) instances, respectively. Automated visual fields were performed in 49 encounters (24%), and the autorefractor was used 34 times (16%). The B-scan was utilized in 14 examinations (6%). Over 26% of all patients brought to the exam room presented for papilledema evaluation or were found to have disc edema.

Conclusions, including unique features of the case:

A dedicated, well-equipped, pediatric inpatient ophthalmology exam room is a valuable resource and assists in the diagnosis and management of complex patients. This model may be replicable at other institutions to enhance inpatient neuro-ophthalmic care.

References: None provided.

Keywords: Pediatric neuro-ophthalmology

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Congenital Horner's Syndrome due to Cervical Extension of Thymic Tissue

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Introduction:

Horner's syndrome in infancy warrants careful evaluation for structural or neurologic causes, including birth trauma, carotid pathology, and neoplasms. Congenital cases are uncommon; identification of benign etiologies is critical to avoid unnecessary interventions. We describe a congenital Horner's secondary to superior cervical extension of thymic tissue, an anatomic variant infrequently reported in the literature.

Description of Cases:

An ex-full-term, healthy 3-month-old female presented with persistent right upper eyelid ptosis since birth. Examination demonstrated right-sided miosis more apparent in dim light, right upper and lower lid ptosis, and full ductions, consistent with Horner's syndrome. There was no heterochromia or palpable face/neck masses. There were no perinatal complications. Head/neck MRI/MRA revealed no abnormalities. However, chest MRI demonstrated superior cervical extension of the thymus along the right carotid artery. There were no radiologic signs of malignant transformation, such as lobulated borders, enhancement, or necrosis, suggesting this variant likely accounted for oculosympathetic disruption in a benign manner. Autoimmune myasthenia gravis as cause of ptosis, though extremely rare in infants, was considered a possibility given the large thymus, but there was no evidence of thymoma, and the ptosis did not fluctuate. Furthermore, anisocoria more apparent in dark alongside ptosis rendered physiologic anisocoria unlikely. The patient's neuro-ophthalmic findings remained stable through seven months. Observation was recommended given expected thymic involution over time, with concurrent amblyopia surveillance.

Conclusions, including unique features of the case:

While thymic cysts and thymomas can rarely cause acquired Horner's syndrome, and while ectopic thymic tissue can cause a congenital Horner's, this is the first report – to our knowledge – of benign thymic tissue contiguously extending into the neck, affecting the sympathetic pathway along the carotid artery. Awareness of this normal variant, presumably due to incomplete thymic descent during fetal development, may prevent unnecessary work-up and guide appropriate reassurance and monitoring.

References: 1) Modabber M, Saint-Martin C, Khan A, Zakrzewski H, Toffoli D. Infantile Horner syndrome due to ectopic cervical thymus gland. *Can J Ophthalmol*. 2019 Feb;54(1):e10-e12. doi: 10.1016/j.jcjo.2018.03.019. Epub 2018 May 21. PMID: 30851785. 2) Berroth ML, Morozova LV, Pollock JM. Ectopic thymus as a cause of Horner's syndrome. *Radiol Case Rep*. 2019 Nov 8;15(1):23-25. doi: 10.1016/j.radcr.2019.10.004. PMID: 31737141; PMCID: PMC6849423.

Keywords: Pupil, Pediatric neuro-ophthalmology

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Grant Support: No grant support.

Contact Information: None provided.

The Pupil Has Become the Master: A Wax on Wax Off Phenomenon

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Introduction:

Understanding the topographical organization of the oculomotor nerve (CN III) is critical: central somatic fibers control eye movements, while peripheral parasympathetic fibers mediate pupillary constriction. Mydriasis in CN III palsy often suggests a compressive lesion, such as an aneurysm. Though CT/MR angiography is less invasive, its sensitivity drops for aneurysms under 3 mm. We present a case of transient pupil-involving CN III palsy that resolved rapidly with blood pressure control.

Description of Cases:

A 50-year-old Hispanic woman with hypertension presented in hypertensive emergency with acute-onset binocular diplopia and right ptosis. BP on admission was 188/79. Examination revealed right mydriasis, ptosis, hypotropia, and exotropia, with full abduction; the remainder of the exam was unremarkable. MRI brain/orbits and CTA head were unremarkable. Her mydriasis was resolved by day 1, with marked motility improvement by day 3 as blood pressure stabilized. Due to concern for a compressive lesion, digital subtraction angiography was performed and revealed a 1.4 × 1.6 mm right P1 PCA aneurysm, not amenable to intervention. By discharge on day 4, symptoms had nearly resolved. The patient was counseled on lifestyle changes and blood pressure control, with outpatient aneurysm monitoring planned.

Conclusions, including unique features of the case:

Pupil-involving CN III palsy with transient mydriasis due to a cerebral aneurysm has not yet been reported in the literature. Clinicians should be aware of cases presenting with transient pupillary dilation in the setting of hypertension, and consider escalation of diagnostic workup if initial imaging is unremarkable. This case underscores the importance of maintaining a high index of suspicion to avoid missing a potentially life-threatening diagnosis.

References: 1. Rinkel GJ, Djibuti M, Algra A, van Gijn J.; Prevalence and risk of rupture of intracranial aneurysms: a systematic review. *Stroke*. 29, 251-256, 1998. 2. Ikawa F, Morita A, Tominari S, Nakayama T, Shiokawa Y, Date I, Nozaki K, Miyamoto S, Kayama T, Arai H; Rupture risk of small unruptured cerebral aneurysms. *Journal of Neurosurgery*. 132, 69-78, 2019. 3. Gasparotti R, Liserre R.; Intracranial aneurysms. *European Radiology*. 15, 441-447, 2005.

Keywords: Pupil, Ocular motility, Neuroimaging, Vascular disorders, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Congenital oculomotor nerve palsy with aberrant eyelid movements and pupillary spasms: A case report

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Introduction:

We report a case of congenital oculomotor nerve palsy presenting with aberrant eyelid movements and an involuntary pupillary reaction.

Description of Cases:

A 24-year-old woman presented with mild anisocoria with no significant medical history. Her ocular history included a history of strabismus and levator muscle surgery. Examination revealed exotropia, hypotropia, and ocular motility impairment, consistent with right oculomotor nerve palsy. Pupillary examination revealed mild anisocoria with the right pupil being unreactive to dim light, followed by involuntary pupillary spasms unassociated with eye position. Twitch-like movements of the upper eyelid were also observed during the spasm phase. Orbital magnetic resonance imaging revealed atrophy of the extraocular muscles, particularly the medial rectus. No intracranial lesions were found and blood tests excluded conditions such as thyroid eye disease. Based on these findings, congenital oculomotor nerve palsy with aberrant regeneration was diagnosed. The patient remained asymptomatic and was managed conservatively. Six months later, no complications due to pupillary spasms or restriction of ocular motility were observed.

Conclusions, including unique features of the case:

This case highlights an unusual pupillary response in congenital oculomotor nerve palsy characterized by involuntary pupillary spasms accompanied by upper eyelid twitching, which has not been previously reported. The prognosis was likely favorable for asymptomatic patients without associated underlying causes.

References: None provided.

Keywords: Pupil, Ocular motility, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Small Patients, Big Mysteries: Diagnostic & Management Dilemmas that Test the Experts of AAPOS & NANOS [1.50 CME]

Moderators: Jason Peragallo, MD (live from AAPOS), MD & Rob Avery, DO (live at NANOS)

Panelists (live at NANOS): Alexis Flowers MD; Grant Liu; MD, Ellen Mitchell, MD

Panelists (live from AAPOS): Elena Bitrian, MD; Stefanie Davidson, MD; Efren Gonzalez, MD

This combined AAPOS and NANOS workshop will discuss pediatric ophthalmology cases in which the diagnosis, findings, and / or treatment pose a clinical dilemma to even an experienced pediatric ophthalmologist. These cases may include rare diagnoses or more common diagnoses with unusual presentations and / or atypical courses. Discussion will include the experiences with similar cases of a panel of seasoned pediatric ophthalmologists, as well as audience participants, and consideration of alternative evaluation and treatment plans.

Upon completion of this session, participants should be able to:

- (1) To share experiences and strategies for the diagnosis and management of challenging non-strabismus pediatric ophthalmology cases.
- (2) The practitioner in the audience is expected to gain new insights into the clinical reasoning behind each diagnosis and the purpose of any intervention
- (3) Be able to describe the treatment and approach to pediatric neuro-ophthalmic disease

**Two Eyes, Two Images, Two Subspecialties:
A Strabismus Case Symposium Featuring Experts from AAPOS and NANOS [1.5 CME]**

Moderators: Stacy Pineles, MD (Live from AAPOS) & Nicholas J. Volpe, MD (live at NANOS)

Panelists (live at NANOS): ; Jane Edmond, MD; Mays El Dairi, MD; Veeral Shah, MD, PhD

Panelists (live from AAPOS): Janet Alexander, MD; Ramesh Kekunnaya, MD; Federico Velez, MD

The workshop will consist of case-based presentations of patients with interesting and/or difficult forms of strabismus. Each panelist will present a difficult strabismus case for discussion by other panelists and the audience. The cases will be related to Neuro-Ophthalmology, as well as craniofacial and complicated childhood strabismus cases. Panelists will discuss the differential diagnoses and potential treatment options.

Upon completion of this session, participants should be able to:

- (1) Describe complicated patterns of strabismus due to neurological diseases
- (2) Discuss various surgical approaches to complex paralytic strabismus
- (3) Discuss surgical approaches to multiplanar nystagmus

Bugs, Brains and Blindness [1.5 CME]

Moderators: Drew Carey, MD & Nora S. Lincoff, MD

Updates in Neuro-Infectious Disease, Caleb McEntire, MD

Updates in Infectious Uveitis, Lucia Sobrin, MD, MPH

Case for Discussion, Jorge Cárdenas-Belaunzarán, MD, MSc

Case for Discussion, Deena Tajifirouz, MD

The diagnosis and management of neuro-ophthalmic manifestations of infectious diseases and infectious uveitides are a complex and evolving challenge. The clinical spectrum, causative agents, and therapeutic strategies are continuously changing, influenced by factors such as emerging pathogens, drug resistance, the increasing population of immunocompromised patients, as well as spread of old and novel pathogens in an increasingly interconnected world. This session aims to provide neuro-ophthalmologists with a practical, case-based update on the latest developments in the diagnosis and treatment of these vision-threatening and potentially life-threatening conditions.

Upon completion of this session, participants should be able to:

- (1) Upon completion of this session, participants should be able to: assess when patients with visual complications from neuro-infectious disease warrant IV anti-microbial treatment vs oral therapies
- (2) Upon completion of this session, participants should be able to: identify clues on the eye exam that point to infectious causes of uveitis in patients presenting to neuro-ophthalmic clinic
- (3) Upon completion of this session, participants should be able to: formulate an evidence-based diagnostic plan to assess patients for neuro-infectious organisms

The Cryptozoology of Neuroinfectious Disease: What is Fact and Fiction?

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Learning Objectives

- The attendee will be able to describe the cranial nerve manifestations and neuro-ophthalmologic manifestations of Lyme disease
- The attendee will be able to clinically use a novel clinical scoring system to distinguish Lyme disease facial palsy from Bell's palsy
- The attendee will be able to describe the presentation of "sick building syndrome" and chronic mold exposure, including which portions of presentation are firmly evidence-based versus speculative
- The attendee will be able to describe effective and ineffective treatments for "chronic Lyme"/post-treatment Lyme disease syndrome.

CME Questions

1. Which of the following is suggestive of Bell's palsy rather than Lyme disease facial palsy?
 - A. Fever
 - B. Holocephalic headache
 - C. Auricular pain
 - D. Body aches
 - E. Fatigue
2. Which of the following statements is fact rather than fiction?
 - A. There are non-CLIA-certified Lyme tests available commercially with good evidence for sensitive and specific Lyme detection
 - B. Visual contrast sensitivity testing is well validated for diagnosis of sick building syndrome
 - C. Seronegative Lyme disease is a fairly common entity
 - D. Lyme disease cannot cause optic neuritis
3. Which of the below treatments has a valid evidence base for treatment of post-treatment Lyme disease syndrome (PTLDS) in some cases?
 - A. Long-term intravenous ceftriaxone therapy
 - B. Chelation therapies
 - C. Insomnia-focused cognitive behavioral therapy
 - D. Hyperbaric oxygen therapies
 - E. Infrared sauna therapy

Talk Outline:

- Lyme Neuroborreliosis Overview
 - Epidemiology by geographic region (USA, Western Europe, etc.)
 - Common CNS manifestations by region
- Cranial Neuropathies and Ocular Involvement
 - Facial nerve palsy: most common cranial neuropathy (~5–10% of Lyme cases; bilateral in up to 20%).
 - Oculomotor and abducens palsies: rare (1–2% of Lyme neuroborreliosis cases).
 - FACT OR FICTION: Lyme Optic Neuritis
 - Optic neuritis is likely real in a few cases, but is rare and often overdiagnosed; many cases likely represent uveitis or papilledema from secondary inflammation
 - Diagnostic criteria (Sibony et al., J Neuro-Ophthalmol 2005)
 - Serologic testing: STTT v MTTT
 - CSF findings, including antibody index
 - Neuroimaging Findings (role of MRI primarily to exclude other etiologies; only rarely diagnostic)
- Treatment
 - Doxy v ceftriaxone
 - **Avoid corticosteroids in suspected Lyme facial palsy (may worsen outcomes).**
- FACE DROPS Clinical Scoring Tool
 - Developed from 285 cases at MEEI and MGH to distinguish Lyme facial palsy (LDFP) from Bell's palsy (BP).
 - Seven predictors (e.g., fatigue, headache, seasonal timing, tick exposure).
 - Score ≥ 5 → predictive of LDFP; ≤ 4 → predictive of BP.
 - Accuracy: ~96.7%.
 - Clinical implications:
 - LDFP → treat with antibiotics, no steroids.
 - BP → steroids ± antivirals (valacyclovir).
- Post-Treatment Lyme Disease Syndrome (PTLDS)
 - Occurs in ~5–15% after adequate antibiotic therapy.
 - Discussion: can Lyme persist after acute treatment?
 - Spirochetes can persist in muscle, most “Chronic Lyme” likely misdiagnosis
 - Diagnosis: is a positive Lyme serology meaningful in this context?
 - **FACT OR FICTION:** <https://igenex.com/> testing, including “AcuDart”
 - Symptoms: fatigue, musculoskeletal pain, cognitive complaints.
 - Not due to persistent infection; prolonged antibiotics not recommended.
 - Supportive management focuses on treating comorbid fatigue, pain, and dysautonomia.

Mold Exposure/Sick Building Syndrome

- Description and diagnosis:
 - o Various names for this syndrome including Chronic Inflammatory Response Syndrome (CIRS), SBS: syndromes that link indoor mold exposure to cognitive and neurologic
 - o One frequently used screening tool in this context is the Visual Contrast Sensitivity (VCS) test, proposed to detect “biotoxin exposure.”
- **FACT OR FICTION: VCS Test:**
 - o VCS assesses the ability to distinguish fine differences in shading (“contrast”)—a neurological component of vision.
 - o Claims that biotoxins from mold impair contrast detection within 24–36 hours of exposure.
 - o Review of literature around supposed “92% accuracy” rate cited by proponents lacks any peer-reviewed data or publicly available supporting evidence.
- Other Visual Findings in the Literature:
 - o No controlled studies confirm direct neuro-ophthalmologic impairment (e.g., decreased visual acuity, optic neuropathy, or retinal damage) due to indoor mold exposure.
 - o Reports of “brain fog” or transient blurred vision in mold-exposed individuals are non-specific and may relate to allergic or systemic inflammatory responses rather than ocular pathology.
- Debunking:
 - o Visual contrast testing (VCS) has not been scientifically validated as a biomarker for mold exposure or “biotoxin illness.”
 - o No evidence exists that indoor mold exposure causes permanent visual acuity loss or specific neuro-ophthalmologic deficits.
 - o Claims linking mold exposure to measurable visual dysfunction remain unsupported by peer-reviewed neurologic or ophthalmologic data.

Update in Infectious Uveitis

Lucia Sobrin, MD, MPH

Learning Objectives

1. Identify clinical scenarios where varicella zoster virus should be considered as a cause of optic neuritis.
2. Describe the diagnostic and therapeutic approach to a patient with suspected posterior segment inflammation due to syphilis.
3. Discuss the diagnosis and management of Bartonella neuroretinitis.

CME Questions

1. Which of the following statements is false regarding characteristics of patients with varicella zoster virus (VZV) reactivation involving the cranial nerves and central nervous system?
 - a. Optic perineuritis is a frequent manifestation in VZV-associated vision loss among immunocompetent patients.
 - b. Immunosuppressed patients have greater neuraxis involvement than immunocompetent patients
 - c. At initial presentation, acute retinal necrosis is seen in the majority of patients with VZV-related optic perineuritis.
 - d. The spinal cord and nerve roots are the least common site of involvement.
2. Which of the following statements is false regarding ocular syphilis?
 - a. Uveitis and optic neuritis are the most common ocular manifestations of syphilis.
 - b. Ocular syphilis can occur in any stage of syphilis and can manifest in any part of the eye.
 - c. Many clinical laboratories screen for syphilis by using a “reverse screening algorithm”: nontreponemal test first, then a treponemal test for positive samples.
 - d. Treponemal tests remain positive for life regardless of treatment while nontreponemal titers spontaneously decrease over time.
3. Which of the following statements is false regarding neuroretinitis?
 - a. Other conditions that can induce optic disc edema with macular star exudate aside from neuroretinitis are hypertensive retinopathy and papilledema from increased intracranial pressure.
 - b. The findings that are characteristic of the neuroretinitis are optic nerve edema and stellate macular exudates secondary to the optic nerve inflammation.
 - c. The single most common infectious organism associated with the development of neuroretinitis is Bartonella.
 - d. The macular star is most often present immediately at the time of symptom onset.

Key Words

1. Optic perineuritis
2. Acute retinal necrosis
3. Syphilis
4. Neuroretinitis
5. Bartonella

Highlights

This lecture will cover common causes of infectious uveitis and their varied presentations, including associated optic nerve and central nervous system presentations. Through a case-based presentation format, the important clues to infectious uveitis will be covered. The importance of prompt diagnosis and treatment for vision preservation will be emphasized.

Summary

Infectious uveitis can lead to blindness rapidly. It is therefore important to identify this diagnosis and the specific causative organism so that the correct antimicrobial therapy can be instituted without delay. In the United States of America, some common causes of infectious uveitis are syphilis, toxoplasmosis, Bartonella and the herpes viruses, including varicella zoster virus. The typical presentations for these entities will be reviewed, as well as the most effective diagnostic and treatment strategies for each. Sometimes these ocular infections can present to neuro-ophthalmologists because the optic nerve is a site of disease and other ocular manifestations are either missed or not present early on in course. The talk will review case studies of such presentations where the optic nerve abnormalities were the most prominent location of disease. The features on examination and imaging that should be carefully examined in order to not miss the diagnosis of an infectious etiology will be highlighted.

CME Answers

1. c
2. c
3. d

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Bugs, Brains, and Blindness Symposium

Mystery case 1

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LEARNING OBJECTIVES

1. Construct a differential diagnosis for chronic disorders affecting the extraparenchymal space that present with progressive ocular motor dysfunction.
2. Recognize key neuroimaging patterns associated with inflammatory or infectious processes involving the ocular motor system.
3. Evaluate diagnostic strategies and approaches in patients with CNS disease when initial laboratory and CSF studies are non-diagnostic.

KEYWORDS

1. Leptomeningeal enhancement
2. Ocular motor disorders
3. Posterior fossa pathology

History & Exam

A 44-year-old female presented to our clinic in November 2024, one year after her initial evaluation by the neurosurgical team.

Her history began in early 2023, when a general practitioner ordered a head CT scan for new-onset, intermittent headaches. The scan revealed a mass lesion, and she was referred to a neurosurgeon for managing possible intracranial hypertension. Neurosurgery, in turn, referred her to neuro-ophthalmology after she reported binocular diplopia and no signs of intracranial hypertension were discovered. However, she didn't schedule her neuro-ophthalmology appointment immediately.

The patient is a civil engineer who has spent several decades working in rural communities. About two years before her first general practitioner consultation, she noticed occasional horizontal binocular diplopia and unrelated bilateral frontal headaches. During 2024, the headaches remained occasional and self-limited, but the diplopia became constant—initially in right gaze, later also in primary position, and she acquired a compensatory right-head turn.

On examination, best-corrected visual acuity was 20/20 in both eyes. Color vision (Ishihara) was 8/8 in each eye. There was no relative afferent pupillary defect. In primary gaze, she showed a 20-prism-diopter esotropia and a mild right head tilt. Smooth pursuit testing revealed limited abduction of the right eye, with mildly slowed abducting saccades; all other ocular movements were full, and no nystagmus was observed. Anterior segments were normal. Both optic discs had a physiologic appearance with a cup-to-disc ratio of 0.3.

Her 2023 brain MRI revealed images of a conglomerate cystic-like lesions in the right cerebellopontine angle, accompanied by focal leptomeningeal enhancement in the adjacent pons and right middle cerebellar peduncle, suggestive of arachnoiditis. A spinal tap was performed. CSF analysis showed no pleocytosis or erythrocytes, normal glucose, LDH, ADA, and protein levels, negative VDRL, and negative anti-T. solium cysticercus IgG, and cryptococcal antigen.

Based on radiological appearance and previous history, an infectious disease was still high in the differential diagnosis, mainly, a tuberculous meningitis, a subarachnoid (racemose) neurocysticercosis, fungal meningitis (cryptococcosis) but also leptomeningeal carcinomatosis and neurosarcoidosis.

She was scheduled for follow-up after two weeks with a chest X-ray, quantiferon Tb-gold, serum ACE, and a new spinal tap, however, she returned nearly a year later, in October 2025. At that time, she reported persistent headaches and constant diplopia in primary gaze position. Examination now revealed a 25-prism-diopter esotropia and a mild (−1) abduction deficit in the right eye. No changes were noted in her anterior segments, and the optic nerves remained without papilledema. She also reported new-onset, constant right-sided tinnitus for the past four months. A new brain and orbits MRI was performed.

Recently Recognized, Clinically Relevant: New Conditions Every Neuro-Ophthalmologist Should Know [1.5 CME]

Moderators: Victoria Pelak, MD & Leanne Stunkel, MD

Relapsing Syndromes, *John Chen, MD, PhD*
People With Cancer, *Ali Hamedani, MD, MHS*
Funny Eye Movements, *Janet Rucker, MD*
Diplopia & Optic Neuritis, *Bart K. Chwalisz, MD*

This session will highlight cutting-edge developments in clinical care for neuro-ophthalmologic conditions related to genetic disease, complications of cancer treatments, and autoimmune nodopathies. A comprehensive review of the latest research and knowledge about these conditions will equip participants to provide the best possible clinical care for neuro-ophthalmology patients by incorporating recent updates.

Upon completion of this session, participants should be able to:

- (1) Review new concepts related to selected genetic diseases, including advancements in understanding relapsing autoimmune genetic conditions and eye movement abnormalities that may occur due to genetic disease.
- (2) Identify neuro-ophthalmic complications of cancer treatments and understand how to address these complications and how they affect the overall treatment plan.
- (3) Identify neuro-ophthalmic manifestations of autoimmune nodopathies and initiate diagnostic testing for these conditions.

RELAPSING GENETIC SYNDROMES

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LEARNING OBJECTIVES (3 required)

1. Recognize monogenic autoinflammatory diseases that can present with neuro-ophthalmic manifestation
2. Understand how to make the diagnosis of monogenic autoinflammatory diseases
3. Discuss the treatment options for monogenic autoinflammatory diseases

CME QUESTIONS (3 required)

1. What is the most common neuro-ophthalmic manifestation of early onset cryopyrin-associated periodic syndromes (CAPS)?
 - A. Papilledema
 - B. Retinal vasculitis
 - C. Optic neuritis
 - D. Diplopia
2. What is the typical demographic for VEXAS syndrome?
 - A. Children
 - B. Teenagers
 - C. Young adult female
 - D. Older adult male
3. What is the first line therapy for CAPS and TRAPS?
 - A. IL-1 inhibitors
 - B. Rituximab
 - C. TNF inhibitors
 - D. Cyclophosphamide

KEYWORDS (5 Max)

1. Monogenic autoinflammatory diseases
2. Neuro-ophthalmic manifestations

HIGHLIGHTS

Neuro-ophthalmic complications are increasingly recognized across the spectrum of monogenic autoinflammatory diseases. These disorders can present with relapsing vision-threatening ocular phenotypes that provide important diagnostic clues and have direct therapeutic implications as targeted cytokine-directed therapies become more widely available.

SUMMARY

Monogenic autoinflammatory diseases are a heterogeneous group of disorders characterized by dysregulated innate immune responses, leading to recurrent systemic and organ-specific inflammation. Neuro-ophthalmic and ocular involvement is increasingly recognized across the spectrum of monogenic autoinflammatory diseases, reflecting shared mechanisms of innate immune dysregulation, vasculopathy, granulomatous inflammation, and central nervous system cytokine-mediated injury. Although less common compared with systemic manifestations, ophthalmic features may serve as important diagnostic clues and can lead to irreversible visual loss if not recognized promptly. Below, we summarize the neuro-ophthalmic phenotypes of key monogenic autoinflammatory disorders relevant to clinical practice.

Cryopyrin-Associated Periodic Syndromes (CAPS)

CAPS encompasses a phenotypic continuum of autosomal dominant conditions caused by mutations in the NLRP3 gene leading to constitutive IL-1 β activation, which include neonatal-onset multisystem inflammatory disease/chronic infantile neurologic, cutaneous, and articular syndrome (NOMID/CINCA) (most severe), Muckle–Wells syndrome (MWS) (intermediate severity), and familial cold autoinflammatory syndrome (FCAS) (mildest).¹ Patients typically present with early onset inflammatory episodes of fever, rash, musculoskeletal symptoms, and ocular inflammation, often associated with elevated inflammatory markers. Ocular involvement has been reported to be present in 71% of patients with CAPS.² Patients commonly exhibit conjunctivitis, keratitis, episcleritis, and anterior or posterior uveitis. Neuro-

ophthalmic manifestations are most pronounced in NOMID/CINCA, where chronic aseptic meningitis leads to intracranial hypertension, persistent papilledema, and progressive optic atrophy if untreated.³ Optic nerve edema in CAPS is usually from raised intracranial pressure, but can also occur in the setting of uveitis and papillitis. Rare cases of retinal vasculitis have been reported.³ Early initiation of IL-1 blockade (anakinra or canakinumab) is essential and has dramatically improved outcomes.⁴

Familial Mediterranean Fever (FMF)

FMF is characterized by recurrent episodes of fever and serositis due to MEFV mutations affecting pyrin function. Ocular involvement is generally mild, most commonly manifesting as conjunctivitis or episcleritis during inflammatory flares. Rare cases of anterior uveitis, retinal vasculitis, frosted branch angiitis, vascular occlusion, optic neuritis, and papillitis have been reported.^{3,5-7} Aseptic meningitis and headaches can occur.⁴ More severe or atypical ocular inflammation should prompt evaluation for co-existing autoinflammatory or vasculitic disorders, particularly Behçet disease. Management typically involves optimization of systemic control with colchicine, with escalation to corticosteroids, immunosuppressive agents, or biologic therapy when retinal vasculitis or other severe ophthalmic manifestations are present.

Tumor Necrosis Factor Receptor–Associated Periodic Syndrome (TRAPS)

TRAPS is an autosomal dominantly inherited autoinflammatory disease that presents with prolonged febrile episodes, migratory erythematous rash, serositis, myalgias, and abdominal or chest pain. Ocular involvement is relatively common with conjunctivitis, episcleritis, and painful periorbital edema occurring in up to half of cases and typically parallel febrile flares. Rarely, multifocal choroiditis, panuveitis, and optic neuritis have been reported.³ The underlying TNFRSF1A mutations causes a spontaneous production of cytokines and chemokines, including IL-1 β . IL-1 blockade is considered the most effective targeted therapy, but TNF and IL-6 inhibitors have also been used.³

ROSAH Syndrome

ROSAH syndrome (retinal dystrophy, optic nerve edema, splenomegaly, anhidrosis, headache) is caused by autosomal-dominant gain-of-function mutations in ALPK1 and represents a combined degenerative and inflammatory ocular disease.^{8,9} Patients typically develop cone-rod retinal dystrophy with nyctalopia and progressive visual field constriction. Persistent or recurrent optic disc edema is a hallmark feature and often occurs without concordant intracranial hypertension, suggesting intrinsic optic nerve inflammation or impaired axoplasmic flow. Additional findings include chronic uveitis, vitritis, cystoid macular edema, and occasional retinal vasculitis. Although corticosteroids and targeted immunomodulatory therapy (e.g., anti-IL-6 therapy) may improve optic disc swelling and inflammatory macular changes, they do not reliably halt the underlying retinal degeneration, which drives long-term visual prognosis. ROSAH should be considered in patients presenting with the combination of optic disc edema and hereditary-appearing retinal degeneration, particularly when accompanied by systemic features such as splenomegaly or anhidrosis.

Blau Syndrome

Blau syndrome, caused by autosomal-dominant NOD2 gain-of-function mutations, is defined by the triad of granulomatous arthritis, dermatitis, and uveitis. Ocular involvement typically presents in early childhood and is often severe, bilateral, and chronic. Granulomatous anterior uveitis is the most common manifestation, but intermediate, posterior, and panuveitis also occur. Multifocal choroiditis, papillitis, and retinal vasculitis are well described.^{3,5,10,11} Complications, including cystoid macular edema, cataract, secondary glaucoma, and optic atrophy, are common and contribute substantially to long-term visual morbidity. Blau-associated uveitis is frequently refractory to topical therapy and requires systemic immunosuppression. TNF inhibitors and other biologics are widely used as steroid-sparing agents, and early aggressive treatment is crucial to prevent irreversible structural damage.

VEXAS Syndrome

VEXAS syndrome (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) is an adult-onset disorder caused by somatic mutations in UBA1, typically presenting in older men with systemic inflammation, chondritis, vasculitic features, and hematologic abnormalities including macrocytic anemia and myelodysplastic changes.¹² Ocular involvement is common and heterogeneous, reflecting the systemic inflammatory milieu. Patients may develop recurrent episcleritis, scleritis, uveitis, dacryoadenitis, periorbital edema, or orbital inflammatory disease such as orbital myositis or optic

perineuritis.^{5,13-15} Ocular and orbital inflammation often parallels systemic disease activity and may be refractory to conventional therapy. Management generally requires systemic glucocorticoids and steroid-sparing immunosuppression, with emerging roles for targeted hematologic therapies. Allogeneic hematopoietic stem cell transplantation is a potential curative therapy. Persistent or unexplained inflammatory eye disease in an older man with cytopenias should prompt evaluation for VEXAS.

Deficiency of Adenosine Deaminase 2 (DADA2)

DADA2 is a systemic vasculopathy and autoinflammatory disorder caused by biallelic ADA2 mutations inherited in an autosomal recessive pattern leading to endothelial dysfunction, immune dysregulation, and a predisposition to early-onset stroke. Ocular involvement reflects its underlying small- and medium-vessel vasculitis, with reported manifestations including retinal vasculitis, retinal artery occlusions, optic neuropathy (rare), and neuro-ophthalmic deficits secondary to lacunar strokes affecting visual pathways or efferent pathways.^{3,5,16} Patients may present with visual field deficits, acute visual loss, diplopia, or chronic ischemic changes on fundus examination. Because stroke risk is high in untreated DADA2, early recognition is critical. TNF inhibitors reduce vascular events and can stabilize both systemic and ocular manifestations, making them first-line therapy for the vasculitic phenotype.

Summary

Across these monogenic autoinflammatory disorders, the neuro-ophthalmic manifestations reflect shared mechanisms of cytokine excess, granulomatous inflammation, and vasculopathy. Early recognition is essential, as many conditions now have targeted therapies, such as IL-1 blockade in CAPS, TRAPS, and FMF; TNF inhibition in DADA2 and Blau syndrome; and tailored immunosuppression in VEXAS, that can prevent irreversible visual loss. Close collaboration between ophthalmology, neurology, rheumatology, immunology, and hematology is essential to optimize outcomes.

Table:

Disease	Ocular Manifestations	Other manifestations and key features	First line treatment(s)
CAPS	Conjunctivitis, keratitis, episcleritis, uveitis, papilledema. Rare: papillitis, retinal vasculitis	Recurrent episodes of fever, rash, aseptic meningitis	IL-1 inhibitors
FMF	Conjunctivitis, episcleritis. Rare: anterior uveitis, retinal vasculitis, frosted branch angiitis, vascular occlusion, optic neuritis, and papillitis	Recurrent episodes of fever and serositis	Colchicine, IL-1 inhibitors if colchicine-resistant or intolerant
TRAPS	Periorbital edema, conjunctivitis, episcleritis. Rare: multifocal choroiditis, panuveitis, and optic neuritis	Prolonged febrile episodes, migratory erythematous rash, serositis, myalgias, and abdominal or chest pain	IL-1 inhibitors
ROSAH	Cone-rod retinal dystrophy and optic disc edema. Rare: uveitis, vitritis, cystoid macular edema, retinal vasculitis	Splenomegaly, anhidrosis, headache	Corticosteroids and steroid-sparing immunosuppression
Blau syndrome	Uveitis, cataract, multifocal choroiditis, papillitis, and retinal vasculitis	Triad of recurrent granulomatous uveitis, arthritis, and dermatitis	TNF inhibitors
VEXAS	Episcleritis, scleritis, uveitis, dacryoadenitis, periorbital edema, orbital inflammation	Affects older men often with chondritis, macrocytic anemia, and myelodysplastic changes	Corticosteroids and steroid-sparing immunosuppression. Allogeneic hematopoietic stem cell transplantation

Disease	Ocular Manifestations	Other manifestations and key features	First line treatment(s)
DADA2	Retinal vasculitis, retinal artery occlusion, diplopia. Rare: optic neuropathy	Early onset lacunar strokes, recurrent fevers and rash	TNF inhibitors

CME ANSWERS

1. A
2. D
3. A

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NEURO-OPHTHALMIC COMPLICATIONS OF NEW CANCER THERAPIES

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LEARNING OBJECTIVES

1. To understand the mechanisms of immune checkpoint inhibitor and chimeric antigen receptor T-cell treatments for cancer.
2. To review the approach to treating immune checkpoint inhibitor-related neuro-ophthalmic adverse effects.
3. To describe neuro-ophthalmic sequelae of immune effector cell-associated neurotoxicity.

CME QUESTIONS

4. Which immune checkpoint inhibitor-related adverse effect may be treated symptomatically while continuing immune checkpoint inhibitor treatment?
 - a. Mild anterior uveitis responsive to topical corticosteroids
 - b. Bilateral panuveitis with optic disc and macular edema
 - c. Myasthenic syndrome with ophthalmoparesis, dysarthria, and dysphagia
 - d. 3M syndrome (myasthenia, myositis, and myocarditis) requiring invasive ventilation and hemodynamic support
5. A 64 year-old man with a 2-year history of seropositive ocular myasthenia gravis (OMG) is diagnosed with non-small cell lung cancer. After consultation with his oncologist, he is offered first-line treatment with pembrolizumab monotherapy. What is the average likelihood that his OMG symptoms will worsen during the course of his treatment?
 - a. 10%
 - b. 40%
 - c. 65%
 - d. 90%
6. A 58 year-old woman receives BCMA-targeted chimeric antigen receptor (CAR) T-cell therapy for multiple myeloma. Which neuro-ophthalmic complication is she most likely to experience?
 - a. Bilateral tonic pupil
 - b. Facial nerve palsy
 - c. Optic neuropathy
 - d. Thyroid orbitopathy

KEYWORDS

1. Immune checkpoint inhibitor
2. Chimeric antigen receptor T-cell
3. Myasthenia gravis
4. Paraneoplastic syndrome
5. Immune effector cell-associated neurotoxicity syndrome

SUMMARY

Cancer treatment has been dramatically transformed in recent years. Many advances in cancer treatment focus on harnessing the power of the body's own immune system because 1) immune cells play a major role in detecting and eliminating cancerous cells, and 2) cancers grow and spread by evading these immunologic processes. However, when the immune system is augmented – either selectively (that is, directed at a specific molecular target) or non-selectively – this

heightened activity has the potential to target other healthy tissues, causing a range of symptoms including some which may be present to the neuro-ophthalmologist.

Immune checkpoint inhibitors (ICI) are monoclonal antibodies which target CTLA-4 (e.g. ipilimumab, tremilimumab), PD-1 (e.g. pembrolizumab, nivolumab, cemiplimab, dostarlimab), or its ligand, PDL-1 (e.g. atezolizumab, durvalumab, avelumab). These proteins inhibit T-cell activity and are overexpressed by tumor cells, so blocking them via monoclonal antibodies upregulates T-cell responses. While the ensuing immune response has proven highly effective in treating a number of solid organ malignancies, it can also cause toxicity affecting virtually any organ in the body. An ICI-related myasthenic syndrome may present to the neuro-ophthalmologist as ocular myasthenia gravis (MG) with typical symptoms of diplopia and ptosis and is similarly acetylcholine receptor antibody-negative in approximately 50%, but generalization is rapid and often requires inpatient treatment¹. Another key distinction between ICI-related myasthenic syndrome and typical autoimmune myasthenia gravis is that it can co-occur with myositis and myocarditis (so-called “3M syndrome”), so screening for these in cases of suspected ICI-related myasthenic syndrome is important. Uveitis is also common and affects up to 1% of ICI-treated patients. Optic neuritis – including a neuromyelitis optica-like presentation – is less common but has also been reported. Other syndromes include aseptic meningitis, encephalitis, acute or chronic inflammatory demyelinating polyneuropathies, giant cell arteritis, and thyroid orbitopathy. Median onset is usually within 4-6 weeks of treatment, but there are reports of presentations occurring more than a year after ICI treatment. ICI toxicity is more common with PD1-directed treatment than CTLA-4, and combination treatment increases this risk even further (12% incidence in an analysis of 9,208 patients from 59 clinical trials)². Additional information about ICI-related adverse events can be found elsewhere, including in recorded talks by Drs. Lynne Gordon, Tariq Bhatti, Zaghay Al-Zubidi, and Andrew Lee on the NANOS Neuro-Ophthalmology Virtual Education Library (NOVEL) website (<https://novel.utah.edu/>).

A more recently recognized complication of ICI treatment is the **unmasking of latent autoimmune or paraneoplastic disease**. In 2017-2018, the French Reference Centre observed a 112% increase in the diagnosis of anti-Ma2 antibody syndromes, and this corresponded to the years when ICI became widely disseminated in France³. Since then, antibody-mediated paraneoplastic syndromes (e.g. anti-Hu, anti-Ma2, anti-CV2/CRMP5 antibodies) have consistently been observed to present after ICI treatment, and it is thought that immunotherapy unmasked their predisposition to cancer-related autoimmunity⁴. These antibodies are sometimes detectable before treatment, and testing has been proposed as a tool for risk stratification, but paraneoplastic syndromes remain rare, limiting the utility of widespread screening⁴. Neuro-ophthalmic manifestations include ocular motor abnormalities in paraneoplastic cerebellar ataxia, brainstem encephalitis, opsoclonus myoclonus ataxia syndrome, and optic neuritis associated with CV2/CRMP5 antibodies.

The treatment of ICI-related adverse events is similar to when such conditions occur in the absence of ICI treatment and may consist of oral or intravenous corticosteroids, intravenous immune globulin, plasmapheresis, and steroid-sparing immunosuppression. A major question for the treating oncologist is whether ICI-related adverse events are severe enough to merit discontinuation of the offending agent, potentially depriving the patient of a highly effective treatment for their life-threatening malignancy. **New guidelines from the American Society of Clinical Oncology and National Comprehensive Cancer Network** grade ICI-related complications on a scale of 1 (mild) to 4 (severe/life-threatening). In general, ICI treatment is continued for grade 1, temporarily held for grade 2, and permanently discontinued for grade 3 or 4⁵. However, most neurologic sequelae of ICI therapy do not have a grade 1 designation, and even the mildest symptoms are considered to be grade 2 toxicity. Treatment is often required for 6-12 months, but up to a quarter may require lifelong immunosuppression despite ICI discontinuation⁵. **Cancer immunotherapy can also worsen existing neuro-ophthalmic diseases** in addition to causing new ones. In previous studies, the majority of people who had MG prior to their cancer diagnosis experience exacerbations during immunotherapy, with half requiring hospitalization⁶. Multiple sclerosis (MS) relapse risk is lower, especially in older patients with inactive disease.

ICI's produce a generalized T-cell response, and the non-selective nature of this effect is responsible for the adverse events discussed above. To produce a stronger but more focused T-cell response, **targeted T-cell therapies** have been developed in the form of **chimeric antigen receptor T-cells (CAR-T)** and **bispecific T-cell engagers (BITE)**. CAR-T cells are patient-derived immune cells that have been genetically engineered to express a cell surface protein whose extracellular component targets a tumor marker of interest (thereby drawing the T-cell in closer proximity to its

target) and whose intracellular component initiates T-cell signaling and activation when binding occurs. BITE are fusion proteins that bind to the tumor antigen and T-cells on separate ends, drawing them together indirectly. Anti-CD19 CAR-T cell therapy was approved by the FDA to treat B-cell acute lymphoblastic leukemia in 2017, and since then, similar therapies have been developed for other B-cell malignancies as well as multiple myeloma, with glioblastoma currently under investigation.

To produce CAR-T cells, autologous or allogeneic T-cells are first harvested via leukapheresis. After *in vitro* cultivation and enrichment, the T-cells are transduced with the CAR gene via a lentiviral vector or other gene insertion strategies, and successfully transduced T-cells are isolated and clonally expanded. The patient is conditioned with lymphodepleting chemotherapy before receiving an infusion of the CAR-T cells. When CAR-T cells enter the bloodstream, they proliferate rapidly and seek out their targets. Upon binding to the target tumor antigen, the CAR-T cells are activated and secrete inflammatory cytokines to induce apoptosis of the cancer cells. However, widespread cytokine release and immune system activation can also produce a generalized inflammatory response known as cytokine release syndrome (CRS). In addition to potentially severe systemic symptoms of fever, tachycardia, hypotension, pulmonary edema, and hepatorenal impairment, neurotoxicity is common and is known as **immune effector cell-associated neurotoxicity syndrome (ICANS)**. In general, neuro-ophthalmic manifestations of this syndrome are nonspecific in the setting of encephalopathy but can include papilledema secondary to cerebral edema. BCMA-targeted CAR-T cell therapy for multiple myeloma is associated with cranial neuropathies, usually involving one or both facial nerves but occasionally also the third, fourth, or sixth cranial nerves. A unique delayed parkinsonian syndrome called movement and neurocognitive treatment-emergent toxicity (MNT) can also occur. Because these are delayed and much less common than typical ICANS, the mechanism of BCMA-related CAR-T cell neurotoxicity is thought to be different. BCMA is expressed in the caudate nucleus during development and up to age 30, so it is possible that off-target binding of CAR-T cells occurs within the CNS⁷. However, the majority of people who develop these complications are over age 30, at which point BCMA RNA and protein are undetectable in the brain, so the exact mechanisms for this complication remain unclear.

There are several reports of infiltrative optic neuropathy associated with CD-19 CAR-T cell therapy for B-cell malignancies. Some had pre-existing CNS disease, so it is thought that subclinical leukemic infiltration was present prior to treatment that then became symptomatic following CAR-T cell treatment due to local tissue infiltration and inflammation⁸⁻¹⁰. In other cases, however, no evidence of leukemic infiltration is found, and rapid improvement suggests a purely inflammatory response rather than cell-mediated destruction¹¹. In very rare cases, CAR-T cells may themselves undergo malignant transformation, and in January 2024, the FDA issued a Black Box warning about the risk of secondary T-cell malignancy following CAR T-cell therapy and need for lifelong monitoring. Finally, because CAR-T cell therapy is administered following lymphodepletion, opportunistic infection is also important to consider as a cause of neuro-ophthalmic symptoms in the period immediately after treatment. CRS and ICANS are often treated with intravenous corticosteroids, tocilizumab (an anti-IL-6 monoclonal antibody), or anakinra (an IL-1 receptor antagonist)^{5,12}, though by reducing activity and T-cell response, they also limit CAR-T cell activity against the targeted cancer cells.

On an optimistic note, **cancer immunotherapy is a promising future treatment for other diseases in neuro-ophthalmology**. Progressive multifocal leukoencephalopathy (PML) is an opportunistic central nervous system infection that occurs due to JC virus reactivation in the setting of immunosuppression. In a series of 8 patients, treatment with pembrolizumab to upregulate the immune system and combat viral infection produced clinical stabilization or improvement and cerebrospinal fluid JC viral load reduction in 5 patients¹³. Pembrolizumab and other ICI have since been used to treat PML on a case-by-case basis, but the incidence of immune reconstitution inflammatory syndrome (IRIS) is as high as 20%, and clinical outcomes remain poor (50% mortality at one year)¹⁴. Bruton's tyrosine kinase (BTK) inhibitors, which were initially developed to treat B-cell malignancies, have re-emerged as novel treatments for MS. MS-specific BTK inhibitors (evobrutinib, tolebrutinib, fenebrutinib, remibrutinib) have better CNS penetrance and fewer off-target effects and have demonstrated benefit in phase 3 trials of both relapsing and progressive forms of MS¹⁵. Finally, CAR-T cell therapy is being explored for MG, MS, and neuromyelitis optica spectrum disorder (NMOSD) as a more potent and long-lasting alternative to conventional B-cell depleting monoclonal antibodies¹⁶.

CME ANSWERS

4. A
5. C
6. B

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GENETICS OF FUNNY EYE MOVEMENTS IN ADULTS

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LEARNING OBJECTIVES

Upon completion of this activity, the attendee will be able to:

4. Identify and localize classic eye movement abnormalities associated with adult-onset genetic disorders.
5. Recognize the phenotypes of the new and common genetic disorder spinocerebellar ataxia type 27B (SCA27B).
6. Decide when to send a patient with abnormal eye movements for genetic testing.

CME QUESTIONS

7. Which eye movement disorder is most characteristic of spinocerebellar ataxia type 27B?
 - A. Downbeat nystagmus
 - B. Convergence insufficiency
 - C. Supranuclear gaze palsy
 - D. Abnormal head impulse test
8. Which eye movement disorder is most common with Niemann-Pick type C?
 - A. Hypermetric saccades
 - B. Horizontal supranuclear gaze palsy
 - C. Gaze-evoked nystagmus
 - D. Slow vertical saccades
9. Which genetic condition is associated with progressive ataxia and palatal tremor (PAPT), with which jerk or pendular nystagmus may occur?
 - A. Spinocerebellar ataxia type 6
 - B. Adult-onset Alexander disease
 - C. Episodic ataxia type 2
 - D. Wilson disease

KEYWORDS

6. Downbeat nystagmus
7. Spinocerebellar ataxia type 27B (SCA27B)
8. Cerebellar ataxia, neuropathy, and vestibular areflexia syndrome (CANVAS)
9. Progressive ataxia and palatal tremor
10. Supranuclear gaze palsy

INTRODUCTION

The role of genetic testing in neurological diagnosis has expanded substantially over recent years, including in disorders with ocular motor abnormalities. The advent of whole exome and whole genome sequencing has increased recognition that disorders previously considered pediatric, such as Niemann-Pick type C or Alexander disease, may present in adults, often with phenotypic differences from the childhood subtypes. Further, genetic technical advances continue to identify new diagnoses, such as spinocerebellar ataxia type 27B (SCA27B). This talk is restricted to eye movement abnormalities that guide the differential diagnosis in classic or relatively common adult-onset genetic disorders. A more extensive list is included in the accompanying table. Genetic testing should be considered in any patient with an unexplained cerebellar syndrome, supranuclear gaze palsy, ocular motor apraxia, or ophthalmoplegia – especially with insidious onset and progression over time. A positive family history, though helpful, is not necessary for genetic testing, as many cases are sporadic. Ideally, genetic testing should be obtained through a genetics counselor or genetics physician for: 1) pre-testing counseling regarding implications for family members, impacts on life and long-term disability insurance, out of pocket cost and 2) proper selection of indicated testing (e.g., targeted single gene; panel, for example, ataxia panel; whole exome

or genome testing with or without trinucleotide repeat expansion testing or mitochondrial testing). As a structural framework for considering abnormal eye movements and genetic disorders, four scenarios are discussed in this syllabus: those that predominantly affect 1) the cerebellum, 2) brainstem-cerebellar connections via the triangle of Guillain-Mollaret, 3) brainstem saccadic burst neurons, or 4) extraocular muscles.

HIGHLIGHTS: Eye Movements in Cerebellar Genetic Disorders

Spinocerebellar ataxias (SCAs) have genetic heterogeneity, but have in common progressive ataxia due to cerebellar dysfunction. SCA27B is highlighted here, as it is new, adult-onset (mean in 6th decade, range 30-88)(1), relatively common, and treatable. SCA27B is an autosomal dominant disorder due to an intronic repeat expansion in the fibroblast growth factor-14 (*FGF-14*) gene that was discovered in 2023.(1, 2) There are three typical phenotypes: late-onset ataxia (slowly progressive), late-onset episodic ataxia (often triggered by alcohol or exercise), and idiopathic downbeat nystagmus (up to 48% of which is explained by SCA27B).(3) Patients may present with years-long, neurologically-isolated constant or episodic oscillopsia or diplopia prior to onset of gait imbalance and up to 60% of patients have oscillopsia and/or diplopia during their disease course.(1, 4) Downbeat nystagmus (DBN) is nearly uniform and likely under-reported, since it is often subtle (e.g., detectable only on fundoscopy, in down-lateral gaze, or after head shaking or supine head hanging). DBN is usually due to dysfunction of the cerebellar flocculus and paraflocculus; thus, other ocular motor signs localizing to these structures are also often present, including impaired smooth pursuit, impaired vestibulo-ocular reflex suppression (VORS), and gaze-evoked nystagmus (GEN). Horizontal diplopia is most often due to cerebellar divergence insufficiency (DI);(5) vertical diplopia is due to comitant skew deviation or alternating skew deviation on lateral gaze.(4) Given the subtlety and asymptomatic nature of DBN in many patients with SCA27B,(4) older patients with suspected sagging eye syndrome (DI due to mechanical orbital causes) should be asked about balance and carefully examined for DBN. The above eye movements localize to the cerebellum, but are not specific for SCA27B; however, these findings in an older patient with a typical SCA27B phenotype predict the diagnosis. It is important to be aware that routine ataxia genetic panels and whole genome sequencing fail to detect the intronic repeat expansion of SCA27B. Testing is available only through specific centers in the US and often must be requested. Gait imbalance, oscillopsia from DBN, and occasionally diplopia in SCA27B may respond to treatment with the potassium channel antagonist 4-aminopyridine (4-AP).(1, 3, 4) 4-AP is contraindicated if the patient has a history of seizures and reduced dosing is required with renal dysfunction.

Another pure cerebellar condition with DBN to consider in adults is SCA6.(6) Both SCA6 (due to *CACNA1A* gene trinucleotide repeat expansions) and Episodic Ataxia type 2 (EA2, due to *CACNA1A* loss of function gene variants) can present with episodic ataxia, often responsive to acetazolamide – though age of onset is typically younger than SCA27B.(7) A final cerebellar condition highlighted is the very rare Cerebellar Ataxia, Neuropathy, and Vestibular Areflexia Syndrome (CANVAS) due to *RFC1* gene variants.(8, 9) Patients with CANVAS typically present in mid-to-late adulthood with progressive imbalance and sensory ganglionopathy. They may have a chronic cough. Patients can have DBN, impaired pursuit, and GEN, but other ocular motor features differ from most cerebellar disorders because of severe bilateral vestibular involvement in CANVAS. Exam features that signify a combination of cerebellar and severe bilateral vestibular dysfunction include smooth eye movements during VOR suppression (VORS)(since there is no VOR to suppress) and the hallmark CANVAS sign of visually-enhanced VOR (VVOR) impairment.(10) Pursuit and vestibular movements both contribute to maintenance of visual fixation during slow (low-frequency), predictable rotations of a patient's head. When pursuit and VOR are both impaired, jerky saccadic corrective movements occur during VVOR. Mild VOR abnormalities with high-frequency testing (i.e., the head impulse test) can be detected in many cerebellar diseases that affect the flocculus, without peripheral vestibular involvement, since the flocculus plays a role in modulating the high frequency VOR. Head impulse testing is abnormal in CANVAS also, but the key point is that the vestibular dysfunction in CANVAS is severe and striking evidence of this is found in VORS and VVOR responses. See Table footnotes for information on testing VORS and VVOR. SCA3 (Machado-Joseph disease) and Friedreich ataxia are also in the differential with CANVAS, as they can have bilateral vestibular involvement.(11, 12) See the table below for other ocular motor features of SCA3.

HIGHLIGHTS: Brainstem Eye Movements and Extraocular Muscle in Genetic Disorders

Oculopalatal tremor (OPT) is the classic abnormality after damage (e.g., stroke or cavernoma hemorrhage) within the triangle of Guillain-Mollaret between the deep cerebellar nuclei and medullary inferior olive via the central tegmental tract. Hypertrophic olivary degeneration is seen on MRI and pendular nystagmus in a vertical and/or torsional trajectory accompanies abnormal spontaneous palatal movements. Yet, in some patients, there is no acute event before insidious onset progressive cerebellar ataxia with palatal tremor (PAPT). Patients with PAPT may have the pendular nystagmus of OPT, but may also have other ‘cerebellar eye movements’ described in the above section. Adults with PAPT may have a 4-repeat tauopathy (i.e., progressive supranuclear palsy, PSP), but genetic evaluation is warranted, as PAPT is reported with several genetic conditions (see table). Classic PSP is likely to be neurodegenerative, but can also occur in genetic disorders (see table). When horizontal saccades are very slow in the context of progressive cerebellar ataxia, SCA2 is likely.(13) Lastly, slowly progressive ophthalmoplegia that is not overcome with VOR and is accompanied by marked ptosis raises suspicion for chronic progressive external ophthalmoplegia(14) or, less often, oculopharyngeal muscular dystrophy(15) in adults. The latter is due to DNA triplet repeats or point mutations in the *PABPN1* gene.

SUMMARY TABLE: Clinically Detectable Eye Movement Abnormalities in Some Genetic Conditions in Adults^a

Ocular motor deficit ^b	Genetic associations (typical age range of onset)
Cerebellar	
Downbeat nystagmus	SCA6(6) (40-60), SCA27B(3, 4) (mean 60's, range 30-88), EA2(7) (2-32), Friedreich ataxia(12) (4-40, usually before age 25), ataxia telangiectasia-like disorder(16) (milder and later onset than ataxia telangiectasia), CANVAS(17) (40-70)
Smooth VOR suppression and impaired VVOR ^d	CANVAS(10), SCA3 ^c (11) (typically 30's, range 10-70), +/-Friedreich ataxia(12)
Periodic alternating nystagmus	SCA6, HSP/SPG7(18) (typically 30-45, range 11-72), ataxia telangiectasia(19)
Brainstem	
PAPT with pendular nystagmus or ‘cerebellar eye movements’	Adult-onset Alexander disease(20), GM2 gangliosidosis(21), <i>POLG</i> gene variants(22), SCA20, cerebrotendinous xanthomatosis, and Leigh and Leigh-like syndrome(23)
Pendular nystagmus (without PAPT)	Adult-onset Alexander disease(20), HSP/SPG7(24)
Supranuclear gaze palsy	Niemann-Pick type C (onset usually in childhood/adolescence, but adult-onset reported) (V – especially down), Wilson disease(25) (usually adolescence), Kufor-Rakeb(26) (usually before 20, range 10-29) (V), Leigh and Leigh-like syndrome, SCA2(13) (20-30) (H), HSP/SPG7(27, 28)
Cortical	
Ocular Motor Apraxia	Wilson disease(29) (usually adolescence), Ataxia with ocular motor apraxia type 2(30) (usually before age 25), Huntington's disease
Peripheral	
Extraocular muscle	CPEO (mitochondrial or nuclear gene variants involved in mitochondrial function such as <i>POLG1</i> and <i>SPG7</i> (31)), oculopharyngeal muscular dystrophy(32) (onset after 40)
Other	
Unproven localization ^c	SCA3 (typically 30's, range 10-70)

Abbreviations: SCA spinocerebellar ataxia; EA episodic ataxia; VOR vestibulo-ocular reflex, VVOR visually enhanced vestibulo-ocular reflex, CANVAS cerebellar ataxia, neuropathy, and vestibular areflexia syndrome; PAPT progressive ataxia with palatal tremor; HSP hereditary spastic paraplegia; SPG7 spastic paraplegia 7; V vertical; H horizontal; CPEO chronic progressive external ophthalmoplegia

- Coverage is not comprehensive, selected disorders are highlighted. For example, only the more common spinocerebellar ataxias are included (SCA2, 3, 6, 27B).
- Coverage is not comprehensive, ocular motor disorders that guide differential diagnosis are highlighted. For example, many genetic cerebellar conditions have gaze-evoked nystagmus, impaired smooth pursuit and VOR suppression, saccadic dysmetria, and mild VOR impairment; thus, these findings are insufficient to narrow differential diagnosis.
- SCA3 is reported to have 2 main patterns of ophthalmoplegia: upgaze paresis(33) that is likely supranuclear gaze palsy and/or bilateral impairment of abduction(34) of unclear localization. Some references label it progressive external ophthalmoplegia. Localization of these findings has not been proven.
- Reflective of the severe bilateral, likely peripheral, vestibular loss that occurs with CANVAS. Vestibular deficits are usually less severe in SCA3 and Friedreich ataxia. VOR suppression is performed by having the patient hold their arm straight in the midline in front of them and asking them to keep their eyes on their thumb while the examiner rotates their chair. VVOR is performed by having the patient fixate a stationary central object while the examiner slowly rotates the patient's head horizontal and then vertically.

CME ANSWERS

- A
- D
- B

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DIPLOPIA AND OPTIC NEURITIS FROM AUTOIMMUNE CAUSES

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LEARNING OBJECTIVES (3 required)

7. The attendee will be able to explain to distinguish between typical and atypical optic neuritis
8. The attendee will be able to formulate a differential diagnosis of diplopia and eye movement problems from an autoimmune cause
9. The attendee will be able to describe how to test for some recently described autoimmune conditions of neuro-ophthalmic interest

CME QUESTIONS (3 required)

10. What are some newly described autoimmune causes of optic neuritis/neuropathy
 - a. GFAP
 - b. NMDARE
 - c. IgLON5
 - d. All of the above
 - e. None of the above
11. What statements are true of optic perineuritis (OPN)?
 - a. The differential diagnosis of OPN is fundamentally the same as the differential diagnosis of optic neuritis
 - b. The differential diagnosis of OPN is fundamentally different to the differential diagnosis of optic neuritis
 - c. OPN is a clinico-radiologic diagnosis, and pathologic confirmation is rarely required
 - d. Conditions associated with OPN include infectious, inflammatory and neoplastic conditions
 - e. All of the above
 - f. B, C, and D
12. Some more recently described causes of autoimmune encephalitis involving the brainstem include
 - a. None, autoimmune encephalitis typically spares the brainstem
 - b. IgLON5
 - c. Kelch-like protein 11 antibody disease
 - d. Leucine zipper 4 (LUZP4) antibody disease
 - e. Anti-RGS8 disease
 - f. All of the above

KEYWORDS (5 Max)

11. Optic neuritis
12. Diplopia
13. Autoimmune optic neuropathy
14. Optic perineuritis
15. Diplopia

HIGHLIGHTS

- Although there is an expanding spectrum of autoimmune and paraneoplastic optic neuropathies, the distinction between typical and atypical optic neuritis remains clinically relevant, and NMOSD and MOGAD remain the most important causes of atypical optic neuritis
- Less common autoimmune causes of optic neuritis include the autoimmune encephalitides (including GFAP, NMDARE and IgLON5) and CIDP

- Optic perineuritis has a completely different differential diagnosis than optic neuritis, which includes recognized associations with giant cell arteritis and varicella zoster virus
- Diplopia and other eye movement disorders can be caused by a number of inflammatory and autoimmune conditions that affect the skull base, meninges, CSF space and brainstem
- Autoimmune mimics of progressive supranuclear palsy should be considered in atypical cases
- Recognize the association of myasthenia gravis with other autoimmune disorders, including the newly described association with AMPA antibodies in thymoma

SUMMARY

This talk will highlight new developments in afferent and efferent inflammatory neuroscience-ophthalmic disease. I will discuss the evolution of our understanding of inflammatory optic nerve disorders, contrasting typical optic neuritis with the atypical optic neuritides and related disorders such as optic perineuritis. Optic neuritis from neuromyelitis optica spectrum disorders (NMOSD), collapsin response-mediator protein-5 (CRMP-5) disease and myelin oligodendrocyte glycoprotein antibody disease (MOGAD) are well established examples of atypical optic neuritis and will therefore only be mentioned briefly to highlight important new developments, for instance in the expanding spectrum of disease variants of MOGAD, the strong association between chronic relapsing inflammatory optic neuropathy (CRION) and MOGAD, and new proposed diagnostic criteria. Rarer kinds of antibody-associated optic neuritis will be described, including those associated with glial fibrillary acidic protein (GFAP) antibodies, N-methyl-D aspartate receptor encephalitis, and the newly recognized association with anti-IgLON5 disease. The association of chronic inflammatory demyelinating polyneuropathy (CIDP) with optic neuropathy is probably under-recognized in the neuro-ophthalmic community. The special situation of inflammatory optic neuropathy associated with immune checkpoint inhibitor medications will not be described in detail, as complications of cancer therapy will be covered in a separate talk. Important recently recognized systemic associations of optic perineuritis will be identified, e.g., with giant cell arteritis and varicella zoster virus. I will transition to more recently recognized skull base inflammatory disorders that can cause both afferent and efferent neuro-ophthalmic syndromes, such as IgG4-related disease and newly recognized paraneoplastic granulomatous CNS disorders (due to Kelch-like protein 11 antibody disease and anti-Ma2 antibodies). I will discuss more recently recognized autoimmune and paraneoplastic syndromes causing brainstem encephalitis or cerebellitis such as Kelch-like protein 11 antibody disease, leucine zipper 4 (LUZP4) antibody disease and anti-RGS8 disease (which in addition to more severe cerebellitis may cause a milder syndrome of skew deviation and mild cerebellar dysfunction). I will review autoimmune or paraneoplastic mimics of progressive supranuclear palsy and conclude by mentioning the newly described association of myasthenia gravis occurring in association with AMPA antibodies in thymoma.

CME ANSWERS

10. D
11. F
12. F

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Neuro-Ophthalmology Bootcamp: Vision, Movement, and the Unexpected [1.5 CME]

Moderator: Steven Galetta, MD

Faculty: Ore Ofe Adesina, MD; Valerie Biousse, MD; Julie Falardeau, MD; Deb Friedman, MD, MPH, FAAN; Larry Frohman, MD; Andrew G. Lee, MD; Nancy J. Newman, MD

This trainee focused session will feature a game style format. Teams of residents and fellows will choose from a list of categories and point values to reveal cases that they will rush against time to solve. Come join in this fun session to improve and reinforce your knowledge of fundamentals of clinical neuro-ophthalmology! Everyone is welcome in the audience.

Upon completion of this session, participants should be able to:

- (1) Identify clinical conditions that cause neuro-ophthalmic symptoms
- (2) Approach eye movement evaluations in a systematic way
- (3) Interpret ancillary testing including OCT and visual fields

Scientific Platform Session I – Sunday, March 22nd [2.0 CME]

Moderators: Melinda Chang, MD; Shlomo Dotan, MD; Eric Gaier, MD, PhD

4:00 pm – 4:12 pm	Non-Image-Forming Light Perception and ipRGC Dysfunction In Alzheimer’s Disease: Results from a Combined Retinal and Brain Study , <i>Nicolae Sanda, Jr., MD, PhD</i>
4:12 pm – 4:24 pm	Application of the 2024 McDonald criteria in the International Acute Optic Neuritis Network , <i>Hadas Stiebel-Kalish, MD</i>
4:24 pm – 4:36 pm	Ultrasound, PET/CT, or Temporal Artery Biopsy for Giant Cell Arteritis? A Prospective Diagnostic Accuracy Study (the GAME-study) , <i>Michael Stormly Hansen, MD</i>
4:36 pm – 4:48 pm	Phase 3 Myasthenia Gravis Inebilizumab Trial: Improvement in Myasthenia Gravis Activities of Daily Living and Quantitative Myasthenia Gravis Ocular Domain Scores , <i>Richard J. Nowak, MD</i>
4:48 pm – 5:00 pm	Inebilizumab in IgG4-Related Disease: Safety and Efficacy Results from the Phase 3 MITIGATE Trial , <i>Guy Katz, MD</i>
5:00 pm – 5:12 pm	Towards Whole Eye Transplantation with Electric Field Stimulation , <i>Kimberly K. Gokoffski, MD, PhD</i>
5:12 pm – 5:16 pm	3D Imaging and Filament Tracing of Human Orbital Vasculature and Lymphatic System , <i>Drenushe Krasniqi-Vanmeter, BS</i>
5:16 pm – 5:20 pm	Neurovascular Compression Between the Supraclinoid Internal Carotid Artery and Anterior Optic Pathway: Establishing Clinical and MRI Diagnostic Criteria , <i>Francesco Cutrupi, MD</i>
5:20 pm – 5:24 pm	Targeting Lipid Peroxidation As A Treatment For NAION , <i>Ming Yang, MD, PhD</i>
5:24 pm – 5:28 pm	Investigating CYP27B1-Driven Neuroprotective Pathways in Acute Retinal Ganglionopathy , <i>Kabeer Thaker</i>
5:28 pm – 5:32 pm	Optic Disc Drusen Association to NAION , <i>David Szanto, BA</i>
5:32 pm – 5:36 pm	Anatomical Characterization of Optical Coherence Tomography Abnormalities in Friedreich Ataxia: Data from a 400-Patient Heterogeneous Cohort , <i>David Lynch, MD, PhD</i>
5:36 pm – 5:40 pm	AI-Based Classification of Parkinson’s Disease Using Quantitative Ocular Motor Biomarkers , <i>Erika Han, MD</i>
5:40 pm – 5:44 pm	Features of Transient Vision Loss: A Study of 300 Patients , <i>Mickey Nguyen</i>
5:44 pm – 5:48 pm	Investigating Regional Cerebrospinal Fluid Flow Alterations In Patients Diagnosed With Idiopathic Intracranial Hypertension , <i>Sofia John, BA</i>
5:48 pm – 5:52 pm	Lenadogene Nolpharvovec Gene Therapy for Leber Hereditary Optic Neuropathy in the Real-Life Setting , <i>Chiara La Morgia, MD</i>

Non-image-forming light perception and ipRGC dysfunction in Alzheimer's disease: results from a combined retinal and brain study

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Introduction:

Intrinsically photosensitive retinal ganglion cells (ipRGCs) mediate non-image-forming photoreception, including regulation of circadian entrainment, sleep–wake cycles, and mood. Disruption of sleep and circadian rhythms represents one of the earliest symptoms of Alzheimer's disease (AD), yet the role of ipRGCs in this process remains poorly understood. Expanding upon the preliminary data presented in 2023, this study presents a comprehensive analysis combining ex vivo human retinal electrophysiological recordings, retinal histology, and brain neuropathological analysis.

Methods:

Retinas and brains from 13 elderly subjects (9 males, 4 females; aged 69–103 years) with varying degrees of AD pathology (absent to severe, according to NIA-AA criteria) were analyzed. Fresh retinal explants (extracted < 2 hours postmortem) underwent extracellular electrophysiological recordings using multi-electrode arrays. ipRGC density and morphology were examined by immunohistochemistry, while neuropathological assessment was performed in brain nuclei involved in visual and non-visual light responses.

Results:

Postmortem electrophysiological recordings were successfully obtained in 6 donors. While rod and cone responses were moderately affected, subjects with advanced AD pathology exhibited a pronounced reduction in ipRGC density, confirmed by immunostaining. The surviving ipRGCs displayed morphological abnormalities and hyperexcitability, suggesting functional alteration of non-visual light pathways. These changes may be subtype-specific and correlated with the severity of AD neuropathology in both retina and brain.

Conclusions:

This first ex vivo human study combining electrophysiology, retinal histology, and brain neuropathology characterizes the structural and functional alterations of ipRGC and non-visual light perception circuits in AD. These findings provide mechanistic insights into the early disruption of circadian and sleep regulation in AD. Assessing ipRGC-dependent light responses in vivo may offer a novel biomarker for disease progression.

References: None provided.

Abstract Type: Clinical afferent disease, Basic Science

Keywords: Retina, Miscellaneous

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Application of the 2024 McDonald criteria in the International Acute Optic Neuritis Network

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Introduction:

The 2024 McDonald criteria for multiple sclerosis (MS) incorporate optic nerve lesions as a fifth topography for dissemination in space (DIS), and other additional diagnostic features. We evaluated their performance in acute optic neuritis (ON) patients within the global Acute Optic Neuritis Network (ACON).

Methods:

In this ongoing, prospective, multicenter study (clinicaltrials.gov, identifier: NCT05605951), we applied the 2024 McDonald criteria to 250 patients with a first-ever ON (enrolment period August 2020 – December 2024) from 22 centers in 14 countries across six continents. We included 61 patients with idiopathic ON (iON), 53 with clinically isolated syndrome and 64 with MS according to 2017 McDonald criteria (2017-CIS, 2017-MS), 22 with aquaporin-4-IgG-positive neuromyelitis optica spectrum disorder (AQP4-IgG+NMOSD), and 50 with myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD). We assessed the sensitivity of the 2017 and 2024 McDonald criteria using the MS "at-risk" population (defined by criteria specific for DIS or dissemination in time (DIT) using MRI). Specificity was measured using the AQP4-IgG+NMOSD and MOGAD cohorts.

Results:

All 2017-MS patients (64/64, 100%) fulfilled the 2024 criteria and 33/53 (62%) 2017-CIS patients were reclassified as MS by the 2024 criteria. Additionally, 18% of AQP4-IgG+NMOSD and 14% of MOGAD patients met the 2024 McDonald criteria. The sensitivity of the 2017 and 2024 criteria were 55% (95%-CI 45-64) and 83% (95%-CI 75-89); specificity was 100% (95%-CI 95-100) and 85% (74-92), and diagnostic accuracy was 72% (95%-CI 65-78) and 84% (95%-CI 76-89), respectively. Visual evoked potentials and optic coherence tomography demonstrated higher sensitivity than MRI for the detection of DIS using the 2024 criteria; however, MRI yielded higher specificity. Due to limited use, the impact of new MRI metrics and KFLC were not assessed.

Conclusions:

The 2024 McDonald criteria enhance diagnostic sensitivity in ON-related CIS, enabling earlier MS diagnosis, but reduce specificity in AQP4-IgG+NMOSD and MOGAD.

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Abstract Type: Clinical afferent disease

Keywords: Demyelinating disease, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Optic neuritis, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Neuroimaging

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Contact Information: None provided

Ultrasound, PET/CT, or Temporal Artery Biopsy for Giant Cell Arteritis? A Prospective Diagnostic Accuracy Study (the GAME-study)

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Introduction:

Introduction: To investigate the diagnostic performance of ultrasound, 2-deoxy-2-[18F]fluoro-D-glucose positron emission tomography/computed tomography (2-[18F]FDG PET/CT), and temporal artery biopsy (TAB) in a multimodal approach in giant cell arteritis (GCA).

Methods:

Methods: This prospective single-center diagnostic accuracy study included 110 patients clinically suspected of GCA (ClinicalTrials.gov NCT05248906). Patients underwent ultrasound, 2-[18F]FDG PET/CT, and TAB after clinical examination and blood sampling. Main outcome measures were diagnostic accuracy measures with final clinical expert diagnosis of GCA and non-GCA based on all available information at six-month follow-up as the comparator.

Results:

Results: A total of 61 patients received the GCA diagnosis, 39 were non-GCA, and 3 were inconclusive. 2-[18F]FDG PET/CT had the highest diagnostic odds ratio (111.29 95% CI: 6-2009), followed by TAB (86.92 95% CI: 5-1556%) and ultrasound (39.86 95% CI: 8-213). The overall sensitivity of ultrasound was 82% (95% CI: 66-92%), and specificity was 90% (95% CI: 68-99%). The sensitivity of 2-[18F]FDG PET/CT was 74% (95% CI: 57-87%), and specificity was 100% (95% CI: 83-100%). The sensitivity of TAB was 68% (95% CI: 51-83%), and specificity was 100% (95% CI: 83-100%). When ultrasound was inconclusive, 2-[18F]FDG PET/CT had a higher sensitivity of 75% (95% CI: 35-97%) vs. 38% (95% CI: 9-76%) for TAB and a specificity of 100% (95% CI: 69-100%) vs. 100% (95% CI: 69-100%) for TAB. Inconclusive results were reported in 22 of 99 ultrasounds, 3 of 102 2-[18F]FDG PET/CTs, and 4 of 90 TABs, respectively.

Conclusions:

Conclusions: A high diagnostic accuracy of ultrasound for GCA was found, supporting this as the first imaging modality in suspected GCA. 2-[18F]FDG PET/CT combined a high diagnostic accuracy with fewer inconclusive results, suggesting that 2-[18F]FDG PET/CT may be used as the second-line testing (when ultrasound is inconclusive or negative and GCA is still suspected), reserving TAB for third-line testing.

References: None provided.

Abstract Type: Clinical afferent disease

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Phase 3 Myasthenia Gravis Inebilizumab Trial: Improvement in Myasthenia Gravis Activities of Daily Living and Quantitative Myasthenia Gravis Ocular Domain Scores

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Introduction:

Generalized myasthenia gravis (gMG) is an autoimmune disease characterized by autoreactive B cells producing anti-acetylcholine receptor antibodies (AChR+), anti-muscle-specific kinase antibodies (MuSK+), or other autoantibodies. The phase 3 MG Inebilizumab Trial (MINT) demonstrated that inebilizumab, a monoclonal antibody targeting CD19+ B cells, resulted in greater reductions in MG Activities of Daily Living (MG-ADL) and Quantitative MG (QMG) scores vs placebo in participants with gMG. This post hoc analysis of MINT assessed whether inebilizumab improved MG-ADL and QMG ocular domain scores.

Methods:

MINT (NCT04524273) enrolled participants with AChR+ or MuSK+ gMG, all of whom underwent a protocol-specified glucocorticoid taper to ≤5 mg/day. Participants were randomized 1:1 to inebilizumab 300 mg or placebo for 52 (AChR+) or 26 (MuSK+) weeks (Ws). MG-ADL and QMG ocular domain scores (range, 0–6) were determined.

Results:

Overall, 238 participants were enrolled and randomized (AChR+, n=190; MuSK+, n=48). Mean baseline MG-ADL and QMG ocular domain scores were comparable. Overall, inebilizumab significantly improved MG-ADL ocular domain scores at W26 vs placebo (least squares mean difference [LSMD], -0.4; 95% confidence interval [CI], -0.8 to -0.1; nominal P=0.03) and resulted in numerically greater improvements in the AChR+ (LSMD, -0.4; 95% CI, -0.8 to 0.0; nominal P=0.07) and MuSK+ (LSMD, -0.6; 95% CI, -1.4 to 0.3; nominal P=0.20) populations. Inebilizumab numerically improved QMG ocular domain scores vs placebo at W26 in the overall (LSMD, -0.4; 95% CI, -0.7 to 0.0; nominal P=0.06), AChR+ (LSMD, -0.3; 95% CI, -0.7 to 0.1; P=0.15), and MuSK+ (LSMD, -0.7; 95% CI, -1.6 to 0.2; nominal P=0.15) populations. In the AChR+ population at W52, inebilizumab significantly improved MG-ADL (LSMD, -0.6; 95% CI, -1.1 to -0.2; nominal P=0.003) and QMG (LSMD, -0.6; 95% CI, -1.1 to -0.2; nominal P=0.007) ocular domain scores vs placebo.

Conclusions:

Inebilizumab numerically improved quantitative measures of ocular function in participants with gMG.

References: None provided.

Abstract Type: Clinical Trials

Keywords: Myasthenia, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Ocular motility

Financial Disclosures: Richard J. Nowak: Richard J. Nowak has received research support from Alexion Pharmaceuticals, Amgen Inc., argenx, Grifols, Horizon Therapeutics, Immunovant, Janssen, the Myasthenia Gravis Foundation of America, the National Institutes of Health, and UCB and has served as a consultant/adviser for Alexion Pharmaceuticals, Amgen Inc., argenx, Cabaletta Bio, Cour Pharmaceuticals, CSL Behring, Grifols, Horizon Therapeutics Immunovant, Janssen, and UCB.; Michael Benatar: Michael Benatar has received grant support from the ALS Association, the ALS Recovery Fund, Eli Lilly, the Kimmelman estate, Muscular Dystrophy Association, the National Institutes of Health, and Target ALS. He also reports research support from Alexion Pharmaceuticals and Immunovant and has served as an investigator in clinical trials funded by Biogen, Novartis, and Orphazyme. He has received personal consulting fees from Alaunos Therapeutics, Alector Therapeutics, Alexion Pharmaceuticals, Annexon Biosciences, Arrowhead Pharmaceuticals, Canopy Immunotherapeutics, CorEvitas, Denali Therapeutics, Eli Lilly, Evox Therapeutics, Horizon Therapeutics, Immunovant, Janssen, Merck, Novartis, Roche, Sanofi, Takeda, Trace Neuroscience, UCB, uniQure, VectorY Therapeutics, Voyager Therapeutics, and Woolsey Pharmaceuticals.; Emma Ciafaloni: No; M. Isabel Leite: M. Isabel Leite has received funding from the National Health Service (Myasthenia and Related Disorders Service and National Specialised Commissioning Group for Neuromyelitis

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Inebilizumab in IgG4-Related Disease: Safety and Efficacy Results from the Phase 3 MITIGATE Trial

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Introduction:

IgG4-related disease (IgG4-RD) is a rare systemic fibroinflammatory disease with recurring flares that affect and damage nearly any organ, including the pachymeninges and orbits. B cells play a central role in disease pathophysiology. Inebilizumab, a humanized anti-CD19 monoclonal antibody, depletes B cells in a targeted manner and was evaluated for safety and efficacy in IgG4-RD.

Methods:

MITIGATE (NCT04540497) was a 52-week, randomized, double-blind, placebo-controlled trial at 80 sites in 22 countries. Adults meeting ACR/EULAR classification (score ≥ 20) with multiorgan history and active disease were stratified (newly diagnosed vs recurrent) and randomized 1:1 to inebilizumab 300 mg IV or placebo on Days 1 and 15 and Week 26. Prednisone was normalized to 20 mg/day at randomization and tapered off by Week 8. Primary endpoint was time to first adjudication committee-determined and investigator-treated IgG4-RD flare during the randomized-controlled period (RCP). Key secondary endpoints included annualized flare rate, flare-free, treatment-free complete remission, and flare-free, glucocorticoid-free complete remission at Week 52. Safety was assessed.

Results:

135 participants were randomized and received inebilizumab (n=68) or placebo (n=67). Among these, 38.5% had historic involvement of lacrimal glands, 11.1% orbit, and 0.7% pachymeninges. Baseline demographics and disease characteristics were generally balanced between arms. Inebilizumab significantly reduced flare risk vs placebo (HR 0.13; 95% CI 0.06–0.28; $p < 0.0001$) and met all key secondary endpoints. Subgroup analyses of efficacy in participants with lacrimal, orbital, and pachymeningeal disease will be presented. The most common adverse events ($>10\%$) were COVID-19 (23.5% vs 19.4%), lymphopenia (16.2% vs 9.0%), and urinary tract infection (11.8% vs 6.0%). No deaths occurred; no serious adverse event affected >1 participant. Serious infections included COVID-19, appendicitis, and diverticulitis, and opportunistic infections were herpes zoster.

Conclusions:

MITIGATE, the first randomized, double-blind, placebo-controlled trial in IgG4-RD, demonstrates efficacy and safety of CD19-targeted B-cell depletion with inebilizumab.

References: Stone, J.H., Culver, E.L., Khosroshahi, A., et al. (2025). Inebilizumab for treatment of IgG4-related disease. *New England Journal of Medicine*, 392(12), 1168-1177.

Abstract Type: Clinical Trials

Keywords: Orbit, Orbit/ocular pathology, Skull base, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: Dustin Cavida: D. Cavida is an employee of and stockholder in Amgen Inc.; John Stone: J.H. Stone has received consulting fees from Amgen Inc and was a committee member during the MITIGATE trial.; Emma Culver: E.L. Culver has received consulting fees from Amgen Inc and was a committee member during the MITIGATE trial.; Arezou Khosroshahi: A. Khosroshahi has received consulting fees from Amgen Inc and was a committee member during the MITIGATE trial.; Wen Zhang:

W. Zhang has received consulting fees from Amgen Inc and was a committee member during the MITIGATE trial.; Emanuel Della-Torre: E. Della-Torre has received consulting fees from Amgen Inc and was a committee member during the MITIGATE trial.; Kazuichi Okazaki: K. Okazaki was a committee member during the MITIGATE trial.; Yoshiya Tanaka: Y. Tanaka has received speaking fees and/or honoraria from Chugai, UCB, Abbvie, AstraZeneca, Eli-Lilly, Behringer-Ingelheim, GlaxoSmithKline, Eisai, IQVIA, Daiichi-Sankyo, Otsuka, Taisho, Gilead, Bristol-Mayers was a committee member during the MITIGATE trial for Amgen Inc.; Matthias Löhr: M. Löhr was a committee member during the MITIGATE trial.; Nicolas Schleinitz: N. Schleinitz has received consulting fees from Amgen Inc and was a committee member during the MITIGATE trial.; Lingli Dong: L. Dong was a committee member during the MITIGATE trial.; Hisanori Umehara: H. Umehara was a committee member during the MITIGATE trial.; Marco Lanzillotta: M. Lanzillotta was a committee member during the MITIGATE trial.; Zachary Wallace: Z.S. Wallace has received consulting fees from Amgen Inc, was a committee member during the MITIGATE trial, and is an employee of Amgen Inc and holds stock.; Mikael Ebbo: M. Ebbo was a committee member during the MITIGATE trial.; George Webster: G.J. Webster was a committee member during the MITIGATE trial.; Ferran Martinez Valle: F. M. Valle was a committee member during the MITIGATE trial.; Manu Nayar: M. Nayar was a committee member during the MITIGATE trial.; Vinciane Rebours: V. Rebours was a committee member during the MITIGATE trial.; Cory Perugino: C.A. Perugino has received consulting fees from Amgen Inc. and was a committee member during the MITIGATE trial.; Rong Luo: R. Luo is an employee of Amgen Inc and holds stock.; Sue Cheng: Sue Cheng is an employee of Amgen Inc. and owns stock.; Daniel Cimbora: D. Cimbora is an employee of Amgen Inc and holds stock.

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Contact Information: None provided.

Towards Whole Eye Transplantation with Electric Field Stimulation

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Introduction:

Whole eye transplantation (WET) is an ambitious approach for restoring vision to patients blinded by retinal and optic nerve disease. A recent breakthrough report of a patient who underwent a hemiface transplant one year prior suggested that globes can be successfully transplanted without signs of sympathetic ophthalmia or phthisis. Not surprisingly, the transplanted eye remained blind. Restoration of vision requires strategies that will maintain survival of ocular structures, preserve the retinal neural network, and drive regeneration, myelination, and integration of retinal ganglion cell (RGC) axons.

Methods:

As an early model of globe transplantation, adult Long Evans rats underwent complete optic nerve transection followed by combinatorial treatment with electric field (EF) stimulation and neurotrophic factors. Histologic and electrophysiologic studies were carried out to determine treatment efficacy on promoting RGC survival and directing RGC axon extension past the transection site.

Results:

Two weeks after complete transection, combinatorial treatment was associated with nearly 50% of RGC survival compared to 5% in untreated controls (389 RBPMS+ cells/0.5mm² +/- 88 n = 4 vs 39 +/- 39, n = 2, respectively). Photoreceptor nuclei density was similar (2289 +/- 136/mm retina, n = 4) to normal age matched controls (2346 +/- 163/mm retina, n = 2). Action potentials were recorded from some RGCs (single-cell patch clamping) demonstrated normal responses to current clamping, voltage clamping, and light stimulation (n = 6). Finally, some animals remarkably demonstrated axon extension across the optic transection site (338 and 705 um; n = 2).

Conclusions:

Our results indicate that combinatorial treatment with EF stimulation and neurotrophic factors could be a valuable strategy to help enable WET to restore vision. Combinatorial treatment promotes survival of RGCs and photoreceptors and appears to help maintain the retinal neural network. Further collaborative efforts are geared at improving durability and efficacy of stimulating electrodes.

References: None provided.

Abstract Type: Basic Science

Keywords: Optic neuropathy, Orbit, Optic nerve trauma and treatment

Financial Disclosures: The authors had no disclosures.

Grant Support: ARPA-H

Contact Information: Kimberly Gokoffski, gokoffsk@hs.uci.edu

3D Imaging and Filament Tracing of Human Orbital Vasculature and Lymphatic System

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¹ Cleveland Clinic Lerner College of Medicine, ² Hopital National de la Vision 15-20 and Institut de la Vision, ³ Light Innovation Technology, ⁴ Mass Eye and Ear

Introduction:

This study addresses key gaps in understanding the 3D vascular architecture of the human orbit. Improved characterization of these vessels is critical to understand mechanisms underlying glaucoma and non-arteritic anterior ischemic optic neuropathy (NAION), two major causes of irreversible blindness.

Methods:

Fourteen human orbits from fresh cadavers were studied with light sheet fluorescence microscopy (LSFM) to image orbital vessels, including ophthalmic and posterior ciliary arteries that had been injected with a fluorescent dye (CM-Dil). Orbits were removed en bloc, fixed and optically cleared for LSFM. Imaris software was used to analyze and trace individual vessels with the Filament Tracer; a customized algorithm expedited otherwise laborious manual tracing. Our methods generated digitized data on the volume, diameter, length and spatial location of each vessel, including veins and lymphatics.

Results:

We reconstructed the 3D vascular architecture of the orbital vessels down to 10 microns. For one immunolabeled specimen, we identified 5,884 filaments and 14,944 vessel segments. The mean filament length was 161.6 μm (range 6.1–35,292.5 μm), and the mean segment diameter was 21.5 μm (range 3.8–180.8 μm). The smallest measurable vascular lumina at the optic nerve head were 5–10 μm in diameter. The mean filament volume was 98,864 μm^3 , with a total vascular volume of approximately $5.8 \times 10^7 \mu\text{m}^3$. Five proximal trunks of parent sPCAs were traced and followed to >10 branches entering the region of the optic nerve head. Recent successful staining with endomucin and D2-40 showed novel 3D imaging of veins and lymphatics in human orbits.

Conclusions:

Leveraging LSFM and 3D reconstruction, we generated the first high-resolution 3D maps of human orbital vasculature. This dataset provides unprecedented anatomical framework for our developing model of orbital blood flow and offers a critical foundation for future studies investigating vascular contributions to optic nerve health.

References: None provided.

Abstract Type: Clinical afferent disease, Basic Science, Other

Keywords: Optic neuropathy, Miscellaneous, Orbit

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Grant Support: None.

Contact Information: None provided.

Neurovascular Compression Between the Supraclinoid Internal Carotid Artery and Anterior Optic Pathway: Establishing Clinical and MRI Diagnostic Criteria

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Introduction:

Neurovascular compression syndrome of the anterior optic pathway is a controversial, often misdiagnosed cause of optic neuropathy resulting from neuro-vascular contact (NVC) between the supraclinoid internal carotid artery (ICA) and the optic nerve or chiasm. Accurate diagnosis of this syndrome is challenged by the frequent incidental occurrence of NVC in asymptomatic healthy subjects and by clinical features that mimic glaucoma. We aimed to define objective clinical and MRI morphometric criteria to discriminate pathological compression from benign contact, and to develop a risk-stratification tool.

Methods:

56 subjects who underwent comprehensive neuro-ophthalmological evaluation and high-resolution 3T orbital MRI were included and stratified into three groups based on the presence of optic neuropathy and radiological evidence of NVC: symptomatic NVC (n=20), asymptomatic NVC (n=20), and healthy controls (n=16). Through blinded morphometric analysis, 17 quantitative and qualitative parameters were analyzed grouped into the following domains: NVC severity grade, ICA diameter, sellar-suprasellar and parasellar space dimensions, displacement of vascular and neural structures, chiasmal position and thickness, optic nerve diameters, length and signal intensity. All statistically significant parameters were integrated into a Composite Diagnostic Score and validated using a Random Forest Random Forest artificial intelligence predictive model.

Results:

Symptomatic NVC was characterized by severe neurovascular contact grade, increased supraclinoid ICA diameter (5.29 ± 0.81 mm), marked anatomical spatial restriction with reduced sellar-suprasellar height (8.97 ± 2.52 mm), decreased optic nerve transverse (2.18 ± 0.38 mm) and vertical (2.23 ± 0.55 mm) diameters, increased optic nerve T2 signal, and reduced chiasmal thickness (1.64 ± 0.66 mm). Significant differences were found when comparing Symptomatic NVC with both Asymptomatic NVC and Healthy Controls ($p < 0.05$). The Composite Diagnostic Score classified as moderate or high risk 95% of symptomatic NVC.

Conclusions:

This study establishes objective criteria to diagnose NVCS using high-resolution MRI parameters. The Composite Diagnostic Score represents the first quantifiable tool for risk stratification, improving diagnostic accuracy in this frequently overlooked condition.

References: None provided.

Abstract Type: Clinical efferent disease

Keywords: Neuroimaging, Optic neuropathy

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Targeting Lipid Peroxidation As A Treatment For NAION

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Introduction:

Nonarteritic anterior ischemic optic neuropathy (NAION) is the most common acute optic neuropathy in those older than age 50 (1-3). There is no effective treatment (4). The human optic nerve is 70% to 85% lipids and selectively vulnerable to lipid-mediated oxidative stress and ferroptosis, a form of cell death (5). We investigated evidence of lipid peroxidation and oxidative damage in NAION and the impact of treatment with Ebselen, a glutathione peroxidase mimetic that dampens lipid peroxidation and oxidative damage after experimental NAION.

Methods:

We performed histologic analysis of markers of lipid peroxidation in human NAION eyes and the murine photochemical thrombosis model of NAION. In the animal model, we also performed in vivo scanning laser ophthalmoscope imaging of oxidative stress and measured visual function and structure, and axonal transport using established methods.

Results:

Human NAION exhibits increased retinal 4-hydroxynonenal and 8-oxoG, markers of lipid peroxidation and oxidative stress. Using the NAION model, there is also post-ischemic significant increase in retinal 4-hydroxynonenal and 8-oxoguanine, and malondialdehyde levels at day 1 and day 21 post-ischemia. After NAION, there was also a significant reduction of intra-retinal RGC axonal superoxide signal and impaired axonal transport of intravitreally injected CTB-555/488 along the optic nerve compared with controls. Ebselen treatment (10 mg/kg intraperitoneal) for three weeks after NAION reduced retinal MDA levels, normalized retinal superoxide ($p < 0.01$), and improved axonal transport in the retino-geniculate and retino-collicular pathways by day 21. Optical coherence tomography showed significant preservation of inner retinal thickness ($P = 0.0279$) and increased retinal ganglion cell densities ($P < 0.009$). Additionally, optokinetic responses ($P < 0.0005$) and P1-N2 amplitudes on pattern electroretinogram ($P < 0.002$) improved at days 7, 14, and 21 compared to vehicle-treated eyes.

Conclusions:

Dampening of post-NAION lipid peroxidation using Ebselen led to improved post-ischemic retinal oxidative stress, axonal mitochondrial dysfunction, and impaired axonal transport, resulting in preservation of visual function and structure.

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Abstract Type: Basic Science

Keywords: Stroke, Optic neuropathy, Optic nerve trauma and treatment, Retina, Neuroimaging

Financial Disclosures: The authors had no disclosures.

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Investigating CYP27B1-Driven Neuroprotective Pathways in Acute Retinal Ganglionopathy

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Introduction:

Retinal ganglion cell (RGC) death is the hallmark feature of optic neuropathies. There continues to be a paucity of treatment options for patients with the underlying cellular damage remaining untreated. Therefore, understanding novel avenues of RGC neuroprotection is imperative. The immunomodulatory and neurotropic roles of vitamin D3 are well documented, moreover, local synthesis in the retina may play a role in attenuating RGC degeneration. Employing a transgenic global knockout mouse model for CYP27B1 - the vitamin D3 synthesizing enzyme, we hypothesize that vitamin D3 deficiency will result in greater loss of RGCs upon mechanical crush injury to the optic nerve.

Methods:

Using a unilateral optic nerve crush (ONC) model, differences in progression of injury at 3-, 7- and 14-day timepoints post-crush was investigated in 8 – 12-week-old CYP27B1+/+ (WT) and CYP27B1-/- (KO) mice. Loss of RGCs with progression of injury was determined by staining retinal wholemounts with antibodies against BRN3A and cleaved caspase-3 (N=6). Injury-mediated immune responses were also characterized within the optic nerve and the retina (N=6) using flow cytometry. Differences in gene expression were profiled utilizing qPCR, looking at excitotoxicity, inflammatory and neurotropic factors (N=6).

Results:

A significantly greater loss of RGCs (BRN3A+ cells) was observed in CYP27B1-/- animals compared to their CYP27B1+/+ counterparts, at 3-, 7-, and 14-day post-injury ($p < 0.05$). Cleaved caspase-3 expression was greater in CYP27B1-/- animals at all timepoints ($p < 0.001$). Examining immune cell activation and localization within the optic nerve and retina no difference was observed. Lastly, retinal gene expression profiling revealed an increase in VEGFa and decreased EAAT1 expression in KO mice ($p < 0.05$).

Conclusions:

These results suggest a role for vitamin D3 mediating downstream RGC neuroprotection during ONC-mediated acute injury. We, further aim to define its molecular mechanism through proteomics, ex-vivo cell cultures and cell-specific CYP27B1 KO animals.

References: None provided.

Abstract Type: Basic Science

Keywords: Optic neuropathy, Optic nerve trauma and treatment

Financial Disclosures: Kabeer Thaker: No; Miranda Mathieson: No; Jacob Rullo: Consultant: Pfizer, Amgen, GSK, Abbvie, Pheonix Micron

Grant Support: None.

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Optic Disc Drusen Association to NAION

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Introduction:

Optic disc drusen (ODD) have been proposed as a risk factor for non-arteritic anterior ischemic optic neuropathy (NAION), though their visual impact remains uncertain in older individuals. We hypothesize that ODD are common in eyes with NAION, more frequent in bilateral cases, and may influence vision.

Methods:

We evaluated the eyes of 359 participants from QRK207 who had Spectralis optical coherence tomography (OCT) optic nerve head (ONH) volumes. ODD were assessed from b-scans at presentation and six-month outcome. Vision was evaluated using BCVA and average TD from combined and censored size III and V fields. Statistical comparisons included two-sample t-tests for continuous outcomes and Fisher's exact tests for categorical outcomes.

Results:

ODD were present in 4.7% (17/359) of study eyes at presentation, 4.6% (13/281) of fellow eyes without prior NAION, and 4.8% (14/293) of study eyes at outcome. ODD occurred in 1.6% (1/64) of study eyes with prior fellow eye NAION and 5.7% (13/229) without ($p=0.32$) at outcome. At presentation, study eyes with ODD ($n=17$) tended to have a worse average TD compared to non-ODD eyes ($n=340$; -9.1 dB vs -7.8 dB; $p=0.078$). At outcome, there was no difference (-9.3 dB vs -8.9 dB; $p=0.71$). Eyes with ODD at presentation less frequently (20%) had visual field progression compared to non-ODD eyes (37%, $p=0.50$). Similarly, no significant differences in BCVA were observed at either presentation (64 ± 18 and 68 ± 21 letters; $p=0.45$) or outcome (63 ± 22 and 64 ± 24 letters; $p=0.81$).

Conclusions:

ODD do not appear to be a significant risk factor in patients with NAION aged 50-80 years, but they are more frequent than in the general population. Though eyes with ODD have worse vision at presentation of NAION, visual progression and outcome are not affected.

References: None provided.

Abstract Type: Clinical afferent disease, Clinical Trials

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Optic neuropathy, Visual fields, Neuroimaging, Higher visual functions

Financial Disclosures: David Szanto: No; Patrick Sibony: No; Brian Woods: No; Mark Kupersmith: Mark Kupersmith is consultant to Oculus SA.

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Anatomical Characterization of Optical Coherence Tomography Abnormalities in Friedreich Ataxia: Data from a 400-Patient Heterogeneous Cohort

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Introduction:

Optic neuropathy is a common (though sometimes subclinical) feature of Friedreich Ataxia (FA). In previous studies, RNFL (retinal nerve fiber layer) thicknesses by optical coherence tomography (OCT) in FRDA were predicted by subject age and genetic severity (GAA1 repeat length). RNFL was also decreased in young children with FA, more consistent with hypoplasia than degeneration. This study assessed RNFL and macular ganglion cell thicknesses cross-sectionally and longitudinally.

Methods:

Patients (n=410) with FA, and controls and carriers, were assessed for RNFL and macular ganglion cell thicknesses by OCT. Values were analyzed in the context of disease features and longitudinal changes.

Results:

RNFL thicknesses were symmetric between the 2 eyes in FA patients and markedly lower than control values. FA eyes had the greatest thinning in the superior and inferior quadrants, matching the distribution of thicknesses in control. FA also affected the macular ganglion cell layer, with similar reductions in both eyes and across all sectors. Lower RNFL and ganglion cell thicknesses were associated with worse visual function (visual acuity, low-contrast letter acuity), and with greater disease duration and age. OCT measures were predicted by vision in linear regression models that accounted for age and GAA1 repeat length, demonstrating the effect of disease progression and genetic severity on RNFL thickness. Correlations with visual dysfunction were substantially higher for RNFL values than for ganglion cell values, suggesting that FRDA affects axons primarily. RNFL thicknesses correlated ($r=0.64$, $p=0.0001$) with worse mFARS disability scores, showing that RNFL provides a marker of neurological progression. RNFL values worsened longitudinally, with faster progression in patients with more severe genetic disease.

Conclusions:

The present study demonstrates that RNFL thickness provides a structural marker of progression in FRDA for ongoing clinical trials. The present data also suggest that the primary pathophysiology is a dying-back optic neuropathy rather than a primary ganglion cell disorder.

References: None provided.

Abstract Type: Clinical afferent disease

Keywords: Genetic disease, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Optic neuropathy

Financial Disclosures: David Lynch: No; Victoria Profeta: No; Elliot Goga: No; Courtney Park: No; Mackenzie Wells: Yes; Willa Mazulla: No; Niyati Bhandari: No; Sonal Sharma: No; Kimberly Schadt: No; Rachel Kenney: No; Laura Balcer: No

Grant Support: None.

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AI-Based Classification of Parkinson's Disease Using Quantitative Ocular Motor Biomarkers

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Introduction:

Parkinson's disease (PD) diagnosis relies primarily on clinical examination, which limits accuracy, especially in early disease stages. Objective biomarkers reflecting PD-related neural dysfunction are urgently needed. Ocular motor and pupillary abnormalities have emerged as promising indicators, yet their integration into diagnostic workflows remains limited. This study aimed to develop and evaluate artificial intelligence (AI) models for PD diagnosis based on quantitative ocular motor parameters recorded with a virtual reality (VR)-based medical eye-tracking device.

Methods:

Ninety-nine individuals with idiopathic PD were enrolled in Zurich (Switzerland) and Exeter (UK). Each participant underwent two visits including standardized ocular motor testing with the VR-based medical eye tracker and corresponding clinical examination. Data with poor eye tracking quality or excessive signal loss were excluded. This preliminary analysis included 132 PD examinations. PD participants were matched to controls of similar age and sex using propensity score matching. Standardized mean differences (SMDs) and Welch's tests assessed group differences. A supervised machine learning model was trained to classify PD versus controls using the most discriminative parameters. Site-specific analyses were conducted separately for Zurich and Exeter.

Results:

Parameters showing the largest PD-control differences included saccades (accuracy, velocity, main sequence), vergence, ocular alignment, and pupillary dynamics (constriction/dilation velocity and latency). The classifier achieved strong discrimination between PD and healthy individuals: Zurich—AUC 0.96 (F1 = 0.92, sensitivity = 0.96, specificity = 0.89); Exeter—AUC 0.91 (F1 = 0.84, sensitivity = 0.89, specificity = 0.79).

Conclusions:

Quantitative ocular motor and pupillary metrics robustly distinguished PD from healthy individuals. While still preliminary, these findings highlight the potential of automated eye-tracking and AI analysis to provide objective, reproducible ocular motor biomarkers for PD diagnosis. Ongoing work includes expanding both patient and control cohorts, combining site datasets, and correlating ocular motor measures with clinical outcomes to refine diagnostic accuracy.

References: None provided.

Abstract Type: Clinical efferent disease, Clinical Trials

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Ocular motility, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease, Pupil

Financial Disclosures: Erika Han: No; Ana Coito: Employee of machineMD; Hassan Fadavi: No; Bruno Hauser: Employee machineMD; Pia Massatsch: Employee machineMD; Valentina Stozitzky: Employee gaitQ; Dongli Li: Employee gaitQ; Bettina Balint: No; Helen Dawes: No; Konrad Weber: Medical advisor for the manufacturer MachineMD of the VR eye-tracker used in this study.

Grant Support: Innosuisse - Swiss Innovation Agency (109.813 INT-LS)

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Features of Transient Vision Loss: A Study of 300 Patients

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Introduction:

Transient vision loss (TVL) is often regarded as a visual type of transient ischemic attack (TIA). However, its outcomes and clinical implications are not as well defined. This study aimed to characterize the clinical features, diagnostic yield, and outcomes of patients presenting with acute TVL to a tertiary emergency department.

Methods:

We retrospectively reviewed 300 patients who presented to the Michigan Medicine Emergency Department between 2013 and 2025 with TVL as their primary symptom. Demographic, clinical, ophthalmic, imaging data, and follow-up outcomes within one year were extracted and analyzed.

Results:

The mean patient age was 61 years (range 18–95), with an equal gender distribution. Ischemic risk factors were present in 63% of patients, occurring more frequently in those over age 50 (74% vs. 26%, $p < 0.001$). TVL was monocular in 71%, binocular in 23%, and indeterminate in 6%. Pertinent abnormal findings included hemoglobin A1c (47%), lipid abnormalities (63%), and ESR/CRP elevation (11%). Neurovascular imaging yielded abnormalities in 19% of carotid ultrasounds, 11% of CTAs, and 13% of MRAs, while non-contrast CT brain revealed no acute findings. Ophthalmic pathology was rare ($< 2\%$), including central retinal vein occlusion (2 cases), retinal emboli (1 case), retinal vasculitis (1 case), and posterior vitreous detachment (1 case). Interventions included initiation of statin therapy (27%), antiplatelet agents (24%), and carotid revascularization (5%). Within one year follow-up, major adverse events were uncommon—only one stroke, one subarachnoid hemorrhage, and one retinal vein occlusion occurred.

Conclusions:

Patients presenting with TVL share ischemic risk profiles similar to those with non-visual TIAs but experience significantly fewer adverse vascular outcomes, supporting the concept of TVL as a “TIA-lite.” Ophthalmic and neurovascular investigations rarely yield actionable findings, though medical stroke prevention measures such as lipid and antiplatelet therapy remain substantial.

References: None provided.

Abstract Type: Clinical afferent disease

Keywords: Stroke, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Investigating Regional Cerebrospinal Fluid Flow Alterations In Patients Diagnosed With Idiopathic Intracranial Hypertension

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Introduction:

Idiopathic intracranial hypertension (IIH) is a disease characterized by elevated intracranial pressure of unknown etiology. Proposed mechanisms for the pathophysiology of IIH center around dysregulation of cerebrospinal fluid (CSF) production, circulation, and reabsorption. Advances in analytical techniques applied to low b-value diffusion magnetic resonance imaging (low-b dMRI) has enabled whole-brain mapping of CSF motility through estimation of mean pseudo-diffusivity (M Ψ). The purpose of this study is to understand the relationship between low-b dMRI derived estimates of CSF motility and visual clinical measures and quantitative retinal imaging in IIH patients.

Methods:

52 patients who underwent low-b dMRI on a Siemens 3 T Vida scanner for evaluation of papilledema were identified. Of these, 28 patients diagnosed with IIH by a Neuro-Ophthalmologist underwent pattern-based analysis to estimate M Ψ using the CSF Waterways (CWW) atlas, a data-driven atlas of CSF compartments designed to investigate regional CSF flow alterations. A retrospective chart review was completed to determine papilledema grade, retinal nerve fiber layer (RNFL) thickness, ganglion cell complex thickness, and visual field mean deviation from the neuro-ophthalmology visit closest in time to the MRI. Correlation analysis assessed the relationship between CWW M Ψ and these clinical variables.

Results:

Elevated CSF M Ψ within the Sylvian fissures (CWW-7 and CWW-8) and along the trans-ventricular pathway (CWW-10; third and fourth ventricles) were associated with increased papilledema severity ($r = 0.46$ – 0.52 , $p < 0.05$). A similar positive association was observed between CWW-10 M Ψ and RNFL thickness ($r = 0.46$; $p < 0.05$).

Conclusions:

Preliminary results indicate that localized hyperdynamic CSF motility within the Sylvian fissures, third, and fourth ventricles may be linked to papilledema in IIH. This suggests CSF motility metrics as a possible novel diagnostic aid and prognostic indicator for IIH patients and a mechanism to further evaluate the underlying pathophysiology of this vision threatening disease.

References: 1. Biousse V, Bruce BB, Newman NJ. Update on the pathophysiology and management of idiopathic intracranial hypertension. *J Neurol Neurosurg Psychiatry*. 2012;83(5):488-494. doi:10.1136/jnnp-2011-302029 2. Nazeri A, Hosseini H, Dehkharghanian T, et al. Characterizing the spatial patterns and determinants of cerebrospinal fluid pseudorandom flow in the human brain with low b-value diffusion MRI. *Imaging Neurosci (Camb)*. 2025;3:imag_a_00473. doi:10.1162/imag_a_00473

Abstract Type: Clinical afferent disease, Other

Keywords: High intracranial pressure/headache, Neuroimaging, Pseudotumor cerebri

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Grant Support: None.

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Lenadogene Nolparvovec Gene Therapy for Leber Hereditary Optic Neuropathy in the Real-Life Setting

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Introduction:

Early access program (EAP) provides efficacy and safety data on the use of lenadogene nolparvovec gene therapy (LNGT) in real-life conditions in patients with Leber hereditary optic neuropathy (LHON) caused by the m.11778G>A ND4 variant.

Methods:

LNGT was provided based on patient or physician requests and its use was authorized by local/national regulations in 4 countries (France, Italy, UK and US). Patients received LNGT as a unilateral or bilateral intravitreal injection. Baseline characteristics, efficacy and safety data were collected.

Results:

A total of 63 ND4-LHON patients received LNGT in EAP, mainly in France (35 [55.6%]) and the US (18 [28.6%]). Most (42 [66.7%]) patients received bilateral injections, all but one on the same day. At the time of the first injection, patients were on average (SD) 33.7 (+/-16.6) years old, with 6 (9.5%) children aged 13 or 14 years. The mean (SD) duration of disease at the first injection was 11.4 (+/-9.5) months. Most (84.1%) patients were treated with idebenone at or after LNGT injection. Mean (SD) best-corrected visual acuity (BCVA) at baseline was 1.74 (+/-0.63) LogMAR. BCVA values at 1 year were obtained from 53 (84%) patients; the mean change in BCVA from nadir to 1 year was -0.42 (+/-0.54) LogMAR (+21 ETDRS letters). Clinically relevant recovery (CRR) from nadir was observed in 42.9% (30/70) of treated eyes within 12 months of disease onset, and in 75.0% (27/36) of treated eyes after 12 months of disease onset. The safety of LNGT was comparable to those of the 189 patients from clinical trial studies, with no difference in the incidence of intraocular inflammation between patients treated bilaterally and unilaterally (51.2% vs 52.4%).

Conclusions:

Injection of LNGT in the real-life setting was associated with a clinically meaningful improvement in visual acuity from nadir and a favorable safety profile.

References: None provided.

Abstract Type: Other

Keywords: Optic neuropathy, Genetic disease

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GenSight Biologics: consultant, financial support; Robert Sergott: GenSight Biologics: consultant; Sarah Thornton: No; Sean Donahue: GenSight Biologics: consultant; Hélène Dollfus: No; Thomas Klopstock: Received research support and consultation fees from Santhera Pharmaceuticals, Chiesi, and GenSight Biologics; Claudia Priglinger: No; Rabih Hage: No; Vasily Smirnov: No; Catherine Cochard: No; Marie-Bénédicte Rougier: No; Emilie Tournaire-Marques: No; Pierre Lebranchu: No; Caroline Froment Tilikete: No; Frederic Pollet-Villard: No; Marie-Alice Laville: No; Claudia Prospero Ponce: No; Scott Walter: No; Francis Munier: No; Pauline Zoppe: No; Magali Taiel: Gensight Biologics: employee; José-Alain Sahel: Gensight Biologics: financial support, owner, recipient; allotopic expression: patent.

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Analytical Studies Poster Reception – March 22, 2026 (Sunday)

Poster #	Submission Title	Author	Category
199	Novel Compact Device for Quantitative Measurements of Extraocular Muscle Tensile Strength	Hyunjin Shin	Biomechanics
200	Age-related changes in the biomechanical properties of the human optic nerve sheath	Michael Dattilo	Biomechanics
201	Epidemiology of Visuospatial Impairment In Older Adults: The Harmonized Cognitive Assessment Protocol	Ali Hamedani	Cognition, Mood & Neuro-degenerative Disease
202	Retinal Microcirculatory and Mitochondrial Responses Associated with Cognitive Improvement Following Yoga Exercise in Older Adults	Hong Jiang	Cognition, Mood & Neuro-degenerative Disease
203	Central retinal venular equivalent discriminates Alzheimer's-associated vasculopathy in UK Biobank	Oana Dumitrascu	Cognition, Mood & Neuro-degenerative Disease
204	Task-Evoked Ocular Metrics, Cortical Structure, and Their Interaction: Links to Cognitive Performance in Mild Cognitive Impairment	Julius Opwonya	Cognition, Mood & Neuro-degenerative Disease
205	Robustness of AI-Derived Linguistic Markers of Cognitive Impairment in the Presence of Visual Disease	Sepideh Jamali Dogahe	Cognition, Mood & Neuro-degenerative Disease
206	Hyperreflective Foci by Optical Coherence Tomography (OCT) Distinguishes Patients with Mild Cognitive Impairment (MCI) Due to Alzheimer's Disease From Cognitively Normal Controls	Christian Diaz Curbelo	Cognition, Mood & Neuro-degenerative Disease
207	Impaired vergence in patients with Parkinson's disease	Sun-Uk Lee	Cognition, Mood & Neuro-degenerative Disease

208	Inebilizumab for NMOSD Treatment in a Real-World Cohort: Analysis from the PPD CorEvitas Synergy of Prospective Health and Experimental Research for Emerging Solutions (SPHERES) Registry	Zana Vranic	Cognition, Mood & Neuro-degenerative Disease
209	Scores for Vision-Based Test of Rapid Picture Naming, Mobile Universal Lexicon Evaluation System (MULES), Predict Cognition in an Alzheimer's Disease Research Center (ADRC) Cohort	Laura Balcer	Cognition, Mood & Neuro-degenerative Disease
210	A recurrent missense variant in the <i>PPIB</i> gene underlies adult-onset autosomal dominant optic atrophy	Berthold Pemp	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
211	Data-Driven Structure-Function Model Improves Central Visual Field Mapping in NAION	Ilias Sarbout	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
212	Vision-related Quality of Life In Patients With Pituitary Adenomas	Fernando Botello-Villagrana	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
213	OCT-Based Differentiation of NAION and CRAO: Longitudinal Analysis of Inner Retinal Layer Thinning	Gregory McElroy	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
214	The Utility of the Temporal Raphe Sign on OCT in Differentiating Normal Tension Glaucoma and Chronic NAION	Gina Yu	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
215	Novel OPA1 Mutation Underlying Dominant Optic Atrophy-Plus in a Thai Cohort: Clinical and Genetic Insights	Pawita Kongthanasomboon	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)

			Optic Nerve, and Chiasm)
216	Prevalence of "Disc-at-Risk" for Non-Arteritic Anterior Ischemic Optic Neuropathy in Healthy Eyes	Muhammad Abouhamid	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
217	High-Dose Glucocorticosteroids and Neuroprotection in Acute Optic Neuritis: A Multicenter Retrospective Cohort Study	Sebastian Kuechlin	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
218	Evaluation of Functional and Structural Biomarkers in OPA1 Autosomal Dominant Optic Atrophy - the FALCON Prospective Natural History Study	Patrick Yu-Wai-Man	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
219	EyeStroke protocol with non-mydriatic color fundus photography and optical coherence tomography (NMFP-OCT) in the emergency department (ED): 2.5-year experience	Madhuri Akella	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
220	Assessing Interrater Reliability of OCT Biomarkers in NAION: Comparison Between Experienced and Junior Raters	Sedra Al Yousef	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
221	Early Optical Coherence Tomography Indicators Are Associated with Outcome Vision Loss in Acute Non-Arteritic Anterior Ischemic Optic Neuropathy	Brian Woods	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
222	Clinical Characteristics and Outcomes of Intracranial Germinomas with Visual Pathway Involvement	Kenny Wang	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
223	Informative Censoring in Study Controls Limits the	Diviya Gorsia	Disorders of the Anterior Visual

	Interpretation of the Long-Term Efficacy of Idebenone in Treating Visual Impairment From Leber Hereditary Optic Neuropathy		Pathway (Retina, Optic Nerve, and Chiasm)
224	Propensity-Matched Evaluation of Idebenone Treatment Duration in Leber Hereditary Optic Neuropathy: Revisiting RHODOS Efficacy Outcomes	Diviya Gorsia	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
225	Misleading pale disc: Wolfram syndrome- Genotype phenotype associations	Soveeta Rath	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
226	Exposure to GLP-1 receptor agonists in patients with simultaneous bilateral Non-Arteritic Anterior Ischemic Optic Neuropathy (sNAION)	Sowmya Yennam	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
227	"Better" VA is not Enough: Limited Quality of Vision Improvement in NAION Patients Without Intervention	Nyree Khachikyan	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
228	Long-Term Structural And Functional Outcomes After Hypofractionated Radiosurgery For Optic Nerve Sheath Meningiomas: A 48-Month Monocentric Oct-Based Study	Ludovica Gargiulo	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
229	Ischemic Optic Neuropathy Associated With Semaglutide: Global Population-Based Analysis Of Over 30 Million Safety Reports	Moiz Lakhani	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
230	Spaeth-Richman Contrast Sensitivity Testing for Early Detection of Linezolid-Induced Optic Neuropathy	Uday Parmar	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
231	Increased Axonal Metabolic Stress In NAION: An Imaging	Rishita Pujari	Disorders of the Anterior Visual Pathway (Retina,

	Study Using Flavoprotein Fluorescence Imaging		Optic Nerve, and Chiasm)
232	Genetic Testing in Idiopathic Optic Neuropathy: Diagnostic Yield and Differences in Clinical Presentation	Nagashreyaa Nagajothi	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
233	The Presence of Macular Edema, Ganglion Cell Layer, and Retinal Nerve Fiber Layer Thinning in Optic Neuritis	Blake Archer	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
234	Conventional and AI-Assisted OCT Analyses in Acute Retrobulbar Optic Neuritis: A New Frontier in Early Detection	Ana Banc	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
235	The Use of OCT In Post-Chiasmal and Chiasmal Demyelination: Beyond The Optic Neuritis Universe	André Jorge	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
236	Prevalence And Incidence Of Fellow Eye Involvement In Non-arteritic Anterior Ischemic Optic Neuropathy Patients	Thanthita Mongkolsrisawat	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
237	Prevalence, Clinical and Genetic Characterization Of Patients With Inherited Retinal Dystrophies: A Descriptive Study	Monica Pardo-Bayona	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
238	Vision related quality of life impairment in Ethambutol induced toxic optic neuropathy: A questionnaire based study	Soveeta Rath	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
239	Functional Visual Impairment in Patients with Different Visual Field Defect	ya-Chuan Hsiao	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)

240	Association Normal-Tension Glaucoma and Migraine with Aura and with Chronic Migraine	Meagan Seay	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
241	Clinical Characteristics and Treatment Outcomes of Optic Neuritis in Asians - Preliminary Findings From A Singapore Cohort	Reuben Foo	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
242	Is the Risk of NAION Tied to an Evolutionary Gordian Knot? A Software Analysis of Blood Flow Dynamics at the Optic Nerve Head	Joseph Rizzo	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
243	Strength of Association Between Optic Neuritis and Infectious or Immune-Mediated Inflammatory Diseases: A Population-Representative Study of 30 million People In England (2011-2024)	Tasanee Braithwaite	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
244	PHOMS Prevalence and Functional Implications in Anterior Ischemic Optic Neuropathy Subtypes	Marius Maartensson	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
245	ORION: A Prospective Natural History Study In Patients With Inherited Optic Neuropathies	Rahul Makam	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
246	Discovery of Novel Genetic Variants Associated with Nonarteritic Anterior Ischemic Optic Neuropathy	Uzma Rentia	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
247	The Psychological Experiences of Patients with Acute Vision Loss: A Cross-Sectional Survey of Patients Diagnosed with Anterior Ischemic Optic Neuropathy	Mira Menon	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)

248	RNASEH2B as genetic risk factor in dominant and sporadic optic disc drusen	Yaping Liao	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
249	Optic Nerve Calcification and Altered Plasma Lipidomics in Non-Arteritic Anterior Ischemic Optic Neuropathy	Anas Alkhabaz	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
250	Risk of Nonarteritic Anterior Ischemic Optic Neuropathy in GLP-1 Agonist Users and Associated Social Determinants of Health in the NIH All of Us Research Program	Jainam Shah	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
251	Optic Disc Edema-Associated Secondary Central Retinal Vein Occlusion: A Case Series and Exploratory Analysis	Victoria Leung	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
252	Seeing Through Divides: Geographic, Socioeconomic, and State-Level Disparities in Optic Neuritis Patients at a South Indian Tertiary Center	Roopesh Dinakaran	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
253	Clinical and Systemic Risk Profiles in Non-Arteritic Anterior Ischemic Optic Neuropathy With and Without Glucagon-Like Peptide-1 Receptor Agonist Exposure: A Retrospective Cohort Analysis	Ari August	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
254	Rapid Metabolic Shifts Prior to NAION Among GLP-1RA-Exposed Patients: A Retrospective Cohort Analysis	Roger Sheffmaker	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
255	Equivocal or Atypical Temporal Artery Biopsy Results Require Integration of Histopathology and Multimodal (Including Clinical) Correlation in Neuro-Ophthalmology	Jimena Hathaway	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)

256	Hyperpermeability of the Inner Blood-Retina Barrier in Visual Snow Syndrome	Matthew O'Riordan	Disorders of the Posterior Visual Pathway and Visual Processing
257	Handheld Photopic ERG Reveals Structure-Function Coupling Between PhNR and GCIPL Thickness in Chronic Optic Neuropathy	Yuri Seo	Disorders of the Posterior Visual Pathway and Visual Processing
258	Asymmetric Papilledema in Idiopathic Intracranial Hypertension: Exploring Anatomical and Venous Correlates	Niranjana Kesavamoorthy	Idiopathic Intracranial Hypertension (IIH)
259	Idiopathic Intracranial Hypertension Patients Have an Earlier Mortality Rate Compared to Controls	Jacqueline Shaia	Idiopathic Intracranial Hypertension (IIH)
260	Diagnosis of High Intra-cranial Pressure using Retinal Images Excluding the Optic Nerve Head	Kelvin Li	Idiopathic Intracranial Hypertension (IIH)
261	Familial Standardized Incidence Ratio in Idiopathic Intracranial Hypertension	Judith Warner	Idiopathic Intracranial Hypertension (IIH)
262	Pseudotumor Cerebri and Tetracycline Antibiotic Use: A Matched Analysis	Alison Gibbons	Idiopathic Intracranial Hypertension (IIH)
263	Rethinking Lumbar Punctures In Idiopathic Intracranial Hypertension: An Algorithm	Vineet Kumar	Idiopathic Intracranial Hypertension (IIH)
264	Updates in Glymphatic Imaging in Idiopathic Intracranial Hypertension	Marc Bouffard	Idiopathic Intracranial Hypertension (IIH)
265	Time from Referral to Surgical Intervention and Outcomes in Idiopathic Intracranial Hypertension	Blake Katsev	Idiopathic Intracranial Hypertension (IIH)
266	Seasonal Variation of Idiopathic Intracranial Hypertension	Ruth Huna-Baron	Idiopathic Intracranial Hypertension (IIH)

267	Correlation of ultrasound-derived optic nerve sheath diameter with OCT and MRI features in idiopathic intracranial hypertension	Martin Bertich	Idiopathic Intracranial Hypertension (IIH)
268	Echography Leads, OCT Follows: Defining When OCT-Only Monitoring Is Safe in Idiopathic Intracranial Hypertension	Christoph Mitsch	Idiopathic Intracranial Hypertension (IIH)
269	Trends In Management Of Idiopathic Intracranial Hypertension	Gloria Pan	Idiopathic Intracranial Hypertension (IIH)
270	Evaluating the Prevalence of Optic Disc Edema in Patients Referred to a Neuro-Ophthalmology Clinic with Pulsatile Tinnitus: A Study on Diagnostic Yield and Clinical Correlates	Sari Yordi	Idiopathic Intracranial Hypertension (IIH)
271	Case-Only Study Designs in Neuro-Ophthalmology: An Example Using Pseudotumor Cerebri Syndrome	Christopher Anthony	Idiopathic Intracranial Hypertension (IIH)
272	Advancing Diagnostics in Idiopathic Intracranial Hypertension: A Tri-modal Investigation of Optic Nerve Sheath Measurements	Karthik Kumar Mani	Idiopathic Intracranial Hypertension (IIH)
273	OCT-Based Telemedicine for Papilledema Monitoring in Children	ainat Klein	Idiopathic Intracranial Hypertension (IIH)
274	Big Data for Improved RNFL Segmentation in Papilledema: A Semi-supervised Deep Learning Model Outperforms the Customary Spectral-Domain OCT Software	Mehdi Ounissi	Idiopathic Intracranial Hypertension (IIH)
275	Disparities in Surgical Management of Medically Refractory Idiopathic Intracranial Hypertension Cases at UT Southwestern Medical Center	Mishel Malik	Idiopathic Intracranial Hypertension (IIH)

276	Clinical Profile of IIH - A Comparative Analysis of Patients With and Without Anemia: A Multicentric Study	Padmavathy Maharajan	Idiopathic Intracranial Hypertension (IIH)
277	Tirzepatide for the Reduction of Acetazolamide in IIH (TREAT-IIH) Trial Design	Robert Mallery	Idiopathic Intracranial Hypertension (IIH)
278	Tetracycline and Vitamin A Derivative Exposure in Patients with Established Pseudotumour Cerebri	Verity Moynihan	Idiopathic Intracranial Hypertension (IIH)
279	Fluorescein Angiography Poorly Differentiates Between Mild Cases of True Versus Pseudo-Papilledema	Josh Kruger	Idiopathic Intracranial Hypertension (IIH)
280	The relationship between PHOMS and Intracranial Pressure in Patients with IIH	Kexin Zhang	Idiopathic Intracranial Hypertension (IIH)
281	Innovative Learning: Using Artificial Intelligence to Navigate Simulated Neuro-Ophthalmology Cases	Samir Touma	Miscellaneous
282	Photophobia in Gulf War Illness: Ocular Surface Symptoms as a Window Into Multisystem Disease	Jonghoon Chang	Miscellaneous
283	Utilization and Diagnostic Yield of Neuroimaging in Patients Presenting to Neuro-ophthalmology for Migraine Aura Without Headache: A 10-year Retrospective Study	Carla Dias	Neuro-Imaging
284	Cross-Species Retinal Aging Analysis in Humans and Non-Human Primates Using Deep Learning	Tuyet Thao Nguyen	Neuro-Imaging
285	Botulinum Toxin A Reduces Activation of Neural Pathways of Photophobia in Patients with History of Traumatic Brain Injury	Alex Hattenhauer	Neuro-Imaging
286	Concurrent Neurological Etiologies of Vision Loss in	Suria Sudhakaran Mannil	Neuro-Imaging

	Glaucoma: Diagnostic Yield of MRI Brain and Orbit in Neuro-Ophthalmology Referrals		
287	Optic Pathway Involvement In Posterior Reversible Encephalopathy Syndrome (PRES): Case Report And Literature Review	Shan Uddin	Neuro-Imaging
288	Application of Artificial Intelligence to Magnetic Resonance Imaging for the Identification of the Etiology of Optic Neuritis	Samir Touma	Neuro-Imaging
289	Ophthalmic Conditions in Patients with Multiple Sclerosis	Ha-Neul Yu	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
290	Factors Associated with Surgical Outcomes in Patients with Congenital Fourth Cranial Nerve Palsy	Sujin Kim	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
291	The Obesity Paradox in Korean Diabetic Patients: Higher Body Mass Index Reduces Non-Arteritic Anterior Ischemic Optic Neuropathy Risk	Jaeryung Kim	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
292	External Validation of Predictive Models in Diagnosing Giant Cell Arteritis Among Temporal Artery Biopsy Patients	J. Benjamin Gordon	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
293	Efficacy of Nipocalimab in Adult Patients with Moderate to Severe Ocular Manifestations of Generalized Myasthenia Gravis in Phase 3 VIVACITY-MG3	Margaret Van Horn	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
294	Decreased Complement C3 and Increased C8G in Neuromyelitis Optica Spectrum Disorder: Evidence of Complement-Mediated Pathophysiology	Bo Young Chun	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases

295	Formulation and Ex Vivo Evaluation of Pyridostigmine Bromide Eye Drops for Ocular Myasthenia Gravis Treatment	Kate Lim	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
296	Association between disease-modifying therapies for multiple sclerosis and risk of non-infectious uveitis	Anthony Cordisco	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
297	Ophthalmologic Spectrum and Clinical Outcomes in Idiopathic and IgG4-Related Hypertrophic Pachymeningitis	Akarawit Eiamsamarng	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
298	Frequency of optic nerve enhancement during acute optic neuritis in MOG antibody-associated disease	Stephanie Syc-Mazurek	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
299	Temporal Patterns of Ocular Syphilis: Imaging and Laboratory Correlates Across Symptom Duration	James Rhead	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
300	Prevalence and Prognostic Significance of Autoantibody Profiles in Transformation of Ocular to Generalized Myasthenia Gravis	Ginger Kwak	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
301	Ocular Symptom Burden on Visual Recovery in Neurosyphilis	Rachel Dolan	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
302	Adaptive Optics OCT Reveals Alterations in Macrophage-Like Cell Morphology in Multiple Sclerosis	Sanjana Marikunte	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
303	Does OPA1 Genotype And Visual Outcomes Predict Idebenone Treatment In Dominant Optic Atrophy (DOA)?	Danielle Gauthier	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
304	Extraocular Muscle And Orbital Fat Changes In Treatment Of Thyroid Eye Disease With Monoclonal Antibodies: A Systematic Review and Meta-Analysis	Alexander Kos	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases

305	Silent Partners in Aging: Unraveling Demographic Risk Factors Linking Glaucoma and Alzheimer's Through a Nationwide EHR Analysis	Bhargavee Gnanasambandam	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
306	Factor Associated with The Presence Of Other Autoimmune Diseases in Neuromyelitis Optica Spectrum Disorder Patients who Initially Presented with Optic Neuritis	Nattarat Tang-ananchai	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
307	Interferon-Beta vs. Monoclonal Antibody Therapy in Multiple Sclerosis-Associated Uveitis: A Systematic Review	Armand Ceniza	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
308	Diplopia in Extramedullary Multiple Myeloma: A Comprehensive Retrospective Analysis of Clinical Characteristics, Management, and Prognosis from a US Tertiary Cancer Center	Arsalaan Asad	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
309	Karyopherin Modulation Protects Against Retinal And Cerebellar Degeneration In Spinocerebellar Ataxia Type 1	Dylan Timperman	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
310	Does Leukemic Optic Neuropathy Hold Key Prognostic Insight in Leukemia?	Jessica Tabary	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
311	Left Eye Physiological Increase in IOP may explain why the Right Eye is First affected in Patients with Leber's Hereditary optic neuropathy.	Shenoda Abd Elmaseh	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
312	Bilateral Optic Nerves T2 Hyperintensity in Idiopathic Intracranial Hypertension: Diagnostic Value and Ophthalmological Correlations.	Natalia Shor	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
313	Patterns of Ischemic Cranial Nerve Palsy and Diabetic Retinopathy: An Urban - Rural	Karthik Kumar Mani	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases

	and Socioeconomic Comparison		
314	A Procedure in Decline: Frequency of Temporal Artery Biopsies Since 2017 in a Major Tertiary Ophthalmology Center	Andreas Bendtsen	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
315	Peri-Orbital Arterial Involvement in Giant Cell Arteritis: Rationale for a Novel MRI Protocol	Alexi Gosset	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
316	Clinical Spectrum And Outcomes Of Leukemic Optic Nerve Infiltration: Insights From A Tertiary Cancer Center	Anushka Mandalapu	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
317	Ocular Viability After Brain Death: Evidence of Retinal Dysfunction in Donor Eyes	Jeffrey Gluckstein	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
318	Cytarabine-Induced Bilateral Optic Neuropathy With Moderate Response to Intravenous Steroid Treatment	Ashley Abing	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
319	Risk of Neuro-Ophthalmic Complications in Immune Checkpoint Inhibitor Users in the TriNetX U.S. Database	Sachin Pathuri	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases
320	Systematic "Papilledema Protocol" in an Emergency Department (ED)	Amy (Mung Yan) Lin	Neuro-Ophthalmic Practice
321	Implementation, Evaluation, and Use of Nonmydriatic Ocular Fundus Imaging in the Emergency Department: More than 2 years of Prospective Consecutive Data	Stuart Duffield	Neuro-Ophthalmic Practice
322	Beyond Vision Loss: Innovative Case Management For Improved Outcomes In Leber Hereditary Optic Neuropathy (LHON)	Timothy Theisen	Neuro-Ophthalmic Practice
323	Normative Percentiles and Age-Related Change Points for RNFL and GCIPL Thickness in	Jae Ryong Song	Neuro-Ophthalmic Practice

	Healthy Adults based on Cirrus HD-OCT		
324	Innovative Anesthetic Cream Taping Technique: Efficacy and Safety for Pain Reduction During Pretarsal Botulinum Toxin A Injection in Hemifacial Spasm: A Double-Blind Randomized Controlled Trial	Nutchaya Sukon	Neuro-Ophthalmic Practice
325	Automated Review of Longitudinal Electronic Health Records: Privacy-Preserving Agentic LLMs for identifying incident NAION at Scale	Tuyet Thao Nguyen	Neuro-Ophthalmic Practice
326	Glaucoma Referrals and Diagnostic Overlap in a Neuro-Ophthalmology Service: A Retrospective Review from a Tertiary Eye Center in Brazil	Luciano Simao	Neuro-Ophthalmic Practice
327	Clinical Course and Visual Outcomes of Ocular Motor Cranial Nerve Schwannomas	Kristina Lin	Neuro-Ophthalmic Practice
328	Analysis of code strokes for vision loss	Courtney Francis	Neuro-Ophthalmic Practice
329	Has Temporal Artery Ultrasound replaced Temporal Artery Biopsy in the Diagnosis of Giant Cell Arteritis? Current Opinions and Practice Patterns of NANOS Members	Raghu Mudumbai	Neuro-Ophthalmic Practice
330	Structural Explanations for Discrepancies Between Clinical vs. Optical Coherence Tomography Measurement of the Cup-to-Disc Ratio	Yasaman Anvarinia	Neuro-Ophthalmic Practice
331	Diagnostic Value of Papilledema in Identifying Intracranial Pathology at a Tertiary Referral Center	Nitsan Duvdevan-Strier	Neuro-Ophthalmic Practice
332	Clinical Profile and Visual Outcomes in Indirect Traumatic Optic Neuropathy: A	Shikha BASSI	Neuro-Ophthalmic Practice

	Retrospective Study from a Tertiary Eye Care Hospital		
333	Diagnostic Concordance of ChatGPT-4.0 in Electroretinogram Interpretation Compared with Human Experts	Salma Yassine	New Diagnostic Measurement Techniques
334	Vestibulo-Ocular Reflex Gain Differentiates Spinocerebellar Ataxia Type 27B from CANVAS and Idiopathic Late-Onset Cerebellar Ataxia	Leonardo Ariello	New Diagnostic Measurement Techniques
335	Vision-Based Concussion Testing in a Youth Ice Hockey Cohort: Are There Gender Differences in Pre-Season Scores for Rapid Picture-(MULES) and Number-Naming (SUN)?	Laura Balcer	New Diagnostic Measurement Techniques
336	Association of Rapid Picture and Number Naming Time Scores to Examination Test Results in Occupational Therapy for Vision and Vestibular Physical Therapy in Clinical Practice	Laura Balcer	New Diagnostic Measurement Techniques
337	Reliability of Objective Vision-Based Screening Tools for Concussion in Collegiate Athletes	Laura Balcer	New Diagnostic Measurement Techniques
338	Comprehensive Stereotaxic Mapping of the Rat Superior Colliculus and Visual Cortex with High-Density Electrode Array	Nicholas Householder	New Diagnostic Measurement Techniques
339	Characterizing 18F-FDG Uptake In Extraocular Muscles Of Patients With Parkinson's Disease	Eden Tefera	New Diagnostic Measurement Techniques
340	Pattern-Level Reproducibility of Head-Mounted Smartphone-Based Perimetry in Optic Neuropathies	Mahmoud KhalafAllah	New Diagnostic Measurement Techniques

341	Association Between Prostaglandin Analogue Use and Sagging Eye Syndrome in Older Adults: A Retrospective Case-Control Study	Emma Carpenter	Ocular Motility Disorders and Nystagmus
342	The Prognosis of Diplopia from Brainstem Ischemic Strokes, A Cross-Sectional Study	Sebastian Garza Hernandez	Ocular Motility Disorders and Nystagmus
343	Recurrent Painful Ophthalmoplegic Neuropathy (RPON): Clinical and Radiological Features with Cerebrospinal Fluid MCP-1 Elevation	Shilin Yang	Ocular Motility Disorders and Nystagmus
344	Causes of Isolated Ocular Motor Nerve Palsy - A Population-Based Evaluation	Fradah Gold	Ocular Motility Disorders and Nystagmus
345	Real-Time Detection and Extraocular Muscle Stimulation Framework for Adaptive Management of Acquired Nystagmus	Kenzi Griffith	Ocular Motility Disorders and Nystagmus
346	Eye Movement Disorders in Central Nervous System Demyelinating Diseases - A Retrospective Study	Natthapon Rattanathamsakul	Ocular Motility Disorders and Nystagmus
347	Non-ocular symptoms in early, treatment-naïve ocular myasthenia gravis: the PROMISE-MG study	Ali Hamedani	Ocular Motility Disorders and Nystagmus
348	Smoking Status Is Associated With Delayed Recovery In Patients With Ischemic Cranial Nerve Palsy: a Pilot Study	Ju-Yeun Lee	Ocular Motility Disorders and Nystagmus
349	Binocular Eye-Tracking of Naturalistic Viewing Highlights Eyeblick and Gaze Asymmetries in Strabismus	Olivia Calancie	Ocular Motility Disorders and Nystagmus
350	Feasibility of a Gamified Virtual Reality (VR) System for Ocular Motor, Assessment After Mild Traumatic Brain Injury	Betania Arce	Ocular Motility Disorders and Nystagmus

351	Feasibility of Detecting Oculomotor Alterations in Patients with Huntington's Disease Using Custom, Retina-Based Eye Tracking	Iftee Shahriar	Ocular Motility Disorders and Nystagmus
352	Incidence of Causative Lesions on Neuroimaging in Isolated Sixth Nerve Palsies: a Large Database Study	Alexander Kwok	Ocular Motility Disorders and Nystagmus
353	A Screening Tool For Evaluation of Diplopia	Kathleen Louis-Gray	Ocular Motility Disorders and Nystagmus
354	Vestibular and Ocular Motor Characteristics in Spinocerebellar Ataxia 6 and Episodic Ataxia type 2 - does the same gene equal the same findings?	Mengchen Suo	Ocular Motility Disorders and Nystagmus
355	Strabismus in Pediatric Cerebral Palsy: A Real-World Analysis of Incidence and Surgical Intervention across U.S. Institutions	Adriana Grigorian	Ocular Motility Disorders and Nystagmus
356	Deep Learning-Based Retinal Vessel Segmentation and Analysis of Intensity and Density in Leber's Hereditary Optic Neuropathy	Maryam Golmohammadi	Ocular-Imaging
357	Syphilis Mimicking Papilledema Diagnosed with Non-Mydriatic Ocular Fundus Imaging in the Emergency Department	Wei-Hsuan Lee	Ocular-Imaging
358	Handheld Non-Mydriatic Fundus Camera for Bedside Inpatient Ophthalmology and Neurology Consultations	Daniel Adamkiewicz	Ocular-Imaging
359	Fundus Photography for Differentiating Ocular Tilt Reaction from Trochlear Nerve Palsy	Nitza Goldenberg-Cohen	Ocular-Imaging
360	Retinal Mitochondrial Function in Response to Yoga Exercise in Patients with Parkinson's Disease	Potyra Rosa	Ocular-Imaging

361	Prospective AI-based Fundus Image Identification of Neuro-Ophthalmic Disorders in a Tertiary Emergency Department	Ayse Gungor	Ocular-Imaging
362	Virtual Reality Visual Fields Show Changes Consistent with Atrophy on Optical Coherence Tomography	Emma Proctor	Ocular-Imaging
363	Visible-Light OCT as a Novel and Sensitive Tool for Assessing Retinal Changes in Multiple Sclerosis and Neuromyelitis Optica	Joshua Rodriguez	Ocular-Imaging
364	The First Year of the Multidisciplinary Eye Dystonia Clinic: Demographics, Treatments, and Surgical Outcomes	Ofira Zloto	Orbital and Eyelid Disorders
365	THRIVE-2 Phase 3 Trial of Veligrotug in Chronic Thyroid Eye Disease (TED): Efficacy, Safety, and Quality of Life at 15 Weeks	Yurong Gao	Orbital and Eyelid Disorders
366	Depth of Proptosis Response with Veligrotug: Patient-Level Results from the THRIVE Phase 3 Trial in Active Thyroid Eye Disease (TED)	Yurong Gao	Orbital and Eyelid Disorders
367	Thyroid-Stimulating Immunoglobulins as a Predictive Biomarker for Thyroid Eye Disease	Iris Ben Bassat Mizrahi	Orbital and Eyelid Disorders
368	Clinical Features in Patients with Thyroid Eye Disease according to the Seropositivity for Anti-Acetylcholine Receptor Antibodies	Hee-Young Choi	Orbital and Eyelid Disorders
369	Orbital Volume Dynamics in Chronic, Low CAS Thyroid Eye Disease (TED): Imaging Evidence of Teprotumumab Treatment Response	Elizabeth Conrad	Orbital and Eyelid Disorders

370	Clinical Outcomes of Superior Ophthalmic Vein Approach for Closure of Carotid-Cavernous Fistulas	Lauren Colwell	Orbital and Eyelid Disorders
371	Efficacy of Teprotumumab in Patients with Long Duration and Short Duration Thyroid Eye Disease (TED): Post Hoc Analysis of 4 Randomized Trials and Open-Label Extensions	Elizabeth Conrad	Orbital and Eyelid Disorders
372	Assessing the Burden of Thyroid Eye Disease in US Patients: A Survey-Based Study	Ruth Meakin	Orbital and Eyelid Disorders
373	Diagnosis Journey, Treatment, and Management of Patients with Ocular Myasthenia Gravis: Insights from a U.S. Patient Panel	Cecelia Johnstone	Orbital and Eyelid Disorders
374	Disease Burden, Impact on Daily Functioning, and Psychological Well-being in Patients with Ocular Myasthenia Gravis: Insights from a U.S. Patient Panel	Cecelia Johnstone	Orbital and Eyelid Disorders
375	An Extended Lateral Orbital Approach for Enhanced Visualization of Neurovascular Structures: Anatomical and Educational Insights	Armand Ceniza	Orbital and Eyelid Disorders
376	Six-Month Visual Outcomes in Pediatric Optic Neuritis: A Multicenter Prospective Study from South Korea	Jae Ho Jung	Pediatric Neuro-Ophthalmology
377	Clinical Characteristics of Optic Neuritis in a Young Pediatric Cohort, Less than Eight Years Old	Matthew Debiec	Pediatric Neuro-Ophthalmology
378	Pediatric Idiopathic Intracranial Hypertension in Hong Kong: A 20-year Study	Matthew Lam	Pediatric Neuro-Ophthalmology
379	Temporal Trends in Optic Pathway Glioma Survival: A Population-Based Analysis	Kathryn Huang	Pediatric Neuro-Ophthalmology

380	Visual Outcomes of Idiopathic Infantile Nystagmus in the Pediatric Population	Esha Prakash	Pediatric Neuro-Ophthalmology
381	Using peripapillary retinal nerve fiber thickness to differentiate between real and pseudopapilledema in Chinese children	Carmen Chan	Pediatric Neuro-Ophthalmology
382	Clinical Features and Outcomes of Late-Presenting Craniosynostosis Initially Presenting as Papilledema	Mark Phillips	Pediatric Neuro-Ophthalmology
383	Evaluating Visual Motor Integration In Children With Optic Neuritis	Natalie Brillhart	Pediatric Neuro-Ophthalmology
384	Utilizing Inter-Eye RNFL Thickness Difference via OCT for Detecting Remote Optic Neuritis In Pediatric-Onset Multiple Sclerosis: Validation of a 4 μ m Threshold	Sydney Chatfield	Pediatric Neuro-Ophthalmology
385	An International Questionnaire on Management of Amblyopia	Andrew Garfield	Pediatric Neuro-Ophthalmology
386	Recovery of the Pupillary Light Reflex in Diabetic Retinopathy Assessed by Automatic Pupillometry	Fabienne Fierz	Pupillary Disorders
387	3D Imaging and Filament Tracing of Human Orbital Vasculature and Lymphatic System	Drenushe Krasniqi-Vanmeter	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
388	Neurovascular Compression Between the Supraclinoid Internal Carotid Artery and Anterior Optic Pathway: Establishing Clinical and MRI Diagnostic Criteria	Francesco Cutrupi	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
389	Targeting Lipid Peroxidation As A Treatment For NAION	Ming Yang	Neuro-Ophthalmic Disorders of Neurologic and Systemic Diseases

390	Investigating CYP27B1-Driven Neuroprotective Pathways in Acute Retinal Ganglionopathy	Kabeer Thaker	Disorders of the Anterior Visual Pathway (Retina, Optic Nerve, and Chiasm)
391	Optic Disc Drusen Association to NAION	David Szanto	Neuro-Imaging
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Novel Compact Device for Quantitative Measurements of Extraocular Muscle Tensile Strength

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Introduction:

Understanding the tensile properties of extraocular muscles (EOMs) is crucial for successful strabismus surgery and accurate predictions of surgical outcomes. Assessments of EOM tensile strength are traditionally highly dependent on the expertise of the ophthalmic surgeon. Consequently, the goal of this study was to create a compact, quantitative, and clinically applicable device for assessing EOM tensile strength.

Methods:

In this study, we developed device uses a strabismus hook connected to a strain gauge load cell that measures the tensile force, and includes a tilting sensor to ensure that the hook is pulled at a consistent angle when a force is applied. The performance of the device was tested on 22 EOMs in 11 patients with intermittent exotropia during surgery for resecting the medial rectus (MR) and recessing the lateral rectus (LR) under general anesthesia

Results:

The subjects were aged 4 to 13 years, with a mean age of 9.4 years (range = 4–13 years), and comprised 6 males and 5 females who were scheduled for elective strabismus surgery to correct intermittent exotropia under general anesthesia. Muscle traction was applied to the MR muscle for the same duration (10 sec) and applied force (10 mm) in all cases to ensure that the muscle stimulation was as consistent as possible. Similarly, the tensile force of the LR was measured using the inferior temporal approach. The measured tensile strength did not differ significantly between the MR (284.9±58.3 g) and the LR (278.3±64.6 g) (p = 0.846).

Conclusions:

In this study we developed a novel compact device for quantitatively measuring the preoperative EOM tensile strength, which could aid strabismus surgery planning. By providing objective real-time measurements, this method may help to explain individual differences in muscle elasticity, thickness, and ultrastructural variations, potentially allowing for more-personalized surgical approaches. Assessing the mechanical properties of EOMs in this way could contribute to improved surgical predictability and patient outcomes.

References: None provided.

Keywords: Adult strabismus with a focus on diplopia, Ocular motility, Pediatric neuro-ophthalmology, Graves' disease, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Age-related changes in the biomechanical properties of the human optic nerve sheath

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Introduction:

Although optic nerve sheath (ONS) structural changes have been described in several ophthalmic disorders, such as idiopathic intracranial hypertension (IIH)^{1,2}, ONS biomechanical properties remain poorly understood, particularly in humans where there are limited studies. Although several studies have described ONS biomechanical properties⁴⁻⁶, the effect of age was not assessed. Here, we report human ONS (hONS) biomechanical properties obtained using unconfined microcompression testing.

Methods:

The ONS from 3 male humans (ages 20, 36, and 63 yo) were dissected from the ON. A cylindrical sample of hONS (1 mm diameter), obtained using a biopsy punch, was placed on a custom-made unconfined microcompression device platform in a PBS fluid bath at room temperature. Samples were pre-loaded with a compressive load of 2 mN, allowed to equilibrate, and then subjected to a 3-step stress relaxation protocol at 5%, 10%, and 15% compressive strain. Data from each step were analyzed independently using linear viscoelastic theory to determine hONS material properties.

Results:

The hONS stiffness was 0.88 ± 0.1 N/mm for the 2 younger subjects (20 and 36 yo) and 0.045 N/mm for the 63 yo subject. The stress after relaxation (Maxwell Ideal Einf) was 8.13 ± 1.55 kPa for younger subjects and 4.10 kPa for the 63 yo subject. The time to relaxation (Maxwell Ideal Tau) was 23.31 ± 12.42 seconds for the younger subjects and 9.00 seconds for the 63 yo subject.

Conclusions:

Younger subjects ONSs tended to be stiffer, relax more slowly, and retain a higher stress after relaxation compared to the older subject ONS. Although we have a small sample size, this data suggests that human ONS biomechanical properties change with age. Further understanding of this difference may provide insights into the pathophysiology of IIH and may lead to the development of novel IIH treatments.

References: None provided.

Keywords: Pseudotumor cerebri, Miscellaneous

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Grant Support: None.

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Epidemiology of Visuospatial Impairment In Older Adults: The Harmonized Cognitive Assessment Protocol

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Introduction:

Visuospatial impairment occurs in neurodegenerative diseases such as Alzheimer's disease and posterior cortical atrophy, but less is known its prevalence in the general older adult population - including those with mild cognitive impairment (MCI) - and its effects on daily functioning and quality of life. Our objective was to determine the prevalence of visuospatial impairment in a nationally representative sample of older adults and identify self- and informant-reported functional measures associated with visuospatial dysfunction.

Methods:

We analyzed data from 3,496 participants aged ≥65 years in the 2016 Harmonized Cognitive Assessment Protocol (HCAP), a sub-study of the nationally representative U.S. Health and Retirement Study. Visuospatial function was assessed using the CERAD constructional praxis and MMSE pentagon copy tasks. Impairment was defined as a factor score >1.5 standard deviations below expected relative to a robust normative sample. Cognitive status was classified by HCAP as normal, mild cognitive impairment (MCI), or dementia. Logistic regression models examined associations between visuospatial impairment and functional outcomes, adjusting for demographic, health, and general cognitive factors.

Results:

Visuospatial impairment was present in 435 participants (11.33%), of whom 49.85% had MCI and 39.97% had dementia. Over half of those with MCI and visuospatial impairment (n=106, 52.71%) had no other cognitive domain affected. Visuospatial impairment was associated with increased odds of self-reported visual difficulty (OR 1.60, 95% CI: 1.20–2.15), difficulty using a map (OR 3.35, 95% CI: 2.35–4.80), and informant-reported navigation difficulties, including getting lost in the community (OR 3.05, 95% CI: 2.16–4.31). Associations with driving, map use, and getting lost at home remained significant after adjusting for general cognition.

Conclusions:

Visuospatial impairment is common among older adults and frequently occurs in isolation in MCI. It is strongly associated with functional limitations, particularly in navigation and driving. These findings underscore the importance of assessing visuospatial function in older adults.

References: None provided.

Keywords: Higher visual functions

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Retinal Microcirculatory and Mitochondrial Responses Associated with Cognitive Improvement Following Yoga Exercise in Older Adults

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Introduction:

This study examined whether retinal biomarkers reflect physiological and cognitive adaptations to yoga in older adults, using multimodal retinal imaging to assess neurovascular and mitochondrial responses after a 24-week intervention.

Methods:

Thirty healthy older adults (mean age 72.3 ± 6.1 years; 25 females) participated in three 60-minute yoga sessions per week for 24 weeks. Retinal vessel density and structure were measured by optical coherence tomography angiography (OCTA), retinal blood flow (RBF) by the Retinal Function Imager (RFI), and mitochondrial activity by macular flavoprotein fluorescence (FPF) using the OcuMet Beacon. Cognitive performance was evaluated at baseline and follow-up with the NIH Cognition Toolbox, Trail Making Tests (TMT-A/B), and Hopkins Verbal Learning Test (HVLT). Linear mixed models assessed longitudinal change, and Spearman correlations examined ocular–cognitive associations controlling for age, sex, and lens status.

Results:

Retinal microcirculatory measures improved significantly: RBF rose from 2.21 ± 0.47 to 2.72 ± 0.93 nl/s ($p = 0.002$); tissue perfusion from 1.91 ± 0.54 to 2.38 ± 0.90 nl/s/mm³ ($p = 0.004$); and capillary flow from 0.115 ± 0.026 to 0.141 ± 0.050 nl/s/mm ($p = 0.004$). Macular FPF decreased from 31.7 ± 10.2 to 30.1 ± 9.8 gsu ($p = 0.041$), indicating improved mitochondrial efficiency. Foveal avascular zone change correlated with FPF ($p = 0.49$, $p = 0.01$), suggesting coordinated vascular–metabolic remodeling. Cognitive gains paralleled ocular improvements: Flanker scores correlated with RBF ($p = 0.38$, $p = 0.04$); Total Recall with perfusion ($p = 0.40$, $p = 0.04$) and capillary flow ($p = 0.41$, $p = 0.03$); and List Sorting with optic-nerve FPF ($p = -0.61$, $p = 0.003$).

Conclusions:

Yoga enhanced retinal microcirculation and mitochondrial function, changes that aligned with improved cognition. These results support the retina as a sensitive, non-invasive biomarker for tracking neurovascular and metabolic adaptations to lifestyle-based cognitive interventions in aging.

References: None provided.

Keywords: Vascular disorders, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Retina, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

Financial Disclosures: Hong Jiang: Ed and Ethel Moor Alzheimer's Disease Research Program (Florida Health, 20A05; Mariam Moarefi; Kylie Joy Martinez; Giovana Rosa Gameiro; Brooke Marie Fitzgerald; Andrew Hoover; Collin Rich: employee at OcuSciences; Joseph F Signorile: UM Aging Team Science Award; Natalie C. Ebner; Jianhua Wang: This study was supported by NIH Center Grant P30 EY014801 NINDS 1R01NS111115 UM Aging Team Science Award

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Contact Information: None provided.

Central retinal venular equivalent discriminates Alzheimer's-associated vasculopathy in UK Biobank

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Introduction:

The relationship between retinal vascular dysfunction and Alzheimer's disease (AD) has been reported. Herein, we investigate the association between AD and automatically quantified retinal arteries and veins diameters in UK Biobank.

Methods:

We quantified central retinal vein equivalent (CRVE) and artery equivalent (CRAE) in Hubbard zones B and C in 1039 UK Biobank right eyes with macula-centered fundus photographs (220 AD, 202 Parkinson's disease (PD), 516 normal controls (NC)). Group-level adjusted mean differences for AD vs NC and AD vs PD with 95% confidence intervals (CI) were constructed using regression modeling, adjusting for between-group confounders where appropriate (age, gender, hypertension, diabetes mellitus (DM), APOE4 carrier).

Results:

AD subjects were significantly older than NC (mean (SD) age 64.9(4.4) vs 55.9(8.1) years, $p < 0.001$), had similar genders and incidence of hypertension (27.7% vs 22.7%, $p = 0.1428$), more DM (6.8% vs 3.5%, $p = 0.04$) and APOE4 carriers (64.4% vs 30.8%, $p < 0.001$). When compared to PD, AD subjects were older (mean (SD) age 64.9 (4.4) vs 62.6 (5.3) years, $p < 0.001$) and more likely to be APOE4 carriers (64.4% vs 29.6%, $p < 0.001$). Between AD and NC, age and DM-adjusted measures showed greater CRVE in Hubbard zone B (mean difference (CI) 2.042 (0.61, 3.47), $p = 0.005$) and C (mean difference (CI) 1.859 (0.41, 3.29), $p = 0.01$). After additional adjustment for APOE4, CRVE in zone B only remained greater in AD ($p = 0.03$). When we compared AD and PD, age, gender and APOE4-adjusted vascular measures also exhibited greater CRVE in AD in zones B ($p = 0.0176$) and C ($p = 0.0018$). CRAE and AV ratio showed non-significant differences between AD and NC, AD and PD, in all zones ($p > 0.05$ for all comparisons).

Conclusions:

CRVE was significantly greater in UK Biobank AD subjects, after adjusting for vascular co-morbidities and APOE4 carriage. Wider retinal venules are indicators of AD-associated retinal vasculopathy and degeneration.

References: None provided.

Keywords: Vascular disorders, Higher visual functions, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Task-Evoked Ocular Metrics, Cortical Structure, and Their Interaction: Links to Cognitive Performance in Mild Cognitive Impairment

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Introduction:

Early detection of Alzheimer's disease (AD) requires biomarkers sensitive to pre-neurodegenerative alterations. Task-evoked oculomotor and pupillary responses during interleaved prosaccade–antisaccade paradigms may provide non-invasive markers of early executive and neuromodulatory dysfunction in mild cognitive impairment (MCI). However, large-scale studies examining these associations and their neuroanatomical correlates remain limited. The primary objective was to determine whether task-evoked ocular metrics are associated with cognitive performance and cortical morphology, and whether these associations are modified by sex and cognitive domain.

Methods:

We analyzed cross-sectional data from a cohort comprising MCI participants (n = 212) and cognitively unimpaired controls (n = 516). Generalized additive models and linear mixed-effects analyses were employed to assess the associations between oculomotor and pupillary metrics, and cortical thickness.

Results:

MCI participants showed broad oculomotor and pupillary deficits. Prosaccade accuracy declined ($\beta = -3.00$, $p = 0.013$) with greater variability ($\beta = +5.36$, $p = 0.002$) and more anticipatory ($\beta = +2.41$, $p = 0.012$) and omission errors ($\beta = +1.73$, $p < 0.001$). Antisaccade performance was further reduced, with fewer correct responses ($\beta = -2.28$, $p < 0.001$), more total ($\beta = +2.25$, $p < 0.001$) and uncorrected errors ($\beta = +1.68$, $p < 0.001$), and slower latencies ($\beta = -11.15$, $p = 0.046$). Pupillary responses were attenuated, showing smaller cue- and target-evoked dilations ($\beta = -0.035$ to -0.027), reduced area under the curve, and delayed peak and minimum diameters. Cue-evoked dilation correlated with frontal cortical thickness. Pupil metrics differed by sex, with women showing larger, faster, and more variable responses, and by cognition, with executive scores most strongly predicting pupil amplitude and constriction kinetics.

Conclusions:

In summary, this study demonstrates that ocular metrics are sensitive to early network dysfunction in AD, reflecting executive and neuromodulatory system alterations. The observed associations with cortical morphology and cognitive performance, and modulation by sex and cognitive domain, support integrating these non-invasive biomarkers into diagnostic and prognostic frameworks for AD.

References: None provided.

Keywords: Pupil, Ocular motility, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc) Eye lid & adnexal disease, Higher visual functions, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Contact Information: None provided.

Robustness of AI-Derived Linguistic Markers of Cognitive Impairment in the Presence of Visual Disease

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Introduction:

Automated analysis of connected speech offers a scalable approach to cognitive screening. Linguistic and semantic features derived from large language models (LLMs) may provide consistent, quantitative markers of cognitive-linguistic impairment. However, picture description depends on visual access, and poor vision could potentially alter how individuals describe a scene. We therefore tested whether reduced vision affects semantic content, measured by semantic deviation, to assess if eye disease changes how patients describe the picture.

Methods:

We analyzed 1,013 picture-description recordings (920 unique adults) annotated by speech-language pathologists for five binary impairments: grammatical errors, semantic errors, nonspecific terms, other cognitive-communication deficits, and word/phrase repetitions. Audio was transcribed with CrisperWhisper. We extracted conventional linguistic features (lexical diversity, sentence length, part-of-speech ratios, readability) and LLM-derived metrics: surprisal (Gemma-7B) and semantic deviation (cosine distance to a control centroid using all-mpnet-base-v2 embeddings). To limit demographic bias, 1:2 optimal propensity matching was applied by age, gender, and education. Models were trained on participants without ON/CAT and tested on those with these conditions.

Results:

Combining conventional and LLM-derived features improved discrimination for multiple impairments (AUC = 0.82–0.86). Model performance in ON/CAT subsets was stable ($\Delta\text{AUC} < 0.05$). Mean semantic deviation did not differ significantly between groups ($p = 0.29$).

Conclusions:

Visual disease did not alter semantic content or linguistic markers, indicating that these AI-derived measures reflect cognition rather than visual access, supporting the robustness and fairness of speech-based cognitive screening.

References: None provided.

Keywords: Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Hyperreflective Foci by Optical Coherence Tomography (OCT) Distinguishes Patients with Mild Cognitive Impairment (MCI) Due to Alzheimer's Disease From Cognitively Normal Controls

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Introduction:

Hyperreflective foci (HRF) are linked to local inflammatory retinal pathologies and various systemic diseases, such as multiple sclerosis. Emerging evidence suggests Alzheimer's Disease (AD) may be linked to specific patterns of HRF distribution, positioning optical coherence tomography (OCT) as a potential noninvasive tool to characterize the earliest stages of AD, including mild cognitive impairment (MCI). We evaluated HRF prevalence and distribution in people with MCI due to AD versus cognitively normal controls.

Methods:

Participants with MCI due to AD, identified by National Institute of Aging Alzheimer's Association (NIA-AA) criteria, Global Clinical Dementia Rating (CDR) scores, and psychometric testing, and cognitively normal controls were recruited through convenience sampling. Each received a Spectral Domain (SD-) OCT scan. HRF presence and distribution by retinal layers was evaluated by 3 independent raters. We performed descriptive statistics, logistic regressions models by patient, generalized estimating equations (GEE) models by eye, and Fisher's exact tests by retinal layer grouping at both the patient and eye levels.

Results:

The MCI group included 21 participants (median age 72 years, range 61-89, 62% female), the control group included 24 participants (75, 65-90, 58% female). HRF were present in 62% of MCI participants vs 28% of controls ($p = 0.04$; OR 3.7 95% CI 1.1 – 13.9) without significant difference at the individual eye level. Age and sex did not predict HRF presence. Outer retinal layers showed the highest HRF prevalence in MCI participants (OR = 5.1, 95% CI: 1.0-34.7 $p = 0.04$).

Conclusions:

HRF were more prevalent in participants with MCI compared to age- and sex-matched controls, especially in the outer retina. This supports the potential of OCT as an objective tool for detecting the earliest stages of AD. Future studies with larger sample sizes and inclusion of various stages of AD may elucidate the role of OCT in tracking disease progression.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Retina

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Impaired vergence in patients with Parkinson's disease

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Introduction:

Patients with Parkinson's disease (PD) frequently report diplopia, even in the absence of overt paralytic strabismus is not found. Increasing evidence suggests that vergence abnormalities, particularly convergence insufficiency, may account for these visual symptoms. However, systematic prospective evaluations of vergence parameters in de novo PD remain limited. We aimed to investigate the relationship between vergence-related disorders in patients with PD, focusing on the prevalence and clinical correlates of convergence insufficiency.

Methods:

We prospectively recruited 79 consecutive patients with de-novo PD mean age $\pm$ standard deviation, 66 ± 10 years; 41 female) between October 2024 and September 2025 at a tertiary referral-based hospital in South Korea. All patients underwent a systematic extrapyramidal neurologic examination for eligibility. Ocular motor assessment included near point of convergence (NPC), ocular alignment using Prism bars, positive (PFV) and negative fusional vergence (NFV). Convergence insufficiency was diagnosed according to the Convergence Insufficiency Treatment Trial criteria. The data were compared with those of 63 age- and sex-matched healthy participants.

Results:

Convergence insufficiency was frequently observed in patients with PD compared to healthy participants (34/79 [43%] vs. 13/63 [21%], $p=0.007$). Multivariable logistic regression analysis showed that convergence insufficiency was associated with the PD (odds ratio: 3.19 [95% confidence interval, 1.47–6.94], $p=0.003$), after controlling other covariates. The near PFV breakpoint was negatively correlated with the Movement Disorder Society-Unified Parkinson's Disease Rating Scale motor part ($r=-0.406$, $p=0.038$), indicating a relationship between reduced vergence capacity and clinical severity of PD.

Conclusions:

Convergence insufficiency is common in patients with PD, and is associated with disease severity. These findings highlights the importance of standardized assessment of the ocular motility in to the clinical evaluation of PD, both for accurate diagnosis of visual complaints and for understanding non-motor manifestations of the disease.

References: None provided.

Keywords: Adult strabismus with a focus on diplopia, Ocular motility, Ocular motility, Miscellaneous

Financial Disclosures: The authors had no disclosures.

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Inebilizumab for NMOSD Treatment in a Real-World Cohort: Analysis from the PPD CorEvitas Synergy of Prospective Health and Experimental Research for Emerging Solutions (SPHERES) Registry

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Introduction:

Neuromyelitis Optica Spectrum Disorder (NMOSD) is a rare autoimmune disease of the central nervous system that impacts the optic nerves and spinal cord, often resulting in irreversible disability. Initiating maintenance therapy early is recommended to prevent relapses and reduce long-term disability. Inebilizumab depletes CD19+ B cells, thereby lowering the risk of relapses.

Methods:

Patients with NMOSD from the US-based PPD™ CorEvitas™ SPHERES Registry enrolled from 6/2/2021 to 2/28/2025 were included. Index visit was defined as the enrollment visit for patients who initiated inebilizumab before joining the registry, or as the treatment initiation visit for those who began inebilizumab at or after enrollment.

Results:

Of the 422 patients prescribed therapy for NMOSD, 68 were treated with inebilizumab. The majority (93%, 63/68) were aquaporin-4 antibody seropositive (AQP4-IgG+). Prior to index visit, 32%, 19%, and 49% of patients had experienced one, two, or three or more relapses, respectively; with a mean±SD of 3.2±2.6 prior relapses. At index visit, inebilizumab users had a mean±SD 5-level EQ-5D (EQ-5D-5L) score of 0.7±0.3 and EQ visual analogue scale (EQ-VAS) score of 70.6±18.9. Disease activity and patient-reported outcomes indicated moderate disease activity, with a mean±SD expanded disability status scale (EDSS) score of 3.5±1.9, and 71% of patients demonstrating normal cognition on the Montreal Cognitive Assessment Blind (MoCA-Blind) score. Among inebilizumab-treated patients, 47% (32/68), 35% (24/68), 12% (8/68), and 6% (4/68) used inebilizumab as first-, second-, third, and fourth- or higher line of therapy, respectively. Of second-line patients treated with inebilizumab, 14 had immediate prior exposure to rituximab, 3 to satralizumab, 2 to non-approved biologics, 3 to glucocorticoid steroids, 1 to immunosuppressant therapy and 1 to immunoglobulin therapy.

Conclusions:

This descriptive analysis of real-world NMOSD patients treated with inebilizumab offers important insights into clinical characteristics and treatment patterns. Additional analysis is underway to understand treatment persistence and long-term outcomes.

References: None provided.

Keywords: Demyelinating disease

Financial Disclosures: Jeffrey Bennett: J.L.Bennett has performed consultative services for Amgen, Genentech, Roche, Chugai, Mitsubishi Tanabe, Novartis, CorEvitas. He has served on Scientific Advisory or Data Safety Monitoring boards for Roche. He has served on a Speakers Bureau for Alexion; has received research support from the NIH, National MS Society, and Alexion; and has received intellectual property interests from a patent on Aquaporin-4 antibody; Dustin Cavida: D. Cavida is an employee of and stockholder in Amgen Inc.; Kristina Patterson: K.R.Patterson is an employee of and stockholder in Amgen Inc.; Jenny Park: J. Park is an employee of and stockholder in Amgen Inc.; Rajvi Wani: R. Wani is an employee of and stockholder in Amgen Inc.; Andrea Meyers: A. Meyers is an employee of and stockholder in Amgen Inc.; Nicole Middaugh: N. Middaugh is an employee of Thermo Fisher Scientific.; C. Jean Choi: C.J.Choi is an employee of Thermo Fisher Scientific; Marie Gurrola: M. Gurrola is an employee of Thermo Fisher Scientific; Michael Levy

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Contact Information: None provided.

Scores for Vision-Based Test of Rapid Picture Naming, Mobile Universal Lexicon Evaluation System (MULES), Predict Cognition in an Alzheimer's Disease Research Center (ADRC) Cohort

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Introduction:

The Mobile Universal Lexicon Evaluation System (MULES) is a picture-based rapid automatized naming (RAN) task that distinguishes patients with various neurological conditions including mild cognitive impairment (MCI) due to Alzheimer's disease. We examined associations of MULES test times with scores on standard ADRC cognitive tests.

Methods:

MCI patients and controls in the NYU ADRC cohort were selected for vision-based testing. The MULES was administered via paper and a tablet-based app. Two trials were administered in each format, and best times were recorded in seconds. Cognitive scales selected for this study included the Mini Mental State Exam (MMSE), NYU Mini Mental State Exam (MMS), NYU Auditory Verbal Learning Test (AVLT), Montreal Cognitive Assessment (MoCA), Craft Story 21 Immediate and Delayed Recall (verbatim and paraphrase scoring), Benson Complex Figure Copy and Recall, Number Span Test Forward and Backward, Category Fluency (Animals and Vegetables), Trail Making Test (parts A and B), Multilingual Naming Test (MINT), and Verbal Fluency: Phonemic Test. Multivariable linear regression analyses accounting for age and education were performed to assess associations between best MULES times and cognitive test scores.

Results:

Among 17 participants (6 MCI, 11 controls), greater (worse) paper MULES time scores were associated with worse scores among subscales for the AVLT ($p=0.022-0.029$) and Craft Story Test ($p=0.031-0.041$), MMS total score ($p=0.001$), MMSE total score (0.046), Benson Figure delayed copy score ($p=0.005$), MINT total score ($p=0.024$), and Category Fluency Test, Vegetables ($p=0.011$). Among 14 participants (5 MCI, 9 controls), worse tablet MULES times were associated with two of the three AVLT subscales associated with paper MULES scores ($p=0.007$, $p=0.017$).

Conclusions:

The MULES assesses visual function, but scores also demonstrate associations with standard cognitive test scores, many of which do not rely on vision. Our data support the potential for the MULES to complement standard test batteries for MCI due to Alzheimer's disease.

References: None provided.

Keywords: Higher visual functions, Ocular motility

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A recurrent missense variant in the *PPIB* gene underlies adult-onset autosomal dominant optic atrophy

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Introduction:

A relatively large number of genes, many of which are implicated in mitochondrial function, are known to be involved in hereditary optic atrophy (OA). For many affected individuals, however, a genetic cause still cannot be identified. Here, we report on autosomal dominant optic atrophy (ADOA) associated with a hitherto unrecognized missense variant within the *PPIB* gene encoding peptidylprolyl isomerase B, which has not previously been linked to OA.

Methods:

In a large pedigree and additional families, exome sequencing (ES) was used to identify a genetic cause in individuals with so far genetically unresolved OA. Detailed clinical phenotyping was performed on all available individuals carrying the identified variant. Subsequently, mitochondrial morphology and function was studied in cultured dermal fibroblasts obtained from five individuals.

Results:

ES revealed a heterozygous missense variant in *PPIB* [NM_000942.5: c.538C>T p.(Arg180Trp)], which segregated with clinically isolated bilateral OA in 19 individuals from 9 families. *PPIB*-associated OA involves an insidious reduction in visual acuity, central scotoma, impaired color vision and inner retinal layer thinning consistent with other ADOAs. Age of symptom onset was mostly in adulthood (median: 36 years), and clinical manifestation varied from mild temporal OA to severe OA. Patient-derived fibroblasts revealed altered mitochondrial morphology as well as subtle respiratory chain defects including reduced basal respiration and decreased amounts of complex I subunits.

Conclusions:

The likely pathogenic *PPIB* missense variant segregates with adult onset ADOA and is associated with mitochondrial dysfunction. While these findings broaden the knowledge of genes implicated in ADOA, future studies are needed to study the exact pathomechanistic role of variants in *PPIB*.

References: None provided.

Keywords: Genetic disease, Optic neuropathy, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease

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Data-Driven Structure–Function Model Improves Central Visual Field Mapping in NAION

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Introduction:

The structure–function relationship between the visual field (VF) and the retinal nerve fiber layer (RNFL) has been formalized by canonical models - Garway-Heath et al. (2000), Jansonius et al. (2009). In non-arteritic ischemic optic neuropathy (NAION), its analysis relied primarily on the Garway-Heath model (Hood et al. 2008) and demonstrated a broadly preserved superior–inferior RNFL–VF organization. Our aim was to further refine these mappings and quantitatively enhance the structure–function relationship in NAION, particularly within the central VF.

Methods:

We analyzed 61 NAION patients from a prospective multicenter cohort (ENDOTHELION group, recruited between 2015 and 2025) and included in the analysis standard automated perimetry (Humphrey 24-2) and peripapillary OCT measurements of retinal nerve fiber layer thickness (RNFL) obtained six months after symptom onset (256 measurements obtained per 1.41° sector, Cirrus; corrected for the disc-fovea angle). We fitted a data-driven structure–function model linking each VF location to the RNFL sectors most predictive of sensitivity. Model performance was assessed using patient-wise cross-validation. Per-point absolute correlations ($|r|$) were compared against those from Garway-Heath and Jansonius models using Wilcoxon signed-rank tests. Anatomical plausibility was evaluated qualitatively with a web-based 3D viewer we developed for interactive exploration of VF–RNFL connections.

Results:

Our model improved VF–RNFL correspondence overall (mean $|r|$ 0.45 vs 0.37 Garway-Heath and 0.34 for Jansonius; $p < 0.0001$). Central six points showed pronounced improvement: mean $|r|$ 0.42 (empirical) vs 0.13 (Garway-Heath) and 0.17 (Jansonius). The learned map consistently reassigned central-inferior and central-superior VF points to superior-temporal and inferior-temporal RNFL sources, respectively, yielding a more eccentric assignment.

Conclusions:

Our empirical NAION structure-function mapping allows refinement of the canonical approaches and, critically, could model central visual loss. This work addresses a long-standing shortfall in central mapping and supports improved alignment between perimetric and structural loss.

References: None provided.

Keywords: Optic neuropathy, Perimetry

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Vision-related Quality of Life In Patients With Pituitary Adenomas

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Introduction:

Visual dysfunction is a symptom of pituitary adenomas (PA). Vision-related quality of life (VR-QOL) has been used to measure clinical outcomes in ophthalmic conditions. The objective of this study was to evaluate the VR-QOL through the 25-item National Eye Institute Visual Function Questionnaire (VFQ-25) in patients with PA.

Methods:

This is a prospective, longitudinal, observational study. We included patients with PA who underwent surgery between April and September 2025. Patients completed the VFQ-25 at baseline and at six weeks postoperatively.

Results:

16 patients were recruited. Mean age of presentation was 51.75 +/- 13.37, 9 (56%) were female. 11 (69%) were non-functioning adenomas, 3 (19%) were growth hormone-secreting adenomas, and 2 (12%) were prolactin-secreting adenomas. Mean tumor size was 31.77 +/- 13.43 mm. 13 (81%) underwent an endonasal transsphenoidal approach, while 3 (19%) underwent a transcranial approach. Mean LogMAR best corrected visual acuity (BCVA) for the right eye (OD) was 0.83 +/- 0.93 before surgery and 0.55 +/- 0.81 after surgery ($p=0.004$); for the left eye (OS) mean LogMAR BCVA was 0.53 +/- 0.73 before surgery and 0.38 +/- 0.73 after surgery ($p=0.063$). We found statistical significance in the following VFQ-25 categories pre- and postoperatively: General vision ($p=0.013$), distance activities ($p=0.048$), peripheral vision ($p=0.013$), dependency ($p=0.039$), and composite score ($p=0.020$). We did not find any statistical significance between the postoperative VFQ-25 composite score and PA subtypes ($p=0.378$) or between surgical approaches ($p=0.545$). Significant correlations with the postoperative VFQ-25 score included preoperative BCVA (OD: $r = -0.510$, $p = 0.043$; OS: $r = -0.463$, $p = 0.031$) and preoperative color vision (OD: $r = 0.510$, $p = 0.043$; OS: $r = 0.313$, $p = 0.002$).

Conclusions:

VR-QOL improved in patients with PA, regardless of the surgical approach or PA subtype. Preoperative BCVA and color vision could help physicians to identify patients likely to achieve a better postoperative VR-QOL.

References: None provided.

Keywords: Visual fields, Perimetry, Skull base, Optic neuropathy

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Grant Support: None.

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OCT-Based Differentiation of NAION and CRAO: Longitudinal Analysis of Inner Retinal Layer Thinning

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Introduction:

NAION and CRAO are both causes of sudden vision loss. When patients present within two weeks of symptom onset, clinical signs such as optic disc or inner retinal edema often allow differentiation. However, as time progresses and edema resolves, both diseases lead to optic atrophy and retinal thinning. It is thought that CRAO results in more significant thinning of the inner retinal layers, particularly the ganglion cell layer, compared to NAION. This study seeks to investigate whether these differences remain detectable months after symptom onset and whether OCT can help distinguish these entities in the chronic phase.

Methods:

Using Epic's SlicerDicer tool patients with CPT codes for OCT retina or OCT optic nerve (92133/92134) and ICD10 codes for ischemic optic neuropathy (H47.011/H47.012/H47.013/H47.019) or central retinal artery occlusion (H34.10/H34.11/H34.12/H34.13) were identified. Charts were reviewed to ensure timeline, image quality, and certainty of diagnosis. Quadrant and average RNFL thickness, superior vs inferior retinal, and GCL layer thicknesses were determined using Spectralis software and Asymmetry Analysis.

Results:

We identified 1968 charts for review. Screening the first 200 charts, 38 suitable NAION cases and 14 CRAO cases have been identified we therefore estimate that we will be able to compare approximately 100 cases for each diagnosis. Preliminary results demonstrate more profound thinning of GCL, RNFL, and retinal thicknesses in CRAO cases. Spectralis' Asymmetry Analysis tool demonstrates on average more asymmetry between superior and inferior retina in cases of NAION.

Conclusions:

Receiver-operator curves will be generated to demonstrate the effectiveness of each parameter and ratios of superior vs total retinal thicknesses and GCL/retina thicknesses to determine which parameters are most effective for discriminating between CRAO and NAION at time points of 3, 6, and 12 months after vision loss. By focusing on patients who presented early and were followed over time, this study will assess whether long-term OCT markers can reliably differentiate NAION from CRAO when traditional clinical signs are no longer visible.

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Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Vascular disorders, Optic neuropathy, Retina

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The Utility of the Temporal Raphe Sign on OCT in Differentiating Normal Tension Glaucoma and Chronic NAION

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Introduction:

Distinguishing glaucomatous optic neuropathy (GON) from non-glaucomatous optic neuropathies (NGON) can be challenging. Optical coherence tomography (OCT) offers objective assessment, and the temporal raphe sign (TRS), a horizontal demarcation between the superior and inferior ganglion cell complex (GCC) seen on GCC thickness maps due to asymmetric atrophy, has been proposed as a distinctive marker of glaucoma over NGON. However, whether TRS contributes discriminative value beyond established biomarkers remains uncertain.

Methods:

This retrospective, single-center cohort study included subjects with NAION or normal-tension glaucoma (NTG) from a tertiary academic center (2020-2023). Inclusion criteria were reliable Zeiss Cirrus OCT and ophthalmic examination. NAION eyes were analyzed ≥6 months post-event to ensure stability. Patients with both diagnoses were excluded. Variables were extracted from electronic health records. For subjects with both eyes affected by NAION or NTG, continuous variables were averaged. Ordinal variables were categorized as 0–2 eyes affected. For univariate analysis, continuous and ordinal variables were analyzed using regression and categorical with Chi-square. Multivariable logistic regression was performed using covariates not highly correlated with each other or outcomes.

Results:

NAION participants (25 [32 eyes]) were similar in age ($p=0.17$) and sex ($p=0.18$) to NTG (48 [81 eyes]). NAION was more often unilaterally impacted (18 NAION vs 15 NTG, $p<0.001$), had smaller C:D ratio ($p<0.001$), worse mean deviation (MD, $p=0.002$), and lower visual field index ($p=0.04$) than NTG on univariate analysis. Frequency of rim pallor, neuroretinal rim notching, rAPD, and TRS also differed (all $p<0.001$). Visual acuity on Snellen chart ($p=0.17$), pattern standard deviation ($p=0.69$), and average RNFL ($p=0.18$) did not differ significantly. Multivariable analysis identified bilateral involvement ($p=0.03$) and MD ($p=0.02$) as independently associated.

Conclusions:

TRS was significantly less frequent in NAION than NTG on univariate analysis, but this association did not persist after adjusting for other biomarkers, indicating OCT findings should augment, rather than replace, clinical and functional assessment to improve diagnostic accuracy and minimize unnecessary testing.

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Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Optic neuropathy, Perimetry, Visual fields

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Novel OPA1 Mutation Underlying Dominant Optic Atrophy-Plus in a Thai Cohort: Clinical and Genetic Insights

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Introduction:

Autosomal dominant optic atrophy-plus (DOA-plus) is a rare condition with limited documentation in Asian populations. This study aimed to characterize DOA-plus in a Thai cohort.

Methods:

A prospective cohort study was conducted at a tertiary university-affiliated center, from November 2020 to December 2021. Patients with suspected DOA-plus and age- and sex-matched controls underwent comprehensive ophthalmological and neurological evaluations. Whole-genome sequencing was then performed to identify pathogenic variants.

Results:

Seven related individuals developed bilateral visual loss between ages 6 and 20 years (best-corrected visual acuity 0.7–1.6 logMAR) and exhibited central or pseudo-bitemporal scotomas. Compared with age- and sex-matched controls, affected individuals showed significantly reduced peripapillary retinal nerve fiber layer thickness (average $61.4 \pm 13.6 \mu\text{m}$ vs $101.3 \pm 11.3 \mu\text{m}$, $p < 0.01$) and macular ganglion cell–inner plexiform layer thickness (average $52.6 \pm 14.4 \mu\text{m}$ vs $83.9 \pm 6.6 \mu\text{m}$, $p < 0.01$), confirming diffuse retinal ganglion cell loss. Additional systemic findings included progressive external ophthalmoplegia, ataxia, peripheral neuropathy, and sensorineural hearing loss. A novel heterozygous missense mutation in the OPA1 gene (c.1317A>C, p.Leu439Phe) was identified in all affected individuals, with incomplete penetrance and variable clinical severity.

Conclusions:

To our knowledge, this is the first genetically confirmed DOA-plus in a Thai family harboring a novel OPA1 mutation. The triad of optic atrophy, progressive external ophthalmoplegia, and neurological features highlights DOA-plus as a diagnostic consideration in syndromic optic neuropathy. Early recognition and genetic testing remain crucial for precise diagnosis, counseling, and management. Larger studies in Asian populations are needed to define prevalence and phenotypic variability.

References: None provided.

Keywords: Genetic disease, Optic neuropathy, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

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Prevalence of “Disc-at-Risk” for Non-Arteritic Anterior Ischemic Optic Neuropathy in Healthy Eyes

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Introduction:

The pathophysiology of non-arteritic anterior ischemic optic neuropathy (NAION) remains unknown, with the most classic risk factor being a crowded optic disc with small cup-to-disc ratio (CDR), so-called “disc-at-risk”. Variations in disc cup size may explain the differences in prevalence of NAION among populations. Recent reports of NAION potentially triggered by medications such as PDE-5 inhibitors or GLP1-RAs have suggested general screening for “disc-at-risk” prior to prescription. Although a few studies have estimated the prevalence of small CDR in fellow eyes of NAION patients, there is little data in healthy eyes across various populations. We aimed to determine the percentage of the general population with small CDRs.

Methods:

Literature search/review for reports on the prevalence of small disc-CDR among normal healthy eyes, defined as CDR ≤ 0.2 vertically/horizontally.

Results:

18 studies spanning 1967-2024 were identified, including more than 55,000 eyes of diverse ethnic backgrounds. Data regarding prevalence of small CDR was retrieved from either visual inspection/manual evaluation of published graphs, or was reported as a proportion. 10 studies used various examination methods to estimate CDR with discrepancies in small CDR prevalence based on techniques used [14.9% using slitlamp vs. 50.7% direct ophthalmoscopy in one study]. The largest (n=4441, predominantly European ancestry) of 7 U.S. studies reported 10.3% with small CDR on stereoscopic disc photographs. A large study (n=17767) from South Korea estimated small CDR in 19.7% (graph-based). None of the studies specifically focused on the prevalence of small CDR in large population samples, nor used optical coherence tomography (OCT) to estimate CDR.

Conclusions:

Despite its pivotal relevance to NAION, limited high-quality data exist regarding the prevalence of small CDR in normal eyes, varying based on race and technique used to measure CDR, highlighting the need for large diverse population studies of optic nerve OCT through large data depositories (biobanks) using validated artificial intelligence algorithms.

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Keywords: Optic neuropathy, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)

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High-Dose Glucocorticosteroids and Neuroprotection in Acute Optic Neuritis: A Multicenter Retrospective Cohort Study

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Introduction:

The seminal Optic Neuritis Treatment Trial lacked structural endpoints, as optical coherence tomography (OCT) was unavailable at that time. To date, we are yet unaware of any large-scale study that has evaluated whether glucocorticosteroids (GCS) mitigate optic atrophy compared to observation only in multiple sclerosis–associated or idiopathic optic neuritis (MS-ON, SI-ON) using OCT.

Methods:

In this international retrospective cohort, participating centers contributed anonymized clinical and OCT data. We included patients aged 18–60 with a first episode of unilateral MS-ON or SI-ON, managed with high-dose GCS or observation alone, and with OCT follow-up between 45 days and 2 years after symptom onset. The primary endpoint was ganglion cell loss in the affected eye, assessed as change in macular ganglion cell and inner plexiform layer thickness (mGCIPLT). Analysis was by treatment group via linear regression with predefined adjustment for sex and baseline high-contrast visual acuity (HCVA).

Results:

We analyzed 431 patients from 15 centers in 8 countries. 331 had received high-dose GCS and 100 were untreated. At baseline, GCS-treated patients had poorer HCVA (median [IQR]: logMAR 0.49 [0.15–1.3] vs. 0.20 [0.00–0.50], $P < .001$). Median time to treatment was 7 days (4–11), and the median dose was 3 g (3–5). Age and sex were balanced between groups. At follow-up, untreated female patients with normal baseline HCVA (logMAR 0) lost a mean 10.3 μm mGCIPLT (95% CI: 4.69–14.6). Male sex was independently associated with an additional 4.34 μm loss (1.03–7.66), and each line of baseline HCVA deficit with an additional 0.82 μm loss (0.60–1.03). There was no significant difference between GCS and observation (estimated effect: 2.73 μm less atrophy with GCS; 95% CI: -1.50–6.97).

Conclusions:

High-dose GCS did not reduce retinal ganglion cell loss compared with observation after adjustment for disease severity predictors.

References: None provided.

Keywords: Optic neuritis, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Demyelinating disease

Financial Disclosures: The authors had no disclosures.

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Evaluation of Functional and Structural Biomarkers in OPA1 Autosomal Dominant Optic Atrophy — the FALCON Prospective Natural History Study

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Introduction:

Autosomal dominant optic atrophy (ADOA) is primarily caused by disease-causing OPA1 variants, resulting in reduced OPA1 protein expression and mitochondrial dysfunction.^{1,2,3} This preferentially affects retinal ganglion cells, causing progressive optic nerve degeneration and visual impairment.³ FALCON was a multicenter natural history study evaluating functional and structural changes in the retina and optic nerve of patients with OPA1 ADOA over 24 months.

Methods:

FALCON enrolled 48 patients (47 analyzed) with ADOA across 10 study sites, aged 8–60 years, and with genetically confirmed heterozygous OPA1 variants. Key outcome measures included change from baseline to 24 months in best-corrected high contrast (HCVA) and low contrast (LCVA) visual acuity, peripapillary retinal nerve fiber layer (pRNFL) thickness, and optic disc flavoprotein fluorescence (FPF).

Results:

At screening, mean patient age was 28.1 years and mean HCVA was 0.57 logMAR. Over 24 months, minimal changes were observed in HCVA and pRNFL thickness. While a modest median decline in LCVA was observed across patients at 24 months (–0.5 ETDRS letter change), 24% (8/33) of patients experienced ≥5 LCVA letter loss with no significant changes in pRNFL thickness. Baseline optic disc FPF varied across sectors and was negatively correlated with pRNFL thickness, ETDRS letter score, and age.

Conclusions:

FALCON is the first natural history study to systematically evaluate functional and structural biomarkers in ADOA. Although OPA1 ADOA is a slowly progressing optic neuropathy, it causes profound visual impairments that worsen with age. The correlation between baseline FPF and visual acuity highlights the link between mitochondrial dysfunction and functional decline. Importantly, our findings indicate that impaired function in the retina and optic nerve occurs before permanent structural loss. LCVA and FPF are promising clinical measures of disease progression that can be used to assess the efficacy of potential disease modifying treatments for ADOA over a shorter time frame.

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Keywords: Genetic disease, Optic neuropathy, Retina

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Grant Support: None.

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EyeStroke protocol with non-mydratic color fundus photography and optical coherence tomography (NMFP-OCT) in the emergency department (ED): 2.5-year experience

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Introduction:

Acute central/branch retinal artery occlusions (CRAO/BRAO) are often missed/delayed in EDs because of limited funduscopy skills/lack of immediate ophthalmology access. We describe CRAO/BRAO patients diagnosed remotely with NMFP-OCT in our ED.

Methods:

Prospective consecutive CRAO/BRAO patients (onset < 1 week) between 06/2023-12/2025 with NMFP-OCT in our ED-Stroke Center.

Results:

Among 78/91 CRAO/BRAO patients seen within 1 week of onset, 12 (15.3%) had vision loss < 4.5 hours, 41 (52.5%) 4.5-≤24 hours, 25 (32 %) >24 hours-1 week [median times from presentation to NMFP-OCT 33 minutes (IQR, 17.75-122 minutes/range, 10-330 minutes), 102 minutes (IQR, 55-181 minutes/range, 12 hours-442 minutes), and 121 minutes (IQR, 94-174 minutes/range, 39-337 minutes), respectively]. Diagnosis was made on: color+OCT, 61/78 eyes [7 visible embolus, 58 retinal whitening]; OCT only, 13/78 eyes [inner retinal hyperreflectivity/thickening/PAMM]; 4/78 uninterpretable imaging. 5/12 patients presenting within 4.5 hours received intravenous thrombolysis [median door-to-needle time, 58 minutes (IQR, 44-140/range, 41-181)]. Brain MRI (74 patients) showed concurrent acute cerebral infarctions in 16/74 (21.6%). Stroke work-up showed ICA stenosis (25/78; 32%); ICA dissection (1/78); aortic arch atheroma (2/78; 2.5%); cardiac source (12/78; 15.3%); temporal arteritis (5/78; 6.4%), hypercoagulable state (4/78; 5.1%); 1 fungal sinusitis; no cause (28/78; 35.8%). 40/78 (51.3%) patients were transferred from outside hospital EDs for "ophthalmologic evaluation"; 26 (33.3%) were referred by outside eye care providers; 12 (15.4%) presented directly to our ED [including 9 of the 12 (75%) who presented within 4.5 hours and 4 of the 5 (80%) who received thrombolysis].

Conclusions:

Despite our EyeStroke protocol facilitated by NMFP-OCT in our ED, only 12/78 (15.3%) of acute CRAO/BRAO patients were diagnosed early enough to be considered for IV-thrombolysis, administered to only 5/12 (41.6%). Rapid workup found a major cause of CRAO/BRAO in 64% and 22% had concurrent cerebral infarctions on MRI. The main barrier was delayed diagnosis/care due to transfer from other institutions/providers, suggesting that wide deployment of NMFP-OCT for remote diagnosis and treatment using existing Telestroke networks is necessary to reduce time to diagnosis, avoid transfers, and improve patient outcomes.

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Keywords: Stroke, Vascular disorders, Retina, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc.) Eyelid & adnexal disease

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Assessing Interrater Reliability of OCT Biomarkers in NAION: Comparison Between Experienced and Junior Raters

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Introduction:

Nonarteritic anterior ischemic optic neuropathy (NAION) is the leading cause of optic nerve-related vision loss in individuals over 50 years. Optical coherence tomography (OCT) of the optic nerve head provides anatomical biomarkers with potentially important clues to pathogenesis, including optic disc drusen (ODD), peripapillary hyperreflective ovoid mass-like structure (PHOMS), anterior lamina cribrosa (ALC), and Bruch's membrane opening (BMO). However, the level of experience required to assess these parameters remains uncertain. In this study, we evaluated the interrater reliability between an experienced and a junior OCT rater.

Methods:

This retrospective observational study included patients diagnosed with NAION at our hospital between August 2021 and August 2023. OCT scans obtained within one month of symptom onset were classified as acute, and those acquired after two months were classified as chronic. Interrater reliabilities for optic disc swelling, ODD, and PHOMS were analysed using Cohen's kappa, while intraclass correlation coefficients (ICC) were used for BMO and ALC.

Results:

Twenty eyes from 19 patients were included. Parameters showing high reliability (ICC or $\kappa > 0.61$) included: optic disc swelling in the acute phase ($\kappa = 1.0$), ODD in the acute ($\kappa = 0.8$) and chronic ($\kappa = 0.7$) phases, BMO in the chronic phase (ICC = 0.7), and ALC in both acute (ICC = 0.9) and chronic (ICC = 0.9) phases. Lower agreement was found for optic disc swelling in the chronic phase ($\kappa = 0.3$), BMO in the acute phase (ICC = 0.59), and PHOMS in both acute ($\kappa = 0$) and chronic ($\kappa = 0.4$) phases.

Conclusions:

ODD showed substantial agreement, making it a reliable parameter compared to PHOMS, which demonstrated no agreement. ALC and BMO in the chronic phase can also be assessed by junior raters, whereas BMO in the acute and optic disc swelling in the chronic phase should be assessed by experienced raters.

References: None provided.

Keywords: Optic neuropathy, Vascular disorders, Neuroimaging

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Early Optical Coherence Tomography Indicators Are Associated with Outcome Vision Loss in Acute Non-Arteritic Anterior Ischemic Optic Neuropathy

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Introduction:

We aim to characterize longitudinal structural changes in non-arteritic anterior ischemic optic neuropathy (NAION) using optical coherence tomography (OCT) and evaluate their relationship with visual outcomes in a large clinical trial cohort.

Methods:

We used OCT data including peripapillary retinal nerve fiber layer thickness (pRNFLT), peripapillary total retinal thickness (pTRT), peripapillary optic nerve head volume (pONHV), and segmentation of the macular ganglion cell-inner plexiform layer (GCIPL) thicknesses from 715 participants (347 Cirrus, 368 Spectralis) in the QRK207 trial (NCT02341560) imaged within 14 days of NAION onset (mean: 8.0 ±SD: 3.2). Imaging was performed at screening, trial enrollment, Month 2, Month 6, and Month 12. We analyzed differences in study and fellow eye ONH, sectoral correlations, and rates of early structural change. We assessed associations with best-corrected visual acuity (BCVA) and visual field (VF) outcomes with regression analyses.

Results:

Study eyes had ONH swelling at screening (mean pRNFLT 241.0 ±74.8 μm; pONHV 6.70 ±1.27 mm³), followed by marked thinning (pRNFLT 56.7 ±14.9 μm; pONHV 2.74 ±0.41 mm³ at Month 6). For study eyes without prior NAION in the fellow eye, increased differences in baseline inter-eye ONH OCT metrics were associated with worse VF sensitivity and BCVA (e.g., inferior pRNFLT vs superior VF at Month 6: rho = -0.35, p< 0.001). Sub-analysis of participants with OCT measurements at both screening and trial enrollment visits (n=182; mean: 3.5 ±2.0 days) showed that GCIPL thinning (-3.0 μm, p< 0.001) was detectable at an early stage. An initial rate of pONHV thickening of 0.3 mm³/day yielded a 4.8-fold higher odds of VF decline by Month 2 (CI 2.8-8.5, p< 0.001, n=222).

Conclusions:

Macular GCIPL thinning is evident at an early stage following NAION onset. Increased baseline inter-eye pRNFLT asymmetry and early ONH volumetric increases in the first days of NAION onset are associated with worse BCVA and VF outcomes.

References: None provided.

Keywords: Optic neuropathy, Vascular disorders

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Clinical Characteristics and Outcomes of Intracranial Germinomas with Visual Pathway Involvement

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Introduction:

Intracranial germinomas are a rare central nervous system (CNS) neoplasm that typically occur in children and adolescents. Diagnosis of intracranial germinomas is challenging, with approximately half of patients with germinoma having delayed diagnosis, which can lead to worse prognosis.⁴ Therefore, it is important for ophthalmologists and neuro-ophthalmologists to be aware of its presentation for timely diagnosis and improved outcomes.

Methods:

This was a single-center retrospective chart review of patients with biopsy-confirmed intracranial germinoma with optic neuropathy at Mayo Clinic from 1/1/1990 to 12/31/24. Medical records were reviewed for demographics, presenting symptoms, diagnosis dates, visual fields, and visual acuity outcomes.

Results:

There were 19 intracranial germinoma patients with visual pathway involvement. Ten patients (52.6%) were female. The mean age with standard deviation (SD) of symptom onset was 16.7 (SD=4.9) years, while the mean age of germinoma diagnosis was 18.2 (SD=5.5) years. With respect to visual pathway involvement, the optic chiasm was most commonly affected (n=15, 78.9%). The most common initial presenting symptoms were headache (n=13, 68.4%) and blurred vision (n=7, 36.8%). Notably, 17 (89.5%) patients also had arginine-vasopressin deficiency/central diabetes insipidus (AVP-D) prior to germinoma diagnosis. With respect to visual acuity outcomes, the initial mean Snellen best corrected visual acuity (BCVA) of all affected eyes was 20/90 (range: 20/15-NLP), while the final mean Snellen BCVA was 20/100 (range: 20/15-NLP). The most common presenting visual field deficit was bitemporal hemianopia (n=7, 36.8%).

Conclusions:

In this study of patients with intracranial germinomas with visual pathway involvement, symptom onset was on average 1.5 years before diagnosis. Arginine-vasopressin deficiency/central DI was very common and occurred prior to vision loss in over 50% of patients. Therefore, in young patients with undifferentiated progressive vision loss, the presence of polydipsia or polyuria, especially prior to onset of vision loss, can be a valuable clue for the potential diagnosis of intracranial germinoma.

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Keywords: Optic neuropathy, Tumors, Paraneoplastic syndromes, Visual fields

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Informative Censoring in Study Controls Limits the Interpretation of the Long-Term Efficacy of Idebenone in Treating Visual Impairment From Leber Hereditary Optic Neuropathy

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Introduction:

Idebenone (IDE; RAXONE®) is approved in the EU for treating visual impairment in Leber hereditary optic neuropathy (LHON). The open-label LEROS study evaluated the efficacy of IDE 900 mg/day over 24 months compared with matched natural history controls (NHC). However, matching NHC to IDE did not account for all confounding factors associated with LHON. A post hoc analysis re-evaluated the efficacy of LEROS using improved controls for selection bias.

Methods:

Stabilized inverse probability of treatment weights from a propensity score model were used to match IDE and NHC subjects. Five prognostic factors were included in the modelling as covariates: sex, age at LHON onset, time from onset at baseline, baseline best-corrected visual acuity in the best seeing eye (best BCVA), and mtDNA mutation type. Response rates were expressed as percentages of weights. Treatment response was defined by the clinically relevant benefit (CRB), comprising either a ≥10-letter EDTRS on-chart improvement in best BCVA, an improvement from off-chart to the ability to read at least 5-letters on-chart, or maintenance of best BCVA below a baseline of 1.0 logMAR.

Results:

At month 12, IDE demonstrated a significantly higher CRB rate (54%; 95% CI: 46%, 63%) than NHC (33%; 95% CI: 23%, 42%). However, CRB rate differences lessened at month 24 (IDE: 53%; 95% CI: 43%, 62%; NHC: 48%; 95% CI: 34%, 61%). An ad hoc analysis suggested the convergence was driven by participants with worsening best BCVA disproportionately lost to follow-up among the NHC group, biasing retention toward those with better vision at month 24. This is called informative censoring. This effect was absent with IDE.

Conclusions:

A clinically meaningful benefit of IDE versus NHC was established at month 12. At month 24, IDE maintained a clinical benefit. However, further interpretation was limited by informative censoring in NHC.

References: None provided.

Keywords: Optic neuropathy, Genetic disease

Financial Disclosures: Alfredo Sadun: Has been a consultant for Chiesi and GenSight Biologics and has received research support from GenSight Biologics and Stealth Therapeutics.; Nancy Newman: Has been a consultant for Chiesi, GenSight, Stoke, Neurophth, and Eli Lilly.; Patrick Yu-Wai-Man: Received research support and consultation fees from Neurophth, Stoke Therapeutics, Santhera Pharmaceuticals, Chiesi, and GenSight Biologics.; Valerio Carelli: Received research support and consultation fees from Santhera Pharmaceuticals, Chiesi, and GenSight Biologics; Rod Gossen: Employee of Chiesi Canada Corp.; Daniela Garavaglia: Employee of Chiesi Farmaceutici S.p.A.; Karen Sison Lance: Employee of Chiesi Canada Corp.; Caroline Fradette: Employee of Chiesi Canada Corp.; Xavier Llòria: Employee of Chiesi Farmaceutici S.p.A.; Thomas Klopstock: Received research support and consultation fees from Santhera Pharmaceuticals, Chiesi, and GenSight Biologics

Grant Support: Chiesi USA, Inc.

Contact Information: None provided.

Propensity-Matched Evaluation of Idebenone Treatment Duration in Leber Hereditary Optic Neuropathy: Revisiting RHODOS Efficacy Outcomes

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Introduction:

Idebenone (IDE; RAXONE®) is approved in the EU for treating visual impairment in Leber hereditary optic neuropathy (LHON). RHODOS was a pivotal Phase 2, randomized, placebo-controlled study that evaluated the efficacy and safety of IDE for visual impairment from LHON. The primary endpoint, defined as the best recovery of logMAR visual acuity (VA) from baseline at Week 24 in either eye, did not significantly differ from placebo. A post hoc analysis tested the hypothesis that the nonsignificant efficacy results of RHODOS were mainly due to the short treatment duration.

Methods:

Participants from a 24-month, open label study in IDE for LHON (LEROS) were matched to the ITT analysis set from RHODOS using a propensity score (PS) matching algorithm. Propensity scores were derived from prognostic covariates of sex, age at symptom onset, time since onset at baseline, baseline best-corrected visual acuity in the best seeing eye (best BCVA), and LHON mtDNA mutation. Treatment response was assessed by clinically relevant benefit (CRB), defined as either a ≥10-letter EDTRS on-chart improvement in best BCVA, an improvement from off-chart to the ability to read at least 5-letters on-chart, or clinically relevant stabilization (CRS) for participants who maintained their baseline best BCVA of < 1.0 logMAR. Results were compared with integrated RHODOS/LEROS efficacy results.

Results:

The CRB, evaluated from the PS matched LEROS analysis set, showed an increase during the first year of treatment—from 26% at Month 6 (12/46) to 45% at Month 12 (19/42). This trend was consistent with respective findings from the integrated ITT set (77/212, 36%; 70/146, 48%). At Month 24, the PS matched LEROS CRB response (42%) also aligned with the integrated CRB response (48%).

Conclusions:

Responder results support the hypothesis that the nonsignificant primary efficacy outcome of RHODOS was due to an insufficient treatment duration.

References: None provided.

Keywords: Optic neuropathy, Genetic disease

Financial Disclosures: Nancy Newman: Has been a consultant for Chiesi, GenSight, Stoke, Neurophth, and Eli Lilly.; Alfredo Sadun: Has been a consultant for Chiesi and GenSight Biologics and has received research support from GenSight Biologics and Stealth Therapeutics.; Patrick Yu-Wai-Man: Received research support and consultation fees from Neurophth, Stoke Therapeutics, Santhera Pharmaceuticals, Chiesi, and GenSight Biologics.; Valerio Carelli: Received research support and consultation fees from Santhera Pharmaceuticals, Chiesi, and GenSight Biologics; Rod Gossen: Employee of Chiesi Canada Corp.; Daniela Garavaglia: Employee of Chiesi Farmaceutici S.p.A.; Karen Sison Lance: Employee of Chiesi Canada Corp.; Caroline Fradette: Employee of Chiesi Canada Corp.; Xavier Llòria: Employee of Chiesi Farmaceutici S.p.A.; Thomas Klopstock: Received research support and consultation fees from Santhera Pharmaceuticals, Chiesi, and GenSight Biologics

Grant Support: Chiesi USA, Inc.

Contact Information: None provided.

Misleading pale disc: Wolfram syndrome- Genotype phenotype associations

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Introduction:

To report various systemic and ophthalmic manifestations in patients with Wolfram syndrome (WS), which were misdiagnosed as glaucoma or idiopathic causes of optic atrophy.

Description of Cases:

Children and adults > 5 years of age) with subtle to significant vision loss, with optic atrophy were included. A retrospective chart analysis with at least 6 months follow up. A detailed neuro-ophthalmic evaluation, neuroimaging and genetic analysis were done in all patients. Eighteen eyes of 9 patients were included. Diminution of vision remained the most common presenting feature with bilateral cataracts detected in 5 patients None of them had keratoconus, dry eyes or any other retinal abnormality. Genetic analysis revealed OPAI AND WFS -1 AND 2 as the most common genes. 66% had an autosomal dominant inheritance. Five children underwent cataract surgery and 3 children were on antiglaucoma medications. Hearing loss was noted only in 3 children and 1 adult. The genitourinary association was seen in 2 patients

Conclusions, including unique features of the case:

Children who had early-onset vision loss and juvenile-onset diabetes mellitus had more severe signs than others. All except one were referred to the vision enhancement centre to support them with low vision aids. Wolfram syndrome may be overlooked due to the variability of symptoms hence this condition should be evaluated in a multidisciplinary manner for early diagnosis and disclosure of all other associated components of the syndrome. WS, a rare, devastating disease that affects different organs and systems, requires a multidisciplinary approach to be successfully treated. A prompt diagnosis decreases morbidity and mortality through prevention and treatment of complications.

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References: None provided.

Keywords: Ocular motility, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Adult strabismus with a focus on diplopia, High intracranial pressure/headache, Optic neuropathy

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Exposure to GLP-1 receptor agonists in patients with simultaneous bilateral Non-Arteritic Anterior Ischemic Optic Neuropathy (sNAION)

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Introduction:

Glucagonlike peptide-1 receptor agonists (GLP-1RA) have recently been implicated as a potential risk factor for NAION, but the association remains unclear. As GLP-1RA medications are increasingly utilized and their indications expand, better knowledge of their potential ophthalmic risks will improve counseling and monitoring of patients. Our study aims to measure rates of GLP-1RA exposure in a population of patients we previously evaluated who presented with simultaneous bilateral non-arteritic anterior ischemic optic neuropathy (sNAION).

Methods:

In this multisite retrospective observational study, we reviewed 25 patients with simultaneous or near-simultaneous NAION from three academic institutions that were originally studied between 2009 and 2020. Demographic information, medical history, use of GLP1-RAs, symptom course, paraclinical evaluation, and visual outcomes were collected for all patients.

Results:

Of the 25 patients, 17 presented with sNAION before the FDA approval of GLP1-RAs and 8 presented after. Of the 8 patients who presented after GLP1-RAs entered the market, none were on the medication prior to their sNAION. 4 of the total 25 patients and more than half of patients with diabetes (4 of 7) were placed on GLP1-RAs, but all were started after their sNAION. No patients had recurrent NAION while on GLP1-RA medication, with a mean duration of treatment of 3 years.

Conclusions:

GLP1-RAs were not a causative factor in any of the 25 cases of sNAION reviewed in our prior study. However, this class of medications is now used at a high rate in patients with diabetes and there were patients in our study group that initiated GLP1-RA medications after their documented sNAION events, suggesting that in this group there was correlation without causation.

References: None provided.

Keywords: Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

"Better" VA is not Enough: Limited Quality of Vision Improvement in NAION Patients Without Intervention

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Introduction:

Non-Arteritic Ischemic Optic Neuropathy (NAION) is the most common cause of acute optic neuropathy in adults over 50, however there are currently no treatments available. As part of the pivotal IONDT study, it was claimed that ~30% of patients improve vision over time without intervention, however the improvement was not shown on overall visual quality.

Methods:

In our study, we processed the data from 96 patients with NAION in Hashemi Eye Care over a period of 8 years. They were followed up at 2, 4, 12 and 24 weeks. The VA change over time was documented and the patients were divided into three distinct categories per visual changes over time to improvement, worsening and stable vision. Right and left eye were processed separately.

Results:

Analysis of visual changes in left eye showed 27% worsened, 45% stable and 28% improved, while for the right eye, 33% worsened, 33% stable and 34% improved. In the IONDT study, they also showed 30% spontaneous improvement in VA by 3 or more lines while they did not specify the final vision being useful. Our study showed that even in the recovery group, only central vision has improved, while the patient is suffering from visual field defect, color vision loss, and low contrast sensitivity.

Conclusions:

Overall, many patients are left with worse quality of vision compared to pre-state of the disease, even if the numerical visual acuity says otherwise. We have to develop better criteria for vision measurement to not discount the visual disability of the patients with reasonable central VA. Statistics for improvement groups in prior studies are skewed, as they do not quantify final VA. In contrary to visual improvement after optic neuritis, the visual recovery after NAION does not restore vision to a pre-injury state, highlighting the importance of developing new treatment modalities.

References: None provided.

Keywords: Optic neuropathy

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Long-Term Structural And Functional Outcomes After Hypofractionated Radiosurgery For Optic Nerve Sheath Meningiomas: A 48-Month Monocentric Oct-Based Study

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Introduction:

Optic nerve sheath meningiomas (ONSMs) are benign, dural-based tumors arising from the optic nerve sheath that lead to progressive compressive optic neuropathy. Hypofractionated stereotactic radiotherapy (HypoFRS) is the eye-preserving standard of care. This study aimed to evaluate long-term functional and structural outcomes following HypoFRS for ONSMs and to identify baseline optical coherence tomography (OCT) predictors of visual prognosis.

Methods:

We retrospectively analyzed 33 patients who underwent CyberKnife hypofractionated radiosurgery (25 Gy in 5 fractions) between May 2011 and May 2019 at the Carlo Besta Neurological Institute. Evaluations included best-corrected visual acuity (BCVA), standard automated perimetry (mean deviation, MD), and spectral-domain OCT of the peripapillary retinal nerve fiber layer (pRNFL) and macular ganglion cell complex (GCC) at baseline, 24 months, and 48 months. Patients were stratified by baseline OCT phenotype (atrophic vs. non-atrophic; optic disc edema vs. normal thickness).

Results:

In affected eyes, BCVA and MD improved at the 24-month follow-up and remained stable through the 48-month follow-up (BCVA $p = 0.095$ – 0.113 ; MD $p < 0.001$), while fellow eyes showed no significant changes. OCT analyses demonstrated a mild decline in pRNFL thickness (particularly in eyes with initial optic disc edema) and a modest thinning of GCC at 24 months, followed by stabilization of both parameters ($p < 0.001$) at 48 months. Eyes treated before the onset of atrophy, especially those with baseline edema or preserved GCC, achieved superior functional and structural outcomes. Exploratory analyses indicated that a baseline GCC thickness $> 70 \mu\text{m}$ was associated with a more favorable long-term prognosis, consistent with structural preservation and functional improvement.

Conclusions:

HypoFRS improves or stabilizes visual function and mitigates progressive neuroretinal atrophy in patients with ONSMs. Baseline GCC may serve as a practical biomarker to guide treatment timing and predict long-term outcomes.

References: None provided.

Keywords: Optic neuropathy, Tumors

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Ischemic Optic Neuropathy Associated With Semaglutide: Global Population-Based Analysis Of Over 30 Million Safety Reports

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Introduction:

Glucagon-like peptide-1 receptor agonists (GLP-1RAs) have transformed cardiometabolic care. However, recent reports have linked semaglutide to non-arteritic anterior ischemic optic neuropathy (NAION), prompting regulatory action by the European Medicines Agency. We conducted the first global, population-based analysis of over 30 million reports to evaluate formulation-specific risk of ischemic optic neuropathy (ION) among patients using semaglutide for diabetes or obesity.

Methods:

We retrieved and deduplicated FDA Adverse Event Reporting System (FAERS) data from December 2017–December 2024. Institutional review board approval and consent were not required for de-identified public data. Reports naming a GLP-1RA as the primary suspect for ION were included. Semaglutide was analyzed in pooled and brand-specific models (Ozempic, Wegovy). Comparator drugs included metformin, insulin, and tirzepatide. Disproportionality was assessed using reporting odds ratios (RORs, 95% CIs) with Bonferroni correction ($p < 0.0056$; $p < 0.0028$ for sex analyses), and Bayesian confirmation ($IC_{025} > 0.3$), thus minimizing false-positive signals.

Results:

Among 30,668,520 reports, 23,678 involved semaglutide (mean age 56.5 ± 11.1 years; 54.1% female). Of these, 3,070 were attributed to Wegovy (mean age 54.7) from 6 countries across 3 continents, and 20,608 to Ozempic (mean age 57.8) from 11 countries across 4 continents. Among 31,774 semaglutide cases, Wegovy demonstrated the strongest signal for ION (ROR = 74.9) versus Ozempic (ROR = 18.8). Sex-stratified analyses revealed markedly higher odds of ION in males (ROR = 116.4).

Conclusions:

Semaglutide was the only agent associated with ischemic optic neuropathy, with the most pronounced signal for Wegovy (ROR = 74.9) followed by Ozempic (ROR = 18.8). Wegovy's higher dose likely intensifies systemic exposure and accelerates metabolic shifts, predisposing to optic nerve hypoperfusion and impaired autoregulation. The absence of signal for tirzepatide supports a GLP-1–specific, dose-dependent mechanism. These findings reveal a robust, reproducible pharmacovigilance signal that warrants prospective validation and ongoing global surveillance.

References: None provided.

Keywords: Optic neuropathy

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Spaeth-Richman Contrast Sensitivity Testing for Early Detection of Linezolid-Induced Optic Neuropathy

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Introduction:

Linezolid, integral to multidrug-resistant tuberculosis therapy, carries a covert risk of optic neuropathy that often escapes early recognition. Traditional measures such as visual acuity or OCT frequently underestimate subclinical functional loss. The Spaeth-Richman Contrast Sensitivity (SPARCS) test offers a reproducible, quadrant-specific evaluation of both central and peripheral visual performance. This study longitudinally assessed contrast sensitivity in patients receiving prolonged linezolid therapy to identify early afferent pathway compromise and compare SPARCS sensitivity against Pelli-Robson and OCT parameters.

Methods:

This prospective observational study enrolled adults receiving linezolid for multidrug-resistant or extensively drug-resistant tuberculosis. Participants underwent baseline, three-month, and six-month neuro-ophthalmic evaluations including best-corrected visual acuity, Ishihara color testing, Pelli-Robson contrast sensitivity, Spaeth-Richman Contrast Sensitivity (SPARCS) testing, and optical coherence tomography of the retinal nerve fiber layer. Mean differences and linear slopes of SPARCS scores were calculated across visits to quantify temporal decline. Correlations between functional and structural parameters were analyzed using Pearson coefficients, and effect sizes were computed with Cohen's *d*. Statistical significance was set at $p < 0.05$.

Results:

Twenty-eight patients (mean age 32.5 ± 13.3 years) completed six-month follow-up. The right eye demonstrated a significant decline in total SPARCS score (mean difference -7.4 ; slope -1.23 points/month; $p = 0.0067$), predominantly in central and inferior quadrants. The left eye remained stable (MD -1.0 ; $p > 0.8$). Pelli-Robson changes were minimal, and RNFL thinning was nonsignificant. SPARCS and RNFL values showed weak correlation ($r \approx -0.1$). Effect size for right-eye decline was large (Cohen's $d = -1.02$), confirming clinically meaningful functional loss.

Conclusions:

SPARCS detected early, quadrant-specific contrast sensitivity loss preceding structural change, highlighting its value as a sensitive, low-cost screening tool for linezolid-induced optic neuropathy surveillance.

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Increased Axonal Metabolic Stress In NAION: An Imaging Study Using Flavoprotein Fluorescence Imaging

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Introduction:

Nonarteritic ischemic optic neuropathy (NAION) is due to hypoperfusion of the anterior optic nerve – a selectively vulnerable region for metabolic stress due to high energy demand and tight compartment. Flavoprotein fluorescence (FPF) imaging is an emerging functional assessment of optic neuropathies and quantifies the increase in autofluorescence due to the accumulation of oxidized flavoproteins. We conducted a retrospective case-control study to compare optic disc and macular FPF with measurements of visual function and structure in chronic NAION.

Methods:

All participants underwent comprehensive assessments of visual function, structure, and FPF imaging. Data was analyzed using custom Python scripts with statistical analysis performed via Mann-Whitney U, Wilcoxon signed-rank tests, ANOVA with Tukey HSD, and Spearman's rho.

Results:

Compared with controls (N=37), NAION eyes (N=77) exhibit significantly higher optic disc FPF ($p < 0.001$) but not macular FPF ($p = 0.266$). NAION eyes also have significantly worse visual acuities, static perimetry mean deviation (MD), and optical coherence tomography peripapillary retinal nerve fiber layer (pRNFL) and macular ganglion cell complex (mGCC) thicknesses (all $p < 0.001$). In NAION eyes, there was significant correlation between optic disc FPF, MD, pRNFL, and mGCC (all $p < 0.001$). A LASSO regression revealed the mGCC thickness as the most important predictor of vision loss, followed by disc FPF (inferior, temporal and superior sectors), and pRNFL (inferior and nasal sectors). In 9 paired eyes from patients with unilateral NAION, disc FPF was significantly worse in the affected eyes compared with the contralateral healthy eyes ($p = 0.039$), which had the same global and sectoral disc FPF scores, visual structure, and function as that of healthy control eyes from participants without NAION.

Conclusions:

NAION patients exhibit increased optic disc FPF, consistent with increased axonal metabolic stress. Optic disc FPF was significantly correlated with visual function and structure. Analysis of paired eyes in patients with unilateral NAION did not reveal evidence of presymptomatic metabolic stress in the contralateral healthy eyes.

References: None provided.

Keywords: Optic neuropathy, Neuroimaging, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease

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Grant Support: None.

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Genetic Testing in Idiopathic Optic Neuropathy: Diagnostic Yield and Differences in Clinical Presentation

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Introduction:

Chronic optic neuropathy classically presents with visual acuity loss, dyschromatopsia, and optic atrophy. Identifying the underlying cause is essential for management; however, many cases remain idiopathic even after comprehensive neuro-ophthalmologic evaluation. Advances in genetic testing now enable detection of hereditary etiologies that may mimic acquired optic neuropathies. This study aimed to determine the diagnostic yield of genetic testing in idiopathic optic neuropathy and to compare clinical characteristics of patients with a confirmed genetic etiology to those with negative testing.

Methods:

A cross-sectional study was conducted on a convenience sample of patients with chronic optic neuropathies who underwent genetic testing following nondiagnostic neuro-ophthalmologic evaluation. Clinical characteristics, including color vision (Ishihara plates), high-contrast visual acuity, low-contrast letter acuity, visual field mean deviation (VFMD), and peripapillary retinal nerve fiber layer (pRNFL) thickness by optical coherence tomography (OCT), were compared between eyes of patients with versus without a confirmed genetic diagnosis. Generalized estimating equation models (GEE) were used to examine whether a confirmed genetic diagnosis was associated with worse scores/measurements. Only clinically affected eyes were included (48 eyes).

Results:

There were 26 patients, all of whom underwent genetic testing. A genetic diagnosis was identified in 11 of 26 patients (42%; 95% CI, 23–61). The most frequent pathogenic variants involved WFS1 and MT-ND4. At initial evaluation, eyes in the genetic group demonstrated less visual field loss (average VFMD –2.2 vs –11.8 dB; difference +9.3 dB; 95% CI, 2.8–15.9; $p = 0.005$). No significant differences were observed for other tests.

Conclusions:

Our results demonstrate that hereditary optic neuropathies can present with subtle or variable phenotypes, supporting the inclusion of genetic testing even in mildly affected idiopathic cases. The visual field was a key test that separated our two groups. Genetic testing may have high yield in patients with idiopathic optic neuropathy.

References: None provided.

Keywords: Optic neuropathy, Genetic disease, Visual fields

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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The Presence of Macular Edema, Ganglion Cell Layer, and Retinal Nerve Fiber Layer Thinning in Optic Neuritis

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Introduction:

Retinal nerve fiber layer (RNFL) and ganglion cell-inner plexiform layer (GCIPL) thinning are well-established sequelae of optic neuritis. There is a less described inflammatory component of optic neuritis (ON) involving the non-myelinated prelaminar and inner nuclear retinal nerve fibers, resulting in microcystic macular edema (MME). MME is postulated to result from Mullerian cell injury during acute inflammation, contributing to additional thinning of the RNFL and GCIPL. MME has been investigated in prevalence and impact on multiple sclerosis (MS) optic neuritis, but less commonly reviewed in myelin oligodendrocyte associated disease (MOGAD), and neuromyelitis optica spectrum disease (NMOSD).

Description of Cases:

A descriptive literature review using PubMed, Web of Science, and Embase (2003–2025), augmented by Elicit, an AI-assisted semantic synthesis platform, screened over 126 million studies via Semantic Scholar and OpenAlex. Thirty-four studies met the inclusion criteria, evaluating RNFL, GCIPL, and MME changes in inflammatory ON. MS: MME prevalence ranged from 4–6%, associated with later disease stage and mild RNFL thinning. MME patients exhibited thicker INL and thinner GCIPL. NMOSD: MME occurred in 5–24% of NMOSD eyes, predominantly within the Inner Nuclear Layer, and was associated with severe, irreversible RNFL and GCIPL loss. Optical Coherence Tomography Angiography (OCTA) demonstrated an average 15% reduction in parafoveal vascular density and an 18% enlargement of the foveal avascular zone in AQP4+ NMOSD, suggesting concurrent microvascular compromise. MOGAD: MME was rarely observed; however, subclinical GCIPL thinning and superficial vascular plexus dropout were identified bilaterally, reflecting diffuse inflammatory and microvascular involvement.

Conclusions, including unique features of the case:

MME represents a biomarker of retinal inflammation across ON subtypes, with a higher prevalence in NMOSD than MOGAD and MS, and may contribute to the severity of RNFL and GCIPL thinning in NMOSD. Recognition of these distinct structural and vascular phenotypes underscores the value of OCT and OCTA as important tools for disease differentiation, monitoring, and prognostication in ON.

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References: None provided.

Keywords: Optic neuritis, Demyelinating disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Retina

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Conventional and AI-Assisted OCT Analyses in Acute Retrobulbar Optic Neuritis: A New Frontier in Early Detection

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Introduction:

Acute retrobulbar optic neuritis (ARON) lacks visible fundus changes, making timely diagnosis challenging. We aimed to analyze the role of OCT in the early detection of ARON.

Methods:

This case-control study included consecutive patients with a first-episode of strictly unilateral ARON from a prospective observational cohort at a single tertiary neurology center. Age- and sex-matched controls were identified retrospectively. Global and sectoral pRNFL thicknesses and macular layer thicknesses were measured using SD-OCT (Spectralis, Heidelberg Engineering) within one month of visual loss. We compared the OCT parameters between ARON eyes, contralateral eyes, and control eyes. To cross-validate the results, we developed a vision transformer pRNFL segmentation model, followed by a binary linear regression AI model to detect ARON-related pRNFL asymmetry by comparing per-degree interocular thickness differences. Averaging across 10° intervals generated 36 pRNFL metrics.

Results:

We included 58 patients (35±10 years, 65.5% women) and 58 controls (36±8 years, 69% women), all with normal optic discs confirmed by fundus photography. Of the patients, 41 (71%) had multiple sclerosis, 3 (5%) NMOSD, 4 (7%) MOGAD, and 10 (17%) idiopathic ARON. Spectralis data revealed significant pRNFL differences between ARON and contralateral eyes in all sectors except temporal. Interocular asymmetry in combined nasal-superior (NS) and nasal-inferior (NI) pRNFL thickness ($p < 0.0001$) was the only parameter that distinguished all patient groups from controls, yielding an AUC of 0.84 (95% CI: 0.77-0.91) with a 19 µm cutoff. ANOVA showed no significant effect of ARON etiology or time since onset on OCT findings ($p = 0.60$). The AI model's post hoc analysis achieved an AUC of 0.89 (95% CI: 0.84-0.94), identifying 12 key 10° regions as critical decision factors, predominantly in the NS and NI sectors.

Conclusions:

OCT interocular asymmetry differentiates inaugural ARON from normal eyes, primarily driven by changes in NS and NI pRNFL sectors.

References: None provided.

Keywords: Optic neuritis, Demyelinating disease

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The Use of OCT In Post-Chiasmal and Chiasmal Demyelination: Beyond The Optic Neuritis Universe

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Introduction:

Optical tomography studies (OCT) in multiple sclerosis (MS) usually classify eyes as having had clinical optic neuritis (ON), subclinical ON, or as otherwise normal. We believe such approach undermines the importance of further including and classifying eyes with signs indicative of retrochiasmal/chiasmal disease (RCD/CD), which could add relevant information about disease status. Objective: to include and analyse eyes with RCD/CD in a large database of MS patients.

Methods:

We included eyes of MS patients who underwent OCT, and had information on disease duration, EDSS, and number of relapses. We further classified them as normal, or with findings indicative of clinical ON (diagnosed >6 months prior), subclinical ON (>7micra inter-eye retinal nerve fiber layer [RNFL] thickness difference and/or >4micra inter-eye ganglion cell layer [GCL] thickness difference), subclinical (non-localizing) involvement (color and/ or statistical RNFL/GCL map abnormalities not fulfilling criteria for subclinical ON, CD and/or RCD), subclinical or clinical CD (bilateral and congruent nasal GCL loss) and/or subclinical or clinical RCD (bilateral and congruent homonymous GCL loss).

Results:

We included 273 eyes. 177 (64.8%) had an abnormal OCT (27.8% clinical visual relapses, 32.9% subclinical visual relapses, 4.0% both) (ON only (n=86, 31.5%), RCD/CD (n=36, 13.1%), non-localizing (n=55, 20.1%)). When comparing between normal, ON and RCD/CD eyes, disease duration in the right eye was different between groups (p=0.020), being greater in RCD/CD (p=0.019) and ON (p=0.029), than in normal eyes. Disease duration in the left eye was near-significantly different between groups (p=0.076), being greater in RCD/CD (p=0.037) than in normal eyes. Relapse rate in the 2 years prior, when using the right eye, was near-significantly different between groups (p=0.086), being greater in RCD/CD (p=0.036) than in ON eyes.

Conclusions:

Retrochiasmal/chiasmal disease in OCT seems to be associated with greater disease duration and number of clinical relapses in the 2 years prior, in MS patients.

References: None provided.

Keywords: Demyelinating disease, Optic neuritis, Neuroimaging

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Prevalence And Incidence Of Fellow Eye Involvement In Non-arteritic Anterior Ischemic Optic Neuropathy Patients

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Introduction:

To the best of our knowledge, there has not been a study dedicated to the prevalence and incidence of fellow eye involvement in non-arteritic anterior ischemic optic neuropathy (NAION) patients in our population. Therefore, our primary objective was to investigate the prevalence and incidence of fellow eye involvement, also, the secondary objective was to identify the possible risk factors for fellow eye involvement in NAION patients.

Methods:

We performed a retrospective review of the medical records of 72 patients who presented with acute, unilateral NAION at the first-ever NAION onset. Only data regarding the first-ever NAION onset in these 72 patients were evaluated. Demographic data along with medical history (age at onset, sex, underlying diseases, and smoking history), and initial ophthalmic findings (best-corrected visual acuity, intraocular pressure, and fellow eye disc-at-risk (cup-to-disc ratio ≤ 0.2)) were reviewed. The development of fellow eye involvement was recorded over a follow-up period of 3 years. Univariate Cox proportional hazard regression analysis was used to calculate the hazard ratio for fellow eye involvement.

Results:

Within 3 years, 11 patients (15.3%) developed fellow eye involvement, with events plateauing after 22.0 months following the first-ever NAION onset. On average, all 72 patients remained free of fellow eye involvement for approximately 31.4 months (mean estimation) within the 3-year window (95% confidence interval: 28.9-34.0 months). The incidence of fellow eye involvement was 0.0588 per person-year. There were no statistically significant risk factors for fellow eye involvement identified.

Conclusions:

The 3-year cumulative prevalence of fellow eye involvement was 15.3% with the incidence rate of 5.9 per 100 person-years. No statistically significant risk factors for fellow eye involvement were identified from our study.

References: None provided.

Keywords: Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Prevalence, Clinical and Genetic Characterization Of Patients With Inherited Retinal Dystrophies: A Descriptive Study

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Introduction:

Inherited retinal dystrophies (IRDs) are genetically and clinically diverse disorders causing progressive, irreversible vision loss. The global incidence is uncertain, though retinitis pigmentosa (RP), the most common, affects about one in 5,000 individuals (1). Due to their genetic complexity—over 270 genes have been identified—epidemiologic data remain limited, particularly in underserved regions (2). Current management emphasizes visual rehabilitation, yet advances offer promising opportunities for targeted molecular treatment (3, 4).

Methods:

This cross-sectional, retrospective study analyzed the prevalence and clinical and genetic characteristics of IRDs in patients evaluated at an ophthalmic center between 2023 and 2024. It aimed to improve understanding of their epidemiologic distribution and genetic diversity, and to contribute knowledge that may guide future gene-based therapies. The study was conducted in accordance with the Declaration of Helsinki and approved by the university's ethics committee (No. 036-24) (5).

Results:

The estimated prevalence of IRDs was 44.1 per 100,000 patients. A total of 166 patients were diagnosed with IRDs. The most prevalent conditions were RP (117; 70.5%), Cone and Cone-Rod Dystrophies (C-CRD) (24; 14.5%), and Stargardt Disease (10; 6.0%). Genetic testing was performed in 86 patients (59.7%), yielding positive results in 70 (81.3%). The remaining patients were diagnosed clinically, supported by multimodal imaging and electrophysiological studies. The most frequent pathogenic variants were RHO (n = 5; RP), ABCA4 (n = 5; C-CRD), NR2E3 (n = 4; RP), and USH2A (n = 4; RP).

Conclusions:

This is the largest epidemiologic study of IRDs in our country. The cohort showed phenotypic and genotypic diversity, with RP as the predominant disorder. Phenotypic variability underscores the need for genetic testing and regional registries to improve diagnostic accuracy and characterize the genetic diversity of IRDs (3, 4). Expanding access to molecular diagnostics and gene-based therapies will be key to improving outcomes globally.

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Keywords: Retina, Genetic disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Vision related quality of life impairment in Ethambutol induced toxic optic neuropathy: A questionnaire based study

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Introduction:

Ethambutol-induced ocular toxicity occurs in almost 1–5% of patients. Ethambutol-induced optic neuropathy poses a significant threat to patient quality of life due to abrupt visual impairment and accompanying functional limitations. The purpose of our study was to evaluate vision-related quality of life (QoL) using a validated questionnaire among patients diagnosed with ethambutol optic neuropathy (EON).

Methods:

A prospective observational study included 30 patients with confirmed ethambutol optic neuropathy (EON) at a tertiary eye care centre. The 25-item Visual Quality of Life Index (VQLI) was administered in person to all ATT patients. Each item scored 1 (excellent) to 5 (poor/severe). Data collected encompassed demographics, tuberculosis features, ATT regimen and duration, and visual function parameters (visual fields, OCT findings, and fundus results).

Results:

The mean ($\pm$ SD) age was 50.3 ± 15.4 years with slight male predominance. Most patients (74.1%) reported gradual visual symptoms (blurred vision, reading difficulty, dyschromatopsia, impaired driving). Mean duration of visual symptoms was 1.5 ± 0.9 months, with a mean interval of 6.1 ± 2.9 months from ATT initiation to onset and 7.6 ± 2.5 months to clinical presentation. Systemic comorbidities occurred in 53.3%, most commonly diabetes mellitus (40%). Automated perimetry (30-2 SITA) was abnormal in 55%, with generalized depression (52.4%), central scotoma (26.2%), and hemianopic defects (12.6%). OCT showed RNFL thinning in 53.6% and GCC thinning in 85.7% of eyes; fundus was normal in 72.4%, while disc margin blurring (20.7%), diffuse atrophy (3.4%), and temporal pallor (3.4%) were less frequent. The mean VQLI was 90 ± 24 , with higher scores indicating worse QoL. The item most linked to poorer QoL was worry about eyesight-related troubles. Patients with better QoL had milder visual dysfunction.

Conclusions:

Ethambutol optic neuropathy significantly impairs vision-related quality of life. Early identification and cessation of ethambutol, combined with regular visual monitoring, are essential to prevent irreversible vision loss and preserve functional vision in patients on anti-tubercular therapy.

References: None provided.

Keywords: Optic neuropathy, Demyelinating disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Functional Visual Impairment in Patients with Different Visual Field Defect

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Introduction:

Visual field defects resulting from optic nerve damage can impair peripheral awareness and interfere with daily functioning. This study aimed to evaluate the association between visual field loss and vision-related quality of life (VRQOL) in glaucoma patients.

Methods:

A total of 73 patients (male: female = 34:39; mean age 60.53 ± 14.41 years) were enrolled. Mean intraocular pressure (IOP) was 13.77 ± 3.89 mmHg in the right eye and 13.98 ± 3.77 mmHg in the left eye. Vision-related quality of life was assessed using the validated Taiwanese version of the NEI VFQ-25(T). Visual field severity was quantified using mean defect (MD), pattern deviation (PD), and corrected pattern deviation (CPD).

Results:

Patients reported substantial reductions in general health and general vision. Near-vision activities were more affected than distance-related tasks. Role difficulties and mild impairment in social functioning were also observed. Among the 30 respondents to driving-related items, mild functional limitations were noted but showed wide variability. Common daily-life challenges included reading difficulties, face recognition problems, shopping obstacles, limitations in electronic device use and public transportation, and fear of falling or using stairs.

Conclusions:

These findings highlight the significant impact of visual field loss on functional independence in glaucoma. Rehabilitation strategies—such as reading aids or mobility-oriented interventions—should be tailored to address specific VRQOL deficits in patients with peripheral visual impairment.

References: None provided.

Keywords: Visual fields, Optic neuropathy, Higher visual functions, Optic nerve trauma and treatment

Financial Disclosures: The authors had no disclosures.

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Association Normal-Tension Glaucoma and Migraine with Aura and with Chronic Migraine

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Introduction:

Previous reports have shown an association between normal-tension glaucoma (NTG) and migraine. The objective of this study was to determine if patients with migraine with aura or patients with chronic migraine, were disproportionately represented in a cohort of patients with NTG.

Methods:

We queried our electronic medical records (EMR) from 2015 to 2025 for patients with ICD-10 codes for NTG. We then determined what proportion of these patients also carried codes for migraine, aura, and chronic migraine. We reviewed charts to ensure that patients had been correctly coded with NTG and are sending the following questionnaires to these patients to more accurately determine what proportion of these patients have migraine with aura and/or chronic migraine: The ID Migraine Questionnaire, The Visual Aura Rating Scale, the HIT-6, and the ICDH3 Criteria for Chronic Migraine.

Results:

We identified 380 patients who carry an ICD code for NTG. In this group, 22 of 380 patients (5.8%) also carry an ICD code for migraine. As of this date we have verified a diagnosis of NTG by chart review in 100 of the 380 patients. 39% of these 100 patients have clinic notes stating they have headache/migraine and 11% of these patients have clinic notes stating they have migraine with aura or migraine aura without headache. The average age of these 39 patients is 64 years (range 41-79) and 31/39 (80%) are female.

Conclusions:

Our preliminary findings confirm previous observations that migraine is increased in patients with NTG. At the Annual Meeting, we will have completed our review of the EMR to confirm a diagnosis of NTG, we will have collected questionnaire results for migraine, migraine with aura, aura without headache, and chronic migraine, and we will present our data and analyses. If accepted, the authors request the abstract committee allow them to resubmit a more developed abstract before the deadline for producing the syllabus.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuropathy, Higher visual functions, High intracranial pressure/headache, Vascular disorders

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Clinical Characteristics and Treatment Outcomes of Optic Neuritis in Asians - Preliminary Findings From A Singapore Cohort

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Introduction:

Optic neuritis (ON) is an inflammatory optic neuropathy causing acute vision loss, often in young and working-age adults. Most existing data, including the landmark Optic Neuritis Treatment Trial, derive from predominantly Caucasian cohorts with multiple sclerosis (MS)-associated ON. Emerging evidence suggests that Asian patients demonstrate distinct clinical phenotypes, serological profiles, and treatment responses. This study aims to characterise the clinical spectrum, diagnostic features, and visual outcomes of ON in an Asian population.

Methods:

Patients aged ≥13 years with a first episode of ON were prospectively recruited from tertiary centres in Singapore. Diagnosis was confirmed clinically by a neuro-ophthalmologist and supported radiologically. Standardised data collection included demographics, clinical features, visual function testing, neuroimaging, serology (AQP4, MOG, autoimmune and infectious markers), and optical coherence tomography (OCT). Visual and structural outcomes were assessed over 12 months.

Results:

Of 35 eligible patients, 28 were enrolled (mean age 43.3 years; 68% female). Ethnic distribution was Chinese 53.6%, Malay 25%, Indian 10.7%, Others 10.7%. Ocular pain occurred in 53.6%, and optic disc swelling in 50%; 17.9% presented bilaterally. Mean presenting visual acuity was 1.24 LogMAR, improving to 0.16 LogMAR at 12 months. Mean Humphrey Visual Field deviation improved from -20.8 dB to -1.9 dB. Final diagnoses included idiopathic ON (53.6%), MOGAD (21.4%), NMOSD (10.7%), MS (10.7%), and infectious ON (3.6%). All patients received intravenous methylprednisolone; seven underwent plasma exchange, and seven received long-term immunotherapy. OCT demonstrated initial RNFL thickening with subsequent thinning corresponding to resolution of oedema.

Conclusions:

Preliminary data suggest that ON in Asian patients exhibits diverse aetiologies and a higher proportion of MOG and AQP4-related disease than in Western cohorts. Visual recovery is substantial but variable across subtypes. Further studies with multi-centre recruitment will enable more robust analysis of prognostic biomarkers and guide population-specific management strategies for optic neuritis in Asia.

References: None provided.

Keywords: Optic neuritis, Demyelinating disease

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Grant Support: None.

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Is the Risk of NAION Tied to an Evolutionary Gordian Knot? A Software Analysis of Blood Flow Dynamics at the Optic Nerve Head

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Introduction:

Human optic nerves receive robust centrifugal pial perfusion that renders them resilient to ischemia over ~80mm length. But, the optic nerve head (ONH) is highly vulnerable to ischemia despite receiving additional blood from the Circle of Zinn-Haller (CZH). We hypothesize and quantitatively assess the risk that ONH hypoperfusion is influenced by asymmetrical flow dynamics at the sPCA trifurcation into the optic nerve, CZH and choroid - an inscrutable Gordian knot of perfusion. The choroid is a capacious, low resistance path that plausibly creates a bias away from the ONH that would be accentuated by hypotension.

Methods:

We utilized a Modelica systems modelling tool ("Dymola") to replicate and validate a mathematical model of a more simple central retinal vessel system utilizing the established fluid:electric analogy (current flow through a network of resistances and capacitances is equivalent to blood flow through vessels with resistances and compliances). We applied this approach to replicate hemodynamics of the sPCA trifurcation zone by populating this tool with anatomical data extracted from our light sheet fluorescent microscopy (LSFM) of human orbits.

Results:

Our modeled CRA flowrates ($[3 \times 10^{-3} - 4.2 \times 10^{-3}]$ mL/s) were higher than published values ($[6.81 \times 10^{-4}]$ mL/s) and we are tuning parameters to approximate those lower values. Using a nonlinear, inverse relationship model, we found anticipated decreases in CRA flowrates ($\sim [5 \times 10^{-4}]$ mL/s) with increased IOP (mimicked by 50% reduction in compliance). With this tool, we are developing a circuit model that incorporates vascular anatomy (extracted from >14,900 LSFM "segments") to represent sPCA hemodynamics and test our hypothesis that flow bias predisposes to ONH hypoperfusion.

Conclusions:

Our model enables testing of our hypothesis that the evolution-derived architecture of a trifurcating sPCA vascular network distributed to perfusion zones of differing resistances/capacitances poses an intrinsic ischemic risk to the ONH. Autoregulation presumably counters flow bias but this response may be insufficient to sustain homeostasis.

References: None provided.

Keywords: Optic neuropathy

Financial Disclosures: Joseph Rizzo: consultant to Life Biosciences; Salwa Anam; Swati umamaheshwaran; Yasaman Anvarinia; Brendan Brinkman; Ted Ahn; Joe baldwin

Grant Support: None.

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Strength of Association Between Optic Neuritis and Infectious or Immune-Mediated Inflammatory Diseases: A Population-Representative Study of 30 million People In England (2011-2024)

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Introduction:

Previous analysis of the incidence trend and systemic disease associations of optic neuritis (ON) in the United Kingdom predated the COVID-19 pandemic, and was underpowered for rare disease associations.¹

Methods:

We performed a population-based analysis of primary care records in England (2013-2024), using the Clinical Practice Research Datalink (CPRD Aurum, n=30 million, protocol 23_003414). Eligible patients were aged >1 year and matched on age, sex, and region. We identified ON and 119 associated disease diagnoses using SNOMED CT codes. The study design included population cohort for incidence; and matched case-control and matched cohort, adjusted for race, for association with infectious and immune-mediated inflammatory diseases [I-MIDs] at baseline [logistic regression] and during follow-up [Cox proportional hazards] in n=9,297 ON cases and 37,188 controls. We defined statistical significance at p< 0.001.

Results:

The incidence of ON in England was stable over 11-years including the COVID-19 pandemic; cumulative incidence 3.5 (95% confidence interval [CI] 3.2-3.8) per 100,000 person years. ON cases were significantly more likely than matched controls to have prior diagnosis of NMOSD (OR 111.0), MS (OR 76.0), CIS (OR 56.8), Behcet's (OR 8.8), GCA (OR 4.5), other vasculitis (OR 2.5) and sarcoidosis (OR 2.1). Incident ON cases were significantly less likely than matched controls to have prior documented COVID-19 (OR 0.2), or prior vaccination for COVID-19 (OR 0.04), or for influenza (OR 0.57). Undifferentiated ON cases had significantly greater hazard of subsequent diagnosis of MS (HR 290.6), CIS (HR 134.0), NMOSD (HR inestimable), GCA (HR 8.7), sarcoidosis (HR 8.2), other vasculitis (HR 4.3), and of infections including COVID-19 (HR 1.7), Herpes Simplex Virus (HR 1.3), and candidiasis (HR 1.3).

Conclusions:

This analysis corroborates and quantifies previous ON associations with an expanded number of systemic diseases in an ~independent population-representative sample from England, and confirms no impact of COVID-19 on epidemiological trend over the pandemic period.

References: Braithwaite T, Subramanian A, Petzold A, et al. Trends in Optic Neuritis Incidence and Prevalence in the UK and Association With Systemic and Neurologic Disease. *JAMA Neurol*;77(12):1514-1523. 2020.

Keywords: Optic neuritis, Demyelinating disease, Pediatric neuro-ophthalmology

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PHOMS Prevalence and Functional Implications in Anterior Ischemic Optic Neuropathy Subtypes

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Introduction:

A peripapillary hyperreflective ovoid mass-like structure (PHOMS) is an optical coherence tomography (OCT) finding associated with axoplasmic stasis in various optic neuropathies. Its prevalence and clinical implications in arteritic (A-AION) versus nonarteritic anterior ischemic optic neuropathy (NA-AION) remain unclear.

Methods:

Patients with A-AION and NA-AION, enrolled from March 2021 to August 2024 in prior prospective studies, were included. All subjects had previously undergone detailed OCT scans of the optic nerve head and macula. High-resolution spectral-domain OCT and visual acuity within one month of diagnosis were available for all included eyes. PHOMS were identified according to the ODDS Consortium criteria. Prevalence of PHOMS was compared between A-AION and NA-AION, and within each subtype OCT parameters and visual acuity were compared between PHOMS-positive and PHOMS-negative eyes.

Results:

22 patients (24 eyes) were included, equally distributed with $n = 11$ (12 eyes) of both subtypes of AION. A PHOMS was present in 41.7% of A-AION eyes and in 25% of NA-AION eyes. Within A-AION, PHOMS-positive eyes demonstrated slightly smaller Bruch's membrane opening diameters ($1442 \pm 71 \mu\text{m}$ vs $1586 \pm 149 \mu\text{m}$, $p = 0.17$) although not reaching significance. In NA-AION, PHOMS-negative eyes showed a trend toward worse perimetric mean deviation ($13.5 \pm 7.5 \text{ dB}$ vs $5.7 \pm 5.7 \text{ dB}$, $p = 0.08$) and slightly lower mGCL volume ($0.89 \pm 0.15 \text{ mm}^3$ vs. $1.03 \pm 0.17 \text{ mm}^3$, $p = 0.19$).

Conclusions:

PHOMS was more frequently observed in A-AION than in NA-AION, suggesting that PHOMS formation may not be exclusive to a predisposing crowded optic disc. Within each AION subtype, PHOMS presence did not significantly impact OCT measurements or visual acuity. These findings indicate that PHOMS likely represents an epiphenomenon of axoplasmic stasis from the ischemic insult.

References: None provided.

Keywords: Optic neuropathy, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Perimetry

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ORION: A Prospective Natural History Study In Patients With Inherited Optic Neuropathies

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Introduction:

Therapeutic trials for inherited optic neuropathies (IONs) require validated outcome measures. Limited prospective evidence exists to guide biomarker selection and patient stratification. This study aimed to longitudinally characterize the visual phenotype in Leber hereditary optic neuropathy (LHON) and autosomal dominant optic atrophy (ADOA).

Methods:

ORION is an ongoing three-year prospective natural history study for adults with LHON or ADOA. Yearly assessments include patient-reported outcome measures (PROMs), best-corrected visual acuity, spatial (s-) and temporal (t-) contrast sensitivity (CS), visual field (VF) deviation, ganglion cell layer (GCL) and retinal nerve fiber layer (RNFL) thickness, and retinal flavoprotein fluorescence (FPF)—a surrogate for metabolic status. Linear mixed models were applied.

Results:

Thirty-eight participants (23 LHON and 15 ADOA) have been assessed, with 18 completed 1-year visits at data cut. Ten LHON patients were enrolled within 12 months of disease onset, while eight ADOA patients were under 40 years. FPF intensity was elevated in LHON and ADOA in the optic rim compared with normative data ($p < 0.001$). Sectorized macular and peripapillary retinal thickness was inversely correlated with FPF intensity ($\beta = -0.169$, $p < 0.001$). In ADOA, macular ($\beta = 0.118$) and peripapillary ($\beta = 0.516$) FPF worsened with age (both $p < 0.001$), but retinal thinning did not. FPF intensity did not vary in acute, dynamic, and chronic LHON phases. Declining visual acuity and mean VF deviations were associated with reductions in s-CS and t-CS (all $p < 0.001$), except at the lowest spatial (1 cycle/degree) and highest temporal (15 Hz) frequencies. These functional measures were correlated with GCL thickness (all $p < 0.05$), but not FPF intensity. Acuity, VF deviation, CS, and GCL thickness were correlated with the composite scores of two separate PROMs (all $p < 0.05$).

Conclusions:

Structural, metabolic, functional, and patient-reported measures of vision are complementary in IONs. Psychophysical tasks can profile rarer retinal cells, while FPF may be a valuable biomarker of metabolic dysfunction.

References: None provided.

Keywords: Optic neuropathy, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Genetic disease

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Discovery of Novel Genetic Variants Associated with Nonarteritic Anterior Ischemic Optic Neuropathy

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Introduction:

Nonarteritic anterior ischemic optic neuropathy (NAION) is the leading cause of acute vision loss in adults over 50, yet the underlying etiology is not known. Here, we investigate whether genetic variation contributes to disease risk in a large cohort of NAION patients.

Methods:

Blood samples collected from NAION patients were genotyped using arrays. Both sample and variant quality control were performed. Related individuals and samples with >5% missing variants were excluded. Variants with >2% missing genotypes, rare variants (minor allele frequency < 1%), and variants with significant deviation from Hardy–Weinberg equilibrium ($p < 1 \times 10^{-8}$) were also excluded. A survey of variants located within 100 kilobases of 76 known optic nerve atrophy genes was performed. These variants were annotated using the Ensembl Variant Effect Predictor (VEP) to determine their predicted impact on gene transcripts and protein sequence.

Results:

A total of 427 NAION cases were included in the analysis, and variants in 76 genomic loci were queried. Multiple variants in genes with disease-relevant functions were identified in the cohort, which have not been previously reported to be associated with NAION. These included variants that alter the amino acid sequence of the mitochondrial membrane protein MFN2 (p.Arg104Trp and p.Tyr752Ter, n=10 and 12, respectively) and the mitochondrial genome maintenance exonuclease MGME1 (p.Thr265Ile, n=10).

Conclusions:

This study has identified novel genetic loci that may contribute to NAION risk. The MFN2 gene is expressed in retinal ganglion cells, and the p.Arg104Trp and p.Tyr752Ter variants have previously been implicated in optic nerve atrophy associated with Charcot-Marie-Tooth disease with variable phenotypic manifestations. Variants in MGME1 can lead to multisystem mitochondrial disease with progressive external ophthalmoplegia and a premature aging phenotype. Taken together, these results suggest that mitochondrial dysfunction may play a pathogenic role in at least some cases of NAION.

References: None provided.

Keywords: Genetic disease, Optic neuropathy

Financial Disclosures: Uzma Rentia; Joseph Rizzo: consultant to Life Biosciences; Leonard Levin: Leonard A. Levin has served as a consultant to Annexon, Dompe, Eyeevensys, Genentech, Janssen Pharmaceuticals, Neuroptika, Oculis, Perfuse, Perceive, Prilenia, Roche, Santen, and UNITY.; Mark Kupersmith: Mark Kupersmith is consultant to Oculis SA.; Amanda Henderson: Amgen (Advisory Boards), Catalist (Advisory Board), Argenx (Sponsored Research); Neil Miller: Amgen (DMC head for clinical trial, Dompé (Advisory board), Lilly (Consultant); Janey Wiggs; Inas Aboobakar

Grant Support: None.

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The Psychological Experiences of Patients with Acute Vision Loss: A Cross-Sectional Survey of Patients Diagnosed with Anterior Ischemic Optic Neuropathy

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Introduction:

Existing research addresses the functional impact of visual impairment among patients with anterior ischemic optic neuropathy (AION) but fails to capture the impact of sudden vision loss on patients' experiences. Our study aims to understand the psychosocial burden of AION to inform patient-centered interventions.

Methods:

This is an ongoing study of patients with acute AION diagnosed within the past year in our neuro-ophthalmology clinics. We abstracted best-corrected visual acuity, perimetric mean deviation, and date of vision loss from medical records. Participants completed validated patient-reported outcome measures including the Vision Core Measure 1 (VCM1), measuring vision-related quality of life, and Patient Health Questionnaire 4 (PHQ-4), screening depression. Patients also responded to open-ended questions regarding coping strategies, sources of support and unmet healthcare needs. Standard descriptive statistics summarized the cohort, and qualitative responses were coded using thematic analysis.

Results:

In these preliminary results, 17 patients met the inclusion criteria of which nine participants (mean age 68 years; five women) were enrolled, including seven with unilateral AION and two with bilateral AION occurring a mean (standard deviation) 8 (4) months prior to enrollment. Mean (SD) vision and perimetric mean deviation in the worse eye were 0.65 logMAR (0.52 logMAR) and -20.7 dB (9.8 dB), respectively. Median (interquartile range) VCM1 scores were 35 (19-46), with higher scores indicating greater impairment. PHQ-4 results indicated 3/9 participants with severe and 1/9 with mild depression. Thematic analysis of open-ended responses revealed that most (7/9) identified family as their primary support. Requests for increased education and psychological care were common (5/9), alongside frequent reports of loss of independence (6/9) and fear of further vision deterioration (3/9).

Conclusions:

Early findings highlight the profound psychosocial impact of vision loss in AION including emotional distress and requests for psychological support. Ongoing recruitment will expand this analysis.

References: None provided.

Keywords: Optic neuropathy, Perimetry, Visual fields

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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RNASEH2B as genetic risk factor in dominant and sporadic optic disc drusen

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Introduction:

Optic disc drusen (ODD) are calcified, acellular deposits that accumulate in the anterior optic nerve, commonly in crowded optic discs and leading to vision loss (1). Family members of patients with ODD have a 10 times higher risk of having ODD than the general population, consistent with genetic risk factors (2-4). The molecular mechanisms driving ODD formation are unknown.

Methods:

We performed whole genome sequencing and analyzed structural dynamics of the wild-type and mutant RNASEH2A–B–C complex using RMSD, RMSF, MM/PBSA, and PCA analyses. Using control and dominant ODD fibroblasts, we examined gene and protein expressions of the RNASEH2A–B–C complex and calcification-associated molecules by RNA sequencing, western blotting, and immunofluorescence.

Results:

We identified 10 ODD patients (4 from 3-generations of a dominant ODD family, 6 sporadic) with heterozygous missense variants in RNASEH2B (Ribonuclease H2, subunit B), a member of the trimeric RNASEH2A–B–C complex involved in degradation of RNA/DNA hybrids and removal of misincorporated ribonucleotides. Nine of ten patients have c.529G>A (p.A177T), the most common pathological variant in Aicardi–Goutières syndrome (AGS), an autosomal recessive disease associated with brain calcification, inflammation, and altered type I interferon signaling (5). In silico analysis of the wildtype and mutant reveals that the RNASEH2B A177T mutation increases deviation and conformational flexibility in the RNASEH2 complex, requiring greater energy for stabilization. Compared with controls, dominant ODD fibroblast exhibits reduced RNASEH2A–B–C expression despite dramatic upregulation of the RNA levels, consistent with a post-transcriptional mechanism or translational dysregulation. Dominant ODD fibroblast shows enhanced hydroxyapatite deposition and upregulation of genes involved in extracellular matrix deposition, inflammatory activation (STING–TBK1–IRF3 axis), and calcium signaling (WNT4, PLCE1).

Conclusions:

RNASEH2B dysfunction is a genetic risk factor for ODD, driving aberrant extracellular matrix remodeling, inflammation, and calcification in the anterior optic nerve compartment, thereby promoting drusen formation and axonal injury. ODD fibroblasts are excellent cellular models for testing treatment of ODD.

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Keywords: Optic neuropathy, Genetic disease

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Optic Nerve Calcification and Altered Plasma Lipidomics in Non-Arteritic Anterior Ischemic Optic Neuropathy

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Introduction:

Non-arteritic anterior ischemic optic neuropathy (NAION) is the most common acute optic neuropathy in adults older than 50. Optic nerve calcification, in the form of optic disc drusen (ODD), is an independent risk factor for NAION, especially in younger patients. Hyperreflective lines, possible precursors to ODD, are sometimes seen on imaging in NAION patients and may represent small areas of ectopic calcification. We performed a retrospective analysis to compare clinical outcomes and plasma lipidomics in NAION patients with and without imaging features of calcification.

Methods:

We analyzed demographic and neuro-ophthalmic assessments in human NAION eyes with and without calcification features on enhanced depth imaging-optical coherence tomography (EDI-OCT). A subset of patients underwent LC/MS-based plasma lipidomic analysis.

Results:

We performed a retrospective analysis of patients with NAION (N=52), ODD-associated NAION (ODD-AION, N=16), and hyperreflective lines associated with NAION (HRL-AION, N=18). HRL-AION patients had similar demographics to NAION patients, with 67% males, while ODD-AION patients were 56% female. ODD-AION (44%) was more likely to occur in patients younger than 50 compared to HRL-AION (11%) and NAION (2%, $p < 0.001$). Final logMAR visual acuity was worse in NAION [0.54 (0.18, 1.48)] compared with ODD-AION [0.18 (0.00, 0.70), $p < 0.05$] and HRL-AION [0.48 (0.10, 0.80), $p > 0.05$]. Comparison of lipidomic profiles of the three groups with ODD plasma showed significantly high levels of lipid species from classes like Acylcarnitines, Ceramides, and Lysophospholipids. Although the three groups had overlapping lipid profiles on principal component analysis, lipid levels were relatively higher in the NAION group.

Conclusions:

Patients with ODD-AION are more likely to be females, have a younger onset of NAION, with better visual acuity. HRL-AION patients are more similar to NAION, with male predominance and older onset of disease. Our study highlights the heterogeneity of NAION and the importance of lipid dysregulation as a major factor regardless of calcification features.

References: Malmqvist L, Li XQ, Hansen MH, et al. Progression Over 5 Years of Prelaminar Hyperreflective Lines to Optic Disc Drusen in the Copenhagen Child Cohort 2000 Eye Study. *J Neuroophthalmol.* 2020;40(3):315-321.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Optic neuropathy, Vascular disorders, Stroke

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Risk of Nonarteritic Anterior Ischemic Optic Neuropathy in GLP-1 Agonist Users and Associated Social Determinants of Health in the NIH All of Us Research Program

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Introduction:

Nonarteritic anterior ischemic optic neuropathy (NAION) causes irreversible vision loss and has been associated with glucagon-like peptide-1 (GLP-1) agonists (1,2). We assessed NAION risk following GLP-1 exposure in patients with type 2 diabetes mellitus (T2DM) or obesity.

Methods:

We retrospectively identified 371,398 adults with EHR data in the NIH All of Us Research Program. GLP-1 users with T2DM (14,930) and/or obesity (16,279) were propensity score-matched 1:1 by age, race, ethnicity, and comorbidities to non-GLP-1 antidiabetic (43,672) and anti-obesity (23,708) medication users. Patients with prior NAION or temporal arteritis were excluded. Cox regression estimated 5-year hazard ratios (HRs); odds ratios (ORs) assessed individual medication risk. Chi-square with post hoc analysis examined social determinants of health (SDOH) from standardized patient surveys.

Results:

Among 28,000 matched patients with T2DM, 23 (0.16%) and 28 (0.20%) NAION cases occurred in the GLP-1 and non-GLP-1 cohorts, respectively. In 28,000 matched patients with obesity, 25 (0.18%) and 30 (0.21%) cases occurred in the GLP-1 and non-GLP-1 cohorts, respectively. GLP-1 agonists overall conferred no increased risk of NAION (T2DM: HR 0.97, $P = 0.82$; obesity: HR 0.95, $P = 0.49$). In sub-group analysis, dulaglutide showed lower risk (T2DM: OR 0.11; obesity: OR 0.15; $P < 0.05$); albiglutide (T2DM: OR 2.41) and exenatide (obesity: OR 1.85) showed higher risk ($P < 0.05$). Mean BMI (37.53 vs 37.33 kg/m²) and HbA1c (8.59% vs 8.06%) were similar among GLP-1 users with or without NAION, respectively ($P > 0.05$). NAION occurred more in individuals with lower income (<\$10,000/year) and fewer than four eye doctor visits ($P < 0.05$).

Conclusions:

We found no increased risk of NAION with GLP-1 use, consistent with some prior research (3). However, increased risk from albiglutide and exenatide warrants investigation. Poor SDOH correlated with greater NAION occurrence, supporting counseling and baseline risk assessment when initiating GLP-1 therapy in socioeconomically disadvantaged patients.

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Keywords: Optic neuropathy, Vascular disorders

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Optic Disc Edema–Associated Secondary Central Retinal Vein Occlusion: A Case Series and Exploratory Analysis

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Introduction:

Severe optic disc edema (ODE) can mechanically impede central retinal venous outflow, potentially leading to central retinal vein occlusion (CRVO). Distinguishing ODE-associated venous changes from primary CRVO with secondary disc edema is challenging.

Methods:

We retrospectively reviewed 2,931 patients with ODE, identifying 432 eyes (14.7%) with moderate-to-severe swelling (RNFL ≥ 150 μm). A subset of 12 patients with ODE followed by CRVO signs ($n=7$) or supportive/ambiguous findings ($n=5$) was analyzed. Data included demographics, RNFL thickness, optic disc features, systemic comorbidities, and temporal development of venous changes. Exploratory case-control analyses compared patients with ODE-associated CRVO to matched controls using Fisher's exact and Wilcoxon rank-sum tests.

Results:

Among primary ODE cases, median age was 34 years (IQR 22.5–41), 92% were female, and median RNFL thickness was 186 μm (IQR 167–247). Etiologies included idiopathic intracranial hypertension, inflammatory optic neuropathies, and chronic papilledema. Secondary CRVO was uncommon, more frequent in females (11/270, 4.1%) than males (1/133, 0.8%), though not statistically significant (Fisher's exact $p = 0.114$, OR 0.18, 95% CI 0.004–1.25), likely due to small event numbers. Median age and RNFL did not differ significantly between eyes with versus without secondary CRVO (Wilcoxon $p = 0.108$ and 0.625). Exploratory case-control comparisons similarly showed no significant differences in age, sex, or RNFL.

Conclusions:

Severe ODE can mechanically contribute to retinal venous congestion and CRVO-like changes, with occurrences trending higher among younger females, although differences were not statistically significant. No other predictors were identified, likely reflecting small sample size and event rarity. This series represents the largest descriptive collection of ODE-associated venous compromise to date and supports the hypothesis that disc swelling alone may precipitate secondary venous obstruction, highlighting the need for prospective studies to clarify risk factors and optimize management.

References: None provided.

Keywords: Optic neuropathy, Vascular disorders, High intracranial pressure/headache, Optic neuritis, Retina

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Grant Support: None.

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Seeing Through Divides: Geographic, Socioeconomic, and State-Level Disparities in Optic Neuritis Patients at a South Indian Tertiary Center

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Introduction:

Optic neuritis (ON) is an acute inflammatory optic neuropathy commonly associated with autoimmune disorders including NMOSD, MOGAD, and ANA disorders. While Western cohorts dominate the literature, South Asian populations exhibit distinct disease patterns due to regional environmental and socioeconomic factors. Few studies address regional disparities within South Asia across urban-rural and socioeconomic strata, limiting targeted interventions. This study examines these disparities to inform equitable healthcare delivery.

Methods:

A retrospective cross-sectional analysis of 119 ON patients from October 2024 to June 2025 was conducted at a tertiary eye care center. Demographics including age, gender, state of origin, urban/rural classification per government database protocols, and socioeconomic status (SES) approximated through paid versus free treatment were collected. Clinical features including ON type and laterality were analyzed using chi-square tests and descriptive statistics.

Results:

Of 119 patients (mean age 43.0 years), 72% were from Tamil Nadu and 28% from Kerala. Geographic analysis revealed 59% rural versus 41% urban patients ($p < 0.01$), contrary to hypothesized urban predominance. Papillitis was most common (48%), followed by retrobulbar neuritis (38%) and other variants (14%), with similar distributions across states suggesting comparable disease manifestation. Socioeconomic analysis demonstrated significant disparity: 85% received paid treatment versus 15% free treatment ($p < 0.001$), suggesting substantial barriers to accessing subsidized care despite institutional availability. Unilateral involvement (LE 44%, RE 35%) predominated over bilateral presentation (21%). No significant age differences emerged between urban/rural or state groups.

Conclusions:

Rural patients and those utilizing paid services were overrepresented, highlighting potential healthcare access inequities and referral patterns. The rural predominance warrants targeted awareness programs and screening in rural communities where disease burden appears concentrated. The socioeconomic disparity despite free treatment availability requires investigation to address systemic barriers. These findings provide critical data for developing geographically-targeted and economically-sensitive interventions to improve early ON diagnosis and health equity in South India.

References: None provided.

Keywords: Optic neuritis

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Grant Support: None.

Contact Information: None provided.

Clinical and Systemic Risk Profiles in Non-Arteritic Anterior Ischemic Optic Neuropathy With and Without Glucagon-Like Peptide-1 Receptor Agonist Exposure: A Retrospective Cohort Analysis

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Introduction:

The relationship between glucagon-like peptide-1 receptor agonist (GLP-1RA) exposure and non-arteritic anterior ischemic optic neuropathy (NAION) remains uncertain. This study aimed to characterize the clinical profile of NAION cases with and without GLP-1RA exposure, including the association of systemic comorbidities.

Methods:

This was a retrospective cohort study at a single tertiary care center. NAION cases were identified by electronic health record search and confirmed by two neuro-ophthalmologists. Patients with NAION during GLP-1RA use were compared to NAION controls without GLP-1RA use. Patient demographics, vascular risk factors, diabetes status, medication use, and visual outcomes were analyzed. Quantitative comparisons were performed using appropriate statistical tests.

Results:

Among 24 GLP-1RA-exposed and 89 control NAION cases, groups were similar in age (61.8 ± 11.0 vs 62.1 ± 12.5 years), race (91.7% vs 94.4% White), and ethnicity (95.8% vs 96.6% non-Hispanic). The GLP-1RA group had more females (54.2% vs 28.1%, $p=0.027$). GLP-1RA-exposed patients had higher rates of diabetes (83.4% vs 31.5%, $p < 0.001$), shorter diabetes duration, and greater use of antidiabetic, antihypertensive, and lipid-lowering agents. Systolic blood pressure and hemoglobin A1c were higher in the GLP-1RA group. No significant differences were found in history of NAION, bilaterality, diabetic retinopathy, tobacco or alcohol use, or visual outcomes.

Conclusions:

NAION patients exposed to GLP-1RA have a greater burden of systemic vascular comorbidities and more advanced diabetes, which may confound the association between GLP-1RA use and NAION risk. Careful adjustment for these factors is necessary in future studies to clarify the independent effect of GLP-1RA exposure on NAION risk.

References: None provided.

Keywords: Optic neuropathy, Vascular disorders, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Rapid Metabolic Shifts Prior to NAION Among GLP-1RA-Exposed Patients: A Retrospective Cohort Analysis

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Introduction:

Conflicting evidence of an association between non-arteritic anterior ischemic optic neuropathy (NAION) and glucagon-like peptide-1 receptor agonists (GLP-1RAs) has been presented. Rapid metabolic changes (body weight, blood glucose, blood pressure) secondary to GLP-1RAs are a plausible mechanism of NAION risk mediation. This study aimed to characterize peri-NAION metabolic changes among GLP-1RA-exposed and control patients.

Methods:

A retrospective cohort analysis was performed at a tertiary care center, and NAION cases were confirmed by two neuro-ophthalmologists. For each NAION event, data included body mass index (BMI) and weight, blood pressure, symptomatic hypotension, and hemoglobin A1c (A1c) values in the 3-12 months prior. GLP-1RA-exposed cases were compared to controls using appropriate statistical tests.

Results:

A total of 25 GLP-1RA-exposed and 89 control NAION cases were analyzed. GLP-1RA cases had higher baseline BMI (42.0 vs. 34.0, $p = 0.041$), and while both GLP-1RA-exposed and control NAION cases experienced weight loss in the three months prior to NAION, the reduction was greater in the GLP-1RA group (mean -6.4 lb vs -2.1 lb, $p = 0.023$). GLP-1RA cases were more likely to experience symptomatic hypotension (17% vs 4%, $p=0.049$). A1c at NAION onset was higher in GLP-1RA cases (6.7 vs. 5.8, $p < 0.001$), as was prior A1c (7.8 vs 6.3, $p = 0.006$). A1c reduction after GLP-1RA initiation was -1.4, with median time of initiation to NAION of 5.3 months.

Conclusions:

NAION cases exposed to GLP-1RAs demonstrate higher BMI but more pronounced peri-event weight loss, increased symptomatic hypotension, and greater glycemic improvement compared to controls. These findings suggest that rapid metabolic and hemodynamic changes may contribute to NAION risk in GLP-1RA users, warranting close monitoring in high-risk patients. Further research is needed to clarify causality and guide risk stratification in this population.

References: None provided.

Keywords: Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Equivocal or Atypical Temporal Artery Biopsy Results Require Integration of Histopathology and Multimodal (Including Clinical) Correlation in Neuro-Ophthalmology

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Introduction:

Indeterminate temporal artery biopsies (TABs) remain a diagnostic challenge in neuro-ophthalmology. Hedges et al. (1983) showed that a “negative” TAB does not exclude giant cell arteritis (GCA), introducing skip lesions. Later studies (McDonnell, 1986; Stacy, 2011) found “healed arteritis” overlaps with arterial injury from other causes. The 2023 Society for Cardiovascular Pathology Consensus (Nair et al.) standardized TAB interpretation but offers limited neuro-ophthalmic guidance. Persistent biopsy-negative cases highlight the need for integrated histopathologic, imaging, and clinical correlation.

Description of Cases:

A review of the literature underscores persistent uncertainty in interpreting temporal artery biopsies (TABs) showing equivocal or healing changes. Active arteritis requires inflammation of the arterial media, whereas adventitial or perivascular inflammation is nonspecific and warrants deeper sectioning to exclude skip lesions. Consensus guidelines redefined “healed arteritis” as “healed arterial injury,” discouraged “temporal arteritis,” and reaffirmed that diagnosis remains morphologic. Giant cells, especially in amyloidosis or calcific arteriopathy, are insufficient without medial inflammation. These refinements clarify diagnostic boundaries but have limited impact in neuro-ophthalmology, where vision loss often coincides with healed or indeterminate biopsies. Advances in vascular ultrasound bridge pathology and clinical assessment: the halo and compression signs indicate active arteritis, whereas persistent intima–media thickening or residual halos suggest healed injury. Integrated with predictors such as CRP elevation, jaw claudication, and ocular ischemia, these findings place TAB results within a continuum of vascular inflammation, yet current algorithms still define only active arteritis, leaving healed lesions unclassified.

Conclusions, including unique features of the case:

Equivocal findings such as periadventitial inflammation and healing changes on TABs represent stages within an evolving spectrum of arterial injury rather than fixed diagnostic categories, overlapping with other diseases. Integrating histopathology with vascular imaging and clinical predictors reframes these features as dynamic markers of disease activity. Recognizing their diagnostic and prognostic value could guide future consensus refinements and support histologic stratification and individualized management in vision-threatening GCA.

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References: None provided.

Keywords: Optic neuropathy, Vascular disorders

Financial Disclosures: J. Tatiana Hathaway; Anna Stagner; Joseph Rizzo: consultant to Life Biosciences

Grant Support: None.

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Hyperpermeability of the Inner Blood-Retina Barrier in Visual Snow Syndrome

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Introduction:

Visual snow syndrome (VSS) is attributed to aberrant visual processing, though the exact mechanisms remain unclear. The potential involvement of inner blood-retinal barrier (iBRB) dysfunction in VSS has not yet been investigated.

Methods:

Twelve participants with VSS underwent fluorescein fundus angiography (FFA) to assess the iBRB integrity. Subclinical extravasation of sodium fluorescein during FFA was quantified by measuring pixel intensity within the retinal parenchyma. Increased pixel intensity, in the context of an intact choroid and iBRB was interpreted as indicating higher iBRB permeability. Cumulative and time-specific median fluorescein signal intensities in the VSS group were compared to those of healthy young adult controls. Additionally, most VSS participants underwent MRI brain scans with gadolinium contrast to assess blood-brain barrier (BBB) integrity.

Results:

No focal fluorescein leakage was observed on FFA in any participant. The cumulative median fluorescein intensity was higher in VSS participants across all ETDRS regions compared to controls, including a 59 % increase in the fovea ($p < 0.0001$), 52 % in the parafovea ($p < 0.0001$), and 48 % in the perifovea ($p < 0.0001$). MRI scans revealed no contrast leakage, confirming BBB integrity in all participants.

Conclusions:

Quantitative FFA analysis revealed increased subclinical fluorescein extravasation in the macula of VSS participants. These findings suggest increased iBRB permeability in VSS, which may contribute to its pathophysiology. Further large-scale studies are needed to validate this hypothesis.

References: None provided.

Keywords: Non-organic visual disorders, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)

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Grant Support: None.

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Handheld Photopic ERG Reveals Structure–Function Coupling Between PhNR and GCIPL Thickness in Chronic Optic Neuropathy

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Introduction:

The photopic negative response (PhNR) of the electroretinogram reflects retinal ganglion cell (RGC) activity, yet its quantitative relationship with structural measures remains unclear. This study evaluated structure–function coupling between handheld PhNR parameters and optical coherence tomography (OCT)–derived metrics in chronic non-glaucomatous optic neuropathy (ON).

Methods:

In this retrospective paired-eye study, 54 eyes of 27 patients with unilateral ON were analyzed. PhNR parameters obtained with a portable RETeval™ device—PhNR72 amplitude, PhNR minimum amplitude, and W-ratio—were correlated with ganglion cell–inner plexiform layer (GCIPL) and retinal nerve fiber layer (RNFL) thickness, and visual-field indices (VFI, MD, PSD). Linear mixed-effects models with subject-specific random intercepts accounted for inter-eye correlation. False-discovery-rate (FDR) correction (row-wise and global) controlled for multiple comparisons.

Results:

Row-wise FDR identified significant associations between W-ratio and GCIPL average, superotemporal, and inferotemporal thickness, and between PhNR minimum amplitude and inferotemporal GCIPL thickness (all $p < 0.05$). After global FDR correction, only the W-ratio–inferotemporal GCIPL relationship remained significant ($p < 0.01$). In contrast, no PhNR parameters correlated with visual-field indices, and PhNR–RNFL associations were observed only in control but not ON eyes, suggesting decoupling once axonal loss stabilized. β coefficients were consistently larger in ON eyes, indicating enhanced PhNR sensitivity to GCIPL thinning in affected eyes.

Conclusions:

Handheld photopic ERG provides a reproducible and objective measure of RGC function in chronic optic neuropathy. The selective PhNR–GCIPL coupling, together with the absence of RNFL and field-level correlations, supports PhNR—particularly the W-ratio—as a structurally anchored biomarker of RGC somal integrity. Portable ERG thus serves as a practical adjunct to OCT for accessible, quantitative evaluation of optic nerve function and disease progression.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Optic neuropathy, Optic neuritis

Financial Disclosures: The authors had no disclosures.

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Contact Information: None provided.

Asymmetric Papilledema in Idiopathic Intracranial Hypertension: Exploring Anatomical and Venous Correlates

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Introduction:

Idiopathic intracranial hypertension (IIH) produces a diffuse elevation in intracranial pressure, yet the resulting papilledema is frequently asymmetric. The mechanisms underlying this asymmetry are not clear. Prior studies suggesting anatomic or vascular asymmetries have been small and inconclusive. This study evaluates bony optic canal size and transverse venous sinus caliber as contributors to asymmetric papilledema.

Methods:

A retrospective chart review was used to identify patients diagnosed with IIH. Symmetry of papilledema was quantified using retinal nerve fiber layer (RNFL) thickness measured by optical coherence tomography (OCT). Bony canal size was measured on coronal CT head sections. Transverse venous sinus stenosis was assessed using the maximum stenosis score (MSS) found on MRV head/MRI brain. The degree of stenosis was scored from 0 (complete stenosis) to 4 (no stenosis).

Results:

88 patients with IIH were included. 71 demonstrated asymmetric papilledema. MRV/MRI data were available for 43 patients, and CT measurements for 22 patients. Correlations were evaluated using Spearman's tests. Right MSS and right RNFL thickness showed a significant negative correlation ($\rho = -0.314$, $P = 0.040$), but the left did not ($\rho = -0.08$, $P = 0.578$). Interestingly, the left MSS had a significant correlation with right RNFL thickness ($\rho = -0.339$, $P = 0.026$), but there was none between the right MSS and left RNFL thickness ($\rho = -0.258$, $P = 0.094$), though a negative trend was detected. Comparing the bony optic canal and the RNFL thickness showed no significant correlation (OD: $\rho = 0.168$, $P = 0.454$, and OS: $\rho = 0.09$, $P = 0.69$).

Conclusions:

A negative correlation was observed between the right RNFL thickness and right MSS, whereas no such correlation was found on the left side. Additionally, there was no correlation between RNFL thickness and the bony optic canal on either side. Further studies are warranted to elucidate why a negative correlation exists between the right RNFL thickness and right MSS but not on the left.

References: None provided.

Keywords: High intracranial pressure/headache

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Idiopathic Intracranial Hypertension Patients Have an Earlier Mortality Rate Compared to Controls

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Introduction:

Idiopathic intracranial hypertension (IIH) is now being considered a neuro-metabolic disorder, due to its high association with obesity, androgen dysregulation and increased cardiovascular incidence. Patients with metabolic disorder have also been shown to have an earlier mortality rate. Due to these findings, it is necessary to evaluate if IIH patients also experience an earlier mortality compared to controls.

Methods:

Patients with an ICD code for IIH (ICD9 348.2, ICD10G93.2) who had died were compared to controls who had died and matched 5:1 based on body-mass index, sex, and race. Patients were excluded if they had any secondary sign of intracranial hypertension including cerebral thromboses and brain tumors. Kaplan Meier analysis was used to evaluate differences in time to death. Causes of death were also evaluated.

Results:

Of the 3,412 IIH patients and 21,512 controls in the base population, 35 IIH patients and 1,418 controls were deceased. Before matching, IIH patients died at an average age of 46.34 (SD 12.27), had an average BMI of 30.33 (SD 7.56), and were 94% female. Controls had an average age of 60.48 average BMI of 29.17 (SD 3.95) and were 70% female. Greedy matching was successful with standardized differences < 0.1. Patients with IIH had an increased risk of early mortality at 2.98 (95% CI 2.04, 4.34). The Kaplan Meier curve showed distinct differences by 50 years of age ($p < 0.0001$). When evaluating cause of death intentional self-harm (hazard ratio 3.64, 95% CI 2.09, 6.71), heart disease (HR 2.91, 95% CI 1.51, 5.75), and endocrine disorders (HR 2.48, 95% CI 1.14, 5.48) all had increased rates among IIH patients compared to controls.

Conclusions:

IIH patients had an earlier mortality rate than controls where IIH patients had increased hazard ratios for suicidality, heart disease, and endocrine disorders.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Pseudotumor cerebri, Optic neuropathy

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Diagnosis of High Intra-cranial Pressure using Retinal Images Excluding the Optic Nerve Head

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Introduction:

While papilledema is the most prominent ophthalmic sign of raised intracranial pressure (ICP), non-optic disc features such as retinal vessel diameter and tortuosity may also reflect high ICP. Machine learning (ML) approaches have been applied for evaluation of papilledema based on optic disc photos. The current study aims to determine the role of non-optic nerve head (ONH) changes in the diagnosis of high ICP by evaluating the performance of a ML model for classification of high vs. normal ICP using retinal images with the ONH excluded.

Methods:

Classification of ICP status was performed using widefield macula-centered retinal images of subjects with idiopathic intracranial hypertension (IIH) and current high ICP (32 subjects, 70 images), and subjects seen for hydroxychloroquine screening (serving as controls, 31 subjects, 62 images). Images were pre-processed to generate ONH-masked and ONH-unmasked retinal images which were analyzed separately. The EfficientNet-B0 model was used for training, validation, and testing of images with a distribution of 70%, 10%, and 20%, respectively. Two neuro-ophthalmologists (graders), who were masked to the clinical diagnosis and model results, independently classified test images as high ICP or control.

Results:

For the ONH-unmasked images, classification accuracies of the DL model, grader 1, and grader 2 were not significantly different (83%, 93%, and 86%, $p=0.38$). For the ONH-masked images, classification accuracies of the model, grader 1, and grader 2 were also not significantly different (79%, 66%, and 76%, $p=0.29$). ONH masking did not significantly impact the performance of the DL model ($p=1.0$) or grader 2 ($p=0.38$), but reduced the performance of grader 1 ($p=0.02$).

Conclusions:

Both expert graders and a DL model demonstrated high performance for classifying elevated and normal ICP retinal images with or without masking of the optic nerve head. This confirms the potential of non-ONH retinal features for diagnosis of high ICP.

References: None provided.

Keywords: High intracranial pressure/headache, Pseudotumor cerebri

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Familial Standardized Incidence Ratio in Idiopathic Intracranial Hypertension

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Introduction:

Idiopathic intracranial hypertension (IIH) is characterized by elevated intracranial pressure of uncertain etiology. The diagnostic criteria of IIH includes raised intracranial pressure, with normal cerebrospinal fluid (CSF) and no other underlying causative etiology. IIH is usually sporadic, without genetic cause discovered with genome-wide association studies (GWAS). However, other methods like the well-described familial standardized incidence ratio (FSIR) allow for evaluation of risk of IIH in members of an individual's family.

Methods:

Databases including the Utah Population Database (UPDB), University of Utah Health (UHealth) Enterprise Data Warehouse (EDW), and Genetic Initiative in Neuro-Ophthalmic Conditions (GINOC) were queried for individuals seen within the UHealth system at our facility from 1995 to 2023 and patients registered in the state of Utah. Patient records were reviewed to confirm/refute a diagnosis of IIH.

Results:

Ten pedigrees were identified as having a high FSIR for familial patients with IIH. A total of 109 subjects were identified as having IIH. Among these 10 pedigrees, the FSIR ranged from 1.87 to 4.91 with significant p-values ranging from 0.0005 to 0.0171. A detailed chart review was performed by a trained neuro-ophthalmologist to confirm IIH diagnoses. Of the 92 patients whose health records were available for review, 57% were confirmed to have a diagnosis of IIH. Compared to 25 other large database studies, this is within range of diagnostic coding accuracy (50.5-97.8%).

Conclusions:

Within a large database study, using familial standardized incidence ratio presents a novel way of analyzing a familial component of idiopathic intracranial hypertension.

References: None provided.

Keywords: High intracranial pressure/headache, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Pseudotumor Cerebri and Tetracycline Antibiotic Use: A Matched Analysis

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Introduction:

Tetracycline antibiotics have long been considered a risk factor for the development of pseudotumor cerebri (PTC). That said, causation has not been established, and data comparing patients with tetracycline-associated PTC to cases without tetracycline use is limited.(1–3) The present study will describe a sample of patients with a PTC diagnosis temporally associated with tetracycline use and compare presenting clinical features, treatment, and visual outcomes to matched controls.

Methods:

ICD-10 codes were used to identify patients with PTC and a history of tetracycline antibiotic use at a tertiary care center from 1/1/2013 to 1/1/2025. Patients who used a tetracycline antibiotic within 90 days prior to presentation were included in the study. These patients will be matched by age, gender, and race to control patients with a diagnosis of PTC and no prior exposure to tetracycline antibiotics. Demographic data, presenting clinical features, initial treatment, and visual outcomes will be compared between cases and controls.

Results:

Twenty patients met study criteria. The majority of cases were female (95.0%) and white (60.0%) with a mean age of 23.0 ± 8.6 years at diagnosis. Mean duration of tetracycline use prior to presentation was 155 days. Median papilledema grade at presentation was 2 [1-3]. All patients discontinued tetracyclines within 60 days of presentation, and the majority (85.0%) were treated initially with ICP-lowering medications. The majority of patients (77.8%) had complete resolution of their papilledema with a mean time to resolution of 335 ± 314 days. Additional analyses will compare demographics, presenting and final visual features (visual acuity, papilledema grade, OCT data, VF data), and clinical course between these cases and matched controls.

Conclusions:

This study will further characterize tetracycline-associated PTC and be the first to perform matched analyses of these cases to non-tetracycline exposed matched controls.

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Keywords: Pseudotumor cerebri

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Rethinking Lumbar Punctures In Idiopathic Intracranial Hypertension: An Algorithm

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Introduction:

Lumbar Puncture (LP) is standard to confirm elevated intracranial pressure (ICP) in Idiopathic Intracranial Hypertension (IIH). There is controversy over the necessity of LP in typical adult IIH presentations. Many patients present with clear clinical and MRI evidence of IIH. Paradoxically, treatment is often initiated even when the initial opening pressure is normal, underscoring if LP truly changes management. We sought to explore if an algorithm could assist in decision-making around LP use in typical IIH cases.

Methods:

A retrospective analysis of 65 consecutive IIH clinic cases was conducted. The literature review identified 292 additional cases meeting inclusion criteria. We performed a meta-analysis of these 357 cases to create an algorithm to determine when LP was absolutely needed and could otherwise be avoided.

Results:

Our 65 clinic cases all underwent formal neuro-ophthalmologic examination including OCT, Humphrey fields and MRI scanning. LP was performed in 62/65 cases. LP altered diagnosis or long-term treatment in 0/62. 2 of 62 cases (LP performed) involved atypical features (both males, one with unilateral disc edema and one with failure to improve with medication). The three cases without an LP improved with treatment. In the 292 literature cases, 68 had no LP and no issues in follow-up. In the remaining 224, LP did not change the diagnosis. We developed a clinical scoring algorithm to quantify levels of suspicion for IIH and standardize decision-making. The algorithm integrated objective criteria (gender, papilledema, MRI findings, BMI, visual field loss, and medication use) to guide when LP may be safely avoided.

Conclusions:

A structured, scored framework to identify when LPs are truly needed in adult IIH cases was created. This algorithm could safely reduce LP use in typical IIH cases. Avoiding LP, although a sea-change in IIH management, could promote diagnostic efficiency, reduce unnecessary procedures, speed treatment, and prioritize patient comfort.

References: 1. Barkatullah, Leishangthem, Moss; MRI findings as markers of idiopathic intracranial hypertension, *Curr Opin Neurol*, 34, 75-83, 2021. 2. Beier, Habil, Korsbæk, Bsteh, et al.; Magnetic Resonance Imaging Signs of Idiopathic Intracranial Hypertension, *JAMA Netw Open*, 7, e2420138, 2024 3. Friedman, Jacobson; Diagnostic criteria for idiopathic intracranial hypertension, *Neurology*, 59, 1492-1495, 2002. 4. Horev, Eliav, Sherer, Biederko, et al.; Radiological signs supporting idiopathic intracranial hypertension in symptomatic patients with lumbar puncture opening pressure < 250 mm, *Scientific Reports*, 14, 19450, 2024. 5. Margolis, DeBusk, Moster, Falardeau, et al.; Lumbar Puncture for Diagnosis of Idiopathic Intracranial Hypertension in Typical Patients, *J Neuroophthalmol*, 41, 375-378, 2021 6. Moss, Margolin, Lee, Van Stavern; Should lumbar puncture be required to diagnose every patient with Idiopathic Intracranial Hypertension?, *J Neuroophthalmol*, 41, 379-384, 2021. 7. Vosoughi, Margolin, Micieli; Can Lumbar Puncture Be Safely Deferred in Patients With Mild Presumed Idiopathic Intracranial Hypertension?, *J Neuroophthalmol*, 42, 505-508, 2022.

Keywords: Pseudotumor cerebri, High intracranial pressure/headache

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Updates in Glymphatic Imaging in Idiopathic Intracranial Hypertension

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Introduction:

Abnormal indices of glymphatic transit (ALPS-indices) in idiopathic intracranial hypertension (IIH) were described at NANOS and in the JNO in 2025. We describe early results reflecting expansion of our existing cohorts, inclusion of participants with secondary intracranial hypertension (SIH), and incorporation of measures of cortical-white matter fluid distribution.

Methods:

Diffusion-derived free water (FW) and ALPS-indices were derived from MRIs of 16 previously unstudied individuals with chronic untreated IIH, SIH, and healthy controls. Gray and white matter FW values were used to compute a Fluid Distribution Index (FDI = GM FW – WM FW). Glymphatic transport efficacy was expressed as the ALPS/FDI ratio, a normalized measure of perivascular diffusion relative to interstitial fluid redistribution. ALPS-indices in newly studied participants were compared to those derived from our existing cohorts.

Results:

Four participants with SIH (all with > Frisen 2 papilledema, ICP >25cm H₂O, and normal brain parenchyma), 3 with chronic (6+ months' duration) untreated IIH, and 8 healthy controls were newly studied. FDI differed across groups ($p=0.05$) with an increased FDI and reduced ALPS/FDI in those with chronic IIH, suggesting cortical fluid accumulation and diminished glymphatic efficiency despite high ALPS-indices. The mean ALPS-index among SIH participants was 1.56 (range 1.38-1.76), which differed from those among our previously-described untreated IIH cohorts with 6+ months' (mean 1.77, $p=0.017$) and < 6 months' (mean 1.26, $p=0.006$) disease duration.

Conclusions:

ALPS/FDI ratios putatively serve as quantitative diffusion MRI markers of fluid redistribution and glymphatic transport efficacy; their reduction in participants with chronic untreated IIH may support our prior hypotheses of homeostatic changes accounting for the duration-dependent evolution in ALPS-indices in individuals with untreated IIH. Additionally, differentiation between individuals with SIH and IIH may offer biologically and diagnostically useful insights. We anticipate expansion of the populations described above and additional ALPS/FDI data by the 2026 NANOS meeting.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), High intracranial pressure/headache, Neuroimaging, Pseudotumor cerebri

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Time from Referral to Surgical Intervention and Outcomes in Idiopathic Intracranial Hypertension

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Introduction:

Idiopathic intracranial hypertension (IIH) is characterized by elevated intracranial pressure without an identifiable cause, and may lead to irreversible vision loss. Surgical treatment options include venous sinus stenting (VSS), optic nerve sheath fenestration (ONSF), and ventriculoperitoneal (VP) shunting. This study evaluated time from referral to surgical intervention, causes of delay, and postoperative visual outcomes across procedures.

Methods:

A retrospective cohort study was conducted at a tertiary academic center from 2014–2025. Patients ≥ 18 years with confirmed IIH who underwent VSS, ONSF, or VP shunt were included. Exclusion criteria included secondary causes of increased intracranial pressure or insufficient documentation. Primary outcome was time from surgical referral to intervention; secondary outcomes included causes of delay, complication rates, reoperations, medication dependence, and visual outcomes at 6 months.

Results:

605 patients were analyzed and 68 (83.8% female, mean age 34.3 ± 9.7 years) were included in the study. 37 underwent VSS, 18 VP shunt, and 13 ONSF. Explicit surgical delays occurred in 13.2%, most often from patient preference. ONSF patients more frequently required reoperation than VSS ($p = 0.0025$) or VP shunt ($p = 0.0023$). Symptom resolution occurred in 66.1% ($p = 0.27$) with no difference among procedures. Persistent medication use was higher in ONSF (66.7%) than VSS (31.4%) or VP shunt (6.2%) ($p = 0.0031$). Mean deviation improved from baseline (OD $p = 0.026$, OS $p = 0.015$), driven by better outcomes in VSS versus VP shunt ($p = 0.008$).

Conclusions:

Explicit surgical delays were uncommon and largely patient-driven. ONSF and inpatient referrals had shorter timelines. VSS achieved superior visual field outcomes than VP shunt, while ONSF had higher reoperation and medication requirements than VSS and VP shunt.

References: None provided.

Keywords: High intracranial pressure/headache, Pseudotumor cerebri, Interventional neuroradiology

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Seasonal Variation of Idiopathic Intracranial Hypertension

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Introduction:

Idiopathic Intracranial Hypertension (IIH), also known as pseudotumor cerebri, It is diagnosed far more frequently among women and has been associated with obesity in females of childbearing age. A potential connection has been suggested between pediatric IIH development and autumn-winter seasons. The relationship between adult IIH and seasonal variations, however, remains unclear. Our purpose was to explore such a potential correlation.

Methods:

A retrospect review of medical records was conducted for all patients diagnosed with IIH at the Neuro-Ophthalmology Unit between December 2009 and December 2022. The collected data included date of symptoms, lumbar puncture opening pressure, body mass index (BMI), medical history, and visual field parameters (mean deviation). Disease severity was evaluated based on the degree of papilledema

Results:

Most (n = 128, 83%) of the 154 patients who met the inclusion criteria were females. Their mean age was 27.8±9.6 years, and their mean BMI was 32.94±5.5. A seasonal distribution analysis revealed a statistically significant increase in the incidence IIH during the summer months (June–August), (33.8%, P=0.03). Irregular menstrual cycles were reported by 13 patients (12.1%), with no seasonal differences (p = 0.52). Seven patients (5.5%) were pregnant at presentation and did not exhibit a seasonal pattern (p = 0.28). Hormonal contraceptive use was reported by 10 (10.9%) patients, also showing no significant seasonal variation (p = 0.08). There was no comparable significant association between seasonality and the severity of other ophthalmological manifestations, such as optic nerve edema or visual field loss

Conclusions:

our findings indicate a significant seasonal variation in adult IIH cases during the summer months unlike pediatric cases, where IIH is more prevalent during autumn and winter. This seasonal trend may be associated with the link between IIH and obesity, as decreased physical activity during the summer months, possibly due to excessive heat, could lead to weight gain

References: None provided.

Keywords: High intracranial pressure/headache, Pseudotumor cerebri

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Contact Information: None provided.

Correlation of ultrasound-derived optic nerve sheath diameter with OCT and MRI features in idiopathic intracranial hypertension

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Introduction:

Ultrasound measurement of the optic nerve sheath diameter (ONSD) has been proposed as a rapid non-invasive surrogate for raised intracranial pressure in diagnosis and monitoring of idiopathic intracranial hypertension (IIH). However, its relationship with MRI-based features of IIH and papilledema remains insufficiently characterized.

Methods:

Thirty-one patients with IIH underwent transbulbar standardized A-scan ultrasound, brain MRI, and optical coherence tomography (OCT) within one month. Univariate linear mixed-effects models were applied using ultrasound-derived ONSD as the dependent variable. Each MRI feature, and peripapillary retinal nerve fiber layer (pRNFL) thickness were evaluated as independent variables, adjusting for CSF opening pressure and time interval between measurements. A Poisson regression assessed the association between ultrasound ONSD and the total number of MRI signs.

Results:

Ultrasound ONSD showed no significant association with CSF opening pressure ($p = 0.34$) or the total number of MRI signs (IRR = 1.06, $p = 0.74$). Among individual MRI parameters, only posterior globe flattening was significantly associated with ultrasound ONSD ($\beta = 0.568$, $p = 0.043$), while optic nerve tortuosity showed a near-significant negative trend ($\beta = -0.572$, $p = 0.064$). In contrast, MRI-derived ONSD, pituitary height, empty sella, and transverse sinus stenosis demonstrated no meaningful associations. A significant positive relationship was observed between ultrasound ONSD and pRNFL thickness ($\beta = 0.275$, $p = 0.007$).

Conclusions:

A-scan ultrasound-derived ONSD correlated more closely with orbital MRI features of IIH than with midline or venous MRI signs. Despite assessing the same anatomical structure, MRI-derived ONSD showed no correlation, likely reflecting the lower precision of MRI due to its limited image resolution. A-scan ultrasound and OCT appear to capture related but distinct, pressure-sensitive changes in the anterior optic nerve. Although further validation in larger, longitudinal cohorts is warranted, A-scan ultrasound may serve as a practical and accessible adjunct for evaluating intracranial pressure in IIH.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), High intracranial pressure/headache, Neuroimaging, Optic neuropathy, Pseudotumor cerebri

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Echography Leads, OCT Follows: Defining When OCT-Only Monitoring Is Safe in Idiopathic Intracranial Hypertension

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Introduction:

In idiopathic intracranial hypertension (IIH), ultrasonographic optic nerve sheath diameter (ONSD) changes within hours–days, whereas peripapillary OCT retinal nerve fiber layer (pRNFL) evolves over days–weeks. When ONSD can be safely discontinued in favor of OCT-only follow-up is uncertain.

Methods:

Longitudinal IIH cohort with paired ONSD (mm) and pRNFL (μm) from baseline (FU0) to FU4 (~6-month intervals), both eyes. Temporal ordering was tested using visit-to-visit lagged regression (cluster-robust SEs), adjusting each outcome for its prior value. Two pre-specified rules for OCT-only at visit k were evaluated: Conservative—ONSD ≤4.5 mm at k–1 and k plus non-increasing pRNFL; Relaxed—ONSD ≤5.0 mm at k plus non-increasing pRNFL. Safety among FU3 switchers was assessed at FU4: failure = ONSD >5.0 mm and/or pRNFL increase (primary), with sensitivity variants.

Results:

Lag analyses showed pressure-first, structure-second dynamics: prior ONSD predicted subsequent pRNFL more strongly than the reverse. Eligibility to switch was 0% at FU2, 5.0%/32.0% (Conservative/Relaxed) at FU3 (n=100), and 0%/43.5% at FU4 (n=46). Safety at FU3→FU4 (primary) was 0/5 failures (0.0%; 95% CI 0.0–43.4) for Conservative and 7/34 (20.6%; 10.3–36.8) for Relaxed. Under stricter definitions, failures were frequent (e.g., pRNFL rise ≥+5 μm: 88.9% Conservative, 65.2% Relaxed).

Conclusions:

The Relaxed rule carries a non-trivial failure risk and should not be adopted for routine OCT-only monitoring. The Conservative rule appears safer but applies to few eyes. ONSD should be retained in early follow-up, and any OCT-only transition restricted to rare cases meeting stringent criteria with clear re-trigger conditions.

References: None provided.

Keywords: High intracranial pressure/headache, Optic neuritis, Vascular disorders

Financial Disclosures: Christoph Mitsch; Martin Bertich; Karl Kircher; Nik Krajnc; Tobias Rakus; Nina Mueller; Stefan Macher; Gabriel Bsteh; Berthold Pemp: received research support from Chiesi, honoraria for lectures and/or consulting from Santen, Novartis and Chiesi

Grant Support: None.

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Trends In Management Of Idiopathic Intracranial Hypertension

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Introduction:

Idiopathic intracranial hypertension (IIH) is characterized by elevated intracranial pressure (ICP) without an identifiable cause. Common symptoms include headache, nausea, neck and back pain, tinnitus, and, in severe cases, irreversible vision loss. Diagnosis follows the modified Dandy criteria, requiring: (1) papilledema, (2) absence of other neurologic abnormalities, (3) negative neuroimaging for secondary causes, (4) elevated lumbar puncture pressure (>25 cm H₂O in adults, >28 cm H₂O in children), and (5) normal cerebrospinal fluid (CSF) composition. Increasingly, patients are diagnosed with IIH without meeting all criteria. This study examines recent trends in IIH diagnosis and management.

Methods:

Patients diagnosed with Benign Intracranial Hypertension (ICD-10 G93.2) between January 2020 and December 2024 were identified using Epic's SlicerDicer database within the Carle Hospital System (n = 1,638) and Epic's Cosmos national database (n = 138,598). Data were segmented by year to evaluate diagnostic and treatment trends. Statistical comparisons between local and national datasets were performed using t-tests.

Results:

Both local (central Illinois) and national data showed more IIH diagnoses than corresponding diagnostic testing. Brain MRI was performed in only 12.86% of national cases versus 0.83% locally (p < 0.001). Lumbar punctures were also underutilized, with higher national rates compared to local (6.40% vs 2.46%, p < 0.001). Treatment patterns revealed fewer local patients received acetazolamide (42.76%) compared to national averages (66.06%, p = 0.015). Analysis controlling for age, gender, BMI, and comorbid Type 2 Diabetes Mellitus showed no significant demographic differences between the two populations.

Conclusions:

Current trends suggest IIH may be increasingly diagnosed clinically rather than through confirmatory testing, as reflected by low imaging and lumbar puncture rates relative to acetazolamide treatment. Alternatively, IIH may be entered as a provisional diagnosis pending further evaluation, explaining the discrepancy between diagnostic coding and testing frequencies.

References: None provided.

Keywords: Pseudotumor cerebri, High intracranial pressure/headache, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Evaluating the Prevalence of Optic Disc Edema in Patients Referred to a Neuro-Ophthalmology Clinic with Pulsatile Tinnitus: A Study on Diagnostic Yield and Clinical Correlates

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Introduction:

Pulsatile tinnitus (PST) is a common referral to neuro-ophthalmology clinics and may be an indicator of elevated intracranial pressure and papilledema. This study aims to evaluate the prevalence of optic disc edema in patients referred for PST. It also aims to investigate demographic and clinical differences between patients with and without optic disc edema among those referred for PST and to assess imaging correlates associated with papilledema.

Methods:

We reviewed 60 consecutive patients referred for evaluation of PST between January 2015 to December 2024 at a tertiary neuro-ophthalmology clinic. Demographics, symptoms at presentation, laterality, and neuroimaging findings were recorded. Imaging findings seen on MRI or CT head that were considered suggestive of elevated intracranial pressure included prominent perioptic CSF, posterior globe flattening, optic nerve tortuosity, empty sella, or venous sinus stenosis. Statistical comparisons were made between patients with and without optic disc edema using descriptive analysis techniques in Microsoft Excel.

Results:

Of 60 patients, 12 (20%) had optic disc edema. Those with optic disc edema were younger (36.5 ± 9.8 years) than those without (47.1 ± 12.0 years; $p = 0.006$). Among 51 patients with head imaging available at evaluation, 10 had optic disc edema leading to eventual diagnosis of papilledema; 9/10 demonstrated at least one typical imaging finding at time of visit, and the remaining case had headache on presentation. Notably, 6 patients exhibited prominent perioptic CSF spaces without optic disc edema.

Conclusions:

In patients presenting with pulsatile tinnitus, 20% had optic disc edema. Optic disc edema was associated with younger age and was nearly always accompanied by either headache or imaging evidence of elevated intracranial pressure. Prominent perioptic CSF spaces alone did not predict optic disc edema. These findings support a combined clinical-imaging approach when evaluating PST as a possible manifestation of intracranial hypertension.

References: None provided.

Keywords: Pseudotumor cerebri, Optic neuropathy, High intracranial pressure/headache, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Case-Only Study Designs in Neuro-Ophthalmology: An Example Using Pseudotumor Cerebri Syndrome

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Introduction:

Cohort and case-control studies are widely used in neuro-ophthalmology, but robust identification of etiologic risk factors is limited by confounding. Selecting a comparable group of people without the exposure or outcome of interest can also cause selection bias. Case-only study designs are highly efficient and only require information about people with the disease of interest. Because cases serve as their own controls, they provide optimal control for confounding. However, these study designs are rarely used in neuro-ophthalmology. Our objective was to illustrate the application of case-only study designs to neuro-ophthalmology using a self-controlled case series (SCCS) of medication-induced pseudotumor cerebri syndrome (PTCS).

Methods:

We identified all female Medicaid beneficiaries aged 12–55 who were diagnosed with PTCS between July 1, 2017, and June 30, 2019. Cases had >2 PTCS diagnoses (ICD-10-CM code G93.2) on different dates and complete Medicaid coverage from 2017-2019. Venous thrombosis and other causes of intracranial hypertension were excluded. Next, we identified all prescriptions for tetracyclines and other relevant medications. SCCS analyses compared each individual's risk of developing PTCS during periods of medication exposure versus non-exposure. Conditional Poisson regression models were used to estimate incidence rate ratios (IRR).

Results:

A total of 4,302 female Medicaid beneficiaries aged 12-55 were diagnosed with PTCS between July 1, 2017, and June 30, 2019 and met study inclusion and exclusion criteria. Among those with at least one tetracycline prescription (n=638), SCCS analysis demonstrated an increased risk of IIH during periods of tetracycline exposure (IRR, 1.79; 95% CI, 1.21–2.63).

Conclusions:

The known association between tetracyclines and PTCS can be demonstrated using a dataset that consists solely of PTCS diagnosis and tetracycline prescription dates. In ongoing work, we will extend this approach to other medications and PTCS, and we propose that broader adoption of case-only study designs will enhance our understanding of uncommon neuro-ophthalmic conditions.

References: None provided.

Keywords: Pseudotumor cerebri, High intracranial pressure/headache, Optic neuropathy, Miscellaneous

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Advancing Diagnostics in Idiopathic Intracranial Hypertension: A Tri-modal Investigation of Optic Nerve Sheath Measurements

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Introduction:

Idiopathic intracranial hypertension (IIH) is characterised by raised intracranial pressure (ICP) without an identifiable cause. Diagnosis follows the Modified Dandy criteria, combining elevated ICP, normal cerebrospinal fluid (CSF) composition, and neuroimaging to exclude secondary causes. Optic nerve sheath diameter (ONSD) reflects ICP effects on the optic nerve. MRI is the standard measurement tool and helps in the initial diagnosis of IIH. This study evaluates the utility of orbital ultrasonography (USG) as a simpler, non-invasive monitoring tool in follow up. Purpose: 1. To assess the correlation of ONSD between USG and MRI in IIH. 2. To evaluate the relationship between CSF opening pressure and ONSD measured by MRI and USG, and the potential of USG as a monitoring tool.

Methods:

This prospective observational study included 50 diagnosed IIH patients. All underwent detailed neuro-ophthalmological examination. ONSD was measured using orbital USG and MRI, and lumbar punctures were performed to record CSF opening and closing pressures. Correlation between USG and MRI ONSD was assessed using Pearson's coefficient, and the relationship between ONSD and CSF pressure was analyzed.

Results:

The cohort had a mean age of 32 years (range 18–55), with 90% female participants. Mean ONSD was 6.8 mm (± 0.5) by USG and 6.6 mm (± 0.6) by MRI. Strong positive correlation was observed between USG and MRI measurements ($r = 0.84$, $p < 0.001$) which signifies a robust association. ONSD also correlated significantly with CSF opening pressure ($r = 0.72$, $p < 0.001$), highlighting the effect of raised ICP on the optic nerve sheath.

Conclusions:

ONSD correlates strongly with CSF pressure in IIH, and USG provides a reliable, non-invasive tool for ONSD measurement. Ocular USG is quick, cost-effective, and suitable for follow-up and ICU monitoring, establishing ONSD as a surrogate marker for elevated intracranial pressure.

References: None provided.

Keywords: Pseudotumor cerebri

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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OCT-Based Telemedicine for Papilledema Monitoring in Children

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Introduction:

Pseudotumor cerebri (PTC) requires frequent monitoring and long-term follow-up owing to its chronic course and the potential risk of vision loss. This requirement imposes a considerable clinical and logistical burden on both patients and healthcare systems. We have previously demonstrated the feasibility of an optical coherence tomography (OCT)–based telemedicine model as an alternative to frontal visits evaluations in adult patients with PTC. However, the applicability and reproducibility of this approach within the pediatric population was not studied. This study aimed to evaluate the reproducibility and safety of telemedicine model for papilledema follow up in pediatric patients.

Methods:

A retrospective cohort of consecutive patients younger than 18 years of age who diagnosed with PTC in a single Neuro-ophthalmology Clinic, at a tertiary referral center, between 2018 and 2025. Intra-examiner decisions were compared between the actual frontal visit recommendations retrieved from the medical record and those given in a demo telemedicine visit based on history and OCT retinal nerve fibre (RNFL) analysis only. The physicians were masked to their previous real-life assessment.

Results:

The cohort included 33 patients, the mean age was 11.6 years, with 51.5% males (n=17) and 48.5% females (n=16). The overall agreement rate between the actual frontal visit recommendations and demo telemedicine visit was 96.9%.

Conclusions:

This study findings indicate that telemedicine-guided management is similar to conventional frontal appointments. Overall, these results support the judicious integration of structured telemedicine pathways into pediatric neuro-ophthalmology practice, complementing traditional visits and promoting a hybrid model of care that optimizes both accessibility and clinical precision.

References: None provided.

Keywords: Pseudotumor cerebri, Pediatric neuro-ophthalmology, High intracranial pressure/headache, Neuroimaging

Financial Disclosures: The authors had no disclosures.

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Big Data for Improved RNFL Segmentation in Papilledema: A Semi-supervised Deep Learning Model Outperforms the Customary Spectral-Domain OCT Software

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Introduction:

Peripapillary OCT segmentation degrades in the setting of retinal nerve fiber layer (RNFL) thickening. We aimed to develop a deep-learning method for automated RNFL segmentation, testing its performance in eyes with papilledema due to confirmed intracranial hypertension.

Methods:

We developed, trained, and tested a semi-supervised AI Vision Transformer (SegFormer) to automatically segment and measure the peripapillary RNFL thickness. The tool was developed on a retrospective dataset of 128,765 patients, encompassing 936,967 peripapillary circle OCT scans (Spectralis, Heidelberg Engineering) acquired between 2009-2025. Training used 807,512 unlabeled scans spanning 50-500 μm RNFL thickness, with adapted methodology to handle noise and artifacts. Testing was performed in an independent set of 640 eyes with confirmed raised intracranial pressure, and the results were compared against the customary software Spectralis. Per-eye mean absolute error (MAE, μm) was reported as median [IQR]. Additionally, in a random subset of 47 papilledema eyes, MAE for both the AI tool and Spectralis software was assessed relative to clinician-annotated data (two independent senior neuro-ophthalmologists).

Results:

Across 640 papilledema scans (320 patients, 30.5 ± 11.8 years; 84% women), inter-method MAE increased with RNFL thickening: RNFL $< 200 \mu\text{m}$ ($n=351$) MAE median $8.85 \mu\text{m}$ [IQR: 9.42]; $200-300 \mu\text{m}$ ($n=189$) $22.93 \mu\text{m}$ [39.27]; $\geq 300 \mu\text{m}$ ($n=100$) $47.55 \mu\text{m}$ [33.92]. In the 47-eye clinician-referenced subset, RNFL MAE by thickness was: $< 200 \mu\text{m}$ ($n=20$) model $6.41 \mu\text{m}$ [4.78] vs Spectralis $11.96 \mu\text{m}$ [13.94]; $200-300 \mu\text{m}$ ($n=19$) $14.11 \mu\text{m}$ [7.85] vs $32.81 \mu\text{m}$ [19.00]; $\geq 300 \mu\text{m}$ ($n=8$) $29.25 \mu\text{m}$ [9.34] vs $89.48 \mu\text{m}$ [82.31].

Conclusions:

Our AI model trained on big data improves RNFL segmentation compared to the Spectralis software, particularly at high RNFL thicknesses. We aim to refine and validate our fully automated AI tool for routine clinical implementation.

References: None provided.

Keywords: Optic neuropathy

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Disparities in Surgical Management of Medically Refractory Idiopathic Intracranial Hypertension Cases at UT Southwestern Medical Center

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Introduction:

Recognizing medically refractory idiopathic intracranial hypertension (IIH) early is critical, since delays in surgery can lead to permanent vision loss. IIH also shows striking socioeconomic disparities, most often affecting obese women of color from low-income backgrounds (Brahma et al). Although cerebrospinal fluid (CSF) shunting is now performed more often than optic nerve sheath fenestration (ONSF), studies suggest underrepresented groups are still more likely to undergo ONSF (Hamedani et al). Because timely surgery and equitable access are both key in preventing visual decline, we examined surgical management patterns and delays in workup among refractory IIH patients at a quaternary care center.

Methods:

We performed a retrospective chart review of IIH patients who had surgery at UT Southwestern Medical Center between 2010 and 2025. We collected data on demographics, visual outcomes before and after surgery, time to presentation, referrals, surgery type, and opening pressure. Statistical tests included two-tailed t-tests, chi-square, and ANOVA with Tukey HSD for post-hoc comparisons.

Results:

A total of 267 procedures from 179 patients were analyzed. Patients who had shunt revisions had lower opening pressures compared to those receiving stents ($p = 0.02$), new shunts ($p = 0.005$), or ONSF ($p < 0.001$). Stent patients tended to present later ($p < 0.001$) and experienced longer delays to subspecialty evaluation ($p < 0.001$) and to surgery ($p = 0.007$ vs. revision; $p < 0.001$ vs. ONSF). Shunt creation and revision also showed longer delays compared to ONSF ($p < 0.001$ and $p = 0.027$). Non-White patients were more likely to undergo ONSF ($p = 0.001$) and less likely to have shunt creation ($p = 0.009$).

Conclusions:

We found significant differences in opening pressure, timing, and race across procedure types, suggesting disparities in how IIH is surgically managed. Expanding this work to include county hospital data will help clarify how these differences affect visual outcomes and access to care.

References: Brahma, V. L. et al. "Socioeconomic and Geographic Disparities in Idiopathic Intracranial Hypertension." *Neurology*, vol. 96, no. 23, 2021, pp. e2854-e60, doi:10.1212/WNL.0000000000012037. Hamedani, A. G. et al. "Trends in the Surgical Treatment of Pseudotumor Cerebri Syndrome in the United States." *JAMA Netw Open*, vol. 3, no. 12, 2020, p. e2029669, doi:10.1001/jamanetworkopen.2020.29669.

Keywords: Pseudotumor cerebri, High intracranial pressure/headache, Neuroimaging, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Visual fields

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Clinical Profile of IIH – A Comparative Analysis of Patients With and Without Anemia: A Multicentric Study

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Introduction:

Idiopathic Intracranial Hypertension (IIH) is a disorder characterised by raised intracranial pressure (ICP) with normal cerebrospinal fluid (CSF) composition and neuroimaging. There is limited literature analysing the clinical characteristics of IIH in patients with anaemia. This study aimed to compare the clinical profile of IIH patients with and without anaemia.

Methods:

This is a prospective study that included patients diagnosed with IIH presenting to neuro-ophthalmology clinics with papilledema for two years. All participants underwent detailed neuro-ophthalmic evaluation, automated perimetry, MRI with venography, and CSF opening pressure measurement. Routine haematological investigations were performed, and patients were categorised into anaemic and non-anaemic groups based on haemoglobin levels. Body Mass Index (BMI) was recorded for all.

Results:

A total of 249 patients were enrolled in the study. Of these, 121 (48.6%) were non-anaemic and 128 (51.4%) were anemic. The mean age of the non-anaemic group was 31.99 ± 8.85 years, and that of the anaemic group was 31.50 ± 9.59 years. The majority of patients in both groups were female — 91.7% in the non-anaemic and 96.1% in the anaemic group. Regarding systemic associations, hypertension (11.6%) and diabetes (5.8%) were more frequent among non-anaemic patients, whereas thyroid disorders (17.18%) were more common among anemic patients. There was no statistically significant difference in BMI distribution between anaemic and non-anaemic groups ($p = 0.767$). The mean deviation (MD) on visual fields averaged -3.97 dB in non-anaemic versus -5.56 dB in moderate to severe anaemic patients, indicating greater field loss in the latter. The mean CSF opening pressure was 32.70 ± 8.16 cm H₂O in the non-anaemic group and 31.87 ± 9.10 cm H₂O in the anaemic group ($p = 0.580$), showing no significant difference.

Conclusions:

Anemia may influence the visual severity in IIH but does not significantly alter overall clinical presentation or systemic associations.

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Keywords: Pseudotumor cerebri, High intracranial pressure/headache, Visual fields

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Grant Support: no

Contact Information: None provided.

Tirzepatide for the Reduction of Acetazolamide in IIH (TREAT-IIH) Trial Design

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Introduction:

The TREAT-IIH trial was developed to better understand the benefits that incretin analogs might offer in treating IIH. Tirzepatide, a dual glucagon-like peptide-1 (GLP-1) and gastric inhibitory protein (GIP) receptor agonist, offers the greatest degree of weight reduction among incretin analogs, and it is unclear if it shares exenatide's ICP-lowering effect. We present the design of TREAT-IIH, a randomized, double-masked, placebo-controlled trial to ascertain the efficacy of tirzepatide as adjunctive therapy to acetazolamide. The study was funded beginning July 2025.

Methods:

Participants will be randomized to receive acetazolamide up to 4g/day with predefined titration parameters plus either tirzepatide or placebo. The study population will be adults with IIH as defined by the modified Dandy criteria. Exclusion criteria include type I diabetes mellitus, pregnancy, post-menopause, prior treatment unless participants requalify after washout, previous ICP-lowering surgery, and perimetric mean deviation (PMD) of -15 dB or worse. An independent adjudication body will evaluate premature withdrawal and treatment failures. The primary outcome will be the difference in mean acetazolamide dose between groups at 9 months. Secondary outcomes include: cumulative acetazolamide dose; acetazolamide and papilledema freedom; IIH remission; time-to-event analyses for cessation of acetazolamide up-titration, beginning of acetazolamide down-titration, and acetazolamide discontinuation; and changes in PMD, papilledema grade, peripapillary retinal nerve fiber layer thickness, ICP, quality-of-life and headache scores, weight, and obstructive sleep apnea indices.

Results:

TREAT-IIH is powered to detect a 300 mg difference in mean daily acetazolamide dose between arms, assuming a standard deviation of 400 mg, and accounting for a single interim analysis in the adaptive design. Estimating 30% loss to follow-up, 90 participants will be enrolled at three academic hospitals.

Conclusions:

TREAT-IIH aims to define the role of tirzepatide in achieving remission of IIH. Enrollment is anticipated in Summer 2026.

References: None provided.

Keywords: Pseudotumor cerebri, High intracranial pressure/headache, Optic neuropathy

Financial Disclosures: Robert Mallery; Bart Chwalisz; Nathan Huey; Marc Bouffard: Clinical trial support for Stoke Therapeutics

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Tetracycline and Vitamin A Derivative Exposure in Patients with Established Pseudotumour Cerebri

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Introduction:

Tetracycline antibiotics and vitamin A derivatives are a rare but well-established cause of drug-associated intracranial hypertension. Given this association, they are avoided in patients with known pseudotumor cerebri (PTC). These medications are commonly used for a range of conditions, including infectious diseases, neoplasms, and dermatologic conditions. To date, no literature has been published on the risk of worsening or recurrent symptoms of raised intracranial pressure (ICP) in patients with known PTC who are later treated with these medications.

Methods:

A retrospective review of medical records was completed, looking at drug exposure history in patients with known PTC. Exposures to tetracycline antibiotics (doxycycline, minocycline) and vitamin A derivatives (tretinoin, isotretinoin) were examined. Patient demographics, presenting examination findings, imaging, cerebrospinal fluid (CSF) opening pressure, and CSF constituents were recorded. Baseline visual acuity, papilledema grade, visual field indices, and retinal nerve fibre layer thickness were compared with findings pre- and post-medication exposure. The presence of worsening headache, visual symptoms, or papilledema at each visit after medication exposure was noted. The primary outcome was recurrence of papilledema or raised intracranial pressure symptoms after drug exposure.

Results:

Forty-one patients diagnosed with PTC had subsequent exposure to tetracycline antibiotics or vitamin A derivatives. Forty (97%) were female, and the average age at diagnosis was 34 years. Of the patients with exposure history, 37 (90%) were exposed to doxycycline, and 4 (10%) to topical tretinoin. Two patients had worsening headache or elevated intracranial pressure symptoms after medication exposure, but did not have worsening of papilledema. Within the cohort, one patient had worsening papilledema in the absence of raised ICP symptoms.

Conclusions:

Worsening of intracranial pressure symptoms and papilledema after exposure to tetracycline antibiotics or vitamin A derivatives was infrequent among patients with established PTC.

References: None provided.

Keywords: Pseudotumor cerebri, High intracranial pressure/headache, Visual fields

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Fluorescein Angiography Poorly Differentiates Between Mild Cases of True Versus Pseudo-Papilledema

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Introduction:

Fluorescein angiography (FA) has been reported as a useful tool in the diagnosis of papilledema. However, its value in mild cases remains uncertain. We hypothesized that FA would perform poorly in mild cases due to the difficulty of distinguishing subtle leakage from staining.

Methods:

A retrospective review was conducted of all patients from the past 10 years who underwent FA for assessment of mild papilledema, defined as fundus features corresponding to Frisen grade 1 or 2. Only cases with a definitive diagnosis of papilledema or pseudopapilledema, established through comprehensive clinical workup, were included. FA images were independently evaluated by five senior retina specialists, masked to clinical details. Each grader assessed the presence of leakage and staining using a five-point Likert scale. Inter-rater reliability was calculated with Fleiss' kappa, and diagnostic accuracy for both leakage and staining detection was determined.

Results:

Thirty-eight eyes (19 patients) were included, with an equal distribution of papilledema and pseudopapilledema. Inter-rater agreement was $\kappa = 0.418$ for leakage and $\kappa = 0.547$ for staining (both $p < 0.001$). For leakage detection, sensitivity was 64.1%, specificity 77.8%, positive predictive value 76.6%, and negative predictive value 65.6% (all $p < 0.001$). For staining detection, sensitivity was 68.9%, specificity 59.1%, positive predictive value 63.3%, and negative predictive value 64.2% (all $p < 0.001$).

Conclusions:

FA is not a reliable method of differentiating papilledema from pseudopapilledema in mild cases due to challenge of differentiating subtle leakage from staining.

References: None provided.

Keywords: Adult strabismus with a focus on diplopia

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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The relationship between PHOMS and Intracranial Pressure in Patients with IIH

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Introduction:

Prior studies have shown that peripapillary hyperreflective ovoid mass-like structures (PHOMS) are more common in the eyes of patients with papilledema than in the eyes of healthy subjects, and it has been hypothesized to play an important role in intracranial pressure surveillance. This study assesses the prevalence of PHOMS at the time of diagnosis of idiopathic intracranial hypertension (IIH) and its relationship with intracranial pressure.

Methods:

Patients diagnosed with IIH based on Modified Dandy Criteria followed by a tertiary center between 2020-2023 were included if they had at least one optic nerve head Enhanced Depth Imaging of Optical Coherence Tomography (EDI-OCT) within 6 weeks of their first lumbar puncture (LP). The prevalence of PHOMS was calculated and two subgroups were made based on the presence of PHOMS in at least one eye (PHOMS/No PHOMS). Baseline clinical characteristics and LP opening pressure (OP) were compared using a t-test.

Results:

Fifty-four patients met the inclusion criteria. 48 (88.89 %) were female and the mean age at diagnosis was 30.95 ± 9.89 (13-71) years. PHOMS were present in 65 eyes, 39 subjects. Prevalence is lower than previously described. A mean OP for the PHOMS group of 31.26 ± 6.87 cm H₂O and a mean OP for the No PHOMS group of 34.36 ± 11.31 cm H₂O was observed ($t = 1.00$, $p = 0.33$).

Conclusions:

We found a high prevalence of PHOMS at the time of diagnosis of IIH (59.26%) Although PHOMS represents a marker of axoplasmic stasis, its presence does not seem to be directly correlated with intracranial pressure, suggesting that anatomic factors may play a role in its development.

References: None provided.

Keywords: Pseudotumor cerebri, High intracranial pressure/headache

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Innovative Learning: Using Artificial Intelligence to Navigate Simulated Neuro-Ophthalmology Cases

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Introduction:

Neuro-ophthalmology is one of the most complex subspecialties within ophthalmology. Because many disorders are rare, residents often have limited clinical exposure to such conditions. Moreover, history-taking plays a pivotal role, and asking the right questions is essential for accurate diagnosis. This study aims to evaluate the effectiveness of an online platform that leverages large language models to simulate clinical cases for ophthalmology and neurology trainees.

Methods:

An interactive platform was developed by two software engineers using GPT-4o, customized with detailed clinical instructions to simulate virtual patients. Neuro-ophthalmology cases were created, allowing users to interact with simulated patients via a chat interface by asking clinical questions. Users then perform virtual examinations (visual acuity, color vision) and order complementary tests (OCT, visual field) through interactive features. After submitting a diagnosis, the AI model validates or corrects it. When the correct diagnosis is reached, a teaching segment is displayed with key learning points and references. A user survey was conducted to assess the platform's usability, educational value, and overall experience.

Results:

Ten simulated cases featuring rare neuro-ophthalmic conditions were developed, such as seronegative giant cell arteritis or syphilitic optic neuritis. Each case required approximately 10 minutes to complete. Users found the interface intuitive and highly appreciated the feedback and teaching components (rated 5/5). The virtual patients effectively reproduced rare conditions, allowing residents to ask relevant clinical questions. The system accurately interpreted queries and generated coherent, informative responses. Overall satisfaction with the platform was high (rated 9/10), and users expressed strong willingness to recommend it to colleagues (rated 9/10).

Conclusions:

Large language model-driven virtual patients represent a promising and innovative tool for neuro-ophthalmology education. Residents found the platform engaging and useful, highlighting its potential to bridge gaps in clinical exposure.

References: None provided.

Keywords: Miscellaneous

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Contact Information: None provided.

Photophobia in Gulf War Illness: Ocular Surface Symptoms as a Window Into Multisystem Disease

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Introduction:

Gulf War Illness (GWI) is a chronic, multi-symptom condition affecting veterans of the 1990–1991 Gulf War. Symptoms span six domains: neurologic/cognitive/mood (N/C/M), fatigue/sleep (F/S), pain, gastrointestinal (GI), respiratory, and skin. Among ophthalmic complaints at the VA, photophobia is notably common. Given its multisystem nature, the pathophysiology of GWI remains unclear. This study investigates photophobia in GWI, using the eye as a window to the brain to explore photosensitivity as a potential marker of central nervous system dysfunction.

Methods:

Twenty-nine Gulf War–era veterans were evaluated (mean age $\pm$ SD = 60.2 $\pm$ 4.8 years; 72.4% male), including 18 deployed and 11 non-deployed. GWI status was determined using the Kansas questionnaire, defining “Kansas-positive” (Kansas+) as moderate or severe symptoms in ≥ 3 domains. Nineteen veterans were Kansas+ and ten were Kansas–. Photophobia and ocular surface symptoms were assessed using the Neuropathic Pain Symptom Inventory–Eye (NPSI-Eye), Visual Light Sensitivity Questionnaire-8 (VLSQ-8), and Ocular Surface Disease Index (OSDI).

Results:

Kansas+ veterans demonstrated significantly higher OSDI scores than Kansas– veterans (33.2 $\pm$ 26 vs 15.5 $\pm$ 12; $P < 0.05$). When stratified by Kansas status and deployment, Games–Howell tests showed significant mean differences between Kansas+ deployed and Kansas– non-deployed veterans in F/S (8.0; 95% CI 3.5–12.4), N/C/M (17.9; 95% CI 10.3–25.6), pain (5.4; 95% CI 2.1–8.7), GI (3.1; 95% CI 0.3–6.0), VLSQ-8 (12.4; 95% CI 1.0–23.8), and OSDI (12.7; 95% CI 1.9–23.5) (all $P < 0.05$). Correlation analyses showed moderate-to-strong associations between OSDI index scores and GI, F/S, N/C/M, and pain ($\rho = 0.51$ – 0.77). VLSQ-8 scores correlated strongly with N/C/M, F/S, and pain ($\rho = 0.71$ – 0.78) and moderately with skin, respiratory, and GI domains ($\rho = 0.46$ – 0.60).

Conclusions:

Kansas+ veterans, particularly those deployed, exhibited greater ocular surface sensitivity and multisystem symptom burden. Photophobia may serve as a biomarker linking ocular and systemic dysfunction in GWI.

References: None provided.

Keywords: Miscellaneous

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Utilization and Diagnostic Yield of Neuroimaging in Patients Presenting to Neuro-ophthalmology for Migraine Aura Without Headache: A 10-year Retrospective Study

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Introduction:

Migraine aura is a complex neurological phenomenon with diagnostic challenges. Patients with visual aura-predominance frequently present to ophthalmology clinics, where neuroimaging is commonly performed to exclude alternative causes of visual symptoms. However, imaging utilization and predictors of abnormal findings are not well-characterized, particularly among patients with migraine aura without headache.¹ This study aimed to describe neuroimaging use and findings in patients with typical versus atypical aura features—the most common drivers of imaging.

Methods:

Single-institution retrospective chart review was conducted for patients experiencing symptoms of migraine aura without headache from 2013-2023. Data regarding demographics, migraine aura characteristics, and MRI findings were collected. The latter were categorized as infarct, infarct-like, white matter change, or mass. The migraine aura was deemed "atypical" with any of the following features: recent pattern change, associated focal neurological deficit, abnormal visual field, optic disc edema, duration < 5min or >60min, or first aura at age>50 years.

Results:

Of the 473 patients identified, 223 (47.1%) had atypical aura features (Atypical group) and 250 (52.9%) had typical features (Typical group). Neuroimaging was ordered at the index event for 136 patients. Imaging order rates did not differ significantly between groups (Typical: 25.2%, n=63; Atypical: 32.7%, n=73; p=0.07). Additionally, there was no significant difference in abnormal image findings between typical and atypical aura groups (Typical: 39.7%, n=23 vs Atypical: 42.4%, n=28; p=0.92). Imaging rarely led to a change in diagnosis; only 1 imaging finding (1 typical) was clinically meaningful.

Conclusions:

Neuroimaging was frequently ordered and obtained for patients with migraine aura without headache. However, clinically meaningful findings were rare. Atypical features did not predict abnormal results, suggesting that current imaging may not effectively distinguish high-risk presentations. Our findings underscore the need for improved criteria to guide imaging decisions in patients who present to neuro-ophthalmology clinics with migraine aura.

References: Evans RW, Burch RC, Frishberg BM, Marmura MJ, Mechtler LL, Silberstein SD, Turner DP. Neuroimaging for Migraine: The American Headache Society Systematic Review and Evidence-Based Guideline. *Headache*. 2, 318-336, 2020.

Keywords: Neuroimaging, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)

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Cross-Species Retinal Aging Analysis in Humans and Non-Human Primates Using Deep Learning

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Introduction:

Deep learning models can predict biological age from retinal fundus photographs, with retinal age gap serving as a biomarker for cardiovascular risk and mortality in humans. Non-human primates are the premier translational model for aging research, but whether retinal aging patterns are conserved across species remains unexplored.

Methods:

We analyzed 2,210 retinal images from 180 rhesus macaques (filtered from 8971 images using AutoMorph) and age-matched human images from the Collaborative University of California Teleophthalmology Initiative, based on a 3:1 age conversion ratio. A DINOv3 vision transformer was fine-tuned using 10-fold cross-validation separately on each dataset. Attention rollout generated saliency maps were anatomically aligned using optic disc and foveal coordinates derived from VascX and then averaged. We compared anatomical region-based saliency distribution (fovea, macula, vessels, optic disc) between the two species, then performed cross-species model validation by training on one species and testing on the other.

Results:

Our model age predictions achieved a mean absolute error (MAE) of 2.2 years ($R^2=0.73$) for macaques and MAE=3.62 years ($R^2=0.86$) for humans. Averaged saliency maps showed qualitatively similar attention patterns between the two species, predominantly highlighting peripapillary regions and retinal vasculature. Quantitative analysis showed greater attention to the optic disc and vasculature in macaques and slightly lower macular attention compared to humans. Cross-species model evaluation demonstrated a correlation of $r=0.741$ when training on primates and testing on humans, and $r=0.597$ for the reverse direction.

Conclusions:

Deep learning models reveal fundamentally similar retinal aging patterns between humans and macaques, supporting the use of nonhuman primates as valuable translational models for aging research and therapeutic development.

References: None provided.

Keywords: Retina

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Grant Support: None.

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Botulinum Toxin A Reduces Activation of Neural Pathways of Photophobia in Patients with History of Traumatic Brain Injury

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Introduction:

Photophobia is a persistent and disabling consequence of traumatic brain injury (TBI), affecting up to 10% of patients one year after injury. Despite its impact, the neural mechanisms underlying photosensitivity remain poorly understood, limiting our ability to predict treatment response. Botulinum toxin A (BoNT-A) has shown promise in reducing pain in migraine and ocular pain syndromes, yet its mechanism of action in TBI-associated photophobia is unclear. Understanding how BoNT-A alters neural activation could reveal biomarkers of response and guide targeted therapy. We investigated whether BoNT-A decreases light-evoked brain activation in patients with TBI and whether these effects are seen selectively in those with objective improvement in photosensitivity.

Methods:

Veterans with a history of TBI and a photosensitivity rating $\geq 4/10$ were recruited from the local Veterans Affairs Hospital. Participants completed questionnaires, Ocular Photosensitivity Analyzer (OPA) testing, and functional magnetic resonance imaging using a bright-screen versus black-screen paradigm. Each received 35 units of BoNT-A across seven forehead sites and repeated identical testing 6 weeks later. Responders were defined as those with $\geq 50\%$ increase in OPA threshold after treatment ($n=5$); non-responders showed $< 50\%$ change ($n=6$). Whole-brain pre- versus post-treatment contrasts were analyzed using FSL software.

Results:

The study cohort ($n=11$) was 81.8% male, 72.7% white, and 63.6% Hispanic, with a mean age of 50 years. Responders showed significantly reduced light-evoked activation after BoNT-A across multiple cortical regions, including the left occipital fusiform gyrus ($Z = 8.34$, $p < 0.001$), right frontal pole ($Z=5.09$, $p < 0.001$), left superior parietal lobule ($Z=5.58$, $p < 0.001$), right superior frontal gyrus ($Z=4.99$, $p < 0.001$), left middle frontal gyrus ($Z=4.71$, $p < 0.001$), right middle frontal ($Z=4.23$, $p < 0.001$), and posterior cingulate gyrus ($Z=4.17$, $p=0.008$). Non-responders demonstrated no significant activation changes.

Conclusions:

BoNT-A reduces light-evoked cortical activation within visual–pain networks in TBI patients who show objective improvement in photosensitivity, suggesting a central neuromodulatory mechanism underlying its clinical benefit.

References: Merezhinskaya N, Mallia RK, Park D, Millian-Morell L, Barker FM, 2nd. Photophobia Associated with Traumatic Brain Injury: A Systematic Review and Meta-analysis. *Optom Vis Sci.* Aug 1 2021;98(8):891-900. doi:10.1097/OPX.0000000000001757

Keywords: Neuroimaging, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Trauma

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Concurrent Neurological Etiologies of Vision Loss in Glaucoma: Diagnostic Yield of MRI Brain and Orbit in Neuro-Ophthalmology Referrals

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Introduction:

Patients with glaucoma may also experience visual loss from an additional underlying neurological disorder. Distinguishing glaucomatous damage from a concurrent non-glaucomatous process can be difficult when the clinical picture is atypical. The use of MRI brain and orbit for these patients has not been clearly defined in terms of its role and diagnostic returns.

Methods:

This retrospective case-series included cases of primary glaucoma referred to neuro-ophthalmology between 06/01/2020 and 06/01/2021 at our center, who underwent MRI of the brain and orbits for evaluation of visual loss not accounted for by glaucomatous optic neuropathy. For eye-level measures, one eye per patient was included. Clinical findings, optical-coherence-tomography (OCT), visual-field results, and MRI brain and orbit studies were analyzed. MRI findings were considered clinically significant (CS) when they contributed to an explanation for the visual deficit. Clinical features were compared between patients with and without CS-MRI findings.

Results:

Among fourteen patients (age 66.4 ± 9.2 years; 50% female), MRI revealed CS non-glaucomatous pathology in 3 (21.4%, one each of compressive optic neuropathy, demyelinating disease, and brain ischemia). A relative afferent pupillary defect (RAPD) and visual field defects atypical for glaucoma were more common in patients with CS- MRI ($p = 0.006$, 0.047 (Fisher's exact). Global RNFL thickness was slightly lower in patients with CS-MRI ($58.2 \pm 6.4 \mu\text{m}$ vs. $72.5 \pm 8.1 \mu\text{m}$; $p = 0.08$), while temporal RNFL thickness was lower in patients with CS-MRI ($49 \pm 5 \mu\text{m}$ vs $62 \pm 7 \mu\text{m}$; $p = 0.03$ (Mann-Whitney)

Conclusions:

Among patients with glaucoma referred to neuro-ophthalmology for concern of additional, non-glaucomatous vision-impacting conditions, MRI identified a contributing cause of vision loss in over one-fifth of cases. The presence of RAPD, visual field pattern atypical for glaucoma, and temporal RNFL thinning on OCT were associated with a CS-imaging result. Careful recognition of these clinical features may enhance diagnostic accuracy and enable earlier identification of concurrent vision-impacting neurologic disease in people with glaucoma.

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Keywords: Neuroimaging, Demyelinating disease, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease, Optic neuropathy, Visual fields

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Optic Pathway Involvement In Posterior Reversible Encephalopathy Syndrome (PRES): Case Report And Literature Review

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Introduction:

PRES is a cerebrovascular syndrome characterized by reversible vasogenic edema of the white matter and acute neurological symptoms including coma, seizures, headache, visual disturbances, and other focal neurologic deficits. It is associated with severe hypertension, renal failure, and use of toxic drugs or agents, including chemotherapeutic and immune-modifying drugs. Although PRES is typically characterized by bilateral, parieto-occipital, and white matter lesions on neuroimaging, unilateral, gray matter, and involvement of other brain regions is possible. We aim to describe a case of PRES with optic chiasm involvement and review five additional cases of PRES with optic pathway involvement.

Description of Cases:

A 43-year-old female patient with a past medical history of acute myeloid leukemia who was admitted for allogeneic stem cell transplant was noted to develop a seizure while speaking to family members. 24-hour vital signs demonstrated a BP range of 136-175 systolic and 75-122 diastolic. A STAT Brain CT demonstrated hypodensities in bilateral occipital lobes and Brain MRI subsequently demonstrated T2 hyperintensities in bilateral occipital lobes and the optic chiasm, suggestive of a diagnosis of PRES. She was also on immunosuppressive therapy with cyclosporine which was discontinued. Three months later she reported that she had inability to see and repeat Brain MRI at that time demonstrated persistent T2 hyperintensities in the optic chiasm. Serum AQP-4 antibody was negative, ruling out optic chiasmitis due to neuromyelitis optica. We also review five additional cases of PRES with involvement of different portions of the optic pathway.

Conclusions, including unique features of the case:

Although PRES is typically characterized by parieto-occipital involvement on neuroimaging, optic pathway involvement is rare. To the best of our knowledge, this is the sixth case of PRES with optic pathway involvement and the third with chiasmal involvement to be reported. Recognition of optic pathway involvement in PRES is essential to ensure prompt diagnosis and management.

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Keywords: Vascular disorders, Neuroimaging, Miscellaneous

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Application of Artificial Intelligence to Magnetic Resonance Imaging for the Identification of the Etiology of Optic Neuritis

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Introduction:

The goal of the study is developing an artificial intelligence model capable of identifying the underlying etiology of optic neuritis based on MRI imaging. The model will be trained to distinguish between multiple sclerosis (MS)–associated optic neuritis, myelin oligodendrocyte glycoprotein antibody–associated disease (MOGAD), and neuromyelitis optica spectrum disorder (NMOSD).

Description of Cases:

For each case of optic neuritis, a standardized set of MRI brain and orbit images and videos will be collected, including axial and coronal FLAIR, STIR, and post-contrast sequences. Artificial intelligence models are being developed in collaboration with a software engineer with AI expertise, leveraging state-of-the-art architectures such as pre-trained convolutional neural networks and transformer-based models. Heatmaps will be generated to visualize regions of interest, enhancing model interpretability and revealing imaging features most relevant for disease classification. A total of 100 cases per etiology (MS, NMO, and MOG) have been identified. The dataset is being partitioned into 70% for training, 10% for validation, and 20% for testing. The model will first undergo self-supervised pretraining on large public datasets of normal brain MRIs to learn generalizable imaging representations. It will then be fine-tuned on our curated optic neuritis dataset to optimize performance for disease-specific classification.

Conclusions, including unique features of the case:

To our knowledge, this represents the first AI model designed to distinguish multiple sclerosis, neuromyelitis optica, and MOG-associated disease using MRI imaging. The generated heatmaps could uncover new distinct radiological patterns specific to each etiology, thereby enhancing diagnostic accuracy.

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References: None provided.

Keywords: Neuroimaging, Optic neuritis

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Grant Support: None.

Contact Information: None provided.

Ophthalmic Conditions in Patients with Multiple Sclerosis

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Introduction:

Multiple sclerosis (MS) is an autoimmune disorder of the central nervous system frequently associated with visual symptoms. However, population-level data on the rates and timing of ophthalmic conditions remain limited. This study examined the prevalence of ophthalmic conditions in individuals with MS versus matched controls and identified associated risk factors.

Methods:

A matched case-control study was conducted using data from the NIH-funded All of Us Research Program. Individuals with MS (n=3,771) were matched 1:3 to controls (n=11,313) by age, sex, and race/ethnicity. Four ophthalmic conditions—optic neuritis, diplopia, nystagmus, and uveitis—were assessed using electronic health records and categorized by timing relative to MS diagnosis. Prevalence and risk factors were analyzed using univariate and multivariate logistic regression, adjusting for sociodemographics, lifestyle, prior brain injury, MS family history, and comorbidities.

Results:

All ophthalmic conditions were significantly more common in MS patients than controls. Optic neuritis was the most frequent (17.0% vs 0.2%; adjusted odds ratio [aOR]= 31.96; p< 0.001), followed by diplopia (10.1% vs 1.0%; aOR=4.88; p< 0.001), uveitis (3.4% vs 0.7%; aOR=2.30; p< 0.001), and nystagmus (2.5% vs 0.2%; aOR=6.97; p< 0.001). Temporal analysis showed that a large proportion of optic neuritis (31.9%), nystagmus (21.9%), diplopia (27.7%), and uveitis (38.3%) preceded MS diagnosis by median days of 178, 504, 279, 788, respectively. Risk factors for optic neuritis among MS patients included comorbid autoimmune disease (aOR=1.55, p< 0.001) and vitamin B deficiency (aOR=1.51, p< 0.001), while hypothyroidism was protective (aOR=0.74, p=0.02).

Conclusions:

Ophthalmic conditions, especially optic neuritis, were more common in MS patients. Uveitis, though rarer, was also more common in MS patients than controls. Large proportions of ophthalmic conditions occurred before MS diagnosis. Certain comorbidities were associated with altered risk for optic neuritis. These findings highlight the importance of recognizing visual disturbances in MS diagnosis and management, identifying patients at increased risk, and fostering collaboration between neurologists and ophthalmologists.

References: None provided.

Keywords: Demyelinating disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Grant Support: None.

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Factors Associated with Surgical Outcomes in Patients with Congenital Fourth Cranial Nerve Palsy

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Introduction:

This study aimed to analyze the surgical outcomes and factors associated with surgical success in children with congenital fourth cranial nerve palsy.

Methods:

A retrospective study was performed for 35 patients who had inferior oblique weakening surgery with at least one year of follow up. Surgical outcomes were grouped as success (hyperphoria/tropia ≤ 5 prism diopters (PD) to hypophoria/tropia ≤ 5 PD), failure (hypertropia > 5 PD or hypotropia > 5 PD) according to the angle of deviation at postoperative one year. We investigated subjects' clinical and demographic factors including magnitude of vertical deviation, stereoacuity at near and distance, and improvement of head tilt. Factors associated with surgical outcomes were then determined through univariate and multivariate analyses.

Results:

Of a total of 35 patients, 27 (77.1%) were assigned to the success group and 8 (22.9%) to the failure group. Univariate analysis revealed that age at surgery, best corrected visual acuity on the left eye, preoperative vertical deviation at distance and near were significantly associated with surgical success for congenital CN4 palsy at postoperative one year. In multivariate analysis, age at surgery was the only factor affecting successful surgical outcome.

Conclusions:

Surgery performed during childhood results in better outcomes than surgery performed in adulthood in patients with congenital CN 4 palsy.

References: None provided.

Keywords: Adult strabismus with a focus on diplopia, Ocular motility

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Grant Support: None.

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The Obesity Paradox in Korean Diabetic Patients: Higher Body Mass Index Reduces Non-Arteritic Anterior Ischemic Optic Neuropathy Risk

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Introduction:

Type 2 diabetes mellitus (T2DM) is a known risk factor for non-arteritic anterior ischemic optic neuropathy (NAION). However, the specific association between obesity indicators, such as body mass index (BMI) and waist circumference (WC), and NAION risk in T2DM patients remains underexplored. This study aimed to investigate this relationship to better understand NAION pathophysiology and inform clinical management strategies.

Methods:

This retrospective nationwide population-based cohort study utilized the Korean National Health Insurance Service database, including 2,178,910 Korean adults with T2DM. Participants were enrolled between 2015–2016 and followed through 2022, with an average follow-up of 5.74 years. NAION cases were identified using ICD-10 code H47.0 with specific healthcare utilization criteria. BMI was categorized into five groups based on Asia-Pacific obesity classification, and WC was categorized using sex-specific criteria. Cox proportional hazards regression models were employed to assess the association between BMI, WC, and NAION risk, adjusting for various confounding factors including age, sex, income, lifestyle, comorbidities, fasting blood glucose, diabetes duration, and medications.

Results:

During 12,512,222.58 person-years of follow-up, 13,524 incident NAION cases were observed. Compared to the reference group (BMI 18.5–23.0 kg/m²), higher BMI categories were associated with a progressively lower NAION risk: BMI 25.0–30.0 kg/m² (HR: 0.917, 95% CI: 0.878–0.958) and BMI ≥30.0 kg/m² (HR: 0.782, 95% CI: 0.725–0.843). Similarly, the highest WC category showed a 12.6% lower NAION risk (HR: 0.874, 95% CI: 0.816–0.935) compared to its reference group (WC 85–90 cm for men and 80–85 cm for women).

Conclusions:

In Korean patients with T2DM, higher BMI and WC are significantly associated with a reduced risk of NAION. These findings challenge traditional views on obesity as a NAION risk factor and provide important insights into NAION pathophysiology in diabetic patients, potentially influencing clinical management, especially concerning the recent discussions around GLP-1 receptor agonist use and NAION risk.

References: None provided.

Keywords: Optic neuropathy, Vascular disorders

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External Validation of Predictive Models in Diagnosing Giant Cell Arteritis Among Temporal Artery Biopsy Patients

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Introduction:

Giant cell arteritis (GCA) is the most common primary vasculitis in the elderly, carrying risks of blindness and systemic complications. The diagnostic gold standard, temporal artery biopsy (TAB), has limited sensitivity and is invasive. Clinical features alone are often insufficient for diagnosis, and glucocorticoid treatment—though lifesaving—can cause significant morbidity. Accurate pre-biopsy prediction tools may guide management, reduce unnecessary biopsies, and prevent complications from delayed or inappropriate corticosteroid use. Logistic regression (LR) and artificial neural network (NN) models developed by Ing et al. have shown promise as clinical prediction tools for GCA risk.

Methods:

We retrospectively reviewed patients evaluated for suspected GCA at the Wake Forest Baptist Eye Clinic who underwent TAB. Demographic, clinical, and laboratory data were collected, and predicted probabilities were generated using Ing et al.'s LR and NN models. Predicted probabilities were compared between biopsy-positive and biopsy-negative groups. Model performance was assessed using Fisher's exact tests, Shapiro-Wilk tests, and receiver operating characteristic (ROC) analysis.

Results:

Of 147 patients, 26 (17.7%) had biopsy-proven GCA. Predictors of positive biopsy included older age, White race, disc edema, jaw claudication, elevated C-reactive protein, and elevated platelet count. Both LR and NN models demonstrated strong predictive capacity, with ROC areas of 0.7786 and 0.7843, respectively. Both models effectively stratified patients by risk, with significantly higher predicted probabilities among biopsy-positive cases. LR yielded a median probability of 30.5% for positives and 12.9% for negatives ($p < 0.0001$), while NN produced 36.7% and 15.9%, respectively ($p < 0.0001$).

Conclusions:

LR and NN models accurately predict pre-biopsy GCA risk in a North Carolinian cohort. These models may reduce unnecessary biopsies and corticosteroid exposure while maintaining diagnostic accuracy, supporting their use as adjunct tools in clinical decision-making.

References: Ing, E. B., Miller, N. R., Nguyen, A., Su, W., et al. Neural network and logistic regression diagnostic prediction models for giant cell arteritis: development and validation. *Clinical ophthalmology* (Auckland, N.Z.), 13, 421–430. 2019

Keywords: Vascular disorders, Visual fields

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Efficacy of Nipocalimab in Adult Patients with Moderate to Severe Ocular Manifestations of Generalized Myasthenia Gravis in Phase 3 VIVACITY-MG3

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Introduction:

In generalized myasthenia gravis (gMG), 15-50% patients have ocular manifestations (ptosis, diplopia) limiting daily-activities and impacting quality-of-life. Nipocalimab+standard-of-care (SOC, nipocalimab) demonstrated sustained efficacy vs placebo+SOC (placebo) in VIVACITY-MG3 (NCT04951622). This analysis evaluated efficacy of nipocalimab vs placebo in the subgroup of patients with moderate-severe ocular manifestations (MSOM).

Methods:

In this post-hoc analysis, MSOM was defined as baseline score of ≥ 2 -points on either diplopia or ptosis items of Myasthenia Gravis-Activities of Daily Living (MG-ADL) scale. Least-squares (LS) mean changes from baseline (CFB) to week 24 (W24) on the MG-ADL-ocular domain (MG-ADL-ocular) and total scores (MG-ADL-total) were analyzed using repeated measures models. Chi-square test statistics were used to evaluate proportion of patients achieving meaningful within-person improvement (MWPI) of ≥ 2 -points at 24-weeks from baseline; logistic regression models were used to examine likelihood (OR) of achieving MWPI.

Results:

At baseline, within MSOM subgroup, nipocalimab (n=54/77) and placebo (n=51/76) arms were comparable in mean age (52.5, 53.5 years), percentage of female patients (63%, 55%) and mean (standard deviation) MG-ADL-ocular (4.1 [1.2]; 3.5 [1.0]) and MG-ADL-total (10.1 [2.8]; 9.4 [1.9]) scores. At W24, the CFB LS mean differences (95% CI) for nipocalimab vs placebo were: MG-ADL-ocular (-1.6 [-2.6, -0.6]; -1.1 [-2.0, -0.2]; p=0.024); and MG-ADL-total (-4.6 [-5.4, -3.7]; -3.2 [-4.1, -2.3], p=0.010), favoring nipocalimab. Greater proportion of patients achieved MWPI at W24 on MG-ADL-ocular (difference=29.3%; OR=3.6; p=0.006) and MG-ADL-total (difference=24.4%; OR=3.5; p=0.01), favoring nipocalimab.

Conclusions:

Nipocalimab-treated patients with gMG and MSOM showed superior improvements on the MG-ADL-ocular and MG-ADL-total scores vs placebo-treated patients and were significantly more likely to achieve MWPI at W24.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Myasthenia

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Contact Information: None provided.

Decreased Complement C3 and Increased C8G in Neuromyelitis Optica Spectrum Disorder: Evidence of Complement-Mediated Pathophysiology

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Introduction:

To evaluate the degree of complement system activation in patients with neuromyelitis optica spectrum disorder (NMOSD) by measuring serum complement components C3 and C8G levels and comparing these with healthy controls.

Methods:

Serum concentrations of C3 and C8G were measured using enzyme-linked immunosorbent assay (ELISA) in 10 patients diagnosed with NMOSD and 16 age- and sex-matched healthy controls. All patients initially presented with optic neuritis as their primary manifestation and were subsequently diagnosed with NMOSD. Statistical differences between groups were analyzed using the Mann-Whitney U test.

Results:

Patients with NMOSD demonstrated markedly decreased serum C3 levels ($18.46 \pm 12.65 \mu\text{g/ml}$) compared with healthy controls ($115.18 \pm 27.52 \mu\text{g/ml}$), representing an 84.0% reduction ($p < 0.001$). In contrast, serum C8G levels were significantly elevated in the patient group ($4.24 \pm 2.32 \mu\text{g/ml}$) compared with controls ($2.22 \pm 1.21 \mu\text{g/ml}$), demonstrating a 91.4% increase ($p < 0.01$). The median C3 levels were $15.44 \mu\text{g/ml}$ (IQR: 11.02-21.13) in patients and $116.97 \mu\text{g/ml}$ (IQR: 100.79-126.32) in controls, while median C8G levels were $3.71 \mu\text{g/ml}$ (IQR: 3.48-5.51) in patients and $2.49 \mu\text{g/ml}$ (IQR: 1.01-3.23) in controls.

Conclusions:

The marked depletion of C3 with significant elevation of C8G observed in NMOSD patients provides compelling evidence for complement-mediated astrocyte injury, which constitutes the core pathophysiology of NMOSD. The dramatic reduction in C3 (84%) indicates extensive complement cascade activation and consumption triggered by AQP4-IgG immune complex formation, whereas the elevated C8G suggests active tissue destruction through increased membrane attack complex (MAC) formation. This distinctive complement profile may serve as a valuable biomarker for monitoring disease activity in NMOSD and may be particularly useful in determining indications for complement inhibitor therapy during acute exacerbations.

References: None provided.

Keywords: Demyelinating disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuritis

Financial Disclosures: The authors had no disclosures.

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Formulation and Ex Vivo Evaluation of Pyridostigmine Bromide Eye Drops for Ocular Myasthenia Gravis Treatment

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Introduction:

Pyridostigmine bromide is the first-line treatment for myasthenia gravis (MG), but its oral administration limits ocular efficacy due to systemic side effects and poor penetration to extraocular muscles and eyelid retractors. Patients with ocular myasthenia gravis (OMG) often continue to experience ptosis and diplopia despite systemic therapy. This study aimed to formulate pyridostigmine as a topical ophthalmic preparation and assess its stability, permeability, and ocular safety using porcine eyes as a preclinical ex vivo model.

Methods:

Pyridostigmine bromide eye drops were prepared and stored at room temperature. Stability was evaluated at 0-, 15-, 30-, and 60-days using UV-Vis spectrophotometry, and pH was measured before and after drug addition to confirm ocular compatibility. Permeability was tested using freshly harvested porcine eyes and a Franz diffusion cell system, with drug recovery quantified spectrophotometrically. Fluorescein staining compared corneal epithelial toxicity between pyridostigmine and phosphate-buffered saline (PBS) controls.

Results:

Pyridostigmine formulations remained chemically stable for up to 60 days. Spectrophotometric analysis confirmed corneal penetration with an average recovery of approximately 0.9 mg per 1 mg applied dose. The natural pig eye model demonstrated greater reproducibility and biological relevance than the Franz diffusion cell. Fluorescein staining revealed no significant epithelial toxicity compared with PBS controls.

Conclusions:

Pyridostigmine bromide can be formulated as a stable, biocompatible ophthalmic solution with measurable corneal penetration in ex vivo models. The natural pig eye system provided reliable translational insights and should be prioritized for future preclinical studies. These findings support the feasibility of a localized pyridostigmine therapy for OMG, warranting further in vivo evaluation.

References: None provided.

Keywords: Myasthenia, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Ocular motility, Orbit

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Association between disease-modifying therapies for multiple sclerosis and risk of non-infectious uveitis

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Introduction:

Multiple sclerosis (MS) patients have an increased risk of non-infectious uveitis (NIU). It is unknown whether MS disease-modifying therapies (DMTs) affect this risk. We sought to assess the comparative risk of NIU in MS after initiating different DMTs.

Methods:

This was a retrospective cohort study of MS patients using a de-identified insurance claims database (Optum Clinformatics™ Data Mart). Inclusion required 3+ MS diagnosis codes from different dates, 1+ DMT prescription, and 2+ years of preceding insurance coverage. Outcomes for interferons, anti-CD20 monoclonal antibodies (mAbs), fumarates, nucleic acid synthesis inhibitors/sphingosine-1-phosphate (S1P) modulators, and natalizumab were compared to glatiramer acetate (GA) as the reference. Incident NIU required an NIU diagnosis code followed by a second code within 120 days for confirmation. In a sensitivity analysis, confirmation required a steroid prescription or ocular injection. Censoring occurred with loss of insurance, intraocular surgery, or DMT change (but patients could contribute multiple treatment periods by changing therapies). Adjusted hazard ratios (aHR) for NIU were calculated using marginal Cox models. To adjust for confounders associated with DMT selection and NIU, propensity scores were computed using multivariable logistic regression.

Results:

There were 43,501 patients contributing 48,221 treatment periods. Median follow-up was 562–703 days across DMT classes. Compared to GA, NIU incidence was lower for interferons (aHR 0.67, 95% CI: 0.50-0.91), anti-CD20 mAbs (aHR 0.66, 95% CI: 0.51-0.85), fumarates (aHR 0.51, 95% CI: 0.36-0.74), and nucleic acid synthesis inhibitors/S1P modulators (aHR 0.14, 95% CI: 0.07-0.29), but not natalizumab (aHR 0.87, 95% CI: 0.61-1.24). The sensitivity analysis found similar results for fumarates (aHR 0.56, 95% CI: 0.38-0.82) and nucleic acid synthesis inhibitors/S1P modulators (aHR 0.16, 95% CI: 0.08-0.33).

Conclusions:

Some MS DMTs may reduce NIU risk. If confirmed in future research, this could enable personalized MS treatment or novel repurposing of MS DMTs for NIU in other patient populations.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Orbit/ocular pathology, Demyelinating disease

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Grant Support: None.

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Ophthalmologic Spectrum and Clinical Outcomes in Idiopathic and IgG4-Related Hypertrophic Pachymeningitis

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Introduction:

This study aimed to explore the ophthalmologic manifestations in patients with hypertrophic pachymeningitis (HP) and to compare the clinical features, laboratory findings, and treatment outcomes between idiopathic and IgG4-related forms of HP.

Methods:

This retrospective study reviewed adult patients diagnosed with HP at Siriraj Hospital, Thailand, between 2017 and 2022. Data were collected on clinical presentations, laboratory results, neuroimaging findings, treatment approaches, and patient outcomes.

Results:

A total of 34 patients (24 women, 10 men) were included, with a mean age of 51.1 years (range 26–80 years). Idiopathic HP was the most common etiology, accounting for 61.8% of cases. Ophthalmic symptoms were present in most patients (85.3%). Diplopia was the most frequent presenting symptom (35.3%), while the most common overall symptom was chronic headache (73.5%), followed by diplopia (50.0%) and decreased vision (35.3%). Eye pain was more common in idiopathic HP ($p = 0.04$). Cranial neuropathy, particularly involving cranial nerves VI, III, and II, was common. Corticosteroids were the initial treatment in most patients, with additional immunosuppressive therapy required in 26 cases due to steroid intolerance or relapse. All patients showed symptomatic improvement within 4 months, and more than half achieved symptom resolution within the first year. Final visual acuity significantly improved from 0.3 to 0.2 logMAR. There was no significant difference in recurrence rates between idiopathic and IgG4-related HP ($p = 0.50$).

Conclusions:

Ocular manifestations are common in HP, with diplopia being the most frequent presenting symptom and eye pain occurring more often in idiopathic cases. These findings highlight the importance of comprehensive ophthalmologic evaluation. Although corticosteroids remain the mainstay of treatment, additional immunosuppressive therapy is frequently required due to relapse or steroid dependence.

References: None provided.

Keywords: Neuro-ophth & infectious disease (eg, AIDS, prion), Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Frequency of optic nerve enhancement during acute optic neuritis in MOG antibody-associated disease

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Introduction:

Optic neuritis (ON) is the most common manifestation of myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD). MRI is routinely used for evaluation of relapses in MOGAD including ON, however, the sensitivity for T1 post-contrast enhancement in orbital MRI in MOGAD associated acute ON has not yet been established.

Methods:

In this retrospective study, patients referred to the Mayo Clinic who met the diagnostic criteria for MOGAD, presented with acute ON, completed MRI with fat suppression of the orbit within 30 days of the onset of visual symptoms, and had adequate clinical data for review were included. Available clinical data and the presence of T1 post-contrast enhancement was evaluated during acute ON.

Results:

The study included 122 patients with MOGAD (median age: 39 years [range, 6-72], 68% female) with 177 acute ON attacks. Bilateral ON occurred in 34/122(28%) of patients. MRIs were completed a median of 6 days (range, 0-26) after the onset of visual loss. Of included attacks, 119/170 (70%) had a visual acuity 20/40 or worse, 77/170(45%) had a visual acuity 20/200 or worse, and 157/173(91%) had pain with eye movements during acute ON. Optic nerve T1 post-contrast enhancement was present in 173/177 ON attacks(97.7%). ON was confirmed in patients without enhancement on MRI by at least one of the following: retinal nerve fiber layer swelling on optical coherence tomography (n=2), enhancement on a second MRI within the acute presentation (11 days later, n=1), and/or new T2 hyperintensity of the optic nerve on a follow-up MRI scan (n=2).

Conclusions:

Contrasted MRI with fat suppression is highly sensitive for the detection of acute ON in MOGAD and can aid in diagnosis. In rare cases, enhancement may not be present in MOGAD acute ON and ancillary testing including OCT and follow-up MRI may be helpful for diagnosis.

References: None provided.

Keywords: Optic neuritis, Demyelinating disease, Optic neuropathy, Neuroimaging

Financial Disclosures: Stephanie Syc-Mazurek; Nanthaya Tisivipat; Natthapon Rattanathamsakul; Paul Farnsworth; Moritz Niederschweiberer; M. Tariq Bhatti; Kevin Chodnicki; Deena Tajfirouz; Sean Pittock: Sean J. Pittock has received personal compensation for serving as a consultant for Roche/Genentech, Sage Therapeutics, Arianys and Astellas. He has received personal compensation for serving on scientific advisory boards or data safety monitoring boards for F. Hoffman-LaRoche AG, Genentech, Arianys and UCB. His institution has received compensation for serving as a consultant for Astellas, Alexion, and Viela Bio/MedImmune. All compensation is paid to Mayo Clinic. He has received research support from Alexion, Viela Bio/MedImmune, Roche/Genentech and Adimmune. He has a patent, Patent# 8,889,102 (Application#12-678350, Neuromyelitis Optica Autoantibodies as a Marker for Neoplasia)-issued; a patent, Patent# 9,891,219B2 (Application#12-573942, Methods for Treating Neuromyelitis Optica (NMO) by Administration of Eculizumab to an individual that is Aquaporin-4 (AQP4)-IgG Autoantibody positive)-issued and from which he has received royalties and a patent for GFAP-IgG; Septin-5-IgG; MAP1B-IgG; Kelch-like protein 11; PDE10A pending.; Eoin P. Flanagan: Dr Flanagan has served on advisory boards for Alexion, Genentech, Horizon Therapeutics and UCB. He has received research support and funding from UCB, Roche and Merck. He received royalties from UpToDate. Dr Flanagan is a site principal investigator in a randomized clinical trial of Rozanolizumab for relapsing myelin oligodendrocyte glycoprotein antibody-associated disease run by UCB. Dr Flanagan is a site principal investigator and a member of the steering committee for a clinical trial of satralizumab for relapsing myelin oligodendrocyte glycoprotein antibody-associated disease run by Roche/Genentech. Dr Flanagan is a Co-Investigator on a study of ravulizumab for neuromyelitis optica spectrum disorder run by Alexion. Dr Flanagan has given educational talks on neuromyelitis optica spectrum disorder funded by Alexion. Dr Flanagan has received funding from the

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Contact Information: None provided.

Temporal Patterns of Ocular Syphilis: Imaging and Laboratory Correlates Across Symptom Duration

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Introduction:

Ocular syphilis has historically been described as a patternless collection of distinct phenotypes. We hypothesized that the disease is less haphazard than this conception implies. To test this, we evaluated whether posterior segment imaging and laboratory findings demonstrate identifiable temporal patterns.

Methods:

The study included 40 patients (73 eyes) diagnosed with ocular syphilis from 2015 to 2025. Posterior segment features were graded across color fundus photography (CF), fluorescein angiography (FA), optical coherence tomography (OCT), and near-infrared reflectance (NIR). Imaging findings were compared across two duration thresholds (≤ 14 vs > 14 days and ≤ 30 vs > 30 days) using Fisher's exact or chi-square tests. Features were classified as time-independent if present in $\geq 40\%$ of both early and delayed groups without $\geq 15\%$ directional skew. Serum rapid plasma reagin (RPR) titers and cerebrospinal fluid (CSF) markers (VDRL, protein, and white blood cell count) were correlated with symptom duration using Spearman analysis.

Results:

OCT macular edema ($p = 0.002$), disc edema ($p = 0.005$), choroidal hyperreflective foci ($p = 0.023$), and NIR geographic reflectivity differences ($p = 0.034$) were significantly more common within 14 days. Before 30 days, disc edema on OCT and CF ($p = 0.006$, 0.007) and NIR linear reflectivity change ($p = 0.031$) were more prevalent. Several features, including OCT subretinal hyperreflective lesions, NIR white dots, FA placoid pattern, and OCT ellipsoid zone (EZ) variable reflectivity, met criteria for time-independence. Some findings (e.g., retinal nerve fiber atrophy) appeared only in delayed presentations, although these occurred too infrequently for statistical significance. RPR titer inversely correlated with duration ($r = -0.445$, $p = 0.004$), while CSF parameters showed mildly negative but nonsignificant trends.

Conclusions:

This study demonstrates that ocular syphilis may be less haphazard than historically described. Despite considerable variety, temporal patterns can be identified. Recognizing early, persistent, and late features may improve diagnostic interpretation and prognostic counseling.

References: Browning DJ, Posterior segment manifestations of ocular syphilis, *Ophthalmology*, 107, 1887–1898, 2000. Oliver GF; Leung EH; Jolley A; Smith JR, Ocular syphilis: A global review, *Eye*, 33, 1913–1924, 2019.

Keywords: Neuro-ophth & infectious disease (eg, AIDS, prion), Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Optic neuritis

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Grant Support: None.

Contact Information: None provided.

Prevalence and Prognostic Significance of Autoantibody Profiles in Transformation of Ocular to Generalized Myasthenia Gravis

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Introduction:

Acetylcholine receptor (AChR) antibodies are found in approximately 50% of patients with Ocular Myasthenia Gravis (OMG) and are associated with an increased risk of the disease progressing to Generalized Myasthenia Gravis (GMG). The relationship between the presence, type, and number of autoantibodies in OMG and the clinical course of the disease remains unclear.

Methods:

We performed a retrospective, single-center chart review of all patients diagnosed with myasthenia gravis (MG) at Froedtert Hospital between January 1, 2016, and August 1, 2023. Clinical data were abstracted from electronic medical records to characterize patient demographics, disease features, treatments, and outcomes.

Results:

A total of 268 patients with a MG diagnosis were included. Among patients with three positive antibodies, a higher proportion developed generalized MG (26 out of 35, or 74.3%) compared with those with fewer or no antibodies. Among those with 0 antibodies, the distribution of patients who did and did not develop GMG is nearly even. Overall, 67.9% of antibody-negative patients did not develop GMG, while 67.9% of antibody-positive patients did develop GMG. There was a statistically significant association between the number of positive antibodies and the development of generalized MG ($p = 0.024$), and Linear-by-Linear Association ($p = 0.003$). Patients with binding antibody positive were significantly more likely to start with or develop GMG (Chi-Square = 29.595, $p < 0.001$).

Conclusions:

Across multiple analyses and outcome measures, antibody positivity—especially the presence of multiple antibodies—is strongly associated with higher likelihood of transformation to GMG.

References: None provided.

Keywords: Myasthenia, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Ocular Symptom Burden on Visual Recovery in Neurosyphilis

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Introduction:

Neurosyphilis can display a wide range of symptoms, which can complicate diagnosis and requires a heightened level of clinical suspicion. While neurosyphilis is known to affect virtually any ocular structure, the specific ocular symptoms, as well as the total eye symptom burden effect on visual recovery, remains poorly characterized.

Methods:

We retrospectively reviewed patients diagnosed and treated for neurosyphilis at a tertiary academic center between 2014-2024. Inclusion criteria required diagnosis confirmed by laboratory and ophthalmologic confirmation, completion of full antibiotic treatment, and documented follow-up visual acuity. Demographics, risk factors, ocular symptoms, systemic features (e.g., hair loss), and baseline and follow-up visual acuity after treatment were extracted. Each ocular symptom (e.g., blurry vision, photophobia, photopsia, vision loss) contributed one point to a composite symptom score. Both eyes were included for analysis to capture within-subject variability. We examined the associations between the primary outcome (Δ logMAR) and symptom scores using mixed-effects multiple regression; a random intercept was included for the patient to account for potential clustering. Age, sex, and marijuana/drug use were included as covariates.

Results:

A total of 49 patients (97 eyes) were included. Mean age was 47.4 ± 11.2 years, and 59.2% were male. All patients had ocular symptoms on initial presentation. Higher total ocular symptom scores were significantly associated with greater visual improvement ($\beta = -0.09$, 95% CI -0.15 to -0.03 , $p=0.005$), indicating that each additional symptom corresponded to a -0.09 logMAR greater recovery in visual acuity after treatment.

Conclusions:

Patients with higher symptom burden demonstrated greater visual improvement following neurosyphilis treatment. This association suggests that symptom burden may reflect earlier recognition and treatment-responsiveness.

References: Reid, Halmagyi, Whyte, McCluskey; Ocular syphilis vs neurosyphilis. are they the same? A guide to investigation and management, Eye, 38, 2337-2349, 2024. Beckman, Rifkin; Ocular syphilis: a case series of four patients and a review of the literature, Annals of Eye Science, 9, 12, 2024.

Keywords: Neuro-ophth & infectious disease (eg, AIDS, prion)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Adaptive Optics OCT Reveals Alterations in Macrophage-Like Cell Morphology in Multiple Sclerosis

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Introduction:

We previously reported use of AO-OCT to visualize MLCs, which are presumed to be retinal microglia, at the vitreomacular interface in MS. Since microglia take on various morphologies in response to environmental conditions, including ramified, rod-like, and amoeboid shapes, visualization of cell morphology with AO-OCT may enable direct quantification of the inflammatory and neurodegenerative state of retinal tissue in MS.

Methods:

Six macular regions in one eye each from nine healthy volunteers (HV) and ten patients with MS (four with a history of optic neuritis (MS-ON) in the imaged eye, six without (MS-no-ON)) were imaged using AO-OCT on a custom-built multi-modal AO device. MLCs were examined directly above the inner limiting membrane (ILM) and labelled based on morphology.

Results:

Total MLC counts in the macular regions were higher in MS (median: MS=32.5, HV=6; $p=0.033$), preferentially in the temporal macula (median: MS=24.5, HV=4; $p=0.007$). Subtype analysis revealed higher rod-like (median: MS=3.5, HV=1; $p=0.010$) and amoeboid (median: MS=18.5, HV=2; $p=0.005$) morphologies temporally in MS, along with higher amoeboid (median: MS=9.5, HV=0; $p=0.046$) morphology nasally. There was no significant difference in ramified MLC count in any retinal location between MS and HV (median: MS=6, HV=1; $p=0.322$). The only difference between MS-ON and MS-no-ON was a higher rod-like appearance (median 12 vs 5, respectively, $p=0.009$).

Conclusions:

Retinal MLCs in activated states are higher in MS as visualized by AO-OCT, particularly in the temporal macula. Our findings add further in vivo evidence of neurodegenerative changes in MS.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Neuroimaging, Demyelinating disease

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Grant Support: Department of Defense Congressionally Directed Medical Research Program (CDMRP), Multiple Sclerosis Research Program (MSRP)

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Does OPA1 Genotype And Visual Outcomes Predict Idebenone Treatment In Dominant Optic Atrophy (DOA)?

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Introduction:

Autosomal dominant optic atrophies (DOA) are inherited diseases of the optic nerve that cause vision loss through retinal ganglion apoptosis due to mitochondrial dysfunction. DOA is commonly caused by pathological variants in the OPA1 gene, which encodes a protein central to mitochondrial function. Although idebenone is an established treatment for Leber's Hereditary Optic Neuropathy, its off-label use in DOA is less understood. We hypothesized that DOA patients with a molecular diagnosis, especially OPA1 variants, or those with worse structural appearances or visual function, may be more likely to use idebenone off-label.

Methods:

Case notes from 39 DOA patients (ages 8-69 years) were reviewed. Patients were arranged as follows: OPA1 (n=15, confirmed OPA1 pathological variant), Unsolved (n=10, genetic testing performed but no pathological variant identified), and Untested (n=14, no genetic testing performed). Idebenone use was defined as having received 300 mg TID for ≥ 12 months. Best corrected visual acuity (BCVA, LogMAR), visual field (VF, mean deviation), and average retinal nerve fiber layer (RNFL, μm) thickness were recorded and compared groupwise. Statistical analysis included Fisher's exact tests, Chi-square tests, and Wilcoxon tests using R software ($\alpha=0.05$).

Results:

Genetic testing was documented in 69% of patients, of whom 38% were OPA1 and 31% were Unsolved. 59% of the cohort were using idebenone off-label. Idebenone use was not significantly associated with genetic testing ($p=1.00$) or with OPA1 mutation ($p=0.985$). Distribution for VA ($W=728$, $p=0.80$), RNFL ($W=753.5$, $p=0.069$), and VF ($W=361$, $p=0.99$) were not significant; therefore, worse structural and visual function relate to idebenone usage.

Conclusions:

Idebenone use was not significantly associated with a molecular diagnosis, OPA1 status, or measures of visual severity, thereby disproving our initial hypothesis. This provides a necessary foundation for larger prospective studies to help determine whether idebenone confers measurable visual benefit in pathological variants of DOA.

References: None provided.

Keywords: Genetic disease, Optic neuropathy

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Extraocular Muscle And Orbital Fat Changes In Treatment Of Thyroid Eye Disease With Monoclonal Antibodies: A Systematic Review and Meta-Analysis

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Introduction:

Imaging provides objective measures of disease activity in thyroid eye disease (TED), yet the impact of biologic therapies on extraocular muscle (EOM) and orbital fat volumes remains undefined. This systematic review and meta-analysis evaluated radiological changes in TED patients receiving monoclonal antibody therapy to inform clinical practice and elucidate potential mechanisms of soft tissue remodeling.

Methods:

The full protocol of this systematic review and meta-analysis was registered on PROSPERO (CRD420251129246). The databases Embase (OVID), Medline, and PubMed were searched from inception to August 18, 2025. Eligible studies reported baseline and follow-up imaging outcomes in TED patients treated with monoclonal antibodies. Fourteen studies were identified, comprising 566 orbits from 304 patients with TED. Data were pooled using random-effects models to estimate mean differences in EOM and orbital fat volumes. Meta-regression was applied to explore associations between clinical indicators and radiographic parameters.

Results:

Six studies assessed radiologic changes after teprotumumab treatment, four after tocilizumab, and four after rituximab. Pooled analysis revealed a mean difference in total EOM volume of -1377.4 mm³ (95% CI: 742.9-2012.0; I²=90.8%; p< 0.001), and an orbital fat volume mean difference of -1731.6 mm³ (95% CI: 461.2-3002.0; I²=82.8%; p< 0.001), representing a 26.7% and 16.2% reduction with treatment, respectively. There was a statistically significant linear relationship between total EOM volume reduction and clinical activity score (CAS) improvement (regression coefficient: 1086 mm³/CAS unit, 95% CI: 850-1322; p< 0.001), as well total orbital fat volume (regression coefficient: 1266 mm³/CAS unit, 95% CI: 504-2029; p=0.001).

Conclusions:

Monoclonal antibody therapy is associated with significant reductions in both EOM and orbital fat volumes in TED. These findings suggest biologics both improve clinical activity and remodel orbital soft tissues, supporting their role in disease modification. Further research is warranted to determine the relationships between long-term radiological and functional outcomes, as well as soft tissue remodeling mechanisms.

References: None provided.

Keywords: Graves' disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Neuroimaging, Orbit, Orbit/ocular pathology

Financial Disclosures: The authors had no disclosures.

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Contact Information: None provided.

Silent Partners in Aging: Unraveling Demographic Risk Factors Linking Glaucoma and Alzheimer's Through a Nationwide EHR Analysis

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Introduction:

Alzheimer's disease and Glaucoma are both chronic progressive diseases that share similar risk factors. The goal of this study is to explore epidemiological patterns in Alzheimer's patients with a past medical history of glaucoma to evaluate which risk factors increase the odds of developing Alzheimer's.

Methods:

Epic Cosmos, a dataset of 280M patients, was queried for patient demographic data, disease staging using relevant ICD-10 codes for primary open angle glaucoma (POAG) and normal tension glaucoma (ICD H40.1X and corresponding codes) or primary angle closure glaucoma (PACG; ICD H40.2X) who developed a diagnosis of Alzheimer's disease (ICD G30.X) between the years 1/2015 - 12/2023. Stratified odds ratios (OR) were calculated.

Results:

Of 703603 POAG patients, 25165 patients developed Alzheimer's Disease (OD 7.10 [7.02 - 7.20], $p < 0.01$). Of 93300 PACG patients, 3092 patients developed Alzheimer's Disease (OD 6.5 [6.27 - 6.73], $p < 0.01$). Amongst POAG patients, female sex (OD 1.30, [1.26 - 1.43], $p < 0.01$), age $> 85+$ (4.85, [4.73 - 4.98], $p < 0.01$), white race (1.19 [1.15 - 1.22], $p < 0.01$), non-hispanic ethnicity (1.32 [1.25 - 1.40], $p < 0.01$) and both intermediate (1.40 [1.36 - 1.44], $p < 0.01$) and severe (1.63, 1.63 - 1.63], $p < 0.01$) disease severity was associated with increased odds. Among PACG patients, female sex (OD [3.31, 3.01 - 3.63], $p < 0.01$), age between 75-85 (OD [1.13, 1.06 - 1.22], $p < 0.01$) or $85+$ (OD [5.88, 5.46 - 6.32], $p < 0.01$), African American race (OD [1.086, 1.00 - 1.17], $p < 0.05$), non-hispanic ethnicity (OD [1.36, 1.19 - 1.54], $p < 0.01$), and severe disease severity (OD [1.39, 1.37 - 1.40], $p < 0.01$).

Conclusions:

In this study, we found that patients with increased age, female gender, non-hispanic ethnicities and severe disease severity were more likely to develop Alzheimer's amongst both POAG and PACG patients. A focus on this population can increase earlier disease intervention and treatment.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Factor Associated with The Presence Of Other Autoimmune Diseases in Neuromyelitis Optica Spectrum Disorder Patients who Initially Presented with Optic Neuritis

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Introduction:

Neuromyelitis optica spectrum disorder (NMOSD) is an autoimmune inflammatory disorder affecting the central nervous system, frequently initially presenting with optic neuritis (ON). Coexistence with other autoimmune diseases has been reported; however, data on factors associated with the presence of such comorbidities among NMOSD patients who initially presented with ON are limited.

Methods:

A retrospective review was conducted on 58 patients diagnosed with NMOSD who initially presented with ON. Demographic data, aquaporin-4 antibody status, non-ON demyelinating events simultaneous with ON onset, clinical characteristics, magnetic resonance imaging characteristics, and the presence of other autoimmune diseases (defined as the presence of at least one other autoimmune disease) were reviewed. In patients who initially presented with bilateral, simultaneous ON, only the eyes with worse best-corrected visual acuity at nadir were reviewed. Factors associated with the presence of other autoimmune diseases were analyzed using univariate and multivariate logistic regression analyses.

Results:

Of the total 58 patients, 19 (32.76%) demonstrated the presence of other autoimmune diseases (17 patients (29.31%) and 2 patients (3.45%) had one and two other autoimmune diseases, respectively). The other autoimmune diseases included autoimmune thyroid diseases (6 patients (10.34%)), systemic lupus erythematosus (6 patients (10.34%)), Sjögren's syndrome (5 patients (8.62%)), immune thrombocytopenia (2 patients (3.45%)), myasthenia gravis (1 patient (1.72%)), and mixed connective tissue disease (1 patient (1.72%)). Age at ON onset ≥ 30 years was significantly associated with the presence of other autoimmune diseases (odds ratio 7.41, 95% confidence interval: 1.48 - 37.06, $p = 0.015$).

Conclusions:

Screening for other autoimmune diseases should be considered in NMOSD patients who initially presented with ON, particularly in those aged at ON onset ≥ 30 years.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuritis, Demyelinating disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Interferon-Beta vs. Monoclonal Antibody Therapy in Multiple Sclerosis-Associated Uveitis: A Systematic Review

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Introduction:

Uveitis is a rare complication of multiple sclerosis (MS). It may present as complaints of floaters or blurred vision, due to a reduction in visual acuity (VA). Traditional management using corticosteroids and immunosuppressants offers limited long-term efficacy. Modern disease-modifying therapies, including interferon-beta (IFN- β) and monoclonal antibodies (mAbs), have emerged as potential treatments that address both neurological and ophthalmological disease components.

Description of Cases:

A systematic review was conducted following PRISMA guidelines. Literature searches of PubMed, EMBASE, and Cochrane Library were performed up to December 2024. Studies evaluating IFN- β or mAb therapy in human patients with MS-associated uveitis (MS-AU) were included. Clinical variables, including visual acuity (VA) before and after treatment, were extracted, converted to LogMAR, and analyzed. Four studies met inclusion criteria for IFN- β and five for mAbs. Among patients treated with IFN- β , 95% (35/37 eyes, 21 patients) had improved or maintained VA after a mean of 34.7 months (range 7.9–78.7), while 100% of mAb-treated patients (19/19 eyes, 10 patients) demonstrated maintained or improved VA after a mean of 25 months (range 8–43). ANOVA comparison revealed no significant difference in VA improvement between IFN- β and mAb treatment groups ($p = 0.665$). Both therapies were associated with reduced intraocular inflammation.

Conclusions, including unique features of the case:

Our findings indicate that IFN- β and mAb therapies yield comparable outcomes in maintaining or improving VA in MS-AU. These treatments may help achieve inflammation control while minimizing steroid exposure. Uveitis can precede the appearance of MS neurological symptoms. Although limited by small sample size and heterogeneous study designs, these results highlight the potential of modern immunotherapies to address both neurological and ocular aspects of MS. Larger controlled studies are warranted to confirm these findings and optimize treatment strategies.

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References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Demyelinating disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Diplopia in Extramedullary Multiple Myeloma: A Comprehensive Retrospective Analysis of Clinical Characteristics, Management, and Prognosis from a US Tertiary Cancer Center

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¹ University of Texas Medical Branch at Galveston, ² Texas A&M University, ³ University of Texas MD Anderson Cancer Center

Introduction:

Diplopia is an uncommon, poorly characterized, but clinically significant manifestation in extramedullary multiple myeloma (EM-MM), often reflecting aggressive disease and associated with poor prognosis. We have conducted the largest retrospective analysis to date, reporting the clinical characteristics, management, and outcomes of patients with EM-MM–related diplopia at a tertiary cancer center.

Methods:

A retrospective chart review identified 250 patients diagnosed with diplopia and MM between 2016 and 2025. After inclusion requiring pathological and imaging confirmation of EM-MM and lesion localization, 52 patients remained. Demographics, myeloma characteristics, disease status, lesion location, ophthalmologic findings, radiation therapy parameters, and outcomes were extracted from patient chart records. Diplopia resolution was categorized as complete, partial, or none. Survival was analyzed using Kaplan–Meier analysis.

Results:

Fifty-two patients (mean age 63.5 years, 52% female) presented with diplopia due to EM-MM; 75% had relapsed/refractory disease and 23% had high-risk cytogenetics. Median interval from myeloma diagnosis to diplopia onset was 961 days. Lesions most frequently involved the skull base (63%), orbit (42%), and cavernous sinus (27%). Cranial nerve VI palsy predominated (63%), especially in skull base and calvarial disease, while proptosis and ptosis were more frequent in orbital involvement. Radiation therapy (median 2000 cGy/8 fractions) was administered to 51 patients, most commonly targeting the skull base and orbit. Diplopia resolved completely in 61% and partially in 12%, with median time to improvement of 61 days. Resolution rates were highest for orbital (75%) and skull base (58%) lesions. Median survival after diplopia onset was 16 months, with 25% alive at two years.

Conclusions:

Extramedullary multiple myeloma (EM-MM) involving sites that affect ocular motility most often presents in relapsed/refractory disease and is associated with cranial nerve palsies and poor survival. Radiation therapy yields meaningful improvement in diplopia, but long-term prognosis remains limited by the aggressiveness of the underlying myeloma present at diplopia manifestation.

References: None provided.

Keywords: Adult strabismus with a focus on diplopia, Tumors, Skull base, Orbit, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None

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Karyopherin Modulation Protects Against Retinal And Cerebellar Degeneration In Spinocerebellar Ataxia Type 1

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Introduction:

Karyopherins are proteins that regulate nucleocytoplasmic transport and alter the localization and accumulation of disease-associated proteins across several neurodegenerative pathologies. Mutant Ataxin-1 (mATXN1), which displays toxicity through its nuclear localization is the disease-driving protein in spinocerebellar ataxia type 1 (SCA1). The neurotoxic effects of this protein lead to neuronal deterioration in both cerebellar and visual system pathways. Retinal abnormalities, including structural macular dysfunction, have been observed in association with SCA1, highlighting the important neuro-ophthalmic involvement in this disease. This study investigates the effects of modulating karyopherin levels on mATXN1-induced neurodegeneration in both retinal and central nervous system tissues. The aim was to uncover possible shared mechanisms and potential therapeutic approaches applicable to this neuro-ophthalmic disease.

Methods:

A well-characterized *Drosophila* model expressing mATXN1 (ATXN1[82Q]) in retinal and central nervous system tissues was studied. Colocalization of mATXN1 with Karyopherin-α (KPNA) was analyzed via immunofluorescence assay. Retinal degeneration and motor impairment were quantified to evaluate how changes in karyopherins influenced mATXN1 induced neurodegeneration. mATXN1 oligomerization was measured using homogeneous time-resolved fluorescence. Pharmacologic inhibition and genetic knockdown of Karyopherin-β1 (KPNB1) were also performed in the DAOY human cell line as well as *Drosophila*.

Results:

mATXN1 colocalized with KPNA in neuronal tissues. Increasing KPNA levels retained mATXN1 in the cytoplasm, reduced oligomer formation, and attenuated both retinal and motor degeneration. Inhibition of KPNB1 increased cytoplasmic KPNA and reduced nuclear mATXN1, while genetic knockdown of its homolog attenuated neurodegeneration in *Drosophila*.

Conclusions:

Karyopherins act as molecular chaperones that modulate mATXN1 localization and aggregation. Enhancing cytoplasmic KPNA reduces nuclear accumulation of toxic mATXN1 species and protects against neurodegeneration in both retinal and cerebellar contexts. These findings identify nucleocytoplasmic transport as a shared pathogenic pathway across visual and motor systems and highlight karyopherin modulation as a potential therapeutic strategy relevant to neuro-ophthalmology.

References: None provided.

Keywords: Genetic disease, Retina, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuropathy

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Grant Support: N/A

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Does Leukemic Optic Neuropathy Hold Key Prognostic Insight in Leukemia?

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Introduction:

Approximately 500,000 Americans are living with or in remission from leukemia. In each subtype, neoplastic leukocytes may directly infiltrate the optic nerve resulting in leukemic optic neuropathy (LON), a condition characterized by optic nerve dysfunction. LON can be an early indicator of central nervous system involvement, often marking the initial presentation of leukemia or signaling recurrence. Given its potential of permanent vision loss, LON is considered a neuro-oncologic emergency. Our study aims to investigate the relationship between the presentation of LON symptoms and leukemia prognosis, shedding light on its potential prognostic value.

Methods:

A retrospective chart review of 548 patient charts and 145 patients met our inclusion criteria of LON from 2010 to 2022. Data collected included demographics, date of leukemia diagnosis, optic nerve presentation, and date of optic nerve involvement with the method of diagnosis and clinical suspicion. Additionally, date and cause of death were also collected. Comparative analyses were run with SPSS software.

Results:

Out of the 145 patients, 79 were analyzed. Among the 79 patients, 41 died of complications related to leukemia, with all deaths occurring within 10 years of both their leukemia and LON diagnoses. Notably, 29 of these deaths occurred within the first year of optic nerve involvement compared to just 8 within the first year after their leukemia diagnosis, while 17 patients had LON involvement at the time of their leukemia diagnosis. LON presentation could potentially serve as a predictor for leukemic outcomes, a novel insight into cancer prognosis.

Conclusions:

Preliminary results suggest a correlation between earlier optic nerve infiltration and a worse leukemia prognosis. Patients with earlier presentations of LON appear to experience higher and rapid mortality than patients with later presentations of LON. Final results will be ready at the time of the conference.

References: Myers KA, Nikolic A, Romanchuk K, et al. Optic neuropathy in the context of leukemia or lymphoma: diagnostic approach to a neuro-oncologic emergency. *Neurooncol Pract.* 4(1), 60-66, 2017. American Cancer Society's Cancer Facts & Figures 2024

Keywords: Optic neuropathy, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Left Eye Physiological Increase in IOP may explain why the Right Eye is First affected in Patients with Leber's Hereditary optic neuropathy.

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Introduction:

Leber's hereditary optic neuropathy (LHON) is a maternally inherited disease due to missense point mutations affecting mitochondrial DNA (mtDNA) genes encoding subunits of respiratory complex I of the electron transport chain (ETC). The left eye has a small but statistically significant physiological increase in the intraocular pressure compared to the right eye, which influences glaucoma symptoms. In this study, we tested the hypothesis that this physiological increase in IOP may influence which eye is first affected in LHON.

Methods:

We retrospectively checked the first affected eye in LHON patients in our clinic. We included all three primary mutations (m.3460G>A, m.11778G>A, m.14484T>C) and other mutations.

Results:

The Total Number of patients was 117. The right eye was first affected in 68 patients, and the left eye was first affected in 49 patients.

Conclusions:

The right eye is slightly more likely to show manifest visual loss in LHON earlier than the left eye. We hypothesize that the slight physiological increase in intraocular pressure in the left eye compared to the right eye causes oxidative stress and hypoxia, which subsequently slightly decreases the mitochondrial mass in the left eye. This chronic oxidative stress may also cause mitochondrial adaptation to a hypoxic environment. Both factors make the right eye more vulnerable to exhibiting symptoms of Leber's hereditary optic neuropathy earlier than the left eye.

References: None provided.

Keywords: Genetic disease, Optic neuropathy

Financial Disclosures: Shenoda Abd Elmaseh; Kim Firn; Danielle Gauthier; Maryam Golmohammadi; Madeline Limb; Alfredo Sadun: Has been a consultant for Chiesi and GenSight Biologics and has received research support from GenSight Biologics and Stealth Therapeutics.

Grant Support: n/A

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Bilateral Optic Nerves T2 Hyperintensity in Idiopathic Intracranial Hypertension: Diagnostic Value and Ophthalmological Correlations.

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Introduction:

Idiopathic intracranial hypertension (IIH) is characterized by increased cerebrospinal fluid (CSF) pressure without secondary cause, leading to headaches, papilledema, and potential visual loss. Although magnetic resonance imaging (MRI) plays a central role in the diagnostic criteria, current radiological signs present relatively modest diagnostic value and do not include a reliable optic nerve biomarker. Objectives: Our aim was to evaluate the diagnostic performance of bilateral posterior optic nerve T2 hyperintensity for IIH compared to established MRI signs, and to explore its potential correlation with clinical and ophthalmological parameters at baseline and short-term follow-up.

Methods:

In this retrospective single-centre study, 30 IIH patients fulfilling diagnostic criteria, and 30 control patients with alternative ophthalmological diseases underwent brain and orbital MRI, and standardized ophthalmological evaluation. To be included, IIH patients had to have a lumbar puncture (LP) within a 3-month interval from MRI. Bilateral canicular and/or apical T2 hyperintensity was defined as the primary imaging marker. Other classical MRI signs of IIH were also recorded. Diagnostic performance was assessed by sensitivity, specificity, predictive values, and ROC analysis. Inter-reader agreement was measured with Cohen's κ .

Results:

Bilateral posterior optic nerve T2 hyperintensity was present in 87% of IIH patients versus 6% of controls, yielding a sensitivity of 87%, specificity of 93%, and AUC of 0.90 (95% CI, 0.82–0.98). Inter-reader agreement was moderate to good ($\kappa = 0.60$). Extended hyperintensity involving both canicular and apical segments correlated with higher papilledema grades and increased pRNFL but not with CSF opening pressure, body mass index, visual acuity. Diagnostic performance was comparable to that of bilateral transverse sinus stenosis (AUC 0.93).

Conclusions:

Bilateral posterior optic nerve T2 hyperintensity emerges as a promising MRI marker of IIH. It probably translates a focal glymphoedema and might reduce the need for invasive LP in clinically typical cases.

References: None provided.

Keywords: High intracranial pressure/headache, Optic neuropathy, Neuroimaging

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Introduction:

Ischemic ocular motor nerve palsies (III, IV, and VI) are frequent neuro-ophthalmic manifestations of diabetes mellitus. Both ocular motor palsy and diabetic retinopathy (DR) share a common microvascular ischemic mechanism. This study is aimed to describe the pattern of DR and socioeconomic distribution among patients presenting with ischemic cranial nerve palsy.

Description of Cases:

A retrospective observational study was conducted between January and April 2025 including 120 patients with isolated ischemic third, fourth, or sixth cranial nerve palsy. Demographic and clinical data, including HbA1C, cholesterol, hypertension, nephropathy, urban vs rural and DR severity were analysed. Socioeconomic status (SES) was categorized as low and moderate-high. Mean age was 59 years; 64% males; sixth nerve palsy was the most frequent (60%), followed by third (23%) and fourth (13%). 88 patients (73.3%) were diabetic. One-third (33%) of diabetics presenting with ischemic cranial nerve palsy had some form of DR, predominantly mild or moderate NPDR, while 9.1% had severe NPDR or PDR. The association between nerve palsy type and DR severity showed a near-significant trend ($H = 5.04$, $p = 0.08$), with higher DR grades observed more often in sixth nerve palsy. A significant relationship existed between SES and nerve palsy type ($\chi^2 = 8.46$, $p = 0.015$), with third nerve palsy more common in lower SES and sixth nerve palsy in higher SES. The mean diabetes duration was longer in lower SES (14.1 years) than in moderate-high SES (9.7 years; $p = 0.052$). Although not statistically significant, severe NPDR and PDR were more common in lower SES, whereas mild to moderate NPDR predominated in moderate-high SES.

Conclusions, including unique features of the case:

The predominance of sixth nerve palsy and the trend toward higher DR grades indicate a shared microvascular ischemic mechanism. Longer diabetes duration and greater DR severity among lower socioeconomic groups likely reflect delayed diagnosis and limited healthcare access.

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References: None provided.

Keywords: Ocular motility, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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A Procedure in Decline: Frequency of Temporal Artery Biopsies Since 2017 in a Major Tertiary Ophthalmology Center

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Introduction:

Giant cell arteritis (GCA) is the most common large vessel vasculitis in the elderly [1] and may cause permanent visual loss and other serious complications [2]. Temporal artery biopsy (TAB) has long been the diagnostic gold standard, but ultrasound (US) and other non-invasive imaging tools are changing the diagnostic setup. Fast Track Clinics (FTCs) with relevantly US-trained personnel allow prompt diagnosis and treatment initiation of GCA, reducing risk of visual loss [3]. An FTC was established in September 2018 at our hospital, and we wished to investigate its impact on TAB use.

Methods:

Data on TABs and patients referred to us with suspected GCA were retrospectively extracted from the regional electronic health record system. Numbers were collected quarterly from January 2017 through September 2025 and grouped into three time periods: (1) Q1 2017 - Q3 2018, before FTC establishment; (2) Q4 2018 - Q4 2023, after FTC establishment and during a prospective GCA study requiring mandatory TAB in 110 suspected GCA cases; (3) Q1 2024 - Q3 2025, after the prospective GCA study. Additionally, a case-cost analysis of performing and analyzing TABs at our center was conducted.

Results:

Before FTC establishment, a median of 34 (IQR 33 to 36) biopsies were performed each quarter, decreasing to 27 (26 to 29; $p = 0.0052$) and 13 (11 to 19; $p < 0.0001$) in the following periods, representing a 62% median reduction. Meanwhile, the median number of patients referred with possible GCA did not decline. The estimated cost of each TAB was ~669 USD, yielding annual savings of ~56,212 USD, excluding US costs.

Conclusions:

The marked decline in TABs suggests a causal relationship with FTC implementation, where US is used as the first-line diagnostic tool.

References: 1. Haugeberg G, Paulsen PQ, Bie RB. Temporal arteritis in Vest Agder County in southern Norway: incidence and clinical findings. *J Rheumatol*. 2000;27(11):2624-2627. <http://www.ncbi.nlm.nih.gov/pubmed/11093444> 2. Tomelleri A, van der Geest KSM, Khurshid MA, et al. Disease stratification in GCA and PMR: state of the art and future perspectives. *Nat Rev Rheumatol*. 2023;19(7):446-459. doi:10.1038/s41584-023-00976-8 3. Diamantopoulos AP, Haugeberg G, Lindland A, Myklebust G. The fast-track ultrasound clinic for early diagnosis of giant cell arteritis significantly reduces permanent visual impairment: Towards a more effective strategy to improve clinical outcome in giant cell arteritis? *Rheumatology (United Kingdom)*. 2016;55(1):66-70. doi:10.1093/rheumatology/kev289

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Peri-Orbital Arterial Involvement in Giant Cell Arteritis: Rationale for a Novel MRI Protocol

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Introduction:

Patients over age 50 presenting with new headache and constitutional symptoms, particularly those with ocular involvement, are routinely screened for temporal arteritis or giant cell arteritis (GCA). MRI “GCA protocols” are commonly performed at initial presentation to assess the temporal arteries. Early recognition is critical, as irreversible blindness results from inflammation of the short posterior ciliary arteries (SPCAs). Despite this, current MRI protocols primarily emphasize evaluation of the temporal arteries. Our study seeks to characterize imaging findings in biopsy-proven GCA and motivate development of a new MRI protocol optimized for evaluation of the orbital vasculature, especially the SPCAs.

Description of Cases:

We retrospectively reviewed all patients with a new diagnosis of GCA at a large tertiary medical center between 2005 and September 2025 (n=102). Among these, 80 (78%) had positive temporal artery biopsies—72 (71%) with active arteritis and 8 (8%) with healed or resolved disease. Of the 72 patients with active GCA, 40 (56%) experienced visual symptoms at diagnosis. Among these, 12 (30%) had MRI brain or orbit studies with post contrast fat-suppression sequences available for review. Independent review by neurologists, radiologists and neuro-ophthalmologists identified peri-neural or optic nerve head enhancement in the majority of cases (n=10, 83%).

Conclusions, including unique features of the case:

Our findings highlight MRI evidence of disease activity beyond the temporal arteries in GCA. However, existing MRI GCA protocols are suboptimal for evaluating the small vascular structures within the orbit – particularly the SPCAs—the vessels most directly implicated in GCA-related blindness. This limitation underscores the need for a refined MRI protocol tailored to the ophthalmic artery, central retinal artery and posterior ciliary circulation.

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References: None provided.

Keywords: Neuroimaging, Optic neuropathy, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Orbit, Vascular disorders

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Clinical Spectrum And Outcomes Of Leukemic Optic Nerve Infiltration: Insights From A Tertiary Cancer Center

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Introduction:

Leukemic optic nerve infiltration (LONI) is a rare yet potentially life-threatening manifestation of hematologic malignancies. Despite its clinical relevance, the incidence, optimal diagnostic methods, and treatment strategies remain poorly understood, largely due to limited number of reported cases. This study provides characterization of clinical presentation, diagnostic patterns, and treatment outcomes in the largest cohort of patients with LONI to date.

Methods:

A retrospective chart review of 548 patient charts was conducted and 145 patients met diagnostic criteria for LONI at a tertiary care center. Data collected included demographics, leukemia subtype, CNS disease history, LONI features/diagnostic methods, treatment regimens, best corrected visual acuity (BCVA) at presentation and follow up, and survival outcomes. Comparative analyses were run with SPSS software.

Results:

79 charts from 2010-2022 (128 affected eyes) were analyzed. LONI was bilateral in 61% of cases and 22% had prior CNS disease. Presenting features included vision loss (27%), eye pain (19%), and relative afferent pupillary defect (35%). Only 57% of imaged patients demonstrated MRI abnormalities, and 47% had remarkable cerebrospinal fluid (CSF) findings. 37% of patients with LONI then received radiation to the orbit/brain. Patients with acute lymphoblastic leukemia (ALL) were more likely to have LONI at relapse than at initial diagnosis ($p < 0.001$), positive CSF results ($p = 0.009$), and vision loss ($p = 0.020$). Patients with prior CNS involvement were more likely to have intracranial infiltration on MRI ($p = 0.039$). Mean presenting BCVA was 0.83 LogMAR, with limited recovery at follow-up.

Conclusions:

Preliminary results indicate that MRI and CSF testing are not reliable diagnostic methods for LONI. Patients with ALL present at relapse at higher rates than other subtypes and have worse visual outcomes. These findings highlight diagnostic limitations, variability in presentation, and need for standardized treatment strategies to prevent irreversible vision loss. Final results will be ready at the time of the conference.

References: None provided.

Keywords: Optic neuropathy, Orbit/ocular pathology, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Ocular Viability After Brain Death: Evidence of Retinal Dysfunction in Donor Eyes

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Introduction:

Enabling visually-functional whole eye transplantation requires a source of viable donor eyes. While it is known that ex vivo outer retinal function can be restored after a period of hypoxia in both human donors and animal models, comprehensive studies of eye viability including retinal ganglion cell (RGC) function in organ donors after brain death have not been performed. We hypothesize that brain dead donors are likely to have optic nerve damage from intracranial disease or retinal damage from ischemia.

Methods:

We evaluated sequential brain-dead donors over age 18 presenting to an organ procurement organization with no known previous sight-limiting injury. Eye examination included dilated fundoscopy, intraocular pressure measurement, pachymetry, and photopic electroretinography with a 3.4 Hz 621 nm flash on a 470 nm background. Patient demographics, cause of brain death, comorbid conditions, and time from brain death to exam were also recorded. Eyes were considered viable for donation if no pathology affecting vision was present and all structural or functional tests fell within the central 90% of healthy control data.

Results:

Since Sept 17, 2025, we evaluated 8 eyes in 4 donors. Donors ranged from 35 to 56 years of age and all were male. One died from trauma, one from ischemic stroke, and two from hypoxia. One CRAO and one BRAO were found. All had cerebral edema on imaging prior to brain death. All electroretinograms except one showed increased latencies in a-waves and b-waves, including those with no visible pathology and normal amplitudes including phNR, a measure of RGC function.

Conclusions:

Although sample size is small, no viable eyes meeting criteria were found. We will continue collecting data including longitudinal studies on donors to determine if prolonged time after brain death or cause of brain death correlates with viability. Future studies will compare in-vivo to ex-vivo function.

References: Abbas, F., Becker, S., Jones, B.W. et al. Revival of light signalling in the postmortem mouse and human retina. *Nature*, 606, 351–357, 2022.

Keywords: Optic neuropathy, Neuro-opth & systemic disease (eg. MS, MG, thyroid), High intracranial pressure/headache

Financial Disclosures: The authors had no disclosures.

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Cytarabine-Induced Bilateral Optic Neuropathy With Moderate Response to Intravenous Steroid Treatment

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Introduction:

Cytarabine, a cytidine analog widely used in the treatment of hematologic malignancies, has been well-documented to cause neurotoxic complications. Very few cases describe optic neuropathy. We present a patient with CNS lymphoma who developed acute, bilateral, painless vision loss following intrathecal (IT) cytarabine administration, with subsequent improvement after intravenous (IV) steroids.

Description of Cases:

A 73-year-old female with CNS lymphoma admitted for an initial dose of IT methotrexate (12 mg) developed acute, bilateral vision loss OU 2 days after. Her visual acuity had declined from 20/20 OD and 20/25 OS to 20/100 OD and 20/50 OS. The following day, the patient's visual acuity worsened to 20/200 OU. Dilated fundus examination revealed bilateral hyperemic optic disc edema with splinter heme OU. IV dexamethasone (40 mg) was then initiated. Following IV steroid treatment, gradual visual improvement was observed. After two days, her visual acuity improved to 20/50 OS while OD remained at 20/200. Given an increase in disc edema and temporal association with initiating IT cytarabine, cytarabine-induced optic neuropathy was strongly suspected. Due to incomplete visual recovery, pulse dose steroids (1g IV Methylprednisolone) was initiated for a 3 day course. Discontinuation of cytarabine was additionally recommended, with plans to transition to an alternative chemotherapeutic regimen.

Conclusions, including unique features of the case:

Although cytarabine has been well-documented to cause neurotoxic complications, we present a rare case of cytarabine-induced optic neuropathy with painless, progressive vision loss. Here we demonstrate that early initiation of high-dose IV steroids may lead to partial visual recovery. Clinicians should prescribe cytarabine with caution and remain alert to visual symptoms in patients initiating this treatment.

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References: None provided.

Keywords: Chemotherapy and radiation injury, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: N/A

Contact Information: None provided.

Risk of Neuro-Ophthalmic Complications in Immune Checkpoint Inhibitor Users in the TriNetX U.S. Database

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Introduction:

Immune checkpoint inhibitors (ICIs) enhance antitumor immunity but may trigger immune-related adverse events (1). Neuro-ophthalmic complications, such as optic neuritis (ON) and myasthenia gravis (MG), have been reported following ICI use (2). This study evaluated the risk of developing neuro-ophthalmic complications after ICI initiation in cancer patients.

Methods:

We queried the TriNetX U.S. network (131,668,565 patients, 2014–2024). Adults with cancer who received ICIs (88,515) were propensity score matched 1:1 to adults with cancer and without ICIs (3,959,368) by age, sex, race, ethnicity, and comorbidities, yielding 88,314 matched pairs. Patients with pre-existing autoimmune disease were excluded. Neuro-ophthalmic complications included MG, ophthalmoplegia, ON, intracranial idiopathic hypertension (IIH), cranial nerve (CN) palsies, and bitemporal hemianopsia. Cox regression estimated 3-year hazard ratios (HRs). Subgroup analyses examined monotherapy by ICI class (PD-1, PD-L1, and CTLA-4 inhibitors) and combination regimens.

Results:

Among 176,682 matched patients, ICI therapy was associated with increased risk of MG (HR: 2.18), ophthalmoplegia (1.74), ON (2.87), IIH (2.81), CN IV palsy (2.51) and bitemporal hemianopsia (2.55) (all $P < 0.05$). CTLA-4 inhibitors were linked to increased risk of ON (1.94) and MG (2.46); PD-L1 inhibitors showed higher risk of MG (3.24), and IIH (3.01) (all $P < 0.05$). PD-1 inhibitors were associated with increased risk of MG (3.03), ophthalmoplegia (1.74), ON (2.77), IIH (2.46), CN IV palsy (3.08), and bitemporal hemianopsia (2.43) (all $P < 0.05$). Combined PD1/CTLA-4 immunotherapy was linked to ON (2.13), MG (2.48), and ophthalmoplegia (1.78) (all $P < 0.05$).

Conclusions:

Consistent with prior literature, ICIs were associated with increased risk of ON, MG, and ophthalmoplegia (3). However, we report previously unexplored risks of IIH, CN IV palsies, and bitemporal hemianopsia, suggesting broad neuro-ophthalmic susceptibility. Risk variation by drug class and regimen warrants investigation. Multidisciplinary collaboration between oncology and ophthalmology may help with detection and management of neuro-ophthalmic complications.

References: 1. Chang EL, Liu R, Keyhanian K, Huynh K, Berkenstock M. Consensus disease definitions for ophthalmic immune-related adverse events of immune checkpoint inhibitors. *J Immunother Cancer*. 2025;13(4):e011049. doi:10.1136/jitc-2024-011049 2. Francis JH, Jaben K, Santomasso BD, Canestraro J, Abramson D. Immune Checkpoint Inhibitor Associated Optic Neuritis. *Ophthalmology*. 2020;127(11):1585-1589. doi:10.1016/j.ophtha.2020.05.003 3. Yu CW, Yau M, Mezey N, Joarder I, Micieli JA. Neuro-ophthalmic Complications of Immune Checkpoint Inhibitors: A Systematic Review. *Eye Brain*. 2020;12:139-167. doi:10.2147/EB.S277760

Keywords: Optic neuritis, Myasthenia, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Grant Support: None.

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Systematic “Papilledema Protocol” in an Emergency Department (ED)

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Introduction:

Increasing ED-Neuro-ophthalmology consultations prompted implementation of a “Papilledema Protocol” to streamline evaluation of patients with signs/symptoms of intracranial hypertension and/or bilateral disc edema [protocol performed in our ED/Clinical Decision Unit (CDU): non-mydratic color-fundus photography/OCT nerve/macula (NMFP-OCT) by ED-staff/remote interpretation by Ophthalmology; Neurology/Neuro-ophthalmology consultations; contrast-MRI brain/orbits; MR-Venogram; lumbar puncture (CSF-opening pressure/analysis); blood pressure; CBC, ±syphilis testing]. We report our >2-year experience evaluating patient final diagnoses and usefulness of tests performed.

Methods:

Prospective quality improvement project of consecutive ED-patients with “Papilledema Protocol” from 6/14/2023-9/21/2025. We collected patient demographics, referral patterns, ancillary testing, final diagnoses, ED/CDU length-of-stay, disposition.

Results:

318 patients with remote diagnosis of “papilledema” on NMFP-OCT underwent “Papilledema Protocol” in our ED/CDU. Referral patterns: presumed papilledema found by outside eye-care-providers (228;72%); papilledema found in our eye clinic (14;4%); symptoms/signs suggesting intracranial hypertension (75;24%); incidental bilateral disc edema in fungemia (1;0.3%). 211 (66.4%) were discharged home from the ED/CDU [median length-of-stay 27.9hours, IQR,24.6-32.2]; 107 (33.6%) were admitted to the hospital. Final diagnoses: idiopathic intracranial hypertension (223;70%) (6 fulminant IIH); cerebral venous thrombosis (7;2.2%); intracranial mass (3;0.9%); subdural hematoma (1); obstructive hydrocephalus (4;1.3%); CSF shunt malfunction (2;0.6%); leptomeningeal process (10;3.1%); stage-IV hypertensive retinopathy (7;2.2%); other anterior optic neuropathies (36;11.3%); pseudopapilledema (24;7.5%). Workup: head-CT (157;49.4%); contrast MRI-brain/orbits (254;79.9%); MRI-brain only (31;9.7%); head-MRV (272;85.5%); LP in ED (263;82.7%); 317 CBC. Disposition: 309/318 (97%) patients required outpatient neuro-ophthalmology follow-up; 4 (1.2 %) patients returned to the ED for same concern within 30 days.

Conclusions:

Remote interpretation of NMFP-OCT obtained in the ED allowed for rapid trigger of “Papilledema Protocol” and expedited care. 77/318 (24.2%) patients with “Papilledema Protocol” in our ED/CDU were diagnosed with severe disorders; 33.6% required admission to the hospital. Only 1.2% of patients returned to the ED within 30 days and 97% received outpatient neuro-ophthalmology follow-up, suggesting appropriate ED/CDU/inpatient care and satisfying continuity of care.

References: None provided.

Keywords: High intracranial pressure/headache, Neuroimaging

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Contact Information: None provided.

Implementation, Evaluation, and Use of Nonmydriatic Ocular Fundus Imaging in the Emergency Department: More than 2 years of Prospective Consecutive Data

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Introduction:

We implemented a table-top non-mydriatic ocular fundus camera combining 45°-true-color photographs and optical coherence tomography nerve/macula (NMFP-OCT) connected to our PACS/electronic health records in our general emergency department (ED) in 06/2023.^{1,2} We have shown that NMFP-OCT performed by ED-staff on patients with vision complaints,^{3,4} headaches,⁵ neurologic disorders,⁶ hypertensive crisis,² with remote interpretation of imaging by ophthalmologists: prevented diagnostic errors;⁸ accelerated triage/patient's discharge;⁷ reduced in-person ophthalmology consultations;^{7,8} reduced burden/increased confidence among trainees.^{1,7,8} This study evaluates the sustainability of this paradigm.

Methods:

Prospective quality improvement project with systematic collection of data on consecutive patients who underwent ED-NMFP-OCT from implementation on 6/14/2023-9/23/2025.

Results:

3692 patients received NMFP-OCT (average, 4.4/day), with increasing rate of 0.126 NMFP-OCT/week. Images ordered by ED-providers for vision complaints (2518/3692;68%), headache (732/3692;20%), other neurologic (309/3692;8%), hypertensive crisis (43/3692;1%), diabetes mellitus (79/3692;2%), other (11/3692;0.3%). Papilledema was ruled-out remotely in 789/981 (80%) patients with concern for intracranial hypertension, avoiding in-person consultations in 93. NMFP-OCT (performed by ED-staff in 89%) was of quality good enough for interpretation in 3256/3692 (88%). 1406/3692 (38%) NMFP-OCT were abnormal: papilledema (245/1406;17.4%); other optic neuropathies (365/1406;26%); CRAO/BRAO (82/1406;5.8%); uveitis/retinitis (115/1406;8.2%), retinal detachment (176/1406;12.5%); vitreous hemorrhage (96/1406;6.8%); other vitreous+retinal abnormalities (230/1406;16.4%); incidental findings (97/1406;6.9%). Camera/connections required rare (< 1/month) routine maintenance lasting < 3hrs, mostly from automated EHR/PACS updates.

Conclusions:

>2 years after implementation in our busy ED, daily NMFP-OCT continues to increase, with ED providers routinely ordering NMFP-OCT based on standard-of-care recommendations for fundus examination. Workflows were adapted to incorporate systematic NMFP-OCT for all patients with vision complaints prior to in-person ophthalmology consultations, and specifically-created protocols ["EyeStroke Alerts",⁹ "Papilledema Concern/Evaluation"].^{7,8} Our large consecutive series confirms that ED-NMFP-OCT is sustainable, scalable, requiring minimal training for replicable use, efficacious for a wide variety of acute clinical presentations, continuing to improve patient care, patient outcomes, and trainee education, making its implementation desirable/likely feasible in other EDs.

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Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), High intracranial pressure/headache, Optic neuropathy, Retina, Stroke

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Beyond Vision Loss: Innovative Case Management For Improved Outcomes In Leber Hereditary Optic Neuropathy (LHON)

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Introduction:

Leber hereditary optic neuropathy (LHON) is a rare, maternally inherited mitochondrial disorder that causes sudden, profound central vision loss through degeneration of retinal ganglion cells and subsequent optic nerve atrophy. Onset can occur throughout one's lifespan. For males, it often occurs in their teens/young adult years, and for females, it occurs later in life. Beyond vision loss, LHON-affected individuals face health-care barriers, financial hardship, and psychosocial challenges. Individuals with LHON vision loss are at increased risk for unintentional injuries, loneliness, depression, anxiety, and lower quality of life.

Description of Cases:

A non-profit organization supporting LHON patients collaborated with a nurse scientist in an IRB-approved qualitative descriptive study aimed at exploring the lived experience of sudden, profound vision loss. Using purposive sampling, 27 U.S. LHON-affected adults participated in gender-specific virtual focus groups/interviews. Data were coded and themes identified: (1) impact of blindness on daily living, (2) impact of sudden, severe vision loss on mental health, and (3) experiences with, and perspectives on, the health care system. Participants described sudden vision loss as profoundly life-changing, with psychological distress, barriers to care, and loss of independence. Access to resources, rehabilitation, and proactive provider support were essential, yet inconsistently delivered.

Conclusions, including unique features of the case:

Innovative care coordination is urgently needed for individuals experiencing sudden blindness. A virtual nurse case manager offers a cost-effective solution by bridging critical gaps in patient education, multidisciplinary care, safety assessments, physical and mental health assessments, referrals for training and rehabilitation, and emotional support. Integrating this role into existing nurse case management programs, such as Medicaid and private insurers like Aetna's care management support program, would centralize LHON-specific expertise, enhance outcome tracking, reduce specialist overutilization, and lower costs for insurers. This role could also monitor emerging trends and inform clinical practice and research efforts.

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References: None provided.

Keywords: Optic neuropathy, Genetic disease

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Normative Percentiles and Age-Related Change Points for RNFL and GCIPL Thickness in Healthy Adults based on Cirrus HD-OCT

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Introduction:

Optical coherence tomography (OCT) is essential for diagnosing glaucoma and optic nerve disease through quantitative retinal nerve fiber layer (RNFL) and ganglion cell-inner plexiform layer (GCIPL) measurements. However, commercial normative databases inadequately represent East Asian populations and lack detailed age stratification, causing false-positives in older adults and missed abnormalities in younger patients. We aimed to identify age-related change points and generate decade-specific normative percentiles for RNFL and GCIPL thickness using Cirrus HD-OCT in a large East Asian cohort.

Methods:

Cross-sectional, population-based study of 8,558 healthy adults from a national health survey (2017-2021). Cirrus HD-OCT imaging used Optic Disc Cube 200×200 protocol for RNFL and Macular Cube 512×128 protocol for GCIPL measurements. Simple linear regression change-point (SLRCP) analysis identified age-related acceleration points. Decade-specific percentiles (5th, 25th, 50th, 75th, 95th) were calculated for ages 20-89 years.

Results:

Cohort included 4,654 women (54.4%) and 3,904 men (45.6%) aged 47.4±13.5 years. Mean RNFL thickness was 95.7±9.1 µm and GCIPL thickness was 82.7±5.8 µm. Linear regression demonstrated significant age-related decline: RNFL at -0.116 µm/year (95% CI, -0.133 to -0.100; P<.001) and GCIPL at -0.044 µm/year (95% CI, -0.055 to -0.034; P<.001). Women showed thicker RNFL (96.6 vs. 94.9 µm; P<.001), while men had thicker GCIPL (83.0 vs. 82.4 µm; P<.001). SLRCP analysis identified change points with accelerated thinning: GCIPL at 50 years (slopes: +0.033 to -0.247 µm/year) and RNFL at 59 years (slopes: -0.084 to -0.201 µm/year). Median RNFL declined from 97 µm (20-29 years) to 87 µm (80-89 years) and GCIPL from 82 µm to 76 µm.

Conclusions:

RNFL and GCIPL demonstrate nonlinear age-related thinning with accelerated decline beginning in the fifth to sixth decades. These decade-specific normative values and change points provide population- and device-specific references for improved diagnostic accuracy in East Asian populations using Cirrus HD-OCT.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Optic neuropathy

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Grant Support: None.

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Innovative Anesthetic Cream Taping Technique: Efficacy and Safety for Pain Reduction During Pretarsal Botulinum Toxin A Injection in Hemifacial Spasm: A Double-Blind Randomized Controlled Trial

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Introduction:

Hemifacial spasm (HFS) is effectively treated with botulinum toxin A (BoNT-A) injection. The pretarsal approach provides superior therapeutic outcomes but is associated with greater pain compared to the preseptal approach. Ready-made anesthetic skin tape has been proven to effectively reduce pain; however, it is unavailable in Thailand. Although anesthetic cream is commonly used, it carries a high risk of chemical eye injury due to its basic pH. Therefore, this study introduced an innovative anesthetic cream taping technique as an alternative, aiming to provide comparable analgesia using accessible materials with safe periocular application. This study aimed to evaluate the efficacy and safety of the novel anesthetic cream taping technique in reducing pain during pretarsal BoNT-A injections in patients with HFS.

Methods:

This randomized, double-blind, placebo-controlled trial included 48 HFS patients assigned to two groups. Each patient received the novel anesthetic tape on one upper eyelid (nasal or temporal) and placebo tapes on the opposite upper and lower eyelids. Tapes were applied for 15 minutes prior to BoNT-A injection using the pretarsal technique. Pain during insertion, injection, and withdrawal was measured using a visual analog scale (VAS); satisfaction and safety outcomes were also recorded.

Results:

Pain scores were significantly lower at the novel anesthetic tape-treated sites compared to placebo across all phases ($P < 0.01$), with overall mean VAS 0.69 in tape-treated sites vs. 4.45 in placebo, 84.5% of pain reduction. Satisfaction scores were significantly higher in the tape-treated group ($P < 0.001$). Subgroup analysis demonstrated that pain scores differed significantly between genders ($P = 0.02$), while no significant differences were found across age, eyelid site, or treatment duration. Mild pruritus occurred in 8.3% of patients; no ocular complications were observed.

Conclusions:

The fifteen-minute novel anesthetic cream taping technique is a safe, well-tolerated, and effective method for reducing pain from pretarsal BoNT-A injections in HFS.

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Keywords: Miscellaneous

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Automated Review of Longitudinal Electronic Health Records: Privacy-Preserving Agentic LLMs for identifying incident NAION at Scale

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Introduction:

Accurate retrospective identification of acute NAION cases is important for research on risk factors, but ICD-10 coding has limited positive predictive value (PPV), and manual EHR review is time intensive. LLM-based automated review of L-EHR with patient privacy preserved may offer scalable, accurate case identification.

Methods:

This retrospective single-center study included 161 subjects with ≥ 1 ION (ischemic optic neuropathy) ICD-10 code(s) in the L-EHR. An expert neuro-ophthalmologist classified each subject for presence of acute NAION based on manual L-EHR review. Four locally-deployed (in order to protect privacy) LLM models via llama.cpp were used to implement four methods of NAION diagnostic classification using unstructured L-EHR data: basic prompting, retrieval-augmented generation (RAG), two-step agentic workflow, and three-step agentic workflow. LLM and expert performance were compared.

Results:

Expert review confirmed acute NAION in 41/161 subjects (25.5%). Agentic LLM workflows substantially outperformed basic and RAG approaches. For direct NAION diagnosis, agentic methods achieved a mean PPV of 86.7%, compared to 61.2% for basic prompting and 60.5% for RAG. Feature extraction with agentic workflows demonstrated high reliability: afferent pupillary defect detection reached 82.6-100% PPV, optic disc edema 78.1-94.1% PPV, and sudden onset 67.0-88.9% PPV across models. Three-step workflows consistently achieved the most balanced performance across all three models.

Conclusions:

Privacy-preserving agentic LLM workflows achieved high PPV for acute NAION case identification among subjects with ≥ 1 ICD-10 code for ION, exceeding ICD-10 code PPV and approaching expert PPV of 100%, while maintaining complete local data control and patient confidentiality. These methods offer a scalable approach for case identification in retrospective clinical research.

References: None provided.

Keywords: Vascular disorders

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Glaucoma Referrals and Diagnostic Overlap in a Neuro-Ophthalmology Service: A Retrospective Review from a Tertiary Eye Center in Brazil

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Introduction:

To evaluate the frequency, clinical characteristics, and diagnostic overlap of glaucoma cases referred to a neuro-ophthalmology service in a tertiary eye hospital.

Methods:

This retrospective observational study included patients evaluated in the neuro-ophthalmology service of our institute from August 2013 to March 2022. Among 903 total records, 852 patients were analyzed because 51 cases were missing the referral source. Demographic and clinical data, including referral origin and glaucoma subtype, were reviewed.

Results:

Of 852 patients, 198 (23.2%) were referred from the glaucoma service, and 31 (3.6%) had confirmed glaucoma. However, 17 out of 31 ($\approx 55\%$) of the patients were originally referred from the glaucoma service. The mean age was 67.4 years (median 70 years), with 13 males (41.9%) and 18 females (58.1%). Glaucoma types included: primary open-angle glaucoma (POAG) in 22 cases (71%), primary angle-closure glaucoma (PACG) in 3 (9.7%), neovascular glaucoma in 2 (6.5%), traumatic glaucoma in 1 (3.2%), and normal-tension glaucoma (NTG) in 1 (3.2%). Six patients (19.4%) presented additional neurological or optic nerve findings: three with simultaneous neurological disorders—two with diplopia (congenital IV nerve palsy and cavernous sinus syndrome) and one with stroke-related visual field defect—and three others with visual loss suspected to result from optic nerve neuropathy coexisting with glaucoma, which was not confirmed until the end of the study.

Conclusions:

Glaucoma accounted for a small but clinically significant proportion of neuro-ophthalmology cases. More than half of glaucoma-related referrals originated from glaucoma specialists, highlighting strong inter-service collaboration and diagnostic overlap between glaucomatous and non-glaucomatous optic neuropathies. Nearly one-fifth of patients exhibited atypical neurological or optic nerve findings, underscoring the importance of comprehensive neuro-ophthalmic evaluation and multidisciplinary management for patients with ocular motility abnormalities or visual loss in the setting of pre-existing glaucoma.

References: None provided.

Keywords: Optic neuropathy

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Contact Information: None provided.

Clinical Course and Visual Outcomes of Ocular Motor Cranial Nerve Schwannomas

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Introduction:

Schwannomas of the oculomotor (CN3), trochlear (CN4), and abducens (CN6) nerves are rare, benign tumors that usually present with slowly progressive, isolated ocular motor nerve palsies. We present tertiary practice patterns and long-term outcomes for these ocular motor cranial nerve Schwannomas, most of whom presented with isolated diplopia.

Description of Cases:

Methods: Schwannomas arising from CN3/4/6 were identified in neurosurgical schwannoma databases, using electronic medical record analytical tools, and via physician recall from 2000-2025. Excluded were asymptomatic or sensory schwannomas and those without adequate ocular data. Lesional characteristics and intervention, visual management, and clinical course were tabulated. Results: 17 schwannomas were identified (average age of 54 ± 18.2): CN3 (n=5, largest dimension mean 7.3mm); CN4 (n=10, mean 4.7mm); CN6 (n=2, mean 10.9mm), arising in cavernous sinus (CN3, n=4; CN4, n=1; CN6, n=2), subarchoid cisterns (CN3, n=2; CN4, n=9), or orbit (CN3, n=1). 12 of 17 cases presented with isolated diplopia. One CN3 tumor had stereotactic radiosurgery (SRS) with strabismus surgery; four were resected: one via endoscopic transphenoidal; two subtotal via endoscopic transphenoidal in one and endoscopic maxillary (+ SRS) in another; and one by transcranial orbitotomy (+ SRS). Of CN4 tumors: one received SRS; one was resected via pterional craniotomy; five were observed leading to strabismus surgery; three were observed without intervention. Of CN6 tumors, both were resected via endoscopic endonasal (+ SRS in one), leading to strabismus surgery. All 17 tumors were radiologically stable over three years, with diplopia effectively managed regardless of intervention. Specifically for trochlear schwannomas, diplopia was reliably eliminated with strabismus surgery and/or prism in the absence of resection or SRS.

Conclusions, including unique features of the case:

Whereas CN3/6 schwannomas frequently warrant treatment with microsurgical resection/SRS and strabismus surgery, nearly all symptomatic CN4 schwannomas were well-managed with strabismus surgery or prism alone and remained radiologically stable after long-term follow up.

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References: None provided.

Keywords: Tumors, Ocular motility, Skull base, Adult strabismus with a focus on diplopia

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Introduction:

Rapid diagnosis of retinal artery occlusions (RAOs) is critical in identifying patients with increased risk of other cerebrovascular events as well as potentially improving visual outcomes. Current limitations largely surround delays in patient presentation and obtaining an ophthalmic evaluation. Non-mydratic ocular fundus photography plus optical coherence tomography (NMFP-OCT) is emerging as a promising tool to reliably and accurately diagnose RAOs, providing ED clinicians the ability to make ultra-rapid diagnoses and stroke alert for patients presenting with acute vision loss. By analyzing prior code strokes for vision loss, we review the current care of patients and how implementation of a NMFP-OCT could change future management protocols.

Methods:

701 patients were identified as direct or transferred code strokes in the past 5 years. 12 of those patients were preliminarily confirmed to have visual symptoms. Their electronic health records were reviewed to collect data of interest, including final diagnosis, which was entered into a RedCap survey created following IRB approval.

Results:

50% patients were transfers from outside hospital. Zero of 12 patients had RAOs. Only one was determined to have had a true stroke. All patients were managed at a tertiary stroke center.

Conclusions:

Most code strokes with associated vision loss are not RAOs. It is rare for a patient with acute vision loss to present within the thrombolytic time window. Prior to the NANOS meeting, we plan to expand our review to include a larger data set, including timeframe, analysis of diagnosed CRAOs, and time to presentation to identify limitations to initiation of a code stroke protocol. Quantifying the current quality of care and outcomes of patients treated for RAOs at our institution will offer insight into the degree of improvement that can be expected with the integration of an NMFP-OCT in our ED.

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Keywords: Stroke, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)

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Has Temporal Artery Ultrasound replaced Temporal Artery Biopsy in the Diagnosis of Giant Cell Arteritis? Current Opinions and Practice Patterns of NANOS Members

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Introduction:

Temporal Artery Ultrasound (TAUS) is a new diagnostic modality for Giant Cell Arteritis (GCA). Its role continues to evolve and not well defined. We conducted a survey of NANOS membership to analyze current attitudes about the role TAUS plays in the diagnosis of GCA versus the historical gold standard of Temporal Artery Biopsy (TAB) and associated practice patterns preferences.

Methods:

A comprehensive survey was offered to all NANOS members exploring attitudes and preferences relating to TAUS versus TAB. Data collection and statistical analysis were performed.

Results:

There were 151 unique responses (20% response rate) with 2:1 Ophthalmology versus Neurology trained. 67% were at an Academic institution and 19% in Private Practice. 53% stated TAUS was available with median 3 days to obtain, compared to 90% for TAB with median 5 days. 64% of respondents chose TAB as their first diagnostic choice while 33% chose TAUS. 59% stated they rarely or never used TAUS. 52% believe TAB is very sensitive versus 13% for TAUS. 98% felt that a positive TAB precluded the need to obtain TAUS to confirm GCA diagnosis while 58% believed the same for a positive TAUS. 76% negatively viewed the learning curve for accurate TAUS. 64% felt that a negative TAB was sufficient to rule out GCA and forego TAUS while only 14% felt the same about TAUS. 39% initially obtained TAUS for low suspicion GCA compared to 33% TAB. No presenting clinical factors appeared important to prompt getting TAUS over TAB. 61% felt TAB would remain the preferred test in the future with most clinicians indicating a 5-7 period before TAUS could potentially replace TAB.

Conclusions:

Clinicians continue to prefer TAB over TAUS. A clear majority of clinicians feel TAB is more reliable than TAUS for a positive test, a negative test, and when the clinical suspicion for GCA is low. Clinicians continue to consider TAB to be the gold standard test for diagnosing GCA.

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Structural Explanations for Discrepancies Between Clinical vs. Optical Coherence Tomography Measurement of the Cup-to-Disc Ratio

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Introduction:

The cup-to-disc ratio (CDR) is a standard parameter to assess optic nerve anatomy and the risks of non-arteritic anterior ischemic optic neuropathy (NAION) and glaucoma. Discrepancies between clinically estimated and OCT-derived measurements have been reported, but the anatomical reasons for such differences have not been systematically explored across a consecutive patient population.

Methods:

Clinical measurements of CDR were obtained by a single neuro-ophthalmologist in consecutive patients evaluated for various visual disorders but deemed to have normal optic nerves. Patients with refractive errors < -4.00 or > +4.00 diopters were excluded. OCT measurements (Cirrus device, enhanced depth imaging with radial scans) were acquired. A discrepancy of ≥ 0.15 between clinical and OCT CDRs prompted a second clinical evaluation, followed by a review of the OCT to identify potential anatomical or technical sources of discrepancy.

Results:

Our analysis included 357 eyes from 208 patients. A discrepancy of ≥ 0.15 between clinical vs. OCT CDR occurred in 141 eyes (39%), with OCT values being generally higher than clinical values in 83% of cases (mean difference = 0.11). Bland–Altman analysis of the discrepant eyes showed a mean bias of 0.214, with OCT showing larger values (SD 0.092), with 95% limits of agreement falling between 0.03 to 0.39 (i.e. moderate degree of variability). Upon re-evaluation, 53% of those discrepancies were attributed to definable factors: 50% of the discrepancies were due to structural characteristics (e.g. residual glial or mesenchymal tissue or “shelf” within the cup, or a sloped or shallow cup; 16% due to vascular position affecting cup estimation; 4% due to optic nerve head tilt; and 28% to technical errors (especially poorly centered OCT).

Conclusions:

These findings demonstrate common disparities between clinical and OCT-derived CDR measurements. Structural factors accounted for most discrepancies, emphasizing the importance of integrating both clinical and OCT when evaluating optic nerve morphology.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Optic neuropathy

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Diagnostic Value of Papilledema in Identifying Intracranial Pathology at a Tertiary Referral Center

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Introduction:

Papilledema is classically considered a hallmark of raised intracranial pressure (ICP) and intracranial pathology. However, its diagnostic yield remains uncertain. Studies of ophthalmoscopy in pediatric headache [1] and of optic nerve head edema (ONHE) prevalence among emergency department patients [2] show that disc swelling is uncommon, even in cases of significant intracranial disease. We aimed to assess the prevalence and diagnostic performance of fundoscopy in detecting intracranial pathology within a large tertiary referral cohort.

Methods:

We retrospectively analyzed 4,867 consecutive ophthalmology consultations for suspected papilledema between January 2014 and April 2024. Cases were reviewed for the presence or absence of papilledema as well as the final medical diagnosis, including brain tumor, idiopathic intracranial hypertension (IIH), sinus vein thrombosis, meningitis, hydrocephalus, intracranial hemorrhage, brain abscess, and malignant hypertension. Incidence, sensitivity, specificity, and predictive values were calculated.

Results:

A total of 3,967 patients met inclusion criteria; 161 (4.1%) had papilledema. Incidence varied across diagnoses and was highest in IIH (81%, 50/62), and lower in meningitis (11.9%, 14/117), brain tumors (8.9%, 38/426), and sinus vein thrombosis (2.7%, 4/148). Across all intracranial pathologies, papilledema had high specificity 98.2%, but low sensitivity (13.5%). Positive predictive value was 64.6% and negative predictive value 82.4%.

Conclusions:

Papilledema was a highly specific but insensitive marker of intracranial pathology. Fundoscopy remains an indispensable bedside examination-its presence strongly predicts underlying disease-but its absence does not exclude serious pathology. These findings highlight both the importance and limitations of fundoscopy, supporting its role as a complementary, rather than standalone, diagnostic tool that must be interpreted alongside clinical findings and neuroimaging.

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Keywords: High intracranial pressure/headache, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Pseudotumor cerebri, Tumors

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Clinical Profile and Visual Outcomes in Indirect Traumatic Optic Neuropathy: A Retrospective Study from a Tertiary Eye Care Hospital

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Introduction:

Traumatic optic neuropathy (TON) remains one of the most challenging causes of sudden vision loss following head injury, with management strategies ranging from observation to high-dose corticosteroids and optic canal decompression. Despite extensive literature, controversy persists regarding prognostic indicators and treatment efficacy. Purpose: To analyse the clinical characteristics, management patterns, and visual outcomes in patients with TON at a tertiary eye care center.

Methods:

We retrospectively reviewed the records of 65 patients (68 eyes) diagnosed with traumatic optic neuropathy.. Data included demographics, mechanism of injury, initial visual acuity (VA), optic disc findings, neuroimaging characteristics, and management received (observation, corticosteroids, or surgery). Visual outcomes were assessed at 1-month follow-up. An improvement of visual acuity by ≥ 2 -lines was recorded.

Results:

The mean age was 28.28 ± 11.9 years; 89% were male. Road-traffic accidents (77%) were the leading cause, followed by assaults, sports injuries and falls. At presentation the best corrected visual acuity (BCVA) in the affected eye was, no light perception in 52.94% of eyes, 14.71% had perception of light, 10.29% had counting-fingers vision, and 5.88% had $\geq 6/60$ BCVA. Optic canal fracture was noted in 14 eyes (20.90%). Around 52.94% received intravenous methylprednisolone with oral steroids, 13.24% only oral steroids, 4.41% underwent surgical decompression and the remaining eyes were observed. Overall, 27.08% eyes showed ≥ 2 -line improvement, 29.17% showed improvement after intravenous steroids with oral steroids, 12.5% improved in oral steroid group, none improved after the optic canal decompression surgery, 14.29% improved in the observation group. No serious systemic complications occurred with corticosteroid therapy.

Conclusions:

In this cohort of patients with traumatic optic neuropathy, the majority were young males injured in road traffic accidents. Visual improvement of ≥ 2 lines occurred in approximately one-quarter of eyes, with the highest rate observed in those treated with combined intravenous and oral corticosteroids. No visual recovery was seen after optic canal decompression. While, an early high-dose corticosteroid therapy may offer potential benefit, the surgical decompression did not improve outcomes in this series.

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Keywords: Optic nerve trauma and treatment, Optic neuropathy, Trauma

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Diagnostic Concordance of ChatGPT-4.0 in Electroretinogram Interpretation Compared with Human Experts

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Introduction:

Artificial intelligence (AI) tools are increasingly evaluated for clinical applications. We investigated whether ChatGPT-4.0, a large language model, can assist in interpreting full-field and multifocal electroretinograms (ERGs) compared with subspecialist ophthalmologists.

Methods:

A retrospective set of 50 anonymized ERG reports was independently reviewed by two human electrophysiologists. Disagreements were adjudicated by a third expert to establish the consensus gold standard. ChatGPT-4.0 was provided with standardized ERG text inputs and its diagnostic impressions were recorded. Agreement between AI and human consensus was measured using accuracy and Cohen's kappa.

Results:

ChatGPT-4.0 demonstrated 92% accuracy compared with the human consensus. Cohen's kappa was 0.79, indicating substantial agreement. The AI correctly identified all 35 abnormal cases (sensitivity 100%). It misclassified 4 of 15 normal cases as abnormal (specificity 73%). Importantly, no abnormal cases were missed, though AI tended toward over-calling pathology. In the four cases where the AI reported abnormal findings but human raters judged them normal, retrospective review of the clinical notes revealed suspected inherited retinal disorders in each instance

Conclusions:

ChatGPT-4.0 showed high concordance with retinal electrophysiology experts in ERG interpretation, with excellent sensitivity and acceptable specificity. While not a substitute for clinical judgment, AI may serve as a supportive tool to flag potential abnormalities, particularly in high-volume or resource-limited settings. Further research should explore real-time integration, prospective validation, and refinement to reduce false positives.

References: None provided.

Keywords: Pediatric neuro-ophthalmology

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Grant Support: None.

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Vestibulo-Ocular Reflex Gain Differentiates Spinocerebellar Ataxia Type 27B from CANVAS and Idiopathic Late-Onset Cerebellar Ataxia

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Introduction:

Spinocerebellar ataxia type 27B (SCA27B) and CANVAS are recently recognized genetic causes of late-onset cerebellar ataxia (LOCA). Despite advances in genetic testing, most panels fail to detect these intronic repeat expansions, leading to multiple testing, and delayed diagnosis. Oculovestibular abnormalities is common in both disorder, and may help differentiate them from idiopathic LOCA (ILOCA), guiding targeted genetic test. We aimed to characterize oculovestibular function in these groups and determine whether vestibulo-ocular reflex (VOR) gain measured by video head impulse testing (vHIT) can differentiate SCA27B from CANVAS and ILOCA.

Methods:

We retrospectively reviewed 290 individuals evaluated for cerebellar ataxia at the Johns Hopkins Ataxia Center (2023–2025). Subjects with SCA27B (n = 33), CANVAS (n = 10), and ILOCA (n = 16) were included, along with age-matched controls (n = 31). All underwent standardized video-oculography (VOG) and vHIT. Horizontal canal VOR gains were quantified and compared using Kruskal–Wallis and Fisher’s exact tests. Receiver operating characteristic (ROC) curves were generated to determine diagnostic thresholds, with significance set at $p < 0.05$.

Results:

Horizontal VOR gain differed significantly across groups ($p < 0.001$): median VOR gain values were lowest in CANVAS (0.20), mild reduced in SCA27B (0.85), and normal in ILOCA (1.11) and controls (1.12). Bilateral vestibulopathy (VOR < 0.6) occurred in 80% of CANVAS, 18% of SCA27B, and none of ILOCA ($p = 0.024$). A VOR cutoff < 0.70 differentiated the genetic ataxias from ILOCA with 100% specificity, while a VOR cutoff < 0.50 distinguished CANVAS from SCA27B with 91% specificity.

Conclusions:

Ocular motor cerebellar signs occur across idiopathic and genetic cerebellar ataxias groups, whereas reduced VOR gains were common in both CANVAS and SCA27B, and not observed in ILOCA. vHIT metrics may assist in distinguishing these genetic ataxias from ILOCA and each other, supporting potential utility as physiologic biomarkers and guiding targeted genetic testing.

References: 1. Pellerin D, Danzi MC, Wilke C, Renaud M, Fazal S, Dicaire MJ, Scriba CK, Ashton C, Yanick C, Beijer D, Rebelo A, Rocca C, Jaunmuktane Z, Sonnen JA, Larivière R, Genís D, Molina Porcel L, Choquet K, Sakalla R, Provost S, Robertson R, Allard-Chamard X, Tétreault M, Reiling SJ, Nagy S, Nishadham V, Purushottam M, Vengalil S, Bardhan M, Nalini A, Chen Z, Mathieu J, Massie R, Chalk CH, Lafontaine AL, Evoy F, Rioux MF, Ragoussis J, Boycott KM, Dubé MP, Duquette A, Houlden H, Ravenscroft G, Laing NG, Lamont PJ, Saporta MA, Schüle R, Schöls L, La Piana R, Synofzik M, Zuchner S, Brais B. Deep Intronic FGF14 GAA Repeat Expansion in Late-Onset Cerebellar Ataxia. *N Engl J Med*. 2023 Jan 12;388(2):128-141. doi: 10.1056/NEJMoa2207406. Epub 2022 Dec 14. PMID: 36516086; PMCID: PMC10042577. 2. Ariello LE, Gold DR, Mu W, Schubert MC, Allen C, Paul A, Rastall DPW. Ocular Motor and Vestibular Profile in Spinocerebellar Ataxia Type 27B: Toward a Practical Bedside Diagnostic Framework. *Cerebellum*. 2025 Sep 4;24(5):149. doi: 10.1007/s12311-025-01906-y. PMID: 40906330. 3. Ariello LE, Gold DR, Millar JL, Schubert MC, Mu W, Rosenthal L, Rastall DPW. Video head impulse test differentiates RFC1-CANVAS, FGF14-SCA27B, and idiopathic late-onset cerebellar ataxias. *J Neurol*. 2025 Oct 7;272(10):679. doi: 10.1007/s00415-025-13433-1. PMID: 41055766.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Ocular manifestations of vestibular disorders, Vestibular disorders, Genetic disease

Financial Disclosures: The authors had no disclosures.

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Vision-Based Concussion Testing in a Youth Ice Hockey Cohort: Are There Gender Differences in Pre-Season Scores for Rapid Picture- (MULES) and Number-Naming (SUN)?

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Introduction:

Vision comprises 50% of the brain pathways and is frequently involved in sport-related concussion. The Mobile Universal Lexicon Evaluation (MULES) and Staggered Uneven Number (SUN) are accessibly administered rapid automatized naming tasks (aged 5-17 years). Gender, within the context of age-related scores, has not been examined. The goal is to examine gender differences in performance on MULES and SUN tests, accounting for observed patterns across age groups ranging from 5 to 17. We sought to examine potential differences in learning effects.

Methods:

Two pre-season trials of the MULES and SUN were administered to a youth ice hockey league. Informed assent/consents for the athletes and parental/guardian permission for research were obtained. The MULES involves 54 color photographs of objects on two sides of an 8.5x 11-inch laminated sheet. The SUN test has four rows of numbers, with single and double digits named in sequence. The fastest (best) times out of the two trials of each test was recorded as baseline.

Results:

Among 175 athletes, 111 boys (mean age 11.4 years) and 64 girls (mean age 12.4 years), had significant associations of slower pre-season test times with younger age on MULES ($r_s = -0.68$, $p < 0.0001$) and SUN ($r_s = -0.71$, $p < 0.0001$). Faster MULES time and gender were statistically significant ($p = 0.0015$, two-sample t-test) (mean boys=56.5 seconds, mean girls=46.9 seconds). Age-controlled analysis did not show a difference in best MULES score by gender ($p = 0.06$). There was no significant difference by gender for SUN ($p = 0.06$, t-test). (mean girls=71.4 seconds boys=85.0 seconds).

Conclusions:

Gender differences and changes across age groups may indicate that our expectations for pre-season, post-injury and recovery time scores may differ between picture- and number-naming test platforms. Additionally, it raises the question of how injury data may differ between boys and girls, emphasizing the need for further research for vision-based concussion testing.

References: None provided.

Keywords: Trauma, Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Association of Rapid Picture and Number Naming Time Scores to Examination Test Results in Occupational Therapy for Vision and Vestibular Physical Therapy in Clinical Practice

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Introduction:

Occupational therapy (OT) for vision and vestibular physical therapy (PT) are mainstays of evaluation and rehabilitation for patients with neurological conditions. Both standard testing batteries and the Mobile Universal Lexicon Evaluation System (MULES, rapid picture naming) and the Staggered Uneven Number (SUN, rapid number naming) were completed. The purpose of this study was to determine the relation of MULES and SUN time scores to other standard tests.

Methods:

Retrospective chart review of electronic medical records was performed for patients evaluated by OT for vision and vestibular PT for concussion and other neurological conditions. Spearman's rank correlation coefficients were used to assess association between continuous scores on MULES, SUN and other timed tests. Wilcoxon rank-sum tests were used to compare continuous MULES and SUN scores between dichotomously scored (finding present vs. absent) OT and PT measures.

Results:

Among the first 36 patients for whom MULES and SUN were included in the initial evaluations the median MULES test time was 56.9 seconds (range 32.6–170.2) and median SUN time was 62.8 seconds (range 32.9–105.3). There were significant associations of greater (worse) MULES and SUN times with worse times on the Developmental Eye Movements (DEM) test for MULES (card 1: $r_s=0.37$, $P=0.03$) and SUN (card 1: $r_s=0.63$, $P=0.0001$; card 2: $r_s=0.56$, $P=0.0005$; card 3: $r_s=0.61$, $P=0.0001$). Also, participants with abnormal supine head roll test results demonstrated significantly longer SUN times compared to those with normal results ($P=0.0009$, Wilcoxon rank-sum test).

Conclusions:

MULES and SUN are practical, accessible rapid automatized naming tasks that reflect scores for standard OT and PT measures. Continuing retrospective review of these clinical data will determine associations of OT/PT examination findings of convergence insufficiency (near point of convergence), the most common neuro-ophthalmologic abnormality for patients with concussion and other neurological conditions, to timed performance measures of MULES and SUN.

References: None provided.

Keywords: Ocular manifestations of vestibular disorders, Ocular motility, Trauma

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Reliability of Objective Vision-Based Screening Tools for Concussion in Collegiate Athletes

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Introduction:

Visual as well as cognitive dysfunction are common clinical presentations of concussion. Formal clinical neuro-ophthalmic examinations and cognitive assessments have long administration times that require a specialist to perform. The Mobile Universal Lexicon Evaluation System (MULES) and Staggered Uneven Number (SUN) assess many visual networks and performance requires the integration of saccadic eye movements, color perception, visual memory and object and number identification. Rapid and reliable tests are important for assessing concussion on the sideline and in the clinic. MULES and SUN were developed to quickly assess visual function following sports-related concussion both in collegiate and youth athletes. They have also been studied in patients with multiple sclerosis, mild cognitive impairment and Parkinson's disease. We determined reliability and agreement for the MULES and SUN tests over a sports season for a collegiate cohort.

Methods:

Healthy collegiate athletes (n=21, mean age 20 years, 57.1% male) completed the MULES and SUN at two baseline visits, approximately two weeks apart, during the pre-season. The tests were administered again immediately at the post-season. The intra-class correlation coefficient (ICC) using a two-way mixed effects model and absolute agreement were calculated as a measure of reliability and agreement between both 1) the two pre-season assessments and 2) the first pre-season assessment and the post-season assessment. Each side of the MULES and each line of the SUN were analyzed individually.

Results:

For both MULES and SUN, high levels of reliability were demonstrated between the two preseason baseline test scores and for pre-season vs. post-season scores (ICCs of 0.76-0.90, $p < 0.001$ for all).

Conclusions:

MULES and the SUN have excellent reliability for capturing the many aspects of visual function and other dimensions related to cognitive and ocular motor function in healthy collegiate athletes. These freely-accessible and rapid measures will be useful for further implementation to assess collegiate as well as youth athletes.

References: None provided.

Keywords: Trauma, Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Comprehensive Stereotaxic Mapping of the Rat Superior Colliculus and Visual Cortex with High-Density Electrode Array

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Introduction:

Electrophysiological mapping of visual areas provides key insights into visual processing. The binocular zone of the primary visual cortex (V1B) integrates inputs from both eyes, while the superior colliculus receives retinal inputs and integrates multisensory information. The V1B extends along the anterior-posterior axis of the cortical surface, whereas the SC layers stack dorsoventrally over the midbrain. The spatial coverage of standard multi-electrode arrays (MEAs) is limited in these areas due to their complex geometries. To overcome this limitation, we developed custom, high-density MEAs designed to match the anatomy of rat V1B and SC, enabling precise, efficient, and comprehensive neural recordings across their distinct three-dimensional structures.

Methods:

We recorded local field potentials (LFPs) from the rat SC and V1B using custom MEAs while presenting full-field light flash stimuli. Sixty-four evenly distributed recording sites were selected for SC and V1B across anterior-posterior, medial-lateral, and dorsal-ventral axes, based on the Paxinos and Watson stereotaxic atlas. The MEAs were fabricated from a 70/30 platinum-iridium alloy. The SC and V1B MEA consisted of an 8x8 and 16x4 layout, respectively. In both arrays, electrodes were spaced 225 μm apart with unique depth to optimize spatial sampling. Each electrode had a diameter of 75 μm to minimize insertion damage, and an impedance of 10 k Ω to maximize signal-to-noise ratio.

Results:

Light-evoked LFPs were successfully recorded from 64 of 64 channels of both MEAs when inserted in the SC and the V1B, with good signal-to-noise ratio. The custom MEAs achieved complete spatial mapping of both cortical structures with precise anatomical alignment while minimizing tissue disruption.

Conclusions:

Combining the latest MEA fabrication technologies with an open-source brain atlas reference enabled the design of custom MEAs that deliver high-density precise recordings. Future applications include performing MEA recordings with threshold focal, perimetric stimulation to enable structure-function correlation.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Visual fields, Higher visual functions, Miscellaneous

Financial Disclosures: The authors had no disclosures.

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Contact Information: None provided.

Characterizing 18F-FDG Uptake In Extraocular Muscles Of Patients With Parkinson's Disease

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Introduction:

Extraocular motility relies on extensive networks of cerebral regions, making the oculomotor system vulnerable in neurodegenerative disease. The goal of this study was to determine if 18F-Fluorodeoxyglucose (FDG) Positron Emission Tomography (PET) could serve as an effective surrogate marker for extraocular muscle (EOM) metabolism and function in patients with Parkinson's Disease (PD).

Methods:

We performed a retrospective analysis of patients who underwent 18F-FDG PET CT at UCSF between 2012-2023. Subjects who had undergone a complete ophthalmic examination within 2 weeks of their scan with documented normal ocular motility were included as controls as well as PD subjects with a clinical evaluation of disease severity (mild, moderate, severe). Scans were analyzed in the radiology interpretation system Visage to obtain SUVmean and SUVmax FDG uptake values for each EOM.

Results:

We analyzed 857 EOMs from 111 controls and 143 EOMs from 18 PD patients. For the control database, FDG values were distributed across age. Pairwise comparisons of uptake between EOMs revealed that most muscles had similar uptake across the age distribution. All EOM from PD patients demonstrated decreased FDG uptake when compared to age-matched controls. Significant decrements in uptake were primarily found in the medial rectus ($p=.0005$) and superior rectus ($p=.0160$) muscles in patients with moderate PD and severe PD, respectively, when compared to age-matched controls.

Conclusions:

These findings indicate a decrement in EOM FDG uptake in PD compared to controls. Decreased metabolic function of medial rectus and superior rectus may account for convergence insufficiency and limitations of vertical eye movements in this population of patients. A larger, prospective cohort study is needed to build on this finding. Nevertheless, 18F-FDG PET may be a useful modality to identify disease-specific patterns of EOM metabolic dysfunction across a wide range of ocular motility disorders in neurodegenerative disease.

References: None provided.

Keywords: Neuroimaging, Ocular motility

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Pattern-Level Reproducibility of Head-Mounted Smartphone-Based Perimetry in Optic Neuropathies

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Introduction:

Standard automated perimetry (SAP) is essential for evaluating optic neuropathies but limited by cost, low portability, and reduced reliability in advanced disease. Head-mounted devices (HMDs) capable of luminance and size modulation offer portable, low-cost alternatives. Prior work focused on pointwise sensitivity comparisons, which have limited clinical relevance. This study evaluates the reproducibility of HMD-based perimetry, emphasizing pattern-level agreement across testing modalities.

Methods:

Thirty-one participants with glaucoma or other optic neuropathies underwent testing using three perimetric modalities (two tests per modality) in a randomized order: conventional SAP (luminance modulation), head-mounted luminance-modulated perimetry (HMD-L), and head-mounted size-modulated perimetry (HMD-S). Testing used a standardized grid, size V stimuli, and a Bayesian adaptive thresholding algorithm. Age-adjusted sensitivities were derived from modality-specific normative datasets. Total deviation and pattern standard deviation probability maps were generated from these distributions. A defect was defined as ≥ 3 contiguous points with $p \leq 0.05\%$. Within-modality reproducibility required meeting the defect criterion on both tests, while cross-modality agreement required an HMD defect co-localized with a repeatable SAP defect. Additional planned analyses will (1) classify cross-modality reproducibility as complete, partial, or no match; (2) determine which defect patterns are most and least reproducible; and (3) test whether a continuous probability model or a relaxed threshold (e.g., $p \leq 10\%$) improves agreement.

Results:

A total of 186 tests (62 per modality) were analyzed. On SAP, 15 inferior and 11 superior repeatable hemifield defects were identified (overall reproducibility 65%). HMD-L reproduced 11/15 (73%) inferior and 11/11 (100%) superior defects, while HMD-S reproduced 10/15 (66%) inferior and 9/11 (81%) superior defects. Five repeatable deficits were unique to HMD testing. Preliminary screening suggests that arcuate and altitudinal defects appeared most reproducible, and relaxed thresholds may improve concordance for shallow or evolving field loss.

Conclusions:

HMDs demonstrated reproducibility comparable to SAP for clinically meaningful defect patterns. Pattern-level and relaxed thresholds may further refine its role as an accessible tool for monitoring optic neuropathies.

References: None provided.

Keywords: Perimetry, Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Association Between Prostaglandin Analogue Use and Sagging Eye Syndrome in Older Adults: A Retrospective Case-Control Study

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Introduction:

Sagging eye syndrome (SES) is a frequent cause of age-related strabismus. Prostaglandin analogues (PGAs), widely used for glaucoma, can induce periorbital changes (prostaglandin-associated periorbitopathy) that resemble SES features. We evaluated whether PGA use is associated with an increased likelihood of SES.

Methods:

Records of patients aged ≥ 60 years seen between 2012 and 2024 were reviewed. SES was diagnosed by chart documentation, clinical features, or orbital MRI. Age- and sex-matched esotropia patients without SES served as controls. Demographic, systemic, and ophthalmic data were collected. Chi-squared tests, t-tests, and logistic regression assessed associations, with PGA use as the primary exposure.

Results:

One hundred patients were included (50 SES, 50 controls; mean age 76.9 years, 66% female). Primary glaucoma was more common in SES patients (14%) than controls (8%) ($p = 0.046$). PGA use was observed in 14% of SES cases versus 4% of controls ($p = 0.081$). Logistic regression showed higher but nonsignificant odds of SES among PGA users (unadjusted OR 3.28, 95% CI 0.63–17.1; adjusted OR 3.14, 95% CI 0.49–20.2).

Conclusions:

PGA use was associated with a threefold increase in odds of SES, though this did not reach statistical significance. Given overlapping features of prostaglandin-associated periorbitopathy and SES, PGA exposure may represent a secondary risk factor in aging patients. Larger, prospective studies are warranted to clarify this relationship.

References: None provided.

Keywords: Adult strabismus with a focus on diplopia, Ocular motility, Orbit

Financial Disclosures: The authors had no disclosures.

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Contact Information: None provided.

The Prognosis of Diplopia from Brainstem Ischemic Strokes, A Cross-Sectional Study

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Introduction:

Diplopia is the separation of visual images due to ocular misalignment. Brainstem ischemic strokes are a frequent cause of diplopia due to the presence of ocular motor structures in the brainstem. There is little evidence about the prognosis of diplopia after brainstem ischemic strokes.

Methods:

Patients that experienced ischemic infarcts between 2020 and early 2024 were identified via ICD10 codes. A chart review was performed to determine if these patients had brainstem involvement and subsequently experienced new-onset diplopia. Participants with dementia, aphasia, or previously existing diplopia were excluded. A telephone survey was conducted to determine the duration of diplopia, severity of symptoms (intermittent vs persistent), use of aids for diplopia, impact on daily activities, and treatment received. Additional risk factors and demographics that may influence the prognosis were obtained.

Results:

Fifty-six patients were identified with new-onset diplopia after having an acute brainstem infarct. All patients were called and 31 were successfully contacted. Seven patients agreed to and completed the survey. Regarding the participants, the age range is between 47 and 80 years old and each one has at least two cardiovascular risk factors. Specifically, hypertension, obesity, and dyslipidemia were seen in over half of the patients. Three of the seven patients have persistent diplopia that prevents them from performing prior activities. One patient received tPA, and no patients received treatment for their diplopia following their stroke. Regarding the four patients whose diplopia has resolved, only one received treatment that involved an eye patch for 21 days alongside occupational therapy. These four patients only experienced diplopia for a short time, lasting between two days and six weeks.

Conclusions:

The majority of the patients with diplopia after an acute brainstem infarct had complete resolution of the diplopia within six weeks, indicating a relatively good prognosis. Study limitations include its low sample size and retrospective nature.

References: None provided.

Keywords: Adult strabismus with a focus on diplopia, Stroke

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Recurrent Painful Ophthalmoplegic Neuropathy (RPON): Clinical and Radiological Features with Cerebrospinal Fluid MCP-1 Elevation

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Introduction:

Recurrent painful ophthalmoplegic neuropathy (RPON) is a rare disorder, and most knowledge about it derives from isolated case reports. We aimed to characterize RPON through a retrospective case series and a literature review.

Description of Cases:

Methods: Patients diagnosed with RPON at our hospital between January 2018 and June 2025 were retrospectively enrolled. A literature review of previously reported RPON cases was also performed. **Results:** Ten patients were included. The median age at diagnosis was 20 years (range, 5–47 years), with an equal sex distribution (5 males, 5 females). The median interval from disease onset to diagnosis was 7 years (range, 3–20 years). Migrainoid headache was reported in 70.0% (7/10), always ipsilateral to the ophthalmoplegia. The oculomotor nerve was most frequently affected (90.0%, 9/10), while the abducens nerve was involved in one case. All patients (100.0%, 10/10) showed enhancement of the affected cranial nerve on MRI, predominantly nodular (70.0%, 7/10). Cytokine analysis was performed in four patients during the acute episode. All (4/4) had elevated cerebrospinal fluid MCP-1 levels (342.4–349.7 pg/mL). Three (3/4) also showed elevated serum MIP-1 β levels (197.2–215.9 pg/mL). Nine patients (9/10, 90.0%) received glucocorticoids, and six (6/10, 60.0%) exhibited persistent neurological deficits. In the literature review ($n = 44$), the median age was 16 years (range, 17 months–53 years), with 56.8% males (25/44). Migrainoid headache occurred in 59.1% (26/44). The oculomotor nerve was affected in 96.5% (42/44) of cases. Nodular enhancement on MRI was reported in 81.8% (36/44). Glucocorticoid therapy was administered in 68.2% (30/44), and persistent neurological deficits were reported in 18.2% (8/44).

Conclusions, including unique features of the case:

This study provides additional clinical and imaging data on RPON and highlights MCP-1 elevation in CSF as a potential biomarker. The findings suggest that inflammatory chemokine-mediated immune activation may contribute to cranial nerve injury in RPON, offering new insights into its pathogenesis and potential therapeutic targets.

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References: None provided.

Keywords: Ocular motility, Pediatric neuro-ophthalmology

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Causes of Isolated Ocular Motor Nerve Palsy – A Population-Based Evaluation

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Introduction:

Variable frequencies of non-microvascular causes of acute isolated ocular motor nerve palsy have been reported in older patients (1-16.5%), resulting in controversies in initial management. We wish to determine proportions of these non-microvascular causes in our population.

Methods:

ICD10-CM codes for isolated ocular motor nerve palsy were used to extract data from electronic medical records over 10 years (2015-2025). Vasculopathy risk factors (diabetes mellitus, hypertension, hypercholesterolemia, coronary artery disease, cerebrovascular disease, and obesity) were documented. Descriptive frequencies of variables and differences between age groups, etiology, and associated risk factors were calculated. Fisher/X2 and multivariable logistic regression analyses were performed using R-v4.5.1 program. Two-sided P< 0.05 was considered significant.

Results:

Of 280 identified patients, 182 had isolated ocular motor nerve palsy. Mean(SD) age was 54.2(20.4) years and 51.6% were male. 59.9% had VIth, 34.1%, IIIrd, and 5.5%, IVth nerve palsy. Common etiologies were microvascular ischemia (30.2%), cerebrovascular accident (13.2%), and inflammatory/demyelinating disease (8.2%). Older patients (≥50years) were more likely to have microvascular ischemia compared to young counterparts (40.3% vs 11.1%, P< 0.0001). Leading risk factors were hypertension (61.5%), diabetes (49.5%), and hyperlipidemia (33.0%). At least one risk factor was present in older (90.8%) than younger (33.3%) patients (P< 0.0001). Among older patients with ≥1 risk factor (n=108), 37% (95% CI=27.9–46.9) had identifiable, non-trauma, non-microvascular causes; mostly cerebrovascular accident, mass/tumor, and inflammatory/demyelinating disease. Etiologies did not differ by affected nerve (P=0.15). In multivariable regression adjusted for nerve, sex and vascular risk factors: older age (≥50years) (aOR=3.36, 95% CI=1.25–9.87; P=0.02) and diabetes (aOR=2.49, 95% CI=1.13–5.68; P=0.03) independently predicted microvascular etiology.

Conclusions:

In our population, a substantial proportion of patients with vascular risk factors had non-microvascular causes for ocular motor nerve palsy. We support neuroimaging and laboratory testing in the initial evaluation of all patients, including older patients with intercurrent vascular risk factors.

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Keywords: Ocular motility, Neuroimaging, Stroke, Tumors, Demyelinating disease

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Real-Time Detection and Extraocular Muscle Stimulation Framework for Adaptive Management of Acquired Nystagmus

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Introduction:

Acquired nystagmus is a condition marked by involuntary, repetitive eye movements that disrupt visual stability and quality of life. Current treatments, including drugs and surgery, are often ineffective, non-specific, and unable to adapt to changing symptoms. We developed a real-time system that detects nystagmus, computes counteracting vectors, and identifies the extraocular muscles requiring stimulation to restore stable gaze—advancing toward adaptive, closed-loop treatment.

Methods:

The system integrates an eye-tracking module with a webcam to capture real-time ocular motion. Eye movements are processed using MediaPipe's FaceMesh model with Kalman filtering to distinguish pathological oscillations from voluntary gaze shifts. Fourier analysis determines counteracting vectors for stabilization, which are then mapped to corresponding extraocular muscles. A graphical user interface (GUI) displays the muscles in real time, guiding electrode placement and potential stimulation. Bench testing on 50 trial videos evaluated detection accuracy, vector computation, and muscle classification.

Results:

Preliminary testing showed high accuracy, with Fourier transform processing achieving response latencies under 10 ms. Among 50 videos, the system identified 22 true positives, 19 true negatives, 5 false negatives, and 4 false positives. Correlation with OtoSuite velocity values was strong (R^2 : 0.9478 left horizontal, 0.9209 left vertical, 0.9545 right horizontal, 0.9485 right vertical). Counteracting vector simulations accurately identified target muscles and their relative contributions to oscillations. In 50 classification trials of lateral, lateral/inferior, medial, and medial/superior muscles, results included 12 lateral, 4 lateral/inferior, 23 medial, and 8 medial/superior true positives, with minimal misclassification. Synthetic data testing is refining contribution estimates, and the GUI is being finalized for real-time feedback.

Conclusions:

This real-time nystagmus detection and muscle stimulation guidance system represents a significant step toward an adaptive, personalized treatment for acquired nystagmus. By integrating live eye tracking with computational modeling of muscle activation, this technology could improve surgical precision and electrode-based neuromodulation therapies. Future work will focus on integrating direct muscle stimulation and validating efficacy through in vivo testing.

References: None provided.

Keywords: Nystagmus, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Pupil

Financial Disclosures: Kenzi Griffith; Dennis Ngo; Archis Shankaran; Simren Shah; Esha Venkat; Travis Tran; Evan Batten; Immanuel Etoh; Michael Repka; Michelle Zwernemann; Edward Kuwera; Kemar Green: Startup, Neuroagent

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Eye Movement Disorders in Central Nervous System Demyelinating Diseases – A Retrospective Study

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Introduction:

Ophthalmoparesis and abnormal spontaneous eye movements are features of the central nervous system demyelinating diseases. However, they have not been vastly studied and the association between their presence and disease outcome has not been reported. This study is aimed to explore the frequency of eye movement abnormalities among patients diagnosed with central nervous system demyelinating diseases.

Methods:

We retrospectively reviewed medical records of all patients evaluated at a single university-based hospital who were (1) diagnosed with either relapsing-remitting multiple sclerosis (RRMS), neuromyelitis optica spectrum disorder (NMOSD) or myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD), and (2) followed-up in the clinic between November 2023 and October 2024. Data on the eye movement abnormalities were collected.

Results:

Of all 218 patients (RRMS 86, NMOSD 116, MOGAD 16), 84.9% were female, and the median disease duration was 6.2 years. Over a follow-up period of 1667 patient-years, diplopia and oscillopsia were reported in 17.4% and 5.0% of patients. Ophthalmoparesis was observed in 26 patients (11.9%), with the most common types being internuclear ophthalmoplegia (6.0%) and abduction deficits (5.5%). Nystagmus was reported in 35 patients (16.1%), with gaze-evoked nystagmus being the most common pattern (7.8%), followed by vertical (2.3%) and pendular nystagmus (1.8%). RRMS was associated with the presence of ophthalmoparesis ($p=0.003$), nystagmus ($p=0.027$) and infratentorial lesions on MRI ($p<0.001$). The presence of ophthalmoparesis or nystagmus was not associated with the higher EDSS or mRS scores ($p>0.05$).

Conclusions:

Eye movement abnormalities were observed in about one-sixth of patients, with RRMS showing the highest frequency. Presence of these abnormalities did not correlate with worse disability.

References: None provided.

Keywords: Ocular motility, Nystagmus, Adult strabismus with a focus on diplopia, Demyelinating disease

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Non-ocular symptoms in early, treatment-naïve ocular myasthenia gravis: the PROMISE-MG study

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Introduction:

The Myasthenia Gravis Activities of Daily Living (MG-ADL) is a commonly used scale that measures ocular and non-ocular symptoms of myasthenia gravis (MG). While ocular MG (OMG) is defined as having symptoms limited to ptosis and diplopia, previous research has found that OMG patients frequently report non-ocular symptoms on the MG-ADL, a finding that has traditionally been dismissed as nonspecific or due to the limited construct validity of MG-ADL in OMG. Up to 85% of OMG patients progress to generalized MG within 2 years, though robust predictors of generalization are limited. Our objective was to determine if the presence of baseline non-ocular symptoms in OMG is associated with disease progression or corticosteroid requirement, potentially reflecting underlying subclinical generalized disease.

Methods:

PROMISE-MG was a prospective, multicenter observational study of adults with early, treatment-naïve MG. At enrollment, subjects could be taking pyridostigmine for < 3 months, but corticosteroid or steroid-sparing immunotherapy for MG were excluded. MG-ADL and other outcome measures were prospectively measured at baseline and follow-up visits. Treatment and follow-up frequency were determined by the treating clinician. We analyzed subjects with OMG (defined as Myasthenia Gravis Foundation of America [MGFA] class I) at the baseline visit. Using multivariable Cox proportional hazards models, we measured the association between baseline non-ocular MG-ADL items and two outcomes: progression to MGFA class >I and corticosteroid initiation.

Results:

Our sample consisted of 29 OMG patients, of whom 8 (27.6%) reported non-ocular symptoms at baseline. Over one year of follow-up, 15 (51.7%) initiated corticosteroids, and 6 (20.7%) experienced generalization. Baseline non-ocular MG-ADL symptoms were not associated with corticosteroid initiation (HR: 0.80, 95% CI: 0.38-1.68) or generalization (HR: 1.44, 95% CI: 0.75-2.78).

Conclusions:

Non-ocular MG-ADL items are not associated with corticosteroid requirement or generalization and therefore likely do not reflect subclinical generalized disease in OMG patients.

References: None provided.

Keywords: Myasthenia, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: Michael Morano; Pushpa Narayanaswami: Research funding from PCORI, Dianthus, Janssen, UCB, and Alexion, served on DSMB for Sanofi, and served on consultancy/Advisory Boards for Alexion, Argenx, UCB, Janssen, Dianthus, Novartis, GSK, ImmuneAbs, and Amgen.; Ali Hamedani: Research funding from the NEI, consulting for ArgenX.

Grant Support: NEI K23 EY033438

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Smoking Status Is Associated With Delayed Recovery In Patients With Ischemic Cranial Nerve Palsy: a Pilot Study

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Introduction:

Smoking is known to influence the occurrence of ischemic cranial nerve palsy (CNP) but its effect on recovery is less clear. Therefore, we aimed to evaluate the impact of smoking on the potential for full recovery in patients with ischemic CNP.

Methods:

We included patients with ischemic CNP who underwent comprehensive brain imaging and blood tests within 2 weeks after diagnosis. All patients were diagnosed by a single physician at a single institute with an idiopathic/microvascular CNP. Follow-up evaluations were performed regularly until recovery. Patients who were lost to follow-up before achieving recovery were excluded. Recovery was defined as orthotropia in primary gaze with ocular limitation < -1. Patients were classified into early and delayed recovery groups based on the median recovery time for each group. Multivariable logistic regression was performed to identify predictors of delayed recovery, including age, sex, co-morbidities (diabetes mellitus, systemic hypertension, hyperlipidemia), type of CNP, degree of initial ocular limitation, and smoking status. Smoking was categorized according to pack-years (heavy/light) and current status (none/previous/current smoker). Odds ratios (ORs) with 95% confidence intervals (CIs) were reported.

Results:

Among 212 patients, 62 patients (Mean age 63.2 years, 50 males) were included for analysis. The mean time from initial diagnosis to primary recovery was 71 days (IQR, 33–119 days). Smoking was strongly associated with delayed recovery: compared with non-smokers, current smokers had an OR of 18.57 (95% CI: 2.51–137.68), and heavy smokers (≥20 pack-years) had an OR of 19.78 (95% CI: 2.17–180.72) for delayed recovery. Among covariates, diabetes mellitus had a significant association with delayed recovery (OR 24.87, 95% CI: 3.42–180.76).

Conclusions:

Current and heavy smoking are significantly associated with delayed recovery to orthotropia in patients with ischemic CNP. These findings suggest that early identification of smokers and active counseling to cease smoking immediately after diagnosis may contribute to faster recovery outcomes in CNP patients

References: None provided.

Keywords: Adult strabismus with a focus on diplopia, Neuro-opth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: Ju-Yeun Lee; Ji-Min Kweon; Si Young kim; Joseph Rizzo: consultant to Life Biosciences

Grant Support: None.

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Binocular Eye-Tracking of Naturalistic Viewing Highlights Eyeblink and Gaze Asymmetries in Strabismus

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Introduction:

Most eye-tracking studies in strabismus have relied on static fixation tasks that mimic the clinical cover–uncover test (1-2). While such paradigms capture fixation stability, they fail to represent how eyes move dynamically in natural scenes where visual salience continuously changes. To better characterize ocular dynamics in strabismus and underlying brain circuitry, we conducted a Free-Viewing binocular eye-tracking experiment examining fixation, saccades, pupil and eyeblink behavior across different viewing conditions.

Methods:

Adults with strabismus (N = 16) attending ophthalmology clinics participated in a 30-minute study using the EyeLink 1000 Plus (SR Research). Each participant viewed identical 5-minute naturalistic video clips under three conditions: (1) strabismus eye occluded, (2) fellow eye occluded, and (3) binocular viewing. Bilateral eye data were recorded simultaneously, and ocular metrics were extracted continuously. Paired-samples t-tests compared eyes within each condition, complemented by Wilcoxon tests for nonparametric confirmation. A two-way repeated-measures ANOVA (Eye × Viewing Condition) evaluated main and interaction effects with Greenhouse-Geisser corrections and Bonferroni-adjusted p-values. Analyses were performed in MATLAB R2025a (MathWorks, Natick, MA).

Results:

Median blink duration differed significantly between eyes ($p = 0.04$) and across viewing conditions ($p = 9.5 \times 10^{-5}$). The fellow eye consistently exhibited longer blinks than the strabismus eye, most prominently during monocular strabismus viewing (median = 25 ms, $p = 0.009$). During binocular viewing, microsaccade rate was higher in the strabismus eye (0.59) than in the fellow eye (0.54, $p = 0.002$), an effect absent during monocular viewing. Horizontal gaze bias was greater in the strabismus eye ($p = 0.006$) and varied with viewing condition ($p = 0.03$).

Conclusions:

In healthy adults, blink synchrony between eyes is typically < 5 ms (3-4). The present finding of prolonged fellow-eye blinks in strabismus suggests an adaptive mechanism reducing dominant-eye visual input to mitigate retinal disparity. Altered microsaccade rate and horizontal gaze bias further indicate dynamic strategies for maintaining binocular visual processing in strabismus.

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Keywords: Higher visual functions, Ocular motility

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Grant Support: SEAMO AFP Innovation Award

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Feasibility of a Gamified Virtual Reality (VR) System for Ocular Motor, Assessment After Mild Traumatic Brain Injury

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Introduction:

Ocular motor function often reflects subtle neurological dysfunction that may follow mild traumatic brain injury (mTBI). Despite this, clinical assessments continue to depend largely on symptom reports and subjective scales. Immersive platforms, such as virtual reality (VR), provide a way to measure these movements under consistent and realistic conditions. Our group previously developed a VR-based ocular motor battery that captured smooth pursuit and saccadic parameters with good reliability. The present work describes the adaptation of that system into a gamified format aimed at improving participation and collecting richer behavioral data for use in recovery monitoring.

Methods:

In the initial feasibility study, healthy participants (n=10) and individuals with known neurological disorders (n=10) completed a series of tasks (i.e., smooth pursuit, saccades, convergence, fixation). The system yielded high-quality recordings in most trials and stable ocular motor measures across repeated sessions. Insights from this dataset informed development of a gamified platform that introduces scoring, adaptive task difficulty, and combined tasks of previous metrics. Ongoing testing includes healthy adults to examine comfort, engagement, and reproducibility.

Results:

All participants completed testing successfully. Distinct ocular motor differences were observed between cohorts. Healthy subjects demonstrated precise smooth pursuit with target-velocity matching, while symptomatic participants showed low-gain pursuit and corrective saccades. Prolonged saccadic latencies in the symptomatic group correlated strongly with greater symptom burden ($\geq 95\%$), and 19 of 20 participants were correctly classified as healthy or symptomatic. Early trials of the gamified platform indicate improved focus and response consistency compared with prior versions.

Conclusions:

A VR-based platform can objectively quantify ocular motor differences between healthy and symptomatic individuals, with metrics strongly correlating with clinical symptom burden. Gamified VR ocular motor and vestibular testing offers a reliable, engaging, and feasible tool for evaluating cognitive and vestibular function after mTBI. Its interactive design enhances user participation while maintaining precision, supporting its potential use as a digital biomarker for concussion recovery.

References: None provided.

Keywords: Ocular motility, Miscellaneous

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Grant Support: None.

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Feasibility of Detecting Oculomotor Alterations in Patients with Huntington's Disease Using Custom, Retina-Based Eye Tracking

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Introduction:

Huntington's disease (HD) is characterized by efferent neuro-ophthalmic abnormalities. We evaluated whether a brief, 30-minute, customized retinal eye-tracking protocol could reliably detect oculomotor differences between adults with HD and healthy controls.

Methods:

We conducted a prospective cross-sectional study including consecutively recruited HD participants (n = 4) and healthy controls (n = 5). Using a custom, monocular retinal imaging-based eye tracker, we collected data on fixation, saccades, smooth pursuit, and anti-saccades. Primary outcomes included saccade latency, fixation stability, saccadic amplitude, saccadic peak velocity, smooth pursuit gain, and anti-saccade error rate.

Results:

Four participants with HD (two females, two males; mean age 52 ± 17 years) and five controls (all male; mean age 47 ± 18 years) were successfully recruited. Controls consisted of participants' spouses (n = 2) and unrelated individuals (n = 3). The protocol was well-tolerated in participants with premanifest or early HD, while those with advanced disease exhibited substantial difficulty completing some tasks due to chorea. Preliminary inspection of the data suggested trends toward increased saccade latency, reduced fixation stability, decreased saccadic amplitude and peak velocity, impaired smooth pursuit gain, and increased anti-saccade error rates. Full statistical analysis is ongoing.

Conclusions:

This pilot study demonstrates the feasibility of implementing a rapid, retina-based eye-tracking protocol in patients with HD. Early observations suggest this system can capture subtle oculomotor alterations and may provide a more sensitive and efficient assay of HD-related dysfunction than existing methods. Continued recruitment and analysis are underway to determine whether these parameters can differentiate premanifest HD from controls and serve as potential biomarkers for disease monitoring and future interventional trials.

References: None provided.

Keywords: Genetic disease, Ocular motility, Nystagmus, Neuroimaging, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease

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Incidence of Causative Lesions on Neuroimaging in Isolated Sixth Nerve Palsies: a Large Database Study

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Introduction:

The management of isolated sixth nerve (CN VI) palsy is debated, balancing immediate neuroimaging against waiting for spontaneous resolution in three months, particularly in older patients with vasculopathic risk factors. The true incidence of serious underlying pathology remains poorly quantified and is based on small case series. This study leveraged a large electronic health record (EHR) database to determine the real-world diagnostic yield of MRI and identify clinical predictors for causative intracranial lesions.

Methods:

This retrospective epidemiologic study utilized a U.S. federated EHR platform. Patients with isolated CN VI palsy (ICD-10) were identified; patients with a history of other cranial nerve disorders prior to or within six months after were excluded. We focused on patients receiving MRI (CPT code 70533) within one month of diagnosis. Outcomes were new diagnoses of possible etiologies (e.g., stroke, neoplasm, CNS inflammation) by ICD-10 codes within six months post-MRI. Sub-group analysis was performed for age groups (≥ 50 vs < 49).

Results:

Of 25,227 patients with isolated CN VI palsy, 6,294 (age 52.7 $\pm$ 21.9, 51% male) underwent MRI within one month. A new diagnosis of a potential cause was found in 379 (6.2%). The most common etiologies were neoplasm (161 patients), stroke (99), and demyelinating disease (64). When stratified by age, there was no statistically significant difference in overall outcomes (≥ 50 : 5.2% vs < 49 : 4.6%, OR 1.13, $p=0.3$). However, older patients were significantly less likely to have demyelinating disease (0.48% vs 2.43%, OR 0.2, $p<0.0001$) and more likely to have a stroke (2.03% vs 1.22%, OR 1.68, $p=0.02$).

Conclusions:

In this first large data study on MRI yield for isolated CN VI palsy, a minority of patients underwent imaging. The rate of a new, potentially causative and treatable diagnosis was significant (6.2%), consistent with previous studies. Age may be a predictive factor for different etiologies rather than overall risk.

References: 1. Tamhankar MA, Bioussé V, Ying GS, et al. Isolated third, fourth, and sixth cranial nerve palsies from presumed microvascular versus other causes: a prospective study. *Ophthalmology*. 2013;120(11):2264-2269. doi:10.1016/j.ophtha.2013.04.009 2. Murchison AP, Gilbert ME, Savino PJ. Neuroimaging and acute ocular motor mononeuropathies: a prospective study. *Arch Ophthalmol*. 2011;129(3):301-305. doi:10.1001/archophthalmol.2011.25 3. Chou KL, Galetta SL, Liu GT, et al. Acute ocular motor mononeuropathies: prospective study of the roles of neuroimaging and clinical assessment. *J Neurol Sci*. 2004;219(1-2):35-39. doi:10.1016/j.jns.2003.12.003

Keywords: Ocular motility, Neuroimaging

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A Screening Tool For Evaluation of Diplopia

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Introduction:

Diplopia is a common condition that could represent trivial or serious disease. Patients often present initially to clinicians who are not trained to perform an appropriate triage decision or an efficient work-up. In an effort to assist such clinicians, we created a screening tool. It was to be widely available, standardized, and able to be deployed quickly and accurately without advanced training.

Methods:

The screening tool consisted of 8 history-based and 6 examination-based questions, developed from extensive trialing in clinics and at the bedside. In this trial, the tool was administered by ophthalmic technicians who had viewed a 5-minute training video on 61 patients presenting with diplopia to the neuro-ophthalmology clinics at the Kellogg Eye Center, University of Michigan, between 2023 and 2025. The “gold standard diagnosis” was rendered by the attending neuro-ophthalmologists.

Results:

The screening protocol successfully identified whether the 61 cases should be referred emergently, urgently, or non-urgently. It very successfully identified monocular diplopia (3/3, 100%), and somewhat successfully identified the probability of skew deviation (7/10, 70%), 3rd nerve palsies (4/6, 66%), 6th nerve palsies (6/14, 42%, 3 had full ductions), and 4th nerve palsies (3/6, 50%, all with full ductions). It was less successful in identifying comitant misalignments (2/9, 22%), and orbital processes (1/5, 20%). The singleton cases of giant cell arteritis, myasthenia gravis, and internuclear ophthalmoplegia could not be accurately identified. There were 5 cases in which no gold standard diagnosis could be rendered.

Conclusions:

Our screening tool added value in determining appropriate urgency of referral. It was relatively successful in identifying many causes of diplopia and thereby guiding the work-up.

References: None provided.

Keywords: Adult strabismus with a focus on diplopia, Ocular motility, Neuro-opth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Vestibular and Ocular Motor Characteristics in Spinocerebellar Ataxia 6 and Episodic Ataxia type 2 – does the same gene equal the same findings?

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Introduction:

The CACNA1A gene encodes the $\alpha 1A$ subunit of the P/Q-type voltage-gated calcium channel. While loss of function mutations cause EA2, toxic gain of function mutations cause SCA6. We sought to compare vestibular and ocular motor (VOM) findings in these overlapping yet distinct entities.

Methods:

Six patients with EA2 and nine patients with SCA6 were identified retrospectively. All patients had undergone an inter-ictal VOM assessment, including video-oculography (VOG) and video head impulse testing (vHIT).

Results:

The average disease duration was 25.6 ± 12.5 years for EA2 and 19.4 ± 13.1 years for SCA6. EA2 patients had a much earlier disease onset (11.5 ± 9 years old) compared to SCA6 (45.8 ± 16.7 years old). Gaze evoked, rebound and downbeat nystagmus were seen in 100% of the SCA6 patients, compared to six (100%), five (83.3%), and four (66.7%) of EA2 patients respectively. Four SCA6 (44.4%) patients and none of EA2 patients had central positional nystagmus (CPN, apogeotropic nystagmus with supine roll). Smooth pursuit was impaired in all SCA6 patients and four EA2 (66.7%) patients. Skew deviation was found in four SCA6 (44.4%) and none of EA2 patients. Four SCA6 and two EA2 patients had vestibular loss with average gain of 0.77 ± 0.22 and 0.82 ± 0.15 respectively.

Conclusions:

Both SCA6 and EA2 patients had evidence of flocculus/paraflocculus impairment (e.g., GEN, DBN, impaired pursuit and alternating skew). However, CPN was only present in the SCA6 group, suggestive of nodulus/uvula involvement. Periodic alternating nystagmus, another nodulus-localizing finding, was also described in SCA6 only. Reduced vHIT gains probably reflects vestibular nuclei and/or flocculus involvement in both, and may be associated with disease severity. Although the same gene is involved with both disorders, its loss of function (EA2) versus toxic gain of function (SCA6) may influence the regions of the cerebellum most affected, even with comparable disease duration.

References: None provided.

Keywords: Nystagmus, Ocular motility, Ocular manifestations of vestibular disorders, Genetic disease, Vestibular disorders

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Grant Support: None.

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Strabismus in Pediatric Cerebral Palsy: A Real-World Analysis of Incidence and Surgical Intervention across U.S. Institutions

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Introduction:

Cerebral Palsy (CP) is frequently associated with strabismus, however the reported prevalence varies widely from 15% to over 70%. To our knowledge, there are no prior studies exploring this associations using large-scale, real-world data. Our aim is to quantify the prevalence of strabismus in CP and evaluate demographic variation using a national database.

Methods:

This retrospective clinical cohort study used a multicenter data registry. We identified pediatric patients with cerebral palsy using International Classification of Diseases 10th Revision (ICD-10) codes. We excluded patients with hereditary spastic paraplegia. The control group comprised healthy children without ocular or neurological disorders, with documentation of a routine newborn or childhood wellness visit. We determined the incidence of strabismus and primary surgical intervention, using corresponding ICD-10 and current procedural terminology (CPT) codes. We matched both cohorts using propensity score matching (PSM) based on demographics, systemic comorbidities, and pertinent ocular conditions.

Results:

The study group included 56,776 patients, with the mean age being 5 years. There was a non-Hispanic (61.16%), White (54.36%), and male (56.10%) predominance, with 14.05% having epilepsy. After matching, the incidence of cerebral palsy patients with strabismus is 11.47% compared to the control group (0.41%) (Risk ratio: 28.14, 95% CI: 24.60-32.19). The incidence of cerebral palsy patients who underwent primary surgery was 2.20% compared to the control (0.07%) (Risk ratio: 31.03, 95% CI: 22.65-42.5).

Conclusions:

Our results demonstrate that strabismus occurs approximately 30 times more frequently among children with cerebral palsy compared to the general pediatric population. However, surgical correction is undertaken in only a subset of affected patients.

References: None provided.

Keywords: Ocular motility, Pediatric neuro-ophthalmology

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Introduction:

Leber's Hereditary Optic Neuropathy (LHON) is the most common inherited mitochondrial optic neuropathy, characterized by subacute unilateral loss of central vision due to thinning of the retinal nerve fiber layer (RNFL) and death of retinal ganglion cells (RGCs). This study used deep learning to identify vascular changes in LHON-affected compared to normal controls, as well as retinal vessel density and intensity across mutation type, age, and gender.

Methods:

A dataset of 1,084 fundus images (584 LHON, 500 normal) between 2014 and 2025 was analyzed using convolutional neural networks to segment the vessels. Quantitative parameters of vessel intensity, vessel density, and variability were statistically analyzed.

Results:

LHON-affected individuals demonstrated a larger vessel area (mean 47.02 vs. 43.67 px), greater segmentation regions (110,248 vs. 90,896), and increased intensity variability compared to normal controls. m.11778G>A/mt-ND4 had the lowest vessel intensity (mean 139.75), and a weak correlation was observed between vessel brightness and age (Spearman $\rho=0.17$, $p=0.005$), indicating retinal change by age. No significant differences were found in vessel traits by gender.

Conclusions:

Deep learning detected significant LHON-associated vascular remodeling, underscoring mutation-specific differences and potential adaptations with age. The findings emphasize understanding LHON pathophysiology, early detection, and targeted therapies.

References: 1. Watson, E. C., Davis, R. L., Ravishankar, S., et al. (2023). Low disease risk and penetrance in Leber hereditary optic neuropathy. *American journal of human genetics*, 110(1), 166–169. <https://doi.org/10.1016/j.ajhg.2022.11.013> 2. Borrelli, E., Balasubramanian, S., Triolo, G., et al. (2018). Topographic Macular Microvascular Changes and Correlation With Visual Loss in Chronic Leber Hereditary Optic Neuropathy. *American journal of ophthalmology*, 192, 217–228. <https://doi.org/10.1016/j.ajo.2018.05.029> 3. Castillo, L., Berrozpe-Villabona, C., Miserachs-García, S., et al. (2022). Quantitative assessment of macular and circumpapillary retinal vessel density across all stages of Leber hereditary optic neuropathy using swept source optical coherence tomography angiography. *Acta ophthalmologica*, 100(8), e1646–e1656. <https://doi.org/10.1111/aos.15169> 4. Huang KW, Yang YR, Huang ZH, et al. Retinal Vascular Image Segmentation Using Improved UNet Based on Residual Module. *Bioengineering (Basel)*. 2023;10(6):722. Published 2023 Jun 14. doi:10.3390/bioengineering10060722 5. Gegundez-Arias, M. E., Marin-Santos, D., Perez-Borrero, I., et al. (2021). A new deep learning method for blood vessel segmentation in retinal images based on convolutional kernels and modified U-Net model. *Computer methods and programs in biomedicine*, 205, 106081. <https://doi.org/10.1016/j.cmpb.2021.106081> 6. Hoover, A., Kouznetsova, V., & Goldbaum, M. (2000). Locating blood vessels in retinal images by piecewise threshold probing of a matched filter response. *IEEE transactions on medical imaging*, 19(3), 203–210. <https://doi.org/10.1109/42.845178> 7. Zhang, S., Webers, C. A. B., & Berendschot, T. T. J. M. (2024). Computational single fundus image restoration techniques: a review. *Frontiers in ophthalmology*, 4, 1332197. <https://doi.org/10.3389/fopht.2024.1332197> 8. Rossant, F., & Paques, M. (2021). Normalization of series of fundus images to monitor the geographic atrophy growth in dry age-related macular degeneration. *Computer methods and programs in biomedicine*, 208, 106234. <https://doi.org/10.1016/j.cmpb.2021.106234>

Keywords: Optic neuropathy, Neuroimaging, Genetic disease, Retina

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Syphilis Mimicking Papilledema Diagnosed with Non-Mydriatic Ocular Fundus Imaging in the Emergency Department

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Introduction:

Syphilis may present with bilateral anterior optic neuropathy, often with isolated bilateral optic disc edema mimicking papilledema from intracranial hypertension. This often leads to “papilledema workup” in emergency departments (ED) to which such patients are often referred, resulting in delayed or even missed diagnosis since syphilis testing is not systematically performed when papilledema is suspected. We report eight patients referred to our ED for “papilledema” workup who were diagnosed with ocular syphilis because of findings on non-mydriatic ocular fundus photography and optical coherence tomography nerve/macula (NMFP-OCT) performed in the ED.

Methods:

We included all consecutive patients diagnosed with ocular syphilis from our prospective consecutive ED-patient cohort who underwent our institution’s papilledema protocol in our general ED. Clinical findings and usefulness of NMFP-OCT were reviewed.

Results:

From 6/14/2023 to 9/21/2025, 8/318 patients (2.5%) who underwent our papilledema protocol were ultimately diagnosed with ocular syphilis. All had bilateral optic disc edema. Visual acuities ranged from 20/20 to hand motion. 5/8 (63%) patients had outer retinal abnormalities and 7/8 (88%) had vitreous cells, all remotely identified on NMFP-OCT imaging obtained in the ED by ED staff. 6/6 patients with LP performed in the ED had normal CSF-opening pressure; 4/6 (67%) had elevated CSF-nucleated cells [range 7-24]; 3/6 (50%) patients had reactive CSF VDRL. All patients had serologic positive RPR/syphilis IgG-IgM. All patients received 14 days of IV-penicillin G with resolution of disc edema.

Conclusions:

Syphilis may present as seemingly isolated bilateral disc edema in the ED, that may suggest papilledema from intracranial hypertension. Remote interpretation of NMFP-OCT obtained in the ED proved very useful by demonstrating suspicious outer retinal changes and/or vitreous cells, findings that should heighten suspicion for ocular syphilis and trigger confirmatory serologic testing.

References: None provided.

Keywords: Neuro-ophth & infectious disease (eg, AIDS, prion)

Financial Disclosures: Wei-Hsuan Lee; Amy (Mung Yan) Lin; Andrew Pendley; Michael Dattilo; Etienne Benard-Seguin; Matthew Keadey; David Wright; Nancy Newman: Has been a consultant for Chiesi, GenSight, Stoke, Neurophth, and Eli Lilly.; Valérie Biousse: Consultant for Topcon medical

Grant Support: None.

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Handheld Non-Mydriatic Fundus Camera for Bedside Inpatient Ophthalmology and Neurology Consultations

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Introduction:

Bedside ocular funduscopic examination is challenging, both for trainees and staffing attendings who must confirm remote findings. Eyer2 is a handheld non-mydriatic, true-color 45/55-degree field ocular fundus camera, with electronic-health-record compatibility, automated upload of images to the Eyer-Cloud, and artificial intelligence (AI) capabilities. Its reliability when used by non-eye-care providers at bedside is unclear. We assessed the feasibility, usefulness, and generalizability of the Eyer2 and its integrated AI tool for ophthalmology/neuro-ophthalmology/neurology inpatient and emergency department (ED) consultations.

Methods:

We deployed the Eyer2 by trained students/medicine/neurology/ICU/residents/fellows/attendings in varied clinical settings including outpatient clinics, EDs, and inpatient units. Images were acquired in both eyes without pupillary dilation, and automatically uploaded to the Eyer-Cloud, with remote interpretation by ophthalmologists. Image quality was graded as good/adequate/poor. Images were assessed for pathology and AI interpretation accuracy.

Results:

Over 20 weeks, 482 photographs were obtained on 242 patients in the ED (19%), hospital floors (13%), ICU (19%), clinic (43%), elsewhere (5%). 230 images were graded as good (48%), 181 adequate (38%), 71 poor (15%). The most common reason for poor image quality was miosis (68%). 183 images were abnormal (38%), including papilledema (38); diabetic/hypertensive retinopathy (35). The AI tool was activated for 66% of images (AI tool does not activate if poor image quality) with sensitivity 76% and specificity 90% for detecting ocular fundus abnormalities.

Conclusions:

Most Eyer2 fundus photographs provided useful data for remote interpretation, allowing accurate and rapid identification of optic nerve/macula pathology, immediate backup for trainees, and documentation of findings. While image quality varied across user-type and location, the camera generated useful images across multiple different operators and clinical settings. Challenges included a steep learning curve in its use and pupillary miosis, especially in ICUs. The AI interpretation was helpful mostly in good quality photographs by alerting non-ophthalmology-trained providers of potential optic nerve or retinal pathology.

References: 1. Lin MY, Dattilo M, Pendley AM, Yan KY, Keadey MT, Wright DW, Newman NJ, Biousse V. Neuro-ophthalmology consultations in an academic medical center with an emergency department equipped with non-mydriatic fundus imaging. *Ophthalmology*. 2025 Aug 21:S0161-6420(25)00523-8. doi: 10.1016/j.ophtha.2025.08.013. Epub ahead of print. PMID: 40849090. 2. Biousse V, Bruce BB, Newman NJ. Ophthalmoscopy in the 21st century: the 2017 H. Houston Merritt lecture. *Neurology*. (2018) 90:167–75. doi: 10.1212/WNL.0000000000004868 3. Melo GB, Nakayama LF, Cardoso VS, Dos Santos LA, Malerbi FK. Synchronous diagnosis of diabetic retinopathy by a handheld retinal camera, artificial intelligence, and simultaneous specialist confirmation. *Ophthalmol Retina*. 2024;8(11):1083-1092. doi:10.1016/j.oret.2024.05.009

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), High intracranial pressure/headache, Optic neuropathy, Retina

Financial Disclosures: Daniel Adamkiewicz; Lennox Xu; Kevin Yan; Michel Shahid; Dami Taiwo; Stuart Duffield; Mung Yan Lin; Nashwa Abdelhafiz; Madhuri Akella; Pooja Parthatharati; Owen Samuels; Julien Cavanagh; Olivia Groover; Spencer Hutto; Nancy Newman: Has been a consultant for Chiesi, GenSight, Stoke, Neurophth, and Eli Lilly.; Valérie Biousse: Consultant for Topcon medical

Grant Support: None.

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Fundus Photography for Differentiating Ocular Tilt Reaction from Trochlear Nerve Palsy

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Introduction:

Ocular tilt reaction (OTR) and trochlear nerve palsy (TNP) can induce cyclotorsion. This study aimed to assess the utility of fundus photography in distinguishing between these disorders in neurological cases.

Description of Cases:

The database of a neuro-ophthalmology hospital-based clinic was retrospectively searched for patients referred for new-onset vertical diplopia in 2020-2023. Data were collected on demographics, medical history, neurological/neuro-ophthalmological assessments, and findings on laboratory studies, neuroimaging, and fundus photography. The angle between the optic disc and fovea was measured using ImageJ software for each eye. The total value of the torsion was calculated. The cohort included 32 patients, 12 males and 20 females, with a mean age of 47 years (5-79 years). Eight were clinically diagnosed with OTR and 24 with non-traumatic TNP, either unilateral or bilateral. Within the OTR group, 6 patients had photo-documented overt intorsion in one eye and extorsion in other; the remainder had similar but undocumented eye movements. All patients with TNP had documented extorsion in one or both eyes. This was calculated in the TNP group as $23.23^\circ \pm 9.8^\circ$ (range: +4.467 to +28.04). The absolute total extorsion value and the sum of deviation of both eyes was identical. The absolute total value of the OTR group was $25.48 \pm 19.47^\circ$ (range: -16.94 to +50.37) and the mean sum was $11.25^\circ \pm 10.55^\circ$. ($p < 0.0001$).

Conclusions, including unique features of the case:

Fundus photography may be useful for differentiating OTR from TNP in complicated neurological cases. Patients in poor neurological condition might be more amenable to undergoing photography than a full eye examination.

:

References: None provided.

Keywords: Ocular motility, Retina, Ocular manifestations of vestibular disorders, Adult strabismus with a focus on diplopia, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Grant Support: None.

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Retinal Mitochondrial Function in Response to Yoga Exercise in Patients with Parkinson's Disease

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Introduction:

To evaluate retinal mitochondrial function in response to a 24-week yoga exercise program in patients with Parkinson's disease (PD).

Methods:

Twenty individuals with clinically diagnosed PD were enrolled; retinal imaging was successfully completed in 17 participants (mean age 72.2 ± 7.2 years; 9 females). Inclusion criteria included: (1) age ≥ 55 years; (2) Montreal Cognitive Assessment (MoCA) > 18 ; (3) Hoehn & Yahr Stage 1–3; (4) ability to ambulate ≥ 50 feet with or without assistance; and (5) ability to get up and down from the floor with minimal help. Retinal mitochondrial function in the macula and optic nerve head was assessed using OcuMet Beacon flavoprotein fluorescence (FPF) imaging. Participants engaged in three 1-hour yoga sessions per week—including YogaCue and Hatha yoga—for 24 consecutive weeks. Changes in FPF between baseline and post-intervention were analyzed using paired t-tests.

Results:

Among 15 patients with analyzable retinal images, mean macular FPF levels showed a mild decrease from baseline (25.90 ± 5.75) to post-intervention (25.44 ± 6.80), though this change was not statistically significant ($P = 0.46$). Similarly, optic nerve head (ONH) FPF decreased slightly from 33.87 ± 6.00 to 33.75 ± 7.67 ($P = 0.89$). Together, these findings indicate a general trend toward improvement in retinal mitochondrial efficiency following 24 weeks of yoga intervention, although the changes did not reach statistical significance.

Conclusions:

This study provides the first evidence of the feasibility of assessing retinal mitochondrial function to evaluate physiological responses to yoga exercise in PD. Although preliminary, the findings highlight the potential of non-invasive ocular imaging as a biomarker platform to monitor exercise-related neuroprotective effects in Parkinson's disease.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Retina

Financial Disclosures: Potyra Rosa; Andrew Hoover; Amanda Virgets; Kylie Joy Martinez; Collin Rich: employee at OcuSciences; Byron Lam: Research support for Stoke Therapeutics; Joseph F Signorile: UM Aging Team Science Award; Jianhua Wang: This study was supported by NIH Center Grant P30 EY014801 NINDS 1R01NS111115 UM Aging Team Science Award; Hong Jiang: Ed and Ethel Moor Alzheimer's Disease Research Program (Florida Health, 20A05)

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Contact Information: None provided.

Prospective AI-based Fundus Image Identification of Neuro-Ophthalmic Disorders in a Tertiary Emergency Department

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Introduction:

Foundation models represent a new generation of self-supervised artificial intelligence (AI) trained on millions of fundus images, capable of learning visual representations of ophthalmic pathologies. We aimed to refine and prospectively evaluate a large-scale pretrained AI model for classification of neuro-ophthalmic disorders in an emergency department (ED).

Methods:

Prospective clinical study enrolling consecutive patients presenting to a tertiary ophthalmology and neurology ED. We built upon RETFound¹, a vision-transformer-based foundation model pretrained on 1.6 million unlabeled fundus images using a self-supervised contrastive learning framework. To reinforce the model for neuro-ophthalmic multi-class classification, we performed supervised fine-tuning on a curated dataset of 6,240 expert-annotated fundus images (4,256 patients) including papilledema (363 images), pseudopapilledema (129 images), arteritic/non-arteritic anterior ischemic optic neuropathies [A/NAION] (44 images), normal retinas (3,401 images), and “other” retinal and optic nerve conditions (2,303 images). Ground-truth diagnosis were independently established by two expert neuro-ophthalmologists through combined assessment of fundus images and clinical data, with adjudication by a senior expert in cases of disagreement. A novel preprocessing pipeline was developed to enhance inter-device consistency, and synthetic minority oversampling was applied to mitigate class imbalance.

Results:

Among the 4,668 included patients presenting for ophthalmic and/or neurological complaints, this interim analysis evaluated the first 2,000 ED patients (1,164 women, 836 men) diagnosed with papilledema (158 images), pseudopapilledema (53 images), A/NAION (33 images), normal retinas (1,070 images), “other” conditions (2,271 images). The model achieved a micro-averaged AUC of 0.97. Class-wise AUCs (95% CI) were: papilledema 0.97 (0.94–0.99), pseudopapilledema 0.98 (0.89–0.99), A/NAION 0.97 (0.92–0.99), normal retinas 0.93 (0.87–0.97) and “other” conditions 0.92 (0.85–0.99).

Conclusions:

A fine-tuned large-scale vision-transformer-based model achieves high accuracy in identifying neuro-ophthalmic disorders from prospectively collected real-world ED fundus images. Extended multi-class evaluation will be performed in this ongoing prospective study.

References: 1. Zhou Y et al. A foundation model for generalizable disease detection from retinal images. *Nature*. 2023;622(7981):156-163.

Keywords: Retina, Optic neuropathy, Vascular disorders, High intracranial pressure/headache

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Virtual Reality Visual Fields Show Changes Consistent with Atrophy on Optical Coherence Tomography

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Introduction:

Humphrey visual fields (HVF) are the gold standard for monitoring visual field defects. Virtual reality (VR) visual fields are an emerging, portable alternative not yet widely utilized in Neuro-Ophthalmology. There are scant studies comparing VR to HVF or other modalities. Optical coherence tomography (OCT) can objectively document optic atrophy. This study aims to assess areas of atrophy on OCT with visual loss documented on HVF and VR to determine VR's validity in optic neuropathy.

Methods:

Ten patients with documented optic neuropathy were evaluated retrospectively using OCT, VR, and HVF data. We compared quadrant-level OCT atrophy with HVF/VR defects to evaluate how closely VR agreed with OCT and HVF. Specifically, quadrants of atrophy on the OCT were compared to quadrants of visual field loss on HVF and VR testing done on the same day.

Results:

In 9 of 10 cases (90%), atrophy in OCT quadrants was also documented as visual loss in the expected pattern on HVF and VR. In one patient, VR showed slightly more visual field loss than HVF and the location of the defect on VR seemed to correlate better with the location of atrophy on OCT. In this patient, OCT showed nasal and temporal atrophy, VR showed a nasal and temporal field defect, while the HVF showed a visual field loss only in the superior nasal quadrant.

Conclusions:

This pilot study indicates that VR visual fields correlate well with HVF defects and OCT atrophy patterns, achieving 90% quadrant-level concordance across modalities. In one individual, there appeared to be a superior alignment between VR and the OCT based on what would be expected on a visual field exam given the location of the atrophy. Although more data is needed to validate these findings, VR appears to have potential as a reliable, portable and comfortable addition to the standard Neuro-Ophthalmology examination.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Optic neuropathy

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Visible-Light OCT as a Novel and Sensitive Tool for Assessing Retinal Changes in Multiple Sclerosis and Neuromyelitis Optica

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Introduction:

Visible-light optical coherence tomography (OCT) is a new device developed by engineers at our center being examined as part of an NIH Common Fund/ NEI effort known as Oculomics. Visible-light OCT offers higher axial resolution than conventional spectral-domain OCT (SD-OCT). This allows for reliable segmentation of individual retinal layers such as the ganglion cell layer (GCL) and inner plexiform layer (IPL), which have been difficult to separate using SD-OCT platforms. This study assessed whether lower GCL thickness and higher GCL–IPL reflectivity ratios from visible-light OCT are associated with worse visual function and SD-OCT structural measures in people with multiple sclerosis (MS) and neuromyelitis optica (NMO).

Methods:

Seven participants (5 MS, 2 NMO, mean age 30.0 ± 12.4 years) underwent visible-light OCT imaging, with GCL thickness and GCL and IPL reflectivity measured in both eyes. Higher GCL–IPL reflectivity ratios indicate a loss of reflectivity distinction or contrast between the two layers. High-contrast visual acuity (HCVA), Sloan 2.5% low-contrast letter acuity (LCLA) and peripapillary RNFL thickness (pRNFLT) on SD-OCT were obtained. Generalized estimating equation (GEE) models were used to examine for statistical associations, accounting for within-subject clustering across eyes and devices.

Results:

Thinner GCL and reduced GCL–IPL reflectivity discrimination, measured by visible-light OCT, corresponded to worse visual performance and lower SD-OCT pRNFLT. GCL thickness correlated with HCVA ($p=0.01$), 2.5% LCLA ($p = 0.010$), and pRNFLT ($p < 0.001$). Similarly, GCL–IPL reflectivity ratio was associated with HCVA ($p < 0.001$), LCLA ($p=0.047$) and pRNFLT ($p < 0.001$). These results suggest neuroaxonal and reflectivity changes within the inner retina are coupled.

Conclusions:

Visible-light OCT metrics of GCL structure and reflectivity demonstrate significant associations with both visual function and axonal integrity in this MS/NMO cohort. Significant findings in this small sample are very promising in supporting visible-light OCT as a sensitive, layer-specific tool for detecting neurodegenerative changes in neuroinflammatory diseases.

References: Tingwei Zhang, Aaron M. Kho, Glenn Yiu, Vivek J. Srinivasan; Visible Light Optical Coherence Tomography (OCT) Quantifies Subcellular Contributions to Outer Retinal Band 4. *Trans. Vis. Sci. Tech.* 2021;10(3):30. <https://doi.org/10.1167/tvst.10.3.30>.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Neuroimaging, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuritis, Optic nerve trauma and treatment

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The First Year of the Multidisciplinary Eye Dystonia Clinic: Demographics, Treatments, and Surgical Outcomes

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Introduction:

Ocular dystonias such as benign essential blepharospasm (BEB), hemifacial spasm (HFS) etc. require multidisciplinary care from both neurology and ophthalmology specialists. Fragmented management can result in a delayed diagnosis, misdiagnosis, or inappropriate treatment. Therefore, we established a multidisciplinary clinic for ocular movement disorders. The purpose of this current study was to present the first-year outcomes of the multidisciplinary ocular dystonia clinic integrating neurology and ophthalmology specialists.

Methods:

Retrospective review of all patients attending the clinic during its first 16 months. Data included demographics, diagnosis, ocular surface parameters at first and last visits, botulinum toxin injections management and surgical procedures. Statistical analysis used paired tests, ANOVA, and Pearson correlation.

Results:

Seventy-six patients (68.4% female, mean age 60.8±11.7 years) were evaluated. Among them: BEB 44.7%, HFS 28.9%, post-facial palsy synkinesis 13.2%, Meige 10.5%, tics 2.6% patients. The most common treatment was botulinum toxin injections. Sixty-six patients (86.84%) reported a mean good response to the injections (score ≥ 8 out of 10). Dosage of botulinum toxin injections increased over time ($p < 0.01$), with BEB receiving the highest among all the ocular dystonia syndromes. A significant negative correlation was found between injection interval and both Schirmer ($r = -0.642$, $p < 0.01$) and TBUT ($r = -0.516$, $p = 0.05$). PEE scores were highest in post-facial palsy synkinesis ($p < 0.01$), while BEB had the lowest Schirmer values ($p < 0.01$). Eyelids surgery was performed in 39.5% of the patients. Surgical rates were highest in Meige (75%) and post-facial palsy (66.7%). Postoperatively, mean botulinum toxin dosage was significantly reduced ($p = 0.02$), as was the mean number of injection sites ($p = 0.049$).

Conclusions:

The first year of our multidisciplinary ocular dystonia clinic demonstrates the feasibility and benefit of integrated care for this complex ocular dystonia patients. High treatment satisfaction, less ocular surface disease, low complication rates and meaningful reductions in toxin requirements after eyelid surgeries highlight the value of combining neurologic and ophthalmology expertise in a single setting. Our findings support the broader adoption of this model to improve the quality, efficiency, and comprehensiveness of care for patients with ocular dystonia.

References: None provided.

Keywords: Orbit/ocular pathology, Orbit/ocular pathology, Tumors, Retina

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Grant Support: None.

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THRIVE-2 Phase 3 Trial of Veligrotug in Chronic Thyroid Eye Disease (TED): Efficacy, Safety, and Quality of Life at 15 Weeks

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Introduction:

TED, a debilitating autoimmune disorder, is often chronic, with long-lasting effects on vision, appearance, and quality of life (QoL). In the phase 3 randomized controlled trial THRIVE-2 in chronic TED (NCT06021054), we evaluated the efficacy and safety of veligrotug, a full antagonist humanized monoclonal antibody targeting IGF-1R. We also assessed disease-specific QoL using the Graves Ophthalmopathy Quality-of-Life (GO-QOL) questionnaire.

Methods:

Adults with moderate-to-severe chronic TED (onset >15 months, proptosis ≥3 mm above normal, and any clinical activity score [CAS]) were randomized to 5 IV infusions Q3W of 10 mg/kg veligrotug or placebo. Efficacy, treatment-emergent adverse events (AEs), and mean change from baseline (CFB) in GO-QOL outcomes (exploratory endpoint) were assessed through Week 15.

Results:

A total of 188 patients received veligrotug (n=125) or placebo (n=63), with mean disease duration of 70 and 82 months. Veligrotug resulted in improvements in TED symptoms as early as 3 weeks, with statistically greater improvements vs placebo at 15 weeks for primary and all secondary outcomes: proptosis responder rate by Hertel (56% vs 8%, $p < 0.0001$), diplopia response (56% vs 25%, $p = 0.0006$), and diplopia resolution (32% vs 14%, $p = 0.0152$). These significant improvements translated into rapid and clinically meaningful improvements in GO-QOL, exceeding the minimal clinically important change threshold (8 points) over baseline at 15 weeks for veligrotug vs placebo. The GO-QOL overall score mean CFB was 12.5 vs 3.2, with 11.0 vs -1.4 for the visual functioning subscale and 13.8 vs 7.7 for the appearance subscale (nominal $p < 0.01$ for all). Most AEs were mild, with one treatment-related serious AE occurring in each group.

Conclusions:

In patients with chronic TED, 5 IV infusions of 10 mg/kg veligrotug were generally well tolerated and led to rapid and statistically significant treatment effect. Veligrotug resulted in clinically meaningful improvement in GO-QOL, with benefits observed in both appearance and visual functioning subscales.

References: None provided.

Keywords: Graves' disease, Orbit, Orbit/ocular pathology, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: John Mandeville: Research investigator for Viridian Therapeutics, Inc.; Kimberly Cockerham: Research investigator, advisory board member, and consultant for Viridian Therapeutics, Inc. and Tourmaline, a research investigator for Immunovant and Argenx, and a former research investigator and advisory board member for Horizon/Amgen, Genentech/Roche, and Lassen.; Jody Abrams: Research investigator for Viridian Therapeutics, Inc.; advisory board member for Viridian Therapeutics, Inc. and Horizon Therapeutics; consultant for Viridian Therapeutics, Inc. and Horizon Therapeutics; speaker for Horizon Therapeutics.; Mohammad Al Khudari: Research investigator for Viridian Therapeutics, Inc.; Steven Leibowitz: Research investigator and advisory board for Viridian Therapeutics, Inc.; research investigator for Lassen Therapeutics, LLC; served on speaker's bureau at Amgen.; Daniel Lemor: Research investigator for Viridian Therapeutics, Inc.; Amy Patel Jain: Research investigator for Viridian Therapeutics, Inc.; research investigator and speaker bureau for Amgen.; Roger E. Turbin: Research investigator for Viridian Therapeutics, Inc., Horizon Therapeutics, and Medtronic; recipient of grants from Viridian Therapeutics, Inc. and Horizon Therapeutics; advisory board member for Viridian Therapeutics Inc., and Horizon Therapeutics; consultant for Viridian Therapeutics, Inc.; Andrea Kossler: Research investigator for Viridian Therapeutics, Inc.; consultant for Viridian Therapeutics, Inc.;

consultant/contracted research Amgen/Horizon Therapeutics; contracted research Sling; research/consultant Lassen Therapeutics LLC; consultant, Immunovant, Genentech, Argenx, Acelyrin.; William Conroy: Employee of Viridian Therapeutics, Inc.; Abhijit Narvekar: Employee of Viridian Therapeutics, Inc.; Rosa Tang: Research investigator for Viridian Therapeutics, Inc. and Horizon Therapeutics; consultant for Viridian Therapeutics, Inc. and Alexion Pharmaceuticals; speaker for EMD Serono.

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Contact Information: None provided.

Depth of Proptosis Response with Veligrotug: Patient-Level Results from the THRIVE Phase 3 Trial in Active Thyroid Eye Disease (TED)

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Introduction:

Veligrotug, an investigational full antagonist monoclonal antibody to IGF-1 receptor, demonstrated rapid, robust improvements across key clinical domains and quality of life in two phase 3 trials for active and chronic TED. We characterize the magnitude of proptosis response observed in the phase 3 THRIVE trial in active TED (NCT05176639).

Methods:

Adults with moderate-to-severe active TED (onset ≤15 months, proptosis ≥3 mm above normal, and clinical activity score [CAS] ≥3) were randomized to receive 5 IV infusions of veligrotug (10 mg/kg) or placebo 3 weeks apart. Proptosis was measured by Hertel exophthalmometry through Week 15.

Results:

Of 113 patients in the intent-to-treat population, 107 (veligrotug n=69; placebo n=38) had both baseline and Week 15 proptosis measurements. At Week 15, 71% of veligrotug-treated patients were proptosis responders (≥2 mm reduction in study eye without a corresponding increase of ≥2 mm in the fellow eye) vs 5% with placebo. None of the veligrotug-treated patients showed an increase in proptosis, while 21% of placebo patients did. Individual patient data (to be presented) showed the magnitude of treatment effect: in veligrotug group, 55% had a reduction ≥3 mm and 23% achieved a reduction ≥4 mm, compared with 3% and 0% for placebo. At Week 15, proptosis reduction (mean ± SD) in veligrotug responders was 3.7 ± 1.4 mm (veligrotug non-responders: 1.1 ± 0.4 mm). Among veligrotug responders, notable improvement was observed as early as Week 3 (mean reduction: 2.4 ± 1.2 mm). Veligrotug was generally well tolerated, with mostly mild adverse events and overall low treatment discontinuation.

Conclusions:

Five infusions of veligrotug (10 mg/kg, Q3W) was generally well tolerated and led to rapid and robust improvements in proptosis. No veligrotug-treated patients had an increase in proptosis, and in the 71% with a proptosis response, the magnitude of reduction (mean 3.7 mm) was substantial.

References: None provided.

Keywords: Graves' disease, Orbit, Orbit/ocular pathology, Neuro-opth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: Jody Abrams: Research investigator for Viridian Therapeutics, Inc.; advisory board member for Viridian Therapeutics, Inc. and Horizon Therapeutics; consultant for Viridian Therapeutics, Inc. and Horizon Therapeutics; speaker for Horizon Therapeutics.; Steven Leibowitz: Research investigator and advisory board for Viridian Therapeutics, Inc.; research investigator for Lassen Therapeutics, LLC; served on speaker's bureau at Amgen.; Raghu Mudumbai: Research investigator for Viridian Therapeutics, Inc., Nicox Ophthalmics, and Stoke Therapeutics.; Kimberly Cockerham: Research investigator, advisory board member, and consultant for Viridian Therapeutics, Inc. and Tourmaline, a research investigator for Immunovant and Argenx, and a former resesearch investigator and advisory board member for Horizon/Amgen, Genentech/Roche, and Lassen.; Roger E. Turbin: Research investigator for Viridian Therapeutics, Inc., Horizon Therapeutics, and Medtronic; recipient of grants from Viridian Therapeutics, Inc. and Horizon Therapeutics; advisory board member for Viridian Therapeutics Inc., and Horizon Therapeutics; consultant for Viridian Therapeutics, Inc.; Navdeep Nijhawan: Research investigator for Viridian Therapeutics, Inc.; Sandy Zhang-Nunes: Research investigator for Viridian Therapeutics, Inc.; research Investigator for Amgen, consultant for Amgen; serves on speakers bureau or advisory boards for Amgen and Tarsus Pharmaceuticals.; Andrea Kossler: Research investigator for Viridian Therapeutics, Inc.;

consultant for Viridian Therapeutics, Inc.; consultant/contracted research Amgen/Horizon Therapeutics; contracted research Sling; research/consultant Lassen Therapeutics LLC; consultant, Immunovant, Genentech, Argenx, Acelyrin.; Ashley Pajak: Employee of Viridian Therapeutics, Inc.; Abhijit Narvekar: Employee of Viridian Therapeutics, Inc.; Michael T. Yen: Research investigator for Viridian Therapeutics, Inc.; consultant/advisor for Ipsen Innovations and Sling Therapeutics.

Grant Support: None.

Contact Information: None provided.

Thyroid-Stimulating Immunoglobulins as a Predictive Biomarker for Thyroid Eye Disease

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Introduction:

Thyroid function tests, including serum TSH, free T3 and T4, and thyroid autoantibodies (TPOAb, TgAb, TBII), are essential for the diagnosis and management of autoimmune thyroid disorders such as Graves' disease and Hashimoto's thyroiditis. However, these parameters often do not correlate with the onset or severity of Thyroid Eye Disease (TED). Thyroid-stimulating immunoglobulins (TSI), a functional subset of TSH receptor antibodies, have emerged as a potential biomarker reflecting disease activity in TED (1,2) response to treatment (3) and chronicity (3). Evidence regarding their clinical utility as a predictive marker remains limited. This study aimed to evaluate the correlation between TSI levels and TED activity and to assess their prognostic value for disease severity and treatment regimens.

Methods:

A retrospective chart review was conducted for all patients presenting to the TED clinic at our medical center between 2017 and 2022 who had at least one TSI measurement. Data collected included demographics, comprehensive ophthalmic examination, Clinical Activity Score (CAS), laboratory values, and quality-of-life scores (GO-QOL). Correlations between TSI and clinical parameters were analyzed using Pearson correlation, and associations with treatment modalities were assessed.

Results:

Sixty patients were included, 43 (72%) of whom were female. Baseline TSI levels significantly correlated with eyelid retraction, intraocular pressure ($r = 0.369$, $P \leq 0.01$), and CAS ($r = 0.392$, $P = 0.029$). TSI > 500% was significantly associated with systemic medical therapy, including high-dose intravenous corticosteroids ($P = 0.05$), treatment per EUGOGO protocol ($P = 0.02$), and radioactive iodine ($P = 0.03$). Elevated TSI was also correlated with surgical interventions including orbital decompression ($P = 0.016$) and strabismus surgery ($P = 0.024$).

Conclusions:

Higher TSI levels at presentation are associated with more severe clinical manifestations and an increased likelihood of medical and surgical treatment in TED. TSI may serve as a predictive biomarker for disease severity and treatment course. Routine TSI testing should be considered in initial evaluation and longitudinal monitoring.

References: 1. Molecular Biomarkers in Thyroid Eye Disease: A literature Review, Ueland HO et al, Ophthalmic Plast Reconstr Surg. 2023 Dec 4; 39(6 Suppl) :S19-28. 2. A novel bioassay for thyroid-stimulating immunoglobulins: Sensitivity and correlation with clinical severity of Graves' orbitopathy. Lytton, S. D. et al. The Journal of Clinical Endocrinology & Metabolism 2010, 95(5); 2123–2131 3. Prognostic factors for thyroid-stimulating immunoglobulin normalization in moderate-to-severe Graves' orbitopathy, Park, J et al, BMC Ophthalmology 2024; 24(1), 274–283.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Graves' disease, Orbit/ocular pathology, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease

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Grant Support: None.

Contact Information: None provided.

Clinical Features in Patients with Thyroid Eye Disease according to the Seropositivity for Anti-Acetylcholine Receptor Antibodies

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Introduction:

To compare the clinical manifestations of thyroid eye disease (TED) according to the seropositivity for anti-acetylcholine receptor (AChR) antibodies

Methods:

Medical records of the patients diagnosed with TED and tested for AChR antibodies were retrospectively reviewed. Patients were classified into seropositive group and seronegative group according to the seropositivity of AChR antibodies. Clinical findings including eyelid abnormalities, strabismus, and extraocular movement were compared between the groups.

Results:

A total of 74 patients (31 male, 41.9%) were included, and mean age was 52.1 ± 16.1 years. Eight patients (10.8%) were allocated in seropositive group and 64 patients in seronegative group. Asymmetric exophthalmos was observed in 18 patients (24.3%). Eyelid abnormalities were found in 65 patients (87.8%), including lid retraction in 21 (28.4%), lid lag in 9 (12.2%), and ptosis in 15 (20.3%). Ptosis was more common in the seropositive group (50.0% vs 16.7%, $P=0.048$). Strabismus was identified in 43 patients (58.1%), most frequently vertical (50.0%), followed by combined vertical and horizontal strabismus (27.5%), exotropia (18.9%), and esotropia (14.9%). Supraduction limitation (51.4%) was the most common extraocular movement limitation. Adduction limitation was significantly more frequent in the seropositive group (57.1% vs 10.9 %, $P=0.009$)

Conclusions:

Ptosis and adduction limitation were more frequent in patients with AChR antibodies positive TED. The presence of these findings may warrant further evaluation for coexisting ocular myasthenia gravis.

References: None provided.

Keywords: Graves' disease

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Orbital Volume Dynamics in Chronic, Low CAS Thyroid Eye Disease (TED): Imaging Evidence of Teprotumumab Treatment Response

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Introduction:

Teprotumumab has demonstrated efficacy in the treatment of active and chronic thyroid eye disease (TED). Extraocular muscle (EOM) and orbital fat (OF) volumes have been shown to normalize toward control levels in active TED following teprotumumab treatment. This study compared orbital volumes in patients with chronic low CAS TED before and after teprotumumab with non-TED orbits.

Methods:

This post hoc analysis included available data from a subset of teprotumumab patients from the Phase 4 trial (NCT04583735) with magnetic resonance imaging (MRI) pre-teprotumumab at baseline (n=16 female [F], 2 male [M] orbits) and/or post-teprotumumab at Wk24 (n=10 F, 4 M orbits). Patients had clinical activity score (CAS) ≤1, TED duration 2-10 years. EOM and OF volumes were measured bilaterally and compared to non-TED controls (100 orbits; 48 M, 52 F) using Welch's t-tests. Due to sex differences, volumes were assessed in F and M+F using sex-matched controls.

Results:

Mean (SD) EOM and OF volumes were larger in M vs F control orbits [EOM, 2774(523) vs 2136(441) mm³, respectively, p<0.001; OF, 11404(2241) vs 9771(1791) mm³, p<0.001]. Mean (SD) EOM and OF volumes of pre-treatment F TED orbits were significantly larger [EOM, 3296(1743) mm³, p=0.018; OF, 15766(3931) mm³, p<0.001] vs F controls. Post-teprotumumab treatment, there were no significant differences in EOM and OF volumes of F TED [EOM, 2470(826) mm³, p=0.24; OF, 9055(1852) mm³, p=0.28] vs controls. In the combined M+F group, mean (SD) OF volumes were significantly larger in pre-treatment TED orbits vs controls [15464(3798) vs 10555(2170), p<0.001]; EOM volumes were also larger [3170(1680) vs 2442(577), p=0.086]. Post-treatment, OF volumes in TED were significantly smaller [9031(1728), p=0.007] while EOM volumes were similar [2261(804), p=0.427] to controls. Sensitivity analysis in 6 patients with both pre-/post-treatment MRI showed similar results.

Conclusions:

This data suggest that increased EOM and OF volumes noted in active TED persist in chronic TED and, despite longstanding disease and low CAS, can be returned to approximately normal non-TED control volumes with teprotumumab treatment.

References: 1. Jain A et al. Br J Ophthalmol. 2022 Feb;106(2):165-171. 2. Douglas RS et al. J Clin Endocrinol Metab. 2023 Dec 21;109(1):25-35. 3. Ross DS et al. Thyroid. 2016 Oct;26(10):1343-1421.

Keywords: Orbit/ocular pathology, Graves' disease, Orbit, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

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Grant Support: None.

Contact Information: None provided.

Clinical Outcomes of Superior Ophthalmic Vein Approach for Closure of Carotid-Cavernous Fistulas

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Introduction:

Carotid cavernous fistulas (CCF) represent the majority of intracranial fistulas, and patients frequently present with ocular symptoms(1,2,3). CCF closure is frequently performed endovascularly via the inferior petrosal sinus (IPS)(4). If the IPS is inaccessible, the superior ophthalmic vein (SOV) can be accessed. The purpose of this study was to identify clinical outcomes, patient characteristics, and complications for open SOV approach for closure of CCF.

Methods:

Retrospective cohort study performed over 2010 to 2025 for all patients who underwent closure of CCF via SOV approach. Outcomes measured included occlusion result, vision, and any sequelae. Preoperative neuroimaging was reviewed, and the SOV diameter was measured on coronal views. Associations of posterior cortical venous drainage (PCVD) with the SOV diameter (≤ 4 mm compared to >4 mm) and stroke were determined using Fisher's exact test with statistical significance at $p < 0.05$.

Results:

A total of 29 patients were identified. Cannulization of the SOV was achieved in 97% of cases, and there was a complete obliteration rate of 87%. The SOV was cannulized with an SOV as small as 3.1 mm and there was no statistically significant association between SOV width and success of cannulization. Five patients (17%) were noted to have PCVD on cerebral arteriography, which correlated with cerebral congestion on preoperative MRI. The most common periocular sequela was upper eyelid ptosis. Final follow-up vision ranged from 20/20 to NLP (median 20/30). Three (10%) patients required canthotomy and cantholysis for orbital compartment syndrome (OCS) following embolization, one intraoperatively and two immediately post-operatively.

Conclusions:

The SOV approach for closure of CCF was effective and relatively safe, achieving an 87% closure rate. Severe iatrogenic visual loss was uncommon. Patients need to be closely monitored immediately postoperatively for OCS. 17% of patients presenting with periocular findings of CCF also demonstrated PCVD on angiography, predisposing them to potential progressive neurologic deficits.

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Keywords: Orbit, Skull base, Neuroimaging, Vascular disorders

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Efficacy of Teprotumumab in Patients with Long Duration and Short Duration Thyroid Eye Disease (TED): Post Hoc Analysis of 4 Randomized Trials and Open-Label Extensions

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Introduction:

Teprotumumab, an insulin-like growth factor-1 receptor inhibitor, significantly improved signs and symptoms of thyroid eye disease (TED) in 4 placebo-controlled trials. Three involved patients with high inflammation, short duration TED and one trial enrolled patients with low activity, long duration TED. We evaluate pooled efficacy data of teprotumumab in patients with TED < 1-yr and ≥1-year disease duration across clinical trials, independent of disease activity.

Methods:

Data from trials in patients with moderate-severe TED were pooled: phase 2 (NCT01868997) and OPTIC (NCT03298867), OPTIC open-label extension (OPTIC-X [NCT03461211]), OPTIC-J (JRCT2031210453), OPTIC-J open-label extension, Phase 4 (NCT04583735), and Phase 4 open-label extension. Patients were to receive eight infusions of teprotumumab or placebo over 21 weeks, with the final study visit at week 24. Observed proptosis response (≥2 mm-improvement), CAS response (≥2-point improvement in patients with baseline CAS≥3), overall response (proptosis and CAS response in patients with baseline CAS≥3) and diplopia response (Gorman scale ≥1-point improvement in patients with baseline diplopia score >0) is reported among teprotumumab-treated patients with TED diagnosis < 1 year or ≥1 year.

Results:

TED duration was mean(SD) 6.5(2.9) months for the < 1-year TED duration group (n=144) and 46.7(29.5) months and for the ≥1-year group (n=81); 88% (127/144) and 84% (68/81) completed treatment, respectively. At week 24, observed proptosis response was 82% (113/137) for shorter TED duration and 72% (54/75) for longer duration; change from baseline was mean(SD) -3.0(1.7) mm (n=137) and -2.6(1.6) mm (n=75), respectively. The observed overall response rate was 80% (98/123) and 71% (12/17), observed diplopia response rate was 66% (69/104) and 57% (17/30), complete resolution of diplopia was observed in 50% (52/104) and 47% (14/30), respectively.

Conclusions:

Patients treated with teprotumumab had clinically meaningful responses regardless of time since TED diagnosis and level of disease activities across all endpoints, although earlier treatment had higher response rates overall.

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Keywords: Graves' disease, Ocular manifestations of vestibular disorders, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Miscellaneous

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Assessing the Burden of Thyroid Eye Disease in US Patients: A Survey-Based Study

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Introduction:

Thyroid eye disease (TED) is an orbital disorder that adversely affects visual function, ocular appearance, and psychosocial health, resulting in substantial impairment of patients' overall quality of life (QoL). We aimed to assess disease burden of TED and its impact on QoL.

Methods:

A cross-sectional online survey of people living with TED in the United States was conducted (05/2025–09/2025). A market research company recruited respondents and validated eligibility. Questions focused on demographics, patient TED details (including severity), and TED-related treatments (including surgical interventions). QoL was assessed using validated patient-reported outcome measures, including Graves' Ophthalmopathy QoL questionnaire (GO-QoL) and National Eye Institute Visual Functioning Questionnaire-Short Form (VFQ-SF).

Results:

Data were collected from 149 respondents with TED, most of whom reported being in an active stage of TED (n=102). Self-perceived disease severity was available for 145 respondents (mild, n=12; moderate, n=77; severe, n=56). Overall, 119 respondents were receiving treatment, most commonly with oral steroids (n=76) or teprotumumab (n=29). The Go-QoL Visual Functioning (VF), Go-QoL Appearance, and VFQ-SF scores (range 0–100; higher = better) generally decreased as disease severity increased; mean scores: mild (73 [VF], 63 [Appearance], 78 [VFQ-SF]), moderate (65, 65, 74), and severe (59, 59, 70). Differences between the severe and moderate subgroups were statistically significant across all measures. The respondent with the lowest GO-QoL VF score (6/100) was in the active TED group. Maximum number of TED symptoms and surgeries received was higher in the moderate (6 symptoms, 6 surgeries) and severe (6 symptoms, 7 surgeries) disease severity groups vs. the mild group (4 symptoms, 3 surgeries). Additional analyses will be explored, examining QoL by treatment type and symptoms experienced.

Conclusions:

These findings provide evidence that lower QoL, based on GO-QoL and VFQ-SF, is associated with increased self-perceived severity. Patients' QoL may be influenced by their symptoms and management required for their disease.

References: None provided.

Keywords: Graves' disease, Ocular motility, Orbit, Orbit/ocular pathology

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Diagnosis Journey, Treatment, and Management of Patients with Ocular Myasthenia Gravis: Insights from a U.S. Patient Panel

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Introduction:

Ocular myasthenia gravis (oMG) is an autoimmune disease characterized by weakness of the extraocular muscles. This study aimed to explore diagnosis, treatment and management of oMG patients.

Methods:

Twenty three U.S. oMG patients, identified via patient groups, participated in 60-minute qualitative telephone interviews conducted with secure screen-sharing (Feb–Mar 2025). Participants provided a healthcare provider clinical note confirming their diagnosis prior to the interview.

Results:

While 57% of patients sought care within one week of symptom onset, time to diagnosis ranged from 1 day to 12 months (mean: 2.4 months). Neurologists most consistently identified oMG, whereas delays were often linked to initial evaluation by ophthalmologists. Patients reported unmet need in faster access to specialists, shorter diagnostic wait times, and greater provider awareness—26% noted insufficient oMG knowledge among non-neurologists. All patients currently used pyridostigmine; 57% used it with corticosteroids (CS). Overall, 82% (19/23) had received CS since diagnosis, with 2 declining due to safety concerns. Among those treated, 37% were on ≥20 mg/day for extended periods, and 47% (9/19) reported side effects. One patient underwent bilateral ptosis surgery. While many reported treatment satisfaction, only 2 achieved full symptom resolution, with symptoms recurring if treatment was missed. Adjuvant strategies included eye patches and prism glasses (70%), activity adjustments, and lifestyle changes. Most (78%) expressed interest in alternative treatments with greater efficacy and fewer side effects.

Conclusions:

Diagnosis of oMG remains delayed due to fragmented care pathways and limited provider familiarity. Patients underscore the need for accelerated diagnosis, more efficacious treatment options with good tolerability, and enhanced awareness to improve oMG care.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Myasthenia, Ocular motility

Financial Disclosures: Jean McGrath Brodeur: JMB is an employee of argenx; Martina Orlovic: MO is an employee of argenx; Rosa Jimenez: RHJ is an employee of argenx; Jeffrey Guptill: JG is an employee of argenx; Yen Wong: YW is an employee of MedPanel and served as a consultant for argenx; Janet Bernard: JB is an employee of MedPanel and served as a consultant for argenx; Pritikanta Paul; Carolina Barnett-Tapia: CB-T as served as an advisory board member for argenx, Alexion, UCB, and Janssen; been a consultant for argenx, Janssen, and UCB; received research support from US Department of Defense, Muscular Dystrophy Canada, MGNet, Grifols, and Octapharma; and is the primary developer of the MGII and may receive royalties.

Grant Support: None.

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Disease Burden, Impact on Daily Functioning, and Psychological Well-being in Patients with Ocular Myasthenia Gravis: Insights from a U.S. Patient Panel

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Introduction:

Ocular myasthenia gravis (oMG) is a rare autoimmune disorder characterized by fluctuating weakness of the extraocular muscles. This study aimed to examine disease burden, impact on daily functioning, and psychological well-being of oMG patients.

Methods:

Twenty three U.S. oMG patients, identified via patient groups, participated in 60-minute qualitative telephone interviews conducted with secure screen-sharing (Feb–Mar 2025). Participants provided a healthcare provider clinical note confirming their diagnosis prior to the interview.

Results:

Among patients aged 29–80, 83% experienced both ptosis and diplopia. Additional symptoms included eye fatigue, blurred vision, and migraines. Persistent symptoms were reported by 65%, and over half experienced ongoing pain, fatigue, and sleep disturbances. oMG significantly impacted patients' ability to work, leading to reduced productivity, financial strain, and employment changes. A total of 91% (n=21/23) reported disruptions in daily activities such as driving and screen use. Among working-age participants (n=16/23), 94% reported impacts on work—particularly in roles requiring prolonged computer use or visual focus. Emotional effects were nearly universal, including frustration, anxiety, and fear of progression to generalized MG. 65% reported reduced self-confidence and social withdrawal, and 58% experienced stigma or misunderstanding. oMG has a moderate to significant impact on mental health for the majority of patients. 41% described strain in family relationships and only 9% had formal caregiving support.

Conclusions:

oMG imposes a substantial burden on patients, affecting physical function, emotional well-being, daily life and ability to work. Persistent symptoms and disturbance of daily activities highlight the need for improved care pathways and expanded treatment options.

References: None provided.

Keywords: Myasthenia, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Ocular motility

Financial Disclosures: Jen Smrtka: JS is an employee of argenx.; Martina Orlovic: MO is an employee of argenx; Rosa Jimenez: RHJ is an employee of argenx; Jeffrey Guptill: JG is an employee of argenx; Yen Wong: YW is an employee of MedPanel and served as a consultant for argenx; Janet Bernard: JB is an employee of MedPanel and served as a consultant for argenx; Pritikanta Paul; Carolina Barnett-Tapia: CB-T as served as an advisory board member for argenx, Alexion, UCB, and Janssen; been a consultant for argenx, Janssen, and UCB; received research support from US Department of Defense, Muscular Dystrophy Canada, MGNet, Grifols, and Octapharma; and is the primary developer of the MGII and may receive royalties.

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An Extended Lateral Orbital Approach for Enhanced Visualization of Neurovascular Structures: Anatomical and Educational Insights

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Introduction:

Cadaveric dissection remains central to anatomy education. Accurate comprehension of orbital neurovascular anatomy is essential for understanding disorders such as orbital apex syndrome, ischemic optic neuropathy, and cranial nerve III, IV, and VI palsies. Orbital anatomy is typically taught through a superior orbital approach. This study introduces a novel extended lateral orbital approach designed to enhance visualization of the deep orbital neurovascular complex and evaluates its educational utility.

Methods:

Seven cadaveric half-heads were dissected using the extended lateral approach, involving removal of the zygomatic bone, lateral orbital rim, and partial resection of the greater wing of the sphenoid. Stereomicroscopic dissection enabled delineation of the ciliary ganglion, ophthalmic artery branches, and cranial nerves III, IV, and VI. A cross-over study compared the extended lateral and traditional superior exposures. 57 medical and optometry students participated in a comparative anatomy workshop and completed pre- and post-session surveys assessing comprehension of orbital relationships.

Results:

The extended lateral exposure provided direct visualization of the ciliary ganglion, nasociliary nerve, and short posterior ciliary arteries extending to the annulus of Zinn—an area often affected in orbital apex pathology. Students reported significantly improved understanding of orbital neurovascular relationships (64.9% preferred the lateral approach; 11% found both approaches complementary).

Conclusions:

The extended lateral orbital approach enhances access to neurovascular structures critical to neuro-ophthalmic disease and surgical training, providing a valuable model for studying the anatomical basis of cranial neuropathies and orbital apex syndromes. Integration of this approach into anatomy and surgical curricula may improve trainees' spatial understanding of the orbit, bridging the gap between anatomical education and neuro-ophthalmologic practice.

References: None provided.

Keywords: Orbit, Skull base, Orbit/ocular pathology

Financial Disclosures: The authors had no disclosures.

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Six-Month Visual Outcomes in Pediatric Optic Neuritis: A Multicenter Prospective Study from South Korea

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Introduction:

While the Optic Neuritis Treatment Trial (ONTT) has greatly advanced our understanding of optic neuritis (ON) in adults, its relevance to pediatric cases is limited due to the focus on adults with unilateral acute ON and lack of antibody profiling. As such, its conclusions and treatment guidelines may not be directly applicable to children. This study aims to address these gaps by evaluating the causes, clinical features, and early treatment outcomes of pediatric ON using antibody testing.

Methods:

The Korea-Pediatric Optic Neuritis Study (K-PONS) is a prospective, nationwide multicenter cohort study conducted from January 2023 to December 2024 across 31 tertiary centers in South Korea specializing in pediatrics and neuro-ophthalmology. Children under 18 years with a first episode of ON in one or both eyes within two weeks of symptom onset were included. Diagnosis followed ONTT criteria and was confirmed with contrast-enhanced orbital MRI. Comprehensive histories, neuro-ophthalmic exams, and serum testing for AQP4-IgG and MOG-IgG antibodies (via cell-based assays) were performed. Patients were followed at 1, 3, and 6 months.

Results:

Forty-four pediatric patients (mean age 10.7±3.5 years) participated. Bilateral ON occurred in 56.8% and optic disc swelling in 81.8%. The average best-corrected visual acuity (BCVA) at enrollment was 0.99±0.89 logMAR, improving to 0.24±0.52 logMAR at 6 months. Diagnoses at 6 months were MOG-associated demyelination (65.9%), isolated ON (25.0%), acute disseminated encephalomyelitis (6.8%), multiple sclerosis (2.3%), and neuromyelitis optica (0%). At follow-up, 50.0% improved their visual category, 50.0% remained stable, and no patients worsened. Poor initial BCVA was the only significant predictor of poor visual outcome at 6 months ($p = 0.026$).

Conclusions:

Pediatric ON often presents with severe acute visual loss but generally shows favorable recovery. MOG antibody-associated disease emerged as the most frequent underlying cause, and poor initial BCVA was linked to poorer long-term vision. These results highlight the unique features of pediatric ON and provide valuable data for developing targeted treatment approaches in this population.

References: None provided.

Keywords: Pediatric neuro-ophthalmology, Demyelinating disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Optic neuritis, Optic neuropathy

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Grant Support: This research was supported and funded by SNUH Lee Kun-hee Child Cancer & Rare Disease Project, Republic of Korea (grant number: 25C-028-0100)

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Clinical Characteristics of Optic Neuritis in a Young Pediatric Cohort, Less than Eight Years Old

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Introduction:

Pediatric optic neuritis is very rare. Thus, the data we have for the younger age group is limited. We postulate that the characteristics of optic neuritis in the younger pediatric population are different than older adolescents.

Methods:

In this ongoing retrospective study, we identified 88 cases of optic neuritis age < 18 since 2010 presenting to a single neuro-ophthalmologist. Analyzed variables were: symptoms, sex, vision, MRI findings, laterality, Myelin Oligodendrocyte Glycoprotein (MOG)/Neuromyelitis Optica (NMO) titer, visual fields, optical coherence tomography (OCT) of the peripapillary retinal nerve fiber layer (RNFL) and ganglion cell layer (GCL) on presentation and final visit. We compared age ≤8y to >8y.

Results:

33 patients were ≤8y and 55 patients were >8y. Comparing age ≤8y to age >8y: MOG positivity was 59% vs. 29%; NMO positivity was 6% vs. 7.3%; bilateral disease was 73% vs. 36%; female gender was 58% vs. 64% respectively. Higher MOG titer predicted worse vision and anatomic outcome. Alternative diagnoses included: Multiple Sclerosis (MS), Clinically Isolated Syndrome (CIS) and Neuroretinitis.

Conclusions:

Younger children with optic neuritis were more likely to be MOG positive and have bilateral disease. Higher MOG titers predicted worse visual outcome. Further analysis is still ongoing.

References: None provided.

Keywords: Pediatric neuro-ophthalmology, Optic neuritis, Demyelinating disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc) Eyelid & adnexal disease

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Grant Support: N/A

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Pediatric Idiopathic Intracranial Hypertension in Hong Kong: A 20-year Study

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Introduction:

Idiopathic intracranial hypertension (IIH) is a relatively common neuro-ophthalmic diagnosis in Caucasians, with a potential to cause severe visual loss. However, it is much less common in East Asians, even after adjusting for the geographical difference in the prevalence of obesity. Previous studies have suggested IIH to be relatively benign with low risk of progression to fulminant disease in Asians. However, visual outcomes in Asian children with IIH have not been well reported given the rarity of the disease in this population. This retrospective review aims to evaluate the clinical characteristics and visual outcomes of Chinese children with primary IIH.

Methods:

Chinese children with primary IIH who attended a tertiary centre in Hong Kong between January 2004 and December 2023 were identified from clinic databases and data were extracted for analysis.

Results:

Five children (age: 4.0-16.8) diagnosed with IIH were identified over a 20-year period. The mean follow-up duration was 6.1 years. All were asymptomatic and had incidental bilateral disc swelling; none were overweight and two were underweight. Body mass index ranged from 14.5 to 22.0. Mean opening pressure on lumbar puncture was 27.0+/-3.8 cmH₂O. The average thickness of retinal nerve fiber layer (RNFL) on optical coherence tomography (OCT) was 137.2+/-14.6 µm at presentation. Two patients were treated with acetazolamide. At final follow-up, all patients had normal or near normal visual acuity (>=6/9), with an average OCT RNFL thickness of 114.7+/-15.7 µm. Only one patient had visual field loss in one eye, not involving the central vision, and none developed optic atrophy. All children were treatment-free at final follow-up with no recurrence of disc swelling or deterioration of optic nerve function.

Conclusions:

Primary IIH is uncommon in Hong Kong Chinese children, with excellent visual outcomes. Most patients can be managed with either observation or acetazolamide alone.

References: None provided.

Keywords: Pediatric neuro-ophthalmology, High intracranial pressure/headache

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Temporal Trends in Optic Pathway Glioma Survival: A Population-Based Analysis

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Introduction:

Optic pathway gliomas (OPGs) are a cause of significant visual morbidity in neuro-ophthalmology. Historically, their critical location limited treatment efficacy. Modern advances include molecular targeted therapies, precision radiotherapy, and improved surgical navigation. This study evaluated whether advances over the past 3 decades have translated into improved overall survival (OS) for patients with OPGs at a population scale.

Methods:

This population-based retrospective cohort study examined 627 patients diagnosed with optic glioma from the Surveillance, Epidemiology, and End Results Dataset, spanning from 1990 to 2021 with follow-up through death or study termination. Cases were grouped by diagnosis period: earlier (1990-2005) and later (2006-2021). Survival was estimated using the Kaplan-Meier method, and differences in survival by diagnosis period were evaluated according to the Log-Rank Test. Analyses were performed in RStudio.

Results:

A total of 627 cases with malignant optic glioma were analyzed. The time period of the study was divided into two and cases' survival was compared across the diagnosis period. The mean age at diagnosis was 13.4 ±17.6). Cohorts were similar in age (14.5±18.5 vs. 12.8±17.0 years) and sex (49% vs. 55% female). Kaplan-Meier overall survival estimates showed relatively high and stable survival patterns across both diagnostic periods. Ten-year overall survival among the earlier and later cohorts remained relatively high, at 90.1% (95% CI: 86.3-94.0%) and 92.7% (95% CI: 89.9-95.5%), respectively. However, the difference in survival between both diagnostic periods was not statistically significant (Log-Rank P=0.22).

Conclusions:

Overall survival among patients with OPGs has remained stable over the past three decades. Though a statistically significant difference in survival was not observed, findings show a temporal survival divergence. This provides insightful population-level evidence that modern treatment advances may slowly but steadily be altering the trajectory of OPG survival.

References: Louis DN, et al. *Acta Neuropathol.* 2021;142(4):1–25. Parsa CF, et al. *Surv Ophthalmol.* 2005;50(6):545–554. Ostrom QT, et al. *Neuro Oncol.* 2022;24(Suppl 5):v1–v95. National Cancer Institute, SEER Program. SEER Research Data, 1990–2021. <https://seer.cancer.gov> Wen PY, et al. *J Clin Oncol.* 2020;38(12):1413–1429.

Keywords: Pediatric neuro-ophthalmology, Tumors, Orbit/ocular pathology

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Grant Support: None.

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Visual Outcomes of Idiopathic Infantile Nystagmus in the Pediatric Population

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Introduction:

Idiopathic Infantile Nystagmus (IIN) develops within the first six months of life and may impair visual development. This study evaluates long-term visual outcomes and ocular findings of children with IIN.

Methods:

A retrospective chart review was conducted for patients diagnosed with IIN at a quaternary academic ophthalmology department between 2010 and 2025. Demographic, clinical presentation, and ophthalmic examination data were collected from electronic medical records. Patients were excluded if diagnosed with a specific etiology of nystagmus.

Results:

72 patients (42 male) with a mean age of 0.44 years (0.23 Standard Deviation [SD]) at presentation were included. The most frequent investigations were magnetic resonance imaging (61%), optical coherence tomography (21%), electroretinography (18%) and genetic testing (18%). Mean follow-up duration was 3.61 years (SD 3.11). At presentation, 23 patients demonstrated Fix and Follow (F&F) vision and 9 had Blink to Light (BTL) vision. The mean BCVA of the remaining 40 patients was 1.01 LogMAR (SD 0.26). At final appointment, 3 patients had F&F vision and 1 had BTL vision. The mean BCVA of the remaining 68 patients was 0.52 LogMAR (SD 0.32). 40 patients with paired data showed a mean improvement of 0.48 LogMAR ($p < 0.001$, paired t-test). A subgroup of 13 patients with ≥ 5 years follow-up demonstrated a mean improvement of 0.77 LogMAR ($p < 0.001$). 35 patients (49%) required refractive correction, 14 (19%) developed amblyopia and 9 (13%) had strabismus surgery for esotropia ($n=5$), exotropia ($n=1$) and null point correction ($n=3$). Abnormal head posture improved from 30 (42%) to 11 (15%), and 22 (31%) patients were referred for low-vision support.

Conclusions:

Idiopathic infantile nystagmus remains a poorly understood condition. A high percentage of patients in this study required intervention for refractive error, amblyopia and strabismus. This highlights the importance of longitudinal follow up to optimize visual function and improve overall outcomes.

References: None provided.

Keywords: Pediatric neuro-ophthalmology, Nystagmus

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Grant Support: None.

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Using peripapillary retinal nerve fiber thickness to differentiate between real and pseudopapilloedema in Chinese children

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Introduction:

Incidental finding of suspected optic disc swelling in children is a common reason for referral to neuro-ophthalmology clinics in East Asia, where childhood myopia is prevalent and myopia can be associated with pseudopapilloedema. This study aimed to determine whether peripapillary retinal nerve fiber layer (pRNFL) thickness measured by optical coherence tomography (OCT) can help distinguish true papilloedema from pseudopapilloedema in Chinese children.

Methods:

This retrospective study included 10 eyes of 5 paediatric patients with papilloedema secondary to idiopathic intracranial hypertension (IIH) or intracranial tumour, and 24 eyes of 12 children with pseudopapilloedema. The mean ages were 14 ± 3 years in the papilloedema group and 12 ± 2 years in the pseudopapilloedema group. pRNFL thickness was measured using Cirrus OCT. Average and sectoral (superior, inferior, nasal, temporal) RNFL thicknesses were compared between groups using unpaired t tests. Receiver Operating Characteristic (ROC) analysis was performed to assess the diagnostic accuracy of average and sectoral pRNFL parameters.

Results:

The papilloedema group showed significantly greater mean pRNFL thickness than the pseudopapilloedema group (146.0 ± 20.7 vs 120.8 ± 19.1 μm), particularly in the inferior (201.3 ± 64.3 vs 147.6 ± 34.2 μm) and nasal (123.6 ± 34.0 vs 113.6 ± 25.7 μm) sectors ($p = 0.002$, 0.004 , and 0.04 , respectively). Differences in the superior and temporal sectors were not significant ($p = 0.18$ and 0.37). ROC analysis showed significant area under the curve (AUC) values of 0.81 and 0.79 for average and inferior pRNFL thickness, respectively ($p = 0.005$ and 0.008). Combining an average pRNFL > 138 μm and inferior pRNFL > 181.5 μm yielded $>95\%$ specificity and 50% sensitivity.

Conclusions:

OCT derived pRNFL measurements provide a non-invasive, accessible method to triage children with suspected optic disc swelling, aiding differentiation between children with true papilloedema who require urgent neuroimaging/ lumbar puncture, and those with pseudopapilloedema who are suitable for less invasive evaluation such as oral fluorescein angiogram.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Pediatric neuro-ophthalmology, Pseudotumor cerebri

Financial Disclosures: The authors had no disclosures.

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Clinical Features and Outcomes of Late-Presenting Craniosynostosis Initially Presenting as Papilledema

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Introduction:

Craniosynostosis, the premature fusion of cranial sutures, may result in elevated intracranial pressure, papilledema, and eventual optic atrophy. Cranial reconstruction is indicated for craniosynostosis-associated, vision-threatening papilledema. Delayed presentation may be associated with late recognition of craniosynostosis and delayed intervention. We studied time to intervention and ophthalmic outcomes in late-presenting cases of craniosynostosis with papilledema at their index evaluation.

Methods:

Retrospective cohort study comprising subjects with single- or multi-suture syndromic and non-syndromic craniosynostosis who presented for their first visit after 2 years of age and who had papilledema. 21 subjects were reviewed, with 15 subjects who met inclusion criteria.

Results:

Mean age at craniosynostosis diagnosis was 4.53 years old without significant difference between syndromic and non-syndromic cases. The only presenting symptom noted in a subset of cases was headache. 40% of non-syndromic cases were initially diagnosed as idiopathic intracranial hypertension. Mean logMAR visual acuity (VA) at presentation was 0.279 (20/38). Frisen grade 3 papilledema or greater was present in 70% of eyes. No cases had a relative afferent pupillary defect. 3 subjects had evidence of abducens palsy (1 unilateral/2 bilateral). The 1 single-suture case did not exhibit optic atrophy; 66.7% of cases of multi-suture cases demonstrated optic atrophy. Mean time to cranial vault expansion surgery for non-syndromic versus syndromic cases was 182 versus 56.8 days, respectively ($p=0.025$). Mean VA at resolution was 0.193 (20/30).

Conclusions:

Craniosynostosis is a rare but treatable cause of secondary papilledema in younger patients. 2- to 7-year-old children may present with high-grade papilledema without visual symptoms and only mild afferent/efferent dysfunction. The risk of optic atrophy is greatest with multi-suture synostosis. Recognition of the stigmata of craniosynostosis and appropriate treatment can preserve afferent visual function.

References: None provided.

Keywords: High intracranial pressure/headache, Optic neuropathy, Pediatric neuro-ophthalmology, Pseudotumor cerebri

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Evaluating Visual Motor Integration In Children With Optic Neuritis

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Introduction:

In pediatric patients, optic neuritis (ON) can be idiopathic or the first manifestation of demyelinating disorders including MOG antibody associated disease (MOGAD), multiple sclerosis (MS), and neuromyelitis optica spectrum disorder (NMOSD) (1). Previous studies suggest that visual acuity (VA) markedly improves with standardized ON treatment over time (2), but the implications of decreased VA and optic nerve atrophy on neurocognitive performance remain unknown. This study sought to assess predictors of neurocognitive performance measured by the visual perception subtest of the Beery Buktenica Visual Motor Integration test, Sixth Edition (VMI-6 VP), in pediatric ON patients.

Methods:

A retrospective chart review from 2017-2023 collected sociodemographic, neurocognitive, neuroophthalmological, and neurologic data in patients between 5-19 years old. Atrophy scores of retinal nerve fiber layer (RNFL) imaging were calculated using proportion of difference in RNFL thickness from acute hospitalization to three-month post-hospitalization. Logistic regression analysis examined contribution of sex, number of days from symptom onset to steroid treatment, and RNFL atrophy data to predict performance on the VMI-6 VP subtest.

Results:

Data for 22 pediatric patients (15 females, 7 males, mean age 12.52 years (SD=3.97)) were collected. MOGAD, MS, and idiopathic ON were the most common diagnoses. Eleven individuals were diagnosed with bilateral ON and ten individuals with unilateral ON (60% right ON). Mean days to steroid treatment was 12.36 days (SD=19.12) but varied widely, particularly for individuals with left ON. Results of linear regression document a significant overall model [$F(3,5) = 7.71, p=0.025$], accounting for 82.2% of the variance in VMI-6 VP performance. Greater right-sided atrophy was associated with a statistically significant decrease in VMI-6 VP performance.

Conclusions:

RNFL atrophy may be a sensitive predictor of neurocognitive testing of visual perception skills in this small sample. Further research using a larger sample size is recommended to evaluate consistency of findings.

References: 1. Yeh, E. A., Graves, J. S., Benson, L. A., Wassmer, E., & Waldman, A. (2016). Pediatric optic neuritis. *Neurology*, 87(9 Suppl 2), S53–S58. <https://doi.org/10.1212/WNL.0000000000002822> 2. Pineles, S. L., Henderson, R. J., Repka, M. X., Heidary, G., Liu, G. T., Waldman, A. T., Borchert, M. S., Khanna, S., Graves, J. S., Collinge, J. E., Conley, J. A., Davis, P. L., Kraker, R. T., Cotter, S. A., Holmes, J. M., & Pediatric Eye Disease Investigator Group (2022). The Pediatric Optic Neuritis Prospective Outcomes Study: Two-Year Results. *Ophthalmology*, 129(8), 856–864. <https://doi.org/10.1016/j.ophtha.2022.03.021>

Keywords: Pediatric neuro-ophthalmology, Optic neuritis, Visual fields

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Utilizing Inter-Eye RNFL Thickness Difference via OCT for Detecting Remote Optic Neuritis In Pediatric-Onset Multiple Sclerosis: Validation of a 4 μ m Threshold

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Introduction:

Pediatric-onset multiple sclerosis (POMS) accounts for up to 10% of MS cases and frequently presents with optic neuritis (ON). Optical coherence tomography (OCT) enables rapid, noninvasive detection of retinal nerve fiber layer (RNFL) thinning, a marker of optic nerve injury. Adult MS criteria use a 5 μ m inter-eye RNFL difference (IOD) to indicate prior ON, but pediatric patients have greater baseline symmetry, suggesting that a lower threshold may improve diagnostic sensitivity. This study evaluated a 4 μ m IOD cutoff and examined its relationship with volumetric MRI measures of brain atrophy.

Methods:

A cross-sectional case-control study included 20 POMS patients with unilateral ON and 20 age-matched controls. Participants underwent spectral-domain OCT and volumetric brain MRI. Global RNFL thickness, inter-eye RNFL difference, and MRI-derived whole-brain, gray matter, and cerebellar volumes were compared using nonparametric tests, ROC analysis, and correlation modeling.

Results:

ON-affected eyes showed significant RNFL thinning versus controls ($82.9 \pm 21.7 \mu\text{m}$ vs. $99.8 \pm 9.8 \mu\text{m}$, $p = 0.0024$). The median inter-eye RNFL difference was greater in POMS (8.5 μm) than controls (2.5 μm , $p = 0.0024$), with 4 μm identified as the optimal discrimination threshold (AUC = 0.78). RNFL asymmetry correlated with inter-eye visual acuity difference ($r = 0.41$, $p = 0.008$) and inversely with lower gray matter and cerebellar volumes ($p < 0.05$), suggesting that retinal injury parallels broader neuro-axonal loss.

Conclusions:

Inter-eye RNFL difference is a sensitive marker of optic nerve injury in POMS. A 4 μm threshold improves detection of prior ON compared with adult criteria and correlates with broader neurodegenerative changes on MRI. Integrating OCT with volumetric MRI may provide a multimodal approach for early MS diagnosis, allowing clinicians to detect subclinical disease, initiate therapy earlier, and monitor neuroprotective outcomes. Establishing pediatric-specific imaging criteria could ultimately enhance individualized care and improve long-term neurological prognosis in this population.

References: None provided.

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Pediatric neuro-ophthalmology, Demyelinating disease, Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc)yEyelid & adnexal disease, Optic neuritis

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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An International Questionnaire on Management of Amblyopia

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¹ Cooper Medical School, ² University of Leicester School, ³ Karolinska Institutet, ⁴ University College London Medical School, ⁵ General University Hospital of Larissa, ⁶ St. Erik Eye Hospital, ⁷ Cooper University Hospital, ⁸ Ulverscroft Eye Unit, ⁹ Lady Hardinge Medical College, ¹⁰ Karolinska University Hospital

Introduction:

Effectively managing amblyopia during the critical period of visual development is vital. Patching is the golden standard, but worldwide management varies. A questionnaire was conducted to assess international success rates for management of amblyopia.

Methods:

A Qualtrics-based questionnaire presented respondents with case scenarios varying by age (4 or 7 years), amblyopia type (anisometropic, strabismic/mixed), and severity (mild or severe), resulting in 8 distinct scenarios. Respondents indicated treatment modality, starting with glasses, then choosing between patching, atropine, dichoptic therapy, or others. Hours per day of patching, length of glasses wear in weeks, and length of treatment were recorded. Inter-nation differences were quantified. Predicted success rate for each scenario was recorded, as measured by a difference of less than two lines between each eye.

Results:

We compiled 242 responses from ophthalmologists, optometrists, and orthoptists across 42 countries. Success rates for anisometropic amblyopes were: mild 4-year olds (83.3% mean, 16.0% SD), mild 7-year olds (65.8% mean, 21.7% SD), severe 4-year olds (61.0% mean, 24.7% SD), and severe 7-year olds (42.8% mean, 24.3% SD). Success rates for strabismic/mixed amblyopes were: mild 4-year olds (68.7% mean, 21.1% SD), mild 7-year olds (53.1% mean, 23.6% SD), severe 4-year olds (55.8% mean, 25.7% SD), and severe 7-year olds (38.6% mean, 24.8% SD). Older, more severe, and strabismic/mixed amblyopes were prescribed higher patching doses and were less likely to use glasses. Glasses and prescribed patching dose per day differed internationally. 84.4% overall used glasses. Next most-used treatments after glasses were patching (90.8%), others (5.1%), and atropine (4.2%).

Conclusions:

Our research highlights differences in management worldwide, and the value of early intervention as evidenced by decreasing success rates with age.

References: None provided.

Keywords: Pediatric neuro-ophthalmology, Higher visual functions, Miscellaneous

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

Contact Information: None provided.

Recovery of the Pupillary Light Reflex in Diabetic Retinopathy Assessed by Automatic Pupillometry

Fabienne Fierz¹, Marat Shamshiev¹, Dominik Bruegger², Mathias Abegg²

¹ University Hospital Zurich, ² machineMD

Introduction:

Diabetic retinopathy (DR) leads to loss of vascular supply in both the inner and the outer retina, which leads to relative ischemia. Dark adaptation requires high retinal oxygen consumption and is impaired in DR. The pupillary light response (PLR) depends on retinal dark adaptation and may serve as a functional biomarker of retinal ischemia. We hypothesize that the recovery of the PLR after dark adaptation, measured by a virtual reality headset with integrated pupillometry, is delayed in patients with DR compared to healthy controls.

Methods:

We conducted a multi-center, non-interventional pilot study evaluating the recovery of the PLR in patients with DR compared to healthy controls and patients with retinitis pigmentosa (RP) serving as a positive control. Each participant underwent a single 20-minute examination using the PRET™ VR headset (machineMD AG, Bern, Switzerland) delivering alternating bright and dark visual stimuli (dark stimulus duration increased by 100ms/cycle across 50 cycles, followed by 10 cycles for internal validation) while recording pupil size.

Results:

10 patients with DR, 7 patients with RP, and 11 healthy participants were included in the preliminary analysis. Across all three cohorts, PLR amplitude increased with prolonged dark adaptation across 50 cycles. Maximal PLR amplitudes were largest in healthy controls, followed by the RP and DR groups.

Conclusions:

Our study demonstrates that the recovery of PLR during dark adaptation can be measured using automated pupillometry with a VR headset. PLR amplitudes were smallest in patients with DR compared to RP and healthy controls, likely reflecting the oxygen deprivation in DR. Thus, measuring the PLR recovery might serve as a potential tool to screen for diabetic retinopathy requiring treatment.

References: None provided.

Keywords: Diagnostic tests (ERG, VER, OCT, HRT, mfERG, etc), Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Pupil

Financial Disclosures: Fabienne Fierz; Marat Shamshiev; Dominik Bruegger: DB is employed by machineMD and owns shares and stock options in the company; Mathias Abegg: MA is employed by machineMD and owns shares and stock options in the company

Grant Support: None.

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Scientific Platform Session II Monday, March 23rd [2.00 CME]

Moderators: Jeffrey L. Bennett, MD, PhD & Y. Joyce Liao, MD, PhD

- 8:00 am – 8:12 am **Risk of Sequential Non-Arteritic Anterior Ischemic Optic Neuropathy**
Madhura Shah, MD
- 8:12 am – 8:24 am **Partial Epigenetic Reprogramming; Preclinical Profile of ER-100 in a Nonhuman Primate Model of NAION**, *Sharon Rosenzweig-Lipson, PhD*
- 8:24 am – 8:36 am **Topical 15-PGDH inhibitor restores visual function after NAION via dampening of ferroptosis and preservation of mitochondrial function**, *Yaping Joyce Liao, MD, PhD*
- 8:36 am – 8:48 am **Intravenous Pulse Methylprednisolone (IVMP) in management of Ethambutol-induced optic neuropathy (EtON)**, *Vivek Lal, MD*
- 8:48 am – 9:00 am **Improved Low-Contrast Visual Acuity and Reduction in Retinal Ganglion Cell Loss with Privosegtor in Acute Optic Neuritis: Results from a Multicenter, Randomized, Placebo-Controlled, Double-Masked Trial**, *Martin S. Zinkernagel, MD, PhD*
- 9:00 am – 9:12 am **Primary Results of the Phase 3 SatraGO-1 and SatraGO-2 Trials: Efficacy and Safety of Satralizumab in Thyroid Eye Disease**, *Prem S. Subramanian, MD, PhD*
- 9:12 am – 9:24 am **THRIVE Phase 3 Trial of Veligrotug in Active Thyroid Eye Disease (TED): Efficacy, Safety, and Quality of Life at 15 Weeks**, *Madhura Tamhankar, MD*
- 9:24 am – 9:36 am **Strabscan: Interpretable Biometrics-Based Machine Learning for Automated Quantification of Horizontal Manifest Deviations in Pediatric Strabismus**, *Rahul M. Dhodapkar, MD*
- 9:36 am – 9:48 am **Vision In SyndrOmic Neurodevelopmental disorders (VISiON)-15q Study: Eye Tracking to Detect Cerebral/cortical Visual Impairment (CVI) in Children with Dup15q and Angelman Syndrome**, *Melinda Chang, MD*
- 9:48 am – 10:00 am **A Phase 1A Single Ascending Dose Study To Evaluate Safety Of PYC-001; A Peptide-Conjugated Oligonucleotide Designed To Treat OPA1 Mutation-Associated Autosomal Dominant Optic Atrophy**, *Clare L. Fraser, FRANZCO*

Risk of Sequential Non-Arteritic Anterior Ischemic Optic Neuropathy

Madhura Shah¹, Drenushe Krasniqi², J. Tatiana Hathaway³, Tais Estrela⁴, Bardia Abbasi³, Robert Mallery⁵, Dean Cestari⁶, John Gittinger³, Joseph Rizzo³

¹ Weill Cornell, ² Cleveland Clinic, ³ Mass Eye and Ear, ⁴ Mass. Eye and Ear Harvard Medical School, ⁵ Mass General Brigham, Mass Eye and Ear, Harvard Medical School, ⁶ Massachusetts Eye and Ear

Introduction:

Non-arteritic anterior ischemic optic neuropathy (NAION) is an acute optic neuropathy typically presenting as a unilateral event; risk of sequential involvement of the fellow eye has previously been calculated from cohorts of fewer than 400 total patients. This study aimed to estimate the risk of sequential NAION (sNAION) over time in the largest reported cohort of NAION patients.

Methods:

A retrospective chart review identified patients diagnosed with NAION between April 1, 2016, and April 1, 2025 via manual review of charts identified via the broad ICD-10 code for “ischemic optic neuropathy” and text search for “NAION”. Dates of first and second eye involvement were manually extracted via chart review together with comorbid conditions such as age, hypertension, diabetes mellitus, and sleep apnea. Kaplan–Meier survival analysis modeled time to second-eye involvement, with censoring of patients without second eye events (uNAION) at last known follow-up, with mean follow up time of 1.75 years.

Results:

A total of 801 NAION patients were included in the analysis: 133 (16.6%) sNAION and 668 (83.4%) uNAION. The risk of fellow-eye NAION was 5.0% at 1 year, 12.4% at 3 years, 18.7% at 5 years, and 31.3% at 10 years. The corresponding adjusted average annual incidence rates were 5.13%, 4.41%, 4.14%, and 3.75%, respectively. The hazard of a sequential event was greatest within the first year and declined progressively thereafter.

Conclusions:

Our rate of second eye involvement (31.3%) derived from the largest published cohort is the highest reported to date. The risk of sNAION risk is highest in the first year following an initial event, which is therefore a critical period for patient counseling and risk factor modification. Although cumulative risk continues to increase over time, the declining annual incidence suggests decreasing vulnerability with longer follow-up. These findings provide quantitative guidance for prognosis and follow-up strategies after a first NAION episode.

References: None provided.

Abstract Type: Clinical afferent disease

Keywords: Optic neuropathy

Financial Disclosures: Madhura Shah: No; Drenushe Krasniqi: No; J. Tatiana Hathaway: No; Tais Estrela: No; Bardia Abbasi: No; Robert Mallery: No; Dean Cestari: No; John Gittinger: No; Joseph Rizzo: consultant to Life Biosciences

Grant Support: Research to Prevent Blindness Medical Student Grant 2023-24

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Partial Epigenetic Reprogramming; Preclinical Profile of ER-100 in a Nonhuman Primate Model of NAION

Sharon Rosenzweig-Lipson¹, Kasia Broniowska¹, Sadie Crocker¹, Richard Davis¹, Drenushe Krasniqi-Vanmeter², Bruce Ksander², Madhura Shah², Lisa Stanek¹, Michel Wathier¹, Joseph Rizzo³

¹ Life Biosciences, ² Mass Eye and Ear Institute, ³ Mass Eye and Ear

Introduction:

Expression of the transcription factors OCT4, SOX2, and KLF4 (OSK) has been used to reprogram retinal ganglion cells (RGCs) to demonstrate anatomical, physiological and visual efficacy in mouse models of aging, optic nerve crush, and glaucoma (Karg et al., 2023; Lu et al., 2020). Expression of OSK improves vision and visual function, reverses DNA hypermethylation, promotes axon regeneration, and increases RGC survival after optic nerve injury (Karg et al., 2023; Lu et al., 2020). The current studies provide translational evidence of efficacy of ER-100 in a nonhuman primate (NHP) model of NAION and provide support for the advancement of ER-100 to clinical trials in optic neuropathies.

Methods:

NAION was induced using a laser photothrombosis procedure (as per Bernstein et al., 2011) targeted to the optic nerve head. ER-100 was administered intravitreally (IVT) either 28 days before or 1 to 3 days after the laser-induced NAION-like injury. In life assessments included color fundus photography, pattern electroretinogram (pERG), and optical coherence tomography along with histological assessments (immunohistochemistry), retinal architecture, and DNA methylation.

Results:

IVT administration of ER-100 resulted in perifoveal expression of OCT4, SOX2 and KLF4 (10-25% of cells) in the ganglion cell layer. ER-100 reversed NAION-induced epigenetic changes in DNA methylation in an RGC-enriched retinal cell population, improved pERG amplitudes by 2-3 μ V, and mitigated the effects of laser damage on retinal architecture. ER-100 was well tolerated, with only transient, procedure-related and AAV2-associated ocular inflammation that resolved over time, stable intraocular pressure, and no adverse effects on outer retinal function by ffERG.

Conclusions:

Collectively, these findings demonstrate ER-100's ocular target engagement, functional and structural neuroprotection, and favorable safety profile in a clinically relevant NHP model of NAION. Clinical trials evaluating ER-100 in optic neuropathies (open angle glaucoma and NAION) will initiate Q1'2026 as the first ever clinical trials evaluating partial epigenetic reprogramming.

References: Bernstein, S. L., Johnson, M. A. & Miller, N. R. Nonarteritic anterior ischemic optic neuropathy (NAION) and its experimental models. *Progress in Retinal and Eye Research*, 30(3): 167–187., 2011 Karg, M. M., Lu, Y. R., Refaian, N., Cameron, J., Hoffmann, E. et al, Sustained Vision Recovery by OSK Gene Therapy in a Mouse Model of Glaucoma. *Cellular Reprogramming*, 25(6), 288–299, 2023 Lu, Y., Brommer, B., Tian, X., Krishnan, A., Meer, M. et al., Reprogramming to recover youthful epigenetic information and restore vision. *Nature*, 588(7836), 124–129, 2020

Abstract Type: Basic Science, Clinical Trials

Keywords: Optic neuropathy, Neuroimaging, Optic nerve trauma and treatment

Financial Disclosures: Sharon Rosenzweig-Lipson: Employee at Life Biosciences; Kasia Broniowska: employee of Life Biosciences; Sadie Crocker: employee of Life Biosciences; Richard Davis: employee of Life Biosciences; Drenushe Krasniqi-Vanmeter: No; Bruce Ksander: No; Madhura Shah: No; Lisa Stanek: employee at Life Biosciences; Michel Wathier: employee at Life Biosciences; Joseph Rizzo: consultant to Life Biosciences

Grant Support: None.

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Topical 15-PGDH inhibitor restores visual function after NAION via dampening of ferroptosis and preservation of mitochondrial function

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Introduction:

There is no effective treatment for nonarteritic anterior ischemic optic neuropathy (NAION) (1). Inhibition of 15-hydroxyprostaglandin dehydrogenase (15-PGDH), the enzyme that degrades prostaglandins such as prostaglandin E2 (PGE2), leads to decreased inflammation and enhanced regeneration (2-4). We investigated 15-PGDH inhibition as treatment for NAION using a potent inhibitor SW033291 (5).

Methods:

We measured retinal 15-PGDH level in human NAION and in murine photochemical thrombosis model of NAION. We developed a topical formulation of SW033291 and assessed its efficacy on visual function and structure in NAION model.

Results:

Compared with controls, eyes from a NAION patient and murine experimental NAION exhibit marked increase in inner retinal 15-PGDH, leading to the hypothesis that 15-PGDH inhibition may be a novel therapeutic approach for NAION. To overcome the hydrophobicity of a small molecule SW033291 with potent 15-PGDH inhibition and to facilitate future translation, we developed a nano-micellar formulation of SW033291 (SW@NM) for topical delivery to the eye. The optimized particle size and formulation enabled efficient delivery in cultured neurons and in murine retina within 30 minutes. Compared with vehicle-treated NAION eyes, NAION eyes treated with 3-week once per day topical SW@NM exhibited significantly dampened optic disc edema, decreased astrogliosis, decreased retinal 15-PGDH and increased PGE2 levels, and improved retinal mitochondrial function (Seahorse Analyzer). SW@NM treatment after NAION resulted in improved visual function (optokinetic responses, photopic negative responses, pattern electroretinogram) and structure (ganglion cell complex thickness on optical coherence tomography, retinal ganglion cell density, and optic nerve axonal density). Retinal proteomics and Western blotting revealed that mechanistically, treatment led to downregulation of ferroptosis, a cell death mechanism involving lipid peroxidation.

Conclusions:

15-PGDH inhibition preserved retinal and optic nerve structure and improved visual function in experimental NAION by increasing retinal PGE2, enhancing mitochondrial function, and inhibiting ferroptosis. These findings support the use of a topical formulation of SW033291 as treatment of acute NAION.

References: 1. Miller, N. R. and A. C. Arnold. Current concepts in the diagnosis, pathogenesis and management of nonarteritic anterior ischaemic optic neuropathy. *Eye (Lond)* 29(1): 65-79 (2015). 2. D. Liu, L. Wu, R. Breyer, M. P. Mattson, K. Andreasson, Neuroprotection by the PGE2 EP2 receptor in permanent focal cerebral ischemia. *Ann. Neurol.* 57, 758–761 (2005). 3. Y. Zhang, A. Desai, S. Y. Yang, K. B. Bae, M. I. Antczak, S. P. Fink, S. Tiwari, J. E. Willis, N. S. Williams, D. M. Dawson, D. Wald, W.-D. Chen, Z. Wang, L. Kasturi, G. A. Larusch, L. He, F. Cominelli, L. Di Martino, Z. Djuric, G. L. Milne, M. Chance, J. Sanabria, C. Dealwis, D. Mikkola, J. Naidoo, S. Wei, H.-H. Tai, S. L. Gerson, J. M. Ready, B. Posner, J. K. V. Willson, S. D. Markowitz, Inhibition of the prostaglandin-degrading enzyme 15-PGDH potentiates tissue regeneration. *Science* 348, aaa2340 (2015). 4. R. Palla, M. Ravichandran, Y. X. Wang, L. Alexandrova, A. V. Yang, P. Kraft, C. A. Holbrook, C. M. Schürch, A. T. V. Ho, H. M. Blau, Inhibition of prostaglandin-degrading enzyme 15-PGDH rejuvenates aged muscle mass and strength. *Science* 371, eabc8059 (2021). 5. M. I. Antczak, Y. Zhang, C. Wang, J. Doran, J. Naidoo, S. Voruganti, N. S. Williams, S. D. Markowitz, J. M. Ready, Inhibitors of 15-Prostaglandin Dehydrogenase To Potentiate Tissue Repair. *J. Med. Chem.* 60, 3979–4001 (2017).

Abstract Type: Basic Science

Keywords: Optic neuropathy

Financial Disclosures: The authors had no disclosures.

Grant Support: National Eye Institute (P30-026877) and Research to Prevent Blindness, Inc.

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Intravenous Pulse Methylprednisolone (IVMP) in management of Ethambutol-induced optic neuropathy (EtON)

Vivek Lal¹, Aastha Takkar Kapila¹, Karthik Vinay Mahesh¹, Prabhjit Kaur¹, Basavaraj Tigari¹, Paramjeet Singh¹, Selv Kathir¹, Jaspreet Sukhija¹, Shweta Chaurasia¹

¹ PGIMER

Introduction:

Ethambutol-induced optic neuropathy (EtON) is a recognized and potentially devastating adverse effect of ethambutol therapy and may cause irreversible visual loss. Current management relies primarily on discontinuation of ethambutol and supportive supplementation, with unpredictable outcomes. Corticosteroids may mitigate mitochondrial dysfunction and optic nerve inflammation, but robust clinical evidence is lacking. We conducted a randomized controlled trial to evaluate the efficacy and safety of high-dose intravenous methylprednisolone (IVMP) in patients with EtON.

Methods:

This prospective, double-blind, placebo-controlled trial was conducted at a tertiary care center in India between March 2021 and August 2024. The trial was prospectively registered with Clinical Trials Registry of India (CTRI/2021/02/031606). One hundred patients with confirmed EtON were randomized (1:1) using block randomization to receive either IVMP (1 gram/day for 5 days) or placebo, in addition to standard of care. The primary outcome was more than 2-line improvement in best-corrected visual acuity (BCVA) on Snellen's/ logMAR chart at 6 months. Secondary outcomes included changes in visual field parameters—mean deviation (MD) and visual field index (VFI). Safety outcomes and predictors of poor recovery were also analyzed.

Results:

Of the 100 randomized patients, 99 completed follow-up (49 IVMP, 50 placebo). At 6 months, 73.5% patients in the IVMP arm achieved a favorable primary outcome compared with 46.0% in the placebo arm [RR (95% CI): 1.59 (1.14–2.22); $p=0.005$]. Visual field parameters also improved significantly in the IVMP group (MD -9.03 vs -13.55 ; $p=0.009$; VFI 34.72 vs 23.95 ; $p=0.012$). No serious adverse events were occurred. On multivariate analysis, IVMP was the only independent predictor of visual recovery, unaffected by age, sex, comorbidities, ethambutol dose, or delay in presentation.

Conclusions:

Short-term high-dose IVMP significantly improves visual outcomes in EtON with a favorable safety profile and low cost, rendering it a practical and widely accessible therapeutic option. This is the first randomized evidence supporting corticosteroids as a therapeutic option for EtON. External validation in large, multicentre studies is warranted to consolidate these findings.

References: None provided.

Abstract Type: Clinical Trials

Keywords: Neuro-ophth & infectious disease (eg, AIDS, prion), Optic neuritis, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: The authors had no disclosures.

Grant Support: None.

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Improved Low-Contrast Visual Acuity and Reduction in Retinal Ganglion Cell Loss with Privosegtor in Acute Optic Neuritis: Results from a Multicenter, Randomized, Placebo-Controlled, Double-Masked Trial

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¹ Department of Ophthalmology, ² Inselspital, University of Bern, ³ APHP Pitié-Salpêtrière and Sorbonne University, Paris Brain Institute, CIC Neurosciences, ⁴ Foundation A. de Rothschild Hospital, ⁵ CRCSEP Neurologie Pasteur 2, CHU de Nice, Université Côte d'Azur, UMR2CA (URRIS), ⁶ Hospices Civils de Lyon, Lyon 1 University, CRNL, ⁷ New York Eye and Ear Infirmary of Mount Sinai, ⁸ McGill University, ⁹ Health R&D LLC, ¹⁰ Adolphe de Rothschild Foundation Hospital, Paris, France, ¹¹ APHP Pitié-Salpêtrière Hospital and Sorbonne University, ¹² Prexton Therapeutics SA, ¹³ University Hospital Bern, ¹⁴ Hospital del Mar and Pompeu Fabra University

Introduction:

We evaluated the safety and efficacy of privosegtor, a first-in-class peptoid small molecule with potential neuroprotective activity, for individuals with acute optic neuritis (AON).

Methods:

ACUITY (NCT04762017) was a phase 2, multicenter, randomized, double-masked, placebo-controlled study. Adult participants (aquaporin-4 antibody negative) with recent onset of unilateral AON (severe visual loss symptoms within 12 days) were included. Participants received intravenous privosegtor (2 or 3 mg/kg/day) plus intravenous steroid (methylprednisolone) or placebo plus steroid for 5 days. The primary endpoint was safety at Month 6. We measured efficacy, for function with low-contrast visual acuity (LCVA) testing, and for structure with measurement of ganglion cell-inner plexiform layer (GCIPL) and retinal nerve fiber layer (RNFL) thickness. Analyses used mixed model for repeated measures on least-squares (LS) mean change from baseline with SE and 90% CI (nominal p-values).

Results:

Thirty-three participants were randomized (n=36 screened) to receive 2 mg/kg/day privosegtor (n=4), 3 mg/kg/day privosegtor (n=15), or placebo (n=14). Adjusted mean $\pm$ SE LCVA scores improved with 3 mg/kg/day privosegtor versus placebo by 18.2 $\pm$ 5.7 letters (90% CI: 8.4, 27.9) at Month 3 (P=0.004) and 14.8 $\pm$ 5.5 letters (90% CI: 5.4, 24.1) at Month 6 (P=0.012). Thinning in LS mean $\pm$ SE was lower with 3 mg/kg/day privosegtor vs placebo at Month 6 for GCIPL (−12.1 $\pm$ 3.7 μ M [90% CI: −18.3, −5.8] vs −21.1 $\pm$ 4.0 μ M [90% CI: −27.9, −14.3]) and RNFL (−30.2 $\pm$ 4.5 μ M [90% CI: −38.0, −22.5] vs −42.9 $\pm$ 4.7 μ M [90% CI: −51.1, −34.7]), a 43% and 30% relative preservation, respectively. The safety profile was comparable between the two groups.

Conclusions:

Privosegtor (3 mg/kg/day) showed significant improvements in visual function and protection from retinal ganglion cell loss (retinal GCIPL structure preservation) in participants with AON. The drug was well-tolerated. Based on the observed neuroprotection, privosegtor may have therapeutic potential for AON and other neuro-ophthalmic disorders.

References: None provided.

Abstract Type: Clinical Trials

Keywords: Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Demyelinating disease, Orbit/ocular pathology, Optic neuritis, Retina

Financial Disclosures: Martin Zinkernagel: Bayer (C), Janssen (C), Oculis (C), Alcon (C), Roche (C), Novartis (C,I), Sandoz (C), Annexon (C), Abbvie (C), Novago (C), Astellas (C), EURETINA (Board of directors), EU EYE (Board of directors); Sebastian Wolf: Sebastian Wolf is consultant for Celltrion Healthcare, Novartis Pharma, Oculis SA, and Priothera SAS.; Céline Louapre: Céline Louapre has received speaker or consultancy fees from Biogen, Sanofi, Novartis, and Merck, not related to the present study, and is consultant for Oculis.; Sophie Bonnin: Sophie Bonnin is a consultant for Oculis SA.; Louise-Laure Mariani: Louise-Laure Mariani received research support grants from the CNES, INSERM, JNLF, The L'Oreal Foundation, the French Parkinson Association, Fondation of France, Paris Brain Institute, and the Axa Foundation; received honorarium for scientific advice or lectures for Digital Medical Hub, Elivie, Sanofi-

Genzyme, Accure Therapeutics, Owkin, Emeis, and the Paris Brain Institute; and received travel funding from the Movement Disorders Society, ANAIF, Merck, Merz, Medtronic, Teva, and AbbVie, outside of the submitted work.; Mikael Cohen: No; Caroline Froment Tilikete: No; Mark Kupersmith: Mark Kupersmith is consultant to Oculis SA.; Leonard Levin: Leonard A. Levin has served as a consultant to Annexon, Dompe, Eyeveusys, Genentech, Janssen Pharmaceuticals, Neuroptika, Oculis, Perfuse, Perceive, Prilenia, Roche, Santen, and UNITY.; Sabri Markabi: Sabri Markabi is consultant to Oculis SA.; Caroline Papeix: Caroline Papeix has been an advisory board member or conference speaker for Roche, Biogen, Novartis, Amgen, and Alexion.; Valérie Touitou: No; Rossella Medori: No; Marion Munk: No; Pablo Villoslada: Pablo Villoslada holds several patents covering prion protein composition of matter and its use for the treatment of CNS and ophthalmological diseases. He holds stocks or stock options and has received consultancy fees from Oculis SA, Bionure Therapeutics, and Accure Therapeutics as part of the development of this program.

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Primary Results of the Phase 3 SatraGO-1 and SatraGO-2 Trials: Efficacy and Safety of Satralizumab in Thyroid Eye Disease

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Introduction:

Thyroid eye disease (TED) is a complex orbital inflammatory disease that can lead to significant morbidity, including facial disfigurement, reduced quality of life, and sight-threatening complications. Interleukin-6 (IL-6) and its receptor (IL-6R) play a key role in the pathogenesis of TED. Satralizumab, a humanized monoclonal antibody that targets IL-6R, was designed using innovative antibody recycling technology, which allows for longer duration of circulation and subcutaneous dosing. Here, we present Week (W)24 results from the phase 3 SatraGO-1/2 trials.

Methods:

SatraGO-1 (NCT05987423) and SatraGO-2 (NCT06106828) are identical, global, phase 3 trials evaluating the efficacy and safety of satralizumab in patients with moderate-to-severe active TED or chronic inactive TED. Participants were randomized 1:1 to receive subcutaneous satralizumab or placebo at W0, W2, and W4 and then Q4W through W20. The primary endpoint was the proportion of participants with active TED who achieved a proptosis response (≥ 2 -mm reduction in proptosis from baseline in the study eye) at W24.

Results:

The proportion of participants with active TED with a proptosis response was higher for satralizumab (SatraGO-1/2; 49/53%) vs placebo (31/23%; $P=0.0715/0.0011$). The proportion of participants with active TED with diplopia reduction (≥ 1 -grade reduction) was higher for satralizumab (SatraGO-1/2; 44/61%) vs placebo (34/26%; $P=0.3371/0.0044$). The proportion of participants with active TED with Clinical Activity Score (CAS) reduction (≥ 2 -point reduction) was higher for satralizumab (SatraGO-1/2; 78/90%) vs placebo (55/63%; $P=0.0120/0.0009$). Clinical benefits were also observed in the overall (active + inactive) TED population. Overall, the incidence of serious adverse events and treatment discontinuations was low and there were no serious infections.

Conclusions:

Satralizumab showed clinically meaningful improvements across key efficacy endpoints, including proptosis, diplopia, and CAS, and had a favorable safety profile in patients with TED. Satralizumab is the first IL-6R inhibitor with convenient subcutaneous dosing demonstrating efficacy for both active and inactive TED.

References: None provided.

Abstract Type: Clinical Trials

Keywords: Graves' disease, Neuro-ophth & systemic disease (eg. MS, MG, thyroid), Orbit/ocular pathology

Financial Disclosures: Prem Subramanian: Consultant: Amgen, Alumis, Roche/Genentech, Kriya, Tourmaline Bio, Viridian, Research Support: Amgen, Immunovant, Tourmaline Bio, Viridian.; César Briceño: Consultant: Amgen, Argenyx, Roche/Genentech, Regeneron. Research Support: Amgen, Argenyx, Roche/Genentech, Viridian; Oluwatobi Idowu: Employment and Stocks or Stock Options: Genentech, Inc.; Laura Brockwell: Employment and Stocks or Stock Options: Roche Products Ltd.; Thorsten Ruf: Employment and

Stocks or Stock Options: F. Hoffmann-La Roche AG.; Thomas Kuenzel: Employment and Stocks or Stock Options: F. Hoffmann-La Roche Ltd.; Christopher Brittain: Employment and Stocks or Stock Options: Genentech, Inc.; Giulio Barteselli: Employment and Stocks or Stock Options: Genentech, Inc; Santiago Ortiz-Perez: Consultant: Amgen, Roche/Genentech, Inc., Thea Lab.

Grant Support: The SatraGO-1 and SatraGO-2 trials are funded by F. Hoffmann-La Roche Ltd.

Contact Information: None provided.

THRIVE Phase 3 Trial of Veligrotug in Active Thyroid Eye Disease (TED): Efficacy, Safety, and Quality of Life at 15 Weeks

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Introduction:

TED is a debilitating autoimmune disorder that not only impairs visual function but also impacts patients' daily activities and well-being. Veligrotug is a full antagonist humanized monoclonal antibody to IGF-1 receptor being evaluated in TED. Here, we assessed the efficacy, safety, and Graves Ophthalmopathy Quality of Life (GO-QOL) outcomes from the phase 3 THRIVE randomized controlled trial of veligrotug in active TED (NCT05176639).

Methods:

Adults with moderate-to-severe active TED (onset ≤ 15 months, proptosis ≥ 3 mm above normal, and clinical activity score [CAS] ≥ 3) were randomized to 5 IV infusions Q3W of 10 mg/kg veligrotug or placebo. Efficacy, treatment-emergent adverse events (AEs), and mean change from baseline (CFB) in GO-QOL outcomes (exploratory endpoint) were assessed through Week 15.

Results:

A total of 113 patients received veligrotug (n=75) or placebo (n=38). Veligrotug resulted in improvements in TED symptoms as early as 3 weeks, with statistically greater improvements vs placebo at 15 weeks for primary and all secondary outcomes: proptosis responder rate by Hertel (70% vs 5%), mean CAS reduction (3.4 vs 1.7), diplopia response (63% vs 20%), and diplopia resolution (54% vs 12%) ($p < 0.0001$ for all). These significant improvements translated into rapid and clinically meaningful improvements in GO-QOL, exceeding the minimal clinically important change threshold (8 points) over baseline at 15 weeks for veligrotug vs placebo. The GO-QOL overall score mean CFB was 17.3 vs 2.9, with 16.5 vs 2.3 for the visual functioning subscale and 18.1 vs 3.6 for the appearance subscale (nominal $p < 0.001$ for all). Most AEs were mild and there were no treatment-related serious AEs.

Conclusions:

In patients with active TED, veligrotug was generally well tolerated and led to rapid and statistically significant improvements in proptosis, CAS, and diplopia that translated into clinically meaningful improvement in GO-QOL. A 5-infusion regimen of veligrotug may become a potential treatment option in TED.

References: None provided.

Abstract Type: Clinical Trials

Keywords: Graves' disease, Orbit, Orbit/ocular pathology, Neuro-ophth & systemic disease (eg. MS, MG, thyroid)

Financial Disclosures: Madhura Tamhankar: Advisor: Amgen, Roche, Viridian; Royalty: Chapter in UpToDate; Michael T. Yen: Research investigator for Viridian Therapeutics, Inc.; consultant/advisor for Ipsen Innovations and Sling Therapeutics.; Raghu Mudumbai: Research investigator for Viridian Therapeutics, Inc., Nicox Ophthalmics, and Stoke Therapeutics.; Kimberly Cockerham: Research investigator, advisory board member, and consultant for Viridian Therapeutics, Inc. and Tourmaline, a research investigator for Immunovant and Argenx, and a former research investigator and advisory board member for Horizon/Amgen, Genentech/Roche, and Lassen.; Jody Abrams: Research investigator for Viridian Therapeutics, Inc.; advisory board member for Viridian Therapeutics, Inc. and Horizon Therapeutics; consultant for Viridian Therapeutics, Inc. and Horizon Therapeutics; speaker for Horizon Therapeutics.; Roger E. Turbin: Research investigator for Viridian Therapeutics, Inc., Horizon Therapeutics, and Medtronic; recipient of grants from Viridian Therapeutics, Inc. and Horizon Therapeutics; advisory board member for Viridian Therapeutics Inc., and Horizon Therapeutics; consultant for Viridian Therapeutics, Inc.; Navdeep Nijhawan: Research investigator for Viridian Therapeutics, Inc.; Sandy Zhang-Nunes: Research investigator for Viridian Therapeutics, Inc.; research Investigator for Amgen, consultant for Amgen; serves on speakers bureau or advisory boards for Amgen and Tarsus Pharmaceuticals.; Andrea Kossler:

Research investigator for Viridian Therapeutics, Inc.; consultant for Viridian Therapeutics, Inc.; consultant/contracted research Amgen/Horizon Therapeutics; contracted research Sling; research/consultant Lassen Therapueutics LLC; consultant, Immunovant, Genentech, Argenx, Acelyrin.; Ashley Pajak: Employee of Viridian Therapeutics, Inc.; Abhijit Narvekar: Employee of Viridian Therapeutics, Inc.; Steven Leibowitz: Research investigator and advisory board for Viridian Therapeutics, Inc.; research investigator for Lassen Therapeutics, LLC; served on speaker's bureau at Amgen.

Grant Support: None.

Contact Information: None provided.

StrabScan: interpretable biometrics-based machine learning for automated quantification of horizontal manifest deviations in pediatric strabismus

Rahul Dhodapkar¹, Melinda Chang², Sudha Nallasamy², Talia Kolin²

¹ University of Southern California, ² Children's Hospital Los Angeles

Introduction:

The purpose of this study was to develop an interpretable, easily accessible system for the automated measurement of horizontal strabismus in children.

Methods:

A convolutional neural network-based machine-learning model pretrained on 66,000 images of faces was used to extract facial biometric data from 223 photographs of 43 pediatric patients with a manifest horizontal strabismus. The model was also used to extract facial biometrics data from 597 neutral expression images in the Chicago Faces Database to develop a weighted-barycenter model to predict orthotropic primary gaze position from biometric facial landmarks, creating a head-pose and image-scale invariant model robust to natural human variation in facial anatomy. Finally, the predicted angle of deviation was directly calculated from the spatial difference between predicted orthotropic and neural-network-measured central iris position. A single-parameter linear least-squares regression model was fitted to further refine the predictions. The final predicted deviations were compared with deviations measured by a pediatric ophthalmologist using the alternate cover testing. Finally, to improve access to the predictive algorithm, an iOS mobile application was developed.

Results:

Prior to linear model refinement, the model predictions demonstrated a high degree of correlation with ground truth, with Pearson correlation coefficient $r = 0.870$ (95% CI: 0.834 - 0.898, $p < 0.001$). After averaging of all observations per subject, and further refinement of predictions with a linear model, the Pearson correlation coefficient against the test data segment was $r = 0.958$ (95% CI: 0.842 - 0.989; $p < 0.001$), R-squared was 0.917, and root mean squared error (RMSE) was 9.672 prism diopters. These tools were successfully developed into a smartphone application which can process images at 30 frames per second.

Conclusions:

By expanding access to accurate strabismus measurement with a system that only requires a smartphone, we hope to provide additional tools for strabismus care worldwide.

References: 1. Bazarevsky V, Kartynnik Y, Vakunov A, et al. BlazeFace: Sub-millisecond Neural Face Detection on Mobile GPUs. arXiv. Preprint posted online July 11, 2019. <https://arxiv.org/abs/1907.05047>. 2. Ma DS, Correll J, Wittenbrink B. The Chicago face database: A free stimulus set of faces and norming data. Behav Res Methods. 2015 Dec;47(4):1122-1135. doi: 10.3758/s13428-014-0532-5.

Abstract Type: Clinical efferent disease, Pediatric Neuro-Ophthalmology

Keywords: Ocular motility, Pediatric neuro-ophthalmology, Adult strabismus with a focus on diplopia

Financial Disclosures: Rahul Dhodapkar: No; Melinda Chang: Grant support: NIH/NEI K23EY033790; Sudha Nallasamy: No; Talia Kolin: No

Grant Support: None

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Vision In Syndromic Neurodevelopmental disorders (VISiON)-15q Study: Eye Tracking to Detect Cerebral/cortical Visual Impairment (CVI) in Children with Dup15q and Angelman Syndrome

Melinda Chang¹, Katherine Granger¹, Sydney Jacobs¹, Achenbach Anna¹, Charlotte Distefano¹, Shafali Jeste¹

¹ *Children's Hospital Los Angeles*

Introduction:

Cerebral/cortical visual impairment (CVI) is a leading cause of pediatric visual impairment. In developmentally delayed patients, standard pediatric ophthalmologic examination can identify visual deficits such as decreased acuity, but identification of higher-level visual perceptual deficits is challenging. We previously described a method to detect abnormalities of visual attention in children with CVI (Saliency analysis of Eye Tracking in CVI, SET-CVI). In this study, we apply SET-CVI to children with duplications and deletions of chromosome 15q (Dup15q and Angelman syndrome, respectively).

Methods:

We prospectively recruited children with 15q disorders who underwent a complete ophthalmologic examination and eye tracking. Using SET-CVI, we calculated fixation saliency values (FSVs), which quantify visual attention to 15 lower- and higher-level visual characteristics. Hierarchical clustering was performed on FSVs to identify groups of 15q participants based on eye tracking patterns. These groups were compared to previously recruited age-matched typically developing controls and children with definite CVI, using multivariate regression to correct for age and sex.

Results:

We recruited 25 children with 15q disorders (mean age 5.8±3.1 years). Four children were excluded due to insufficient visual acuity for eye tracking analysis (< 3 cpd). Clustering analysis of FSVs divided participants into two groups with low- and high-suspicion of CVI (15q-CVI-LS [n=12] and 15q-CVI-HS [n=9]). FSVs were significantly different between children in the 15q-CVI-HS group and controls at p< 0.001 on 14 of 15 visual characteristics, but did not differ between children in the 15q-CVI-HS and definite CVI groups on 13 of 15 characteristics. Only three children in the 15q-CVI-HS group were diagnosed clinically with CVI.

Conclusions:

Unsupervised machine learning analysis of eye tracking data may identify children with neurogenetic syndromes who exhibit features of CVI, based on abnormal visual attention to lower- and higher-level visual characteristics. This may facilitate diagnosis of CVI in this challenging population.

References: None provided.

Abstract Type: Pediatric Neuro-Ophthalmology

Keywords: Pediatric neuro-ophthalmology

Financial Disclosures: Melinda Chang: Grant support: NIH/NEI K23EY033790; Katherine Granger: No; Sydney Jacobs: No; Achenbach Anna: No; Charlotte Distefano: No; Shafali Jeste: Grant support: The Saban Research Institute (TSRI) Team Science Award

Grant Support: NIH/NEI K23EY033790 The Saban Research Institute (TSRI) Team Science Award

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A Phase 1A Single Ascending Dose Study To Evaluate Safety Of PYC-001; A Peptide-Conjugated Oligonucleotide Designed To Treat OPA1 Mutation-Associated Autosomal Dominant Optic Atrophy

Clare Fraser¹, Doron Hickey², Aishwarya Kundu³, George Mitchell³, Sri Mudumba³

¹ *Sydney University*, ² *Royal Victorian Eye and Ear*, ³ *PYC Therapeutics*

Introduction:

Autosomal Dominant Optic Atrophy (ADOA) is a blinding eye disease caused by haploinsufficiency of the OPA1 gene in the retinal ganglion cells (RGCs). There are no therapeutic options for patients with OPA1-associated ADOA. PYC-001 is a first in class, disease modifying intravitreally injected investigational RNA therapeutic drug, designed to upregulate OPA1 protein expression, thereby addressing the underlying cause of ADOA. A Phase 1 Single Ascending Dose (SAD) first-in-human study named SUNDEW was initiated to evaluate the safety and tolerability of PYC-001.

Methods:

An open-label, SAD study recruited 9 participants with genetically confirmed OPA1 mutation-associated ADOA in 3 dose cohorts (3, 10 and 30 µg). Each subject received an unilateral intravitreal injection of PYC-001 in the worse affected eye and was followed for incidence, severity and relatedness of adverse events. Dose escalation was based on review by a safety review committee (SRC) using 4-week incremental data collected after each cohort dosing. Safety and tolerability were evaluated based on adverse event (ocular and non-ocular) reporting, including clinical chemistry parameters, measures of visual function, functional vision and imaging. Exploratory efficacy was assessed using visual acuity under normal and low contrast conditions.

Results:

No drug related adverse events, and no intraocular inflammation were observed at any visit following injection of PYC-001. Encouraging early improvements in visual acuity were observed in eyes treated with PYC-001 from week 4 onwards. A greater proportion of PYC-001 treated eyes showed clinically meaningful improvements in low-contrast visual acuity as compared to untreated fellow eyes.

Conclusions:

Single intravitreal injection of PYC-001 is safe and well tolerated at all doses assessed to date. Encouraging early improvements in visual acuity were observed. Repeat dose safety and efficacy of PYC-001 in ADOA patients is now being evaluated in a global study named MYRTLE.

References: None provided.

Abstract Type: Clinical Trials

Keywords: Genetic disease, Optic neuropathy

Financial Disclosures: Clare Fraser: No; Doron Hickey: No; Aishwarya Kundu: Employee of PYC Therapeutics; George Mitchell: Employee of PYC Therapeutics; Sri Mudumba: Employee of PYC Therapeutics

Grant Support: None.

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Jacobson Lecture [0.5 CME]

Valerie Biousse, MD (Introduction by Nancy Newman, MD)

Non-mydriatic ocular imaging has been shown to be useful in emergency departments and neurology clinics where it can replace the rarely used direct ophthalmoscope. Recent advancements in technology have made possible direct connection to patients' electronic medical records and remote interpretation by ophthalmologists and neuro-ophthalmologists of imaging obtained in the emergency department and neurology clinics. This presentation will review the major studies performed over the past decade and propose strategies to increase the deployment of ocular imaging outside of eye clinics.

Upon completion of this session, participants should be able to:

- (1) Review recent advancements in non-mydriatic ocular imaging
- (2) Discuss strategies to implement non-mydriatic ocular imaging in the emergency department and in neurology clinics
- (3) Develop outcome measures to evaluate the impact of non-mydriatic ocular imaging in emergency departments and in neurology clinics

Eyes on the Evidence: What's New in Treating Neuro-Ophthalmic Disease? [1.0 CME]

Moderators: Tatiana Bakaeva, MD, PhD & Marc Bouffard, MD

CRAO Treatments, *Valerie Biousse, MD*

Gene Therapies, *Patrick Yu-Wai Man, MD, PhD*

Idiopathic Intracranial Hypertension, *Susan P. Mollan, MBChB, PhD*

Thyroid Eye Disease, *Michael S. Lee, MD*

Health and Neuro-Ophthalmology, *Natalia S. Rost, MD, MPH, FAAN, President, American Academy of Neurology*

This session highlights the latest updates in the management of central retinal artery occlusion, genetic optic neuropathies, idiopathic intracranial hypertension, and thyroid eye disease. The expert speakers will also explore unanswered questions regarding the treatment of those conditions and the necessary next steps to advance our field, including avenues for collaboration with broader initiatives discussed by American Academy of Neurology president Dr. Natalia Rost.

Upon completion of this session, participants should be able to:

- (1) Identify the strengths and limitations of the current evidence for management of CRAO, IIH, genetic optic neuropathies, and TED.
- (2) Discuss ongoing efforts to optimize approaches to the above conditions and identify current unmet needs which should guide further investigation.
- (3) Describe the AAN Brain Health Initiative and identify opportunities for cross-disciplinary collaboration.

“Eyes on the Evidence: What’s New in Treating Neuro-Ophthalmic Disease?”
Latest news in the management of acute central retinal artery occlusion

Valérie Biousse, MD
Professor of Ophthalmology and Neurology
Reunette Harris Chair of Ophthalmic Research
Emory University School of Medicine, Atlanta GA. USA

LEARNING OBJECTIVES (3 required)

10. The attendees will be able to understand best practices for the diagnosis and management of acute central retinal artery occlusion.
11. The attendees will know the results of recent clinical trials evaluating the acute treatment of central retinal artery occlusion.
12. The attendees will be able to discuss the latest recommendations for the treatment of acute central retinal artery occlusion based on the lack of currently available level 1 evidence.

CME QUESTIONS (3 required)

1. The diagnosis of very acute (within 1-3 hours of vision loss) central retinal artery occlusion is best made with:

- A. Dilated funduscopic examination.
- B. Color fundus photography.
- C. Ocular ultrasound looking for a spot sign.
- D. Optical coherence tomography of the macula.
- E. Optical coherence tomography of the optic nerve.

2. Which of the following is true regarding intravenous thrombolysis for acute central retinal artery occlusion:

- A. Current evidence suggests that it should be administered within 4.5 hours of vision loss to have the best chances of visual recovery.
- B. Both alteplase and tenecteplase may be used.
- C. The protocol is identical to the standard thrombolysis protocol used for cerebral infarctions.
- D. Thrombolysis may be administered by stroke neurologists or emergency department providers when the diagnosis of acute central retinal artery occlusion is confirmed remotely on ocular fundus imaging (photographs or optical coherence tomography) even without an in-person ophthalmology consultation.
- E. All of the above.

3. Which of the following is true regarding the treatment of acute central retinal artery occlusion with thrombolysis:

- A. Thrombolysis is standard of care for acute central retinal artery occlusion (level 1 evidence).
- B. Intravenous thrombolysis may be considered within 4.5 hours of vision loss in selected informed patients.
- C. Intra-arterial thrombolysis is more effective than intravenous thrombolysis in patients with acute central retinal artery occlusion.
- D. The recent results of the European randomized clinical trials suggest that intravenous thrombolysis should not be administered to patients with acute central retinal artery occlusion.
- E. Symptomatic cerebral hemorrhage after intravenous thrombolysis was a major concern in the THEIA study.

KEYWORDS (5 Max)

16. Central retinal artery occlusion
17. Optical coherence tomography
18. Stroke
19. Emergency department
20. Thrombolysis

HIGHLIGHTS

Acute central retinal artery occlusion is an emergency requiring multidisciplinary evaluation and treatment in emergency settings affiliated with a Stroke Center. The goals of treatment are to improve visual outcomes and prevent devastating recurrent stroke or other cardiovascular events.

SUMMARY

The acute management of central retinal artery occlusion (CRAO) has evolved over the past decade and has progressively shifted from eye-care providers to stroke neurologists, with emphasis on hyperacute management, expedited diagnostic tests, and aggressive stroke and cardiovascular secondary prevention.¹⁻⁶

Revascularisation of the ischemic retina with thrombolysis is supported by anecdotal cases, open-label studies, and meta-analyses of observational data,^{1,6} suggesting that intravenous thrombolysis is a low-risk therapy in patients with acute CRAO, although many centers continue to choose intra-arterial thrombolysis. Whether to use intravenous or intra-arterial thrombolysis (via direct infusion into the ophthalmic artery) in patients with acute CRAO remains debated. However, most clinicians agree that early treatment, ideally within 4.5 hours of vision loss, should be the goal, which is best accomplished with the intravenous route. Indeed, a few studies have suggested that patients treated shortly after visual loss might have better outcomes than those who receive either delayed treatment, no treatment, or any alternative ophthalmological (so-called conservative) treatment.^{1,6,5} It is however important to note that the true retinal tolerance time to severe ischemia in patients with acute CRAO remains unknown in humans, and may be much shorter than the 240 minutes previously reported by Hayreh in primates.^{1,2}

Although a few retrospective studies suggested that hyperbaric oxygen may be useful in acute central retinal artery occlusion (especially when combined with thrombolysis), there is little data to support its routine use and it is only easily accessible to a few centers.¹

Randomized controlled trials evaluating thrombolysis in patients with acute ischemic stroke are extremely difficult to perform, mostly because of delayed presentation and diagnosis. This issue is even more pronounced for patients with acute CRAO because most patients with isolated monocular visual loss are not immediately referred to emergency departments. Additionally, funduscopic examination is not usually performed by non-eye-care providers and entails time-consuming pharmacological pupillary dilation, delaying the diagnosis of acute central retinal artery occlusion in non-ophthalmic settings; this may be improved by implementation of non-mydriatic color fundus photograph and optical coherence tomography in the emergency department with remote interpretation, avoiding the need for in-person ophthalmology consultation.³⁻⁵

Two multicenter double-blinded randomized controlled phase 3 trial (THEIA from France,⁷ TenCRAO from Norway⁸) have been completed recently, and an additional trial (REVISION from Germany⁹) is ongoing. These 3 trials have relatively similar design and test the hypothesis that intravenous thrombolysis with alteplase or tenecteplase administered within 4.5 hours of vision loss onset is superior to aspirin therapy alone (THEIA and TenCRAO) or placebo (REVISION). Intravenous thrombolysis was used in a manner analogous to protocols used for the treatment of patients with cerebral ischaemic stroke. In both THEIA⁷ and TenCRAO,⁸ patients treated with thrombolysis failed to meet the primary endpoint of an improvement in visual acuity of at least 0.3 logMar from baseline to 1 month, although there was a definite trend for better visual recovery in the thrombolysis arm compared with the aspirin arm. Unfortunately, both studies were largely underpowered and do not allow any definite conclusion. The REVISION trial⁹ should be properly powered and includes a true placebo arm (instead of aspirin). We are anticipating an interim analysis by the end of 2025, which should provide important additional information. Once available, the large amount of data collected by these three similarly designed trials will be combined in a patient-level meta-analysis.¹⁰

Until these results are available, and in anticipation of other potential therapies for acute CRAO, it will be important to continue to support the expansion of multi-disciplinary networks capable of offering off-label intravenous thrombolysis within hours after onset of visual loss, keeping in mind that “time is retina”.^{3-5,11,12} Non-mydriatic ocular imaging (ideally combining color fundus photography and optical coherence tomography) in emergency departments affiliated with stroke

centers is the best way to facilitate an immediate definitive diagnosis of acute CRAO by remote interpretation of ocular imaging by an ophthalmologist, in parallel with activation of an eye stroke alert

CME ANSWERS

- 13. D
- 14. E
- 15. B

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NOVEL THERAPEUTIC APPROACHES FOR INHERITED OPTIC NEUROPATHIES

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LEARNING OBJECTIVES (3 required)

13. Review the latest developments in gene therapy for Leber hereditary optic neuropathy
14. Discuss novel therapeutic approaches for inherited optic neuropathies
15. Appreciate the challenges of conducting clinical trials for inherited optic neuropathies

CME QUESTIONS (3 required)

13. Which of the following is correct with regards to allotopic gene expression for Leber hereditary optic neuropathy (LHON) caused by the m.11778G>A mitochondrial DNA (mtDNA) variant in *MT-ND4*?
 - A. A recoded version of the *MT-ND4* gene is inserted into the nuclear genome
 - B. The adeno-associated virus serotype 2 (AAV-2) was used to deliver the replacement *MT-ND4* gene in phase 3 clinical trials
 - C. The mRNA transcript has a mitochondrial targeting sequence (MTS) to guide its positioning on the mitochondrial surface
 - D. Five-year follow-up data of individuals treated with this gene therapy approach show a sustained improvement in best-corrected visual acuity.
 - E. All of the above
14. Which of the following therapeutic approaches is not currently being explored for autosomal dominant optic atrophy (DOA) caused by pathogenic variants in the nuclear gene *OPA1*?
 - A. Antisense oligonucleotides (ASOs) to increase the level of the wild-type OPA1 protein
 - B. “Cut and paste” strategy using mRNA transplicing
 - C. Gene editing to correct the pathogenic *OPA1* variant
 - D. Mitochondrial transplantation
 - E. Neurotrophic factors to promote retinal ganglion cell survival
15. Which of the following experimental treatments could prevent visual loss from LHON?
 - A. Gene editing to correct the pathogenic variant
 - B. Shifting the level of heteroplasmy (mutant mtDNA) to improve mitochondrial function
 - C. The transfer of whole mitochondria into retinal ganglion cells
 - D. Mitochondrial replacement therapy to prevent the maternal transmission of the pathogenic mtDNA variant
 - E. All of the above

KEYWORDS (5 Max)

21. Autosomal dominant optic atrophy
22. Gene editing
23. Gene therapy
24. Leber hereditary optic neuropathy
25. Mitochondrial transplantation

HIGHLIGHTS

1. Replacement gene therapy for LHON caused by the m.11778G>A mtDNA variant is based on the allotopic expression of the *MT-ND4* gene. Three phase III clinical trials (RESCUE, REVERSE and REFLECT) and a five-year follow-up study (RESTORE) have shown sustained improvement in best-corrected visual acuity compared with the expected natural history.

2. Phase I clinical trials (SUNDEW, MYRTLE and OSPREY) that make use of ASOs to modulate mRNA splicing and increase the level of the wild-type OPA1 protein are currently recruiting patients with *OPA1* DOA.
3. Novel therapeutic approaches are being investigated for inherited optic neuropathies, including targeted gene editing, shifting the level of heteroplasmy (mutant mtDNA) and mitochondrial transplantation.

SUMMARY

(Summary text here)

1. Inherited optic neuropathies

Inherited optic neuropathies are an important cause of visual loss in children and young adults with an estimated prevalence of 1 in 10,000 in the general population. The pathological hallmark of this group of diseases is the selective loss of retinal ganglion cells (RGCs) causing progressive optic nerve degeneration and irreversible visual loss. Inherited optic neuropathies are genetically heterogeneous with an expanding list of causative genes encoded by the mitochondrial and nuclear genomes [1]. The classical paradigms are Leber hereditary optic neuropathy (LHON) and autosomal dominant optic atrophy (DOA). LHON is caused primarily by three pathogenic mitochondrial DNA (mtDNA) variants, namely, m.3460G>A in *MT-ND1*, m.11778G>A in *MT-ND4* and m.14484T>C in *MT-ND6*, with m.11778G>A being by far the most common disease-causing variant. Although DOA is genetically heterogeneous, the predominant causative gene is *OPA1* (3q29), which accounts for ~60% of cases. Mitochondrial dysfunction is central to the pathophysiology of LHON and *OPA1* DOA with increased levels of reactive oxygen species and a bioenergetic crisis contributing to RGC loss. The only approved treatment for LHON is idebenone, which is a short-chain ubiquinone analogue that mitigates these two deleterious consequences, promoting RGC survival. About half of all treated patients experience a visual benefit, but the response is variable and it is not possible to stop the catastrophic loss of RGCs in the subacute phase of the disease. Given the limited treatment options available for inherited optic neuropathies, different strategies are being investigated, ranging from traditional gene replacement therapy to mRNA therapeutics, and potentially groundbreaking approaches based on targeted gene editing and mitochondrial transplantation [2].

2. Mitochondrial gene therapy for LHON

Replacement gene therapy for LHON caused by the m.11778G>A mtDNA variant in *MT-ND4* is at an advanced stage of development. It is based on allotopic gene expression of a recoded version of the *MT-ND4* gene, which is transferred into the nucleus, and the resulting mRNA transcript has a mitochondrial targeting sequence (MTS) that directs its import to the mitochondrial compartment. Three phase III clinical trials (RESCUE, REVERSE and REFLECT) and a five-year follow-up study (RESTORE) have recruited patients with visual loss of up to one year who were treated with an intravitreal injection of the gene therapy construct packaged into an adeno-associated virus serotype 2 (AAV-2) vector. Five years after treatment, an improvement from the nadir of -0.3 logMAR or more was observed in at least one eye in about two thirds of the study participants [3]. However, there are several unanswered questions, in particular, the therapeutic window, the optimal viral titer, and the reasons for the unexpected contralateral response observed in the non-injected fellow eye. These controversies will be explored as part of upcoming studies (REVISE, REVIVE and RECOVER) and an Expanded Access Program (EAP).

3. mRNA therapeutics for *OPA1* DOA

Visual loss in *OPA1* DOA starts insidiously in early childhood. Although disease progression is highly variable, about half of all affected patients will have significant visual impairment by the fifth decade of life. Over 400 pathogenic *OPA1* variants have been reported with about two thirds causing haploinsufficiency i.e. a reduction in the level of the wild-type protein resulting in mitochondrial dysfunction and RGC loss. Given this common disease mechanism, antisense oligonucleotides (ASOs) are being used to modulate translation of the wild-type mRNA transcripts and maximize the production of the native OPA1 protein. Based on promising preclinical data demonstrating the safety and efficacy of this approach, phase I trials (SUNDEW, MYRTLE and OSPREY) have been launched that are recruiting patients with DOA carrying a disease-causing haploinsufficient *OPA1* variant. Another therapeutic approach that is being considered for *OPA1* DOA is a “cut and paste” mRNA transplicing strategy. Treatment trials for this mitochondrial optic neuropathy

pose distinct challenges due to the highly variable rate of visual decline, the transient nature of mRNA transcripts and ASOs, and the uncertainties relating to the frequency of repeat injections.

4. Gene-agnostic therapeutic approaches

Advanced therapies for relatively rare inherited optic neuropathies are time-consuming and expensive. These constraints call for gene-agnostic approaches that are now a reality spearheaded by major advances in gene therapy vector design and delivery, and the availability of molecular tools for precise genetic manipulation. Gene therapy with diffusible neurotrophic factors, such as brain-derived neurotrophic factor (BDNF), is being investigated for glaucoma and late-onset neurodegenerative diseases, and this strategy could be extended to inherited optic neuropathies. A range of molecular tools (mtZFN, mitoTALEN and mitoARCUS) are being optimised that can be used to selectively destroy mutant mtDNA and shift the heteroplasmy to a level that is less or no longer detrimental to mitochondrial function [4]. Furthermore, it is now possible to achieve targeted gene editing for both the mitochondrial and nuclear genomes, using DddA-derived cytosine base editors (DdCBE) and CRISPR technology, respectively. Mitochondrial gene editing would have the advantage of preventing the onset of catastrophic visual loss in LHON by treating unaffected carriers. It could also be used to correct the genetic defect prior to IVF insemination, providing an alternative to mitochondrial replacement therapy for women of childbearing age who carry homoplasmic mtDNA variants [5]. Gene editing is a powerful tool that has been used to generate a mouse model harboring the pathogenic m.11778G>A variant, providing a much-needed in vivo platform for studying disease mechanisms and testing therapies for LHON [6]. Lastly, preliminary studies indicate that the transplantation of whole mitochondria into RGCs can mitigate the mitochondrial dysfunction that characterise inherited optic neuropathies, providing a generic approach to preserve RGCs and vision.

5. Conclusion

Inherited optic neuropathies cause significant visual impairment with a major impact on quality of life. Although several challenges lie ahead, there is cause of cautious optimism with a broad range of therapies now reaching the translational phase, capitalizing on more precise tools for gene and mRNA modification.

CME ANSWERS

- 16. E
- 17. D
- 18. E

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Eyes on the Evidence: What's New in Treating Neuro-Ophthalmic Disease?

Idiopathic intracranial hypertension

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LEARNING OBJECTIVES

1. Summarize the systemic disease associations of idiopathic intracranial hypertension.
2. Describe the controversy in the management of visual failure in of idiopathic intracranial hypertension.
3. Discuss the use of glucagon like peptide – 1 receptor agonists in people living with idiopathic intracranial hypertension

CME QUESTIONS

1. What was the **MOST** common and **LEAST** serious complication of a venous sinus stent?
 - a. Intracerebral hemorrhage
 - b. Mastoiditis
 - c. Stent migration
 - d. Transient ipsilateral headache
2. What is **NOT** a contraindication of the use of glucagon like peptide – 1 receptor agonist?
 - a. Diabetes Mellitus Type 1
 - b. Gastroparesis
 - c. History of thyroid cancer
 - d. Hypertension
3. Which of the following treatments have **NOT** been subject to phase III a randomized control trial for people living with Idiopathic intracranial hypertension?
 - a. Acetazolamide
 - b. Bariatric surgery
 - c. Venous sinus stenting
 - d. Weight watchers diet

KEY WORDS

1. Pseudotumor Cerebri Syndrome (PTSC)
2. Idiopathic Intracranial Hypertension (IIH)
3. Cerebrospinal fluid diversion
4. Dural venous sinus stenting
5. Systemic metabolic disease

Idiopathic intracranial hypertension (IIH) is an increasingly prevalent condition characterised by raised intracranial pressure (ICP), papilloedema and headache with emerging evidence suggesting a systemic metabolic disorder.^{1,2} People with IIH have cited challenges in their care and made recommendations in key areas such as communication regarding the relationship between weight management, disease development and remission.³ A person with IIH may meet many specialists and therefore a coordinated standard approach to care is recommended.⁴ The first consensus guidelines for IIH were published in 2018 and clinical practice is evolving.⁴

Although raised ICP and the neuroophthalmological symptoms represent the core clinical syndrome of IIH, these are secondary to an underlying metabolic disorder. At the population level, people living with IIH are at a higher risk of developing cardiovascular diseases and type 2 diabetes melitus⁵. This is likely linked to the greater degree of insulin resistance in IIH, compared to obese controls, which normalizes following weight loss, indicating that insulin resistance is a modifiable metabolic feature in IIH.^{6,7} Adverse maternal health is observed with reduced fertility, a three-fold increased

risk of gestational diabetes, five-fold increased risk of pre-eclampsia, and increased surgical deliveries.⁸ Abnormal adipocytes located truncally are associated with androgen excess with elevated levels of serum testosterone, cerebrospinal fluid androstenedione and testosterone which may also independently drive cerebrospinal fluid production.^{6,7,9}

Management of IIH is focussed on preserving vision, symptomatic treatment of headache and modifying the underlying risk of living with obesity.⁴ The vast majority of people with IIH are treated medically,¹⁰ only 7% require surgery to save vision and there is no evidence that intracranial intervention alters the metabolic syndrome.^{11,12} All of the interventions, CSF shunting, dural venous sinus stenting (VSS) and optic nerve sheath fenestration, have been shown, to a variable extent, to help improve or stabilise visual function, reduce headache and, indeed, lower intracranial pressure. All have known complications and revision rates.¹³⁻¹⁸ To date, there are no randomized controlled trials directly comparing CSF shunting and VSS, the two most commonly performed procedures, for sight-threatening IIH. Existing studies involved heterogeneous cohorts and often relied on variable, non-standardised outcome measures, with frequent use of binary indicators, such as the presence or absence of papilloedema or headache; this leads to a lack of comparable, high-quality data to support confident clinical decision-making.¹⁹

It is now widely accepted that venous sinus stenosis is a common phenomenon observed in IIH and VSS is increasingly being deployed for IIH. Advances here include the River Stent trial that has recently been published.²⁰ This was a single-arm, open-label study evaluating a specific intracranial stent to treat symptomatic venous sinus stenosis in IIH.²⁰ It should be noted that reduction in ICP following CSF removal has been shown to alleviate the stenosis, indicating that venous sinus stenosis may be a secondary consequence to raised ICP rather than primary etiology.^{21,22}

Two definitions used clinically, although with little validation, are worth mentioning:

1. Fulminant IIH

Fulminant IIH has been defined as those within 4 weeks of their initial IIH diagnosis having escalation of their clinical syndrome requiring surgical intervention.²³ This term is often applied more flexibly without the time limit, since rapid deterioration in IIH can occur at any stage and time-based criteria may delay urgent care.²⁴

2. Medically refractory IIH

Many have used this term to describe patients with ongoing headaches, continued pulsatile tinnitus or mild chronic papilloedema. However, most studies do not specify which symptoms are refractory to treatment, whether patients were resistant to weight loss interventions, or provide details on the medication classes and dosages used for managing intracranial pressure and headaches. In addition, medically refractory disease would probably be less common if there was rapid access to weight management services, as there is evidence that weight loss correlates with reduction in intracranial pressure and headache burden.²⁵ Likewise, targeting medication over use and the success of modern targeted headache treatments should reduce this group of patients.^{26,27,28}

There is no single functional or structural measure that has been validated to define IIH patients as an appropriate intervention candidate, nor indeed any biomarkers to accurately guide prognosis. It may be widely assumed that the Humphrey visual field mean deviation can solely guide clinical decision making, but all neuro-ophthalmologists know that there is discordance between the amount of papilloedema and the visual field findings. One prospective study evaluating CSF diversion in sight threatening disease did compare patients who had a pre-procedural perimetric mean deviation above and below -7dB, and found those that had -7dB or worse, performed worse in the long-term.²⁹ There is no international consensus on the definition of severe papilledema. Sight-Threatening IIH is determined by the experts' clinical judgement (Table 1). Features of severe papilledema include a Frisén grade ≥ 3 , with intraretinal fluid or subretinal fluid tracking toward the macula.²⁹

Table 1, One definition of sight threatening IIH adapted from Hyder et al.²⁹

A	If first visit: presence of severe papilledema (confirmed on fundoscopy and optical coherence tomography imaging) and the loss of visual field noted on a reliably performed visual field
OR	
B	On follow-up: increasing papilledema (confirmed on fundoscopy and optical coherence to tomography imaging) and the increasing loss of visual field noted on a reliably performed visual field
AND	

C	Imminent irreversible visual loss considered definite or probable without intervention from urgent cerebrospinal fluid diversion surgery. Alternative therapeutic approaches would be unlikely to alter the trajectory of irreversibly imminent visual loss (medical therapy with or without weight loss, if appropriate)

Acetazolamide, a carbonic anhydrase inhibitor, first prescribed in 1954 remains the most commonly prescribed medicine for IIH. In 2014, the IIH Treatment Trial (IIHTT) evaluated the use of acetazolamide along with a multicomponent dietary intervention and compared it to placebo combined with the multicomponent dietary intervention in those with active and acutely diagnosed IIH with mild visual loss defined as a mean deviation between -2 to -7dB in either eye. While medicines targeting ICP can reduce papilledema the mainstay of medical management should be weight loss as this has been shown to be associated with disease remission.³¹ Weight loss is challenging as many barriers exist to support patients on their weight loss journey.

The directed use of synthetic incretins at a population level have been shown to be beneficial for both medical and surgically treated patients. One TriNetX study found a reduced odds of undergoing stenting and CSF diversion with glucagon like peptide – 1 receptor agonist (GLP-1 RA) use.³² Two other studies reported less medications used and less coding for headache, visual disturbances, blindness in the GLP-1 RA group.^{33,34} Overall morbidity was also found to be less in one.³⁴ While we await results of randomized clinical trials evaluating GLP-1 RA and dual Glucose-dependent Insulinotropic Polypeptide (GIP)/GLP-1RA in IIH, open label studies have been positively reporting, more weight loss, less headache and less acetazolamide use, with moderate tolerability.³⁵

SUMMARY

Idiopathic intracranial hypertension is one of the most common neuro-ophthalmologic disorders seen neuro-ophthalmologists. Idiopathic intracranial hypertension is characterized by raised intracranial pressure that triggers disabling headaches and can cause permanent visual loss. There are no licensed treatments for the condition and the majority of approaches to managing the disease prioritize resolution of papilledema. There is a spectrum of the disease ranging from mild to severe, and for the majority of patients the visual prognosis is good. However, around 7% require escalation of treatment to save sight, with surgical choice being largely dictated by local expertise. Evidence is emerging that IIH is a systemic metabolic disease and there are a number of different factors that need to be considered. Addressing headache is of key importance to the patient and reducing long-term morbidity of the disease. Options for weight management should be sensitively discussed, and the wide spread use of glucagon like peptide – 1 receptor agonists are gaining positive results for the IIH population.

CME ANSWERS

- 1. D, Transient ipsilateral headache.** While all are potential side effects of VSS, transient ipsilateral headache is a common side effect that is deemed less serious than the rare side effects of intracerebral haemorrhage, mastoiditis and stent migration
- 2. D, Hypertension.** Diabetes Mellitus Type 1, gastroparesis and a history of thyroid cancer are all contraindications for the use of GLP-1 RAs.
- 3. C, Venous sinus stenting.** The IIH Treatment Trial was a multicentre, double-masked, randomised, placebo-controlled trial evaluating the use of acetazolamide and placebo in conjunction with a lifestyle modification program that took place at North American centres. The trial was a landmark publication showing statistically significant improvement in the primary outcome of the perimetric mean deviation of the 24-2 Humphrey Visual field in those in the treatment arm. The IIH weight trial was a randomized clinical trial that enrolled women with active IIH and a body mass index of 35 or higher at five National Health Service hospitals in the United Kingdom. Women were randomised to bariatric surgery or the community weight management (CWM) intervention, Weight Watchers. At both 12 and 24 months intracranial pressure and body weight were significantly lower and quality of life improved in the bariatric surgery as compared with the CWM arm. There has yet to be a phase III RCT evaluating any neurosurgical intervention in people living with IIH.

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What's New in Thyroid Eye Disease Treatments?

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Mackall-Scheie Research Chair in Ophthalmology
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LEARNING OBJECTIVES

1. Discuss recurrence rates of TED following completion of teprotumumab therapy
2. Identify emerging biologics under investigation in TED treatment
3. Compare novel routes of administration and dosing schedules for TED therapies

CME QUESTIONS

1. What percentage of patients with TED experience recurrence following treatment with teprotumumab?
 - A. 2-5
 - B. 10-15
 - C. 20-40
 - D. 50-60
2. Teprotumumab, a therapy for TED, acts primarily by inhibiting which target?
 - A. IGF-1 receptor
 - B. VEGF
 - C. IL-6
 - D. FcRn
3. True or False: Phase 4 studies demonstrated measurable improvement in proptosis among patients with chronic TED treated with teprotumumab

KEYWORDS

1. Thyroid eye disease
 2. Teprotumumab
 3. IGF-1
 4. IL-6
 5. IL-11
 6. FcRn
 7. VEGF
-
- I. What's new with teprotumumab?
 - A. Active and chronic TED
 1. Original findings: active, moderate-to-severe TED
 - a. 80% ≥ 2 mm proptosis reduction compared to 10% placebo
 - b. Diplopia improved in 55-73%
 2. Expanded evidence
 - a. Phase 4 RCT show 62% ≥ 2 mm proptosis improvement in chronic TED
 - b. No difference in diplopia improvement between tepro and placebo in chronic cohort

B. Recurrence rate

1. 29-37% experience reactivation or return of symptoms within 1-2 years
 - a. Vary by definition
 - 2+ mm proptosis
 - 2+ increase in CAS
 - Symptoms
2. How do recurrences present?
 - a. Gradual proptosis (50-70%)
 - b. Extraocular muscle restriction/diplopia (20-40%)
 - c. Pain, swelling, and redness (10-20%)
3. Risk factors
 - a. Smoking
 - b. Age
 - c. Larger extraocular muscle volumes

C. Hearing loss

1. High and middle frequencies
2. Bilateral
3. Gradual onset
4. Onset after mean 3.8 infusion
5. Up to 45% experience auditory symptoms in small retrospective cohorts
 - a. Autophony usually reversible (83%)
 - b. Sensorineural hearing loss by audiometry in 10-50%
6. Risk factors
 - a. Older patients (65+)
 - b. Pre-existing hearing loss
7. Audiogram before, during, and after treatment
 - a. 45% subjectively noted hearing loss despite audiometric changes

D. Future considerations

1. Target patient
 - a. Can we identify patients who are unresponsive or respond best?
 - b. Study design: Observational study of a large group of patients
2. Maintenance therapy
 - a. Can we mitigate relapses with repeated infusions (e.g., every 6 months)?
 - b. Study design: Randomized extension vs. placebo for teprotumumab responders
3. Combination therapy
 - a. Is there a benefit to combining teprotumumab with other therapies especially those who may be poorly responsive or at higher risk of recurrence?
 1. Radiation therapy
 2. Rituximab
 3. Other
 - b. Study design: RCT of tepro + placebo vs. tepro + combination
4. Study endpoint considerations
 - a. Concern for subjective symptoms (pain in CAS) or testing (Hertel exophthalmometry)
 - b. Objective, centralized assessments minimize examiner variability

- a. Imaging-based proptosis
- b. Imaging-based orbital volume
- c. Standardized diplopia field testing
- d. Eyelid metrics using standardized photography with masked readers

II. Emerging therapies in development

- A. Delivery includes intravenous, subcutaneous, sub-Tenons, and oral
- B. Proposed schedules include daily, weekly, Q2w, Q3w, and Q4w
- C. FDA approved
 1. Most therapies are approved for other indications and are being studied or used off label
 2. Some treatments are not approved for any indications and are being studied in TED alone
- D. Targets
 1. Specific receptors involved in fibrosis and inflammation (IGF-1, IL-6, IL-11)
 2. General reduction of IgG levels without broad immunosuppression (FcRn)
 3. General reduction of edema (VEGF)

<u>Drug</u>	<u>Target</u>	<u>Route</u>	<u>Schedule</u>	<u>Status/Notes</u>
Teprotumumab	IGF-1R	IV	Q3w x 8	FDA-approval: TED
Veligrotug	IGF1R	IV	Q3w x5	Higher affinity mAb Phase 3 trials for active and chronic TED completed but not published, but topline data indicate significant benefit
VRDN-003	IGF1R	SQ	Q4w x6	Phase 3 trials completed for active and chronic TED but not published and no topline data available
Linsitinib	IGF-1R	PO	Daily	Failed in the oncology space Benefit in murine model of TED No current Phase 2/3 trials
Tocilizumab	IL-6R	IV or SQ	IV: Q4w SQ: Q1-2w	FDA-approval: GCA One RCT and several small series in TED
Satralizumab	IL-6R	SQ	Q4w	FDA-approval: NMOSD Phase 3 trials for active and chronic TED showed benefit in proptosis/CAS
Sariluzmab	IL-6R	SQ	Q2w	FDA-approval: RA and PMR Small series in TED

Efgartigimod	FcRn	SQ	Qw	Engineered Fc Fragment FDA-approval: GMG Phase 3 trial for active TED ongoing – closed in Dec 2025
Nipocalimab	FcRn	IV	Q2w	High-affinity FcRn inhibitor FDA-approval: None No trials currently
Batoclimab	FcRn	SQ	Qw	FDA-approval: None Phase 2 trials in TED terminated early
Aflibercept	VEGF	ST	Q2w x3	FDA-approval: wet AMD, diabetic retinopathy Phase 2 for active TED
K1-70	TSH-R	IV	?	Phase 1 trial – no SAE, 50% proptosis response
GenSci098 SYD5115 S37a	TSH-R	?	?	Preclinical

*IGF=insulin growth factor, IL = interleukin, FcRn = neonatal Fc receptor, ST = subtenons

CME Answers

1. **A**
2. **D**
3. **True**

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BRIDGING SUBSPECIALTIES: A UNIFIED APPROACH TO BRAIN HEALTH

Natalia S. Rost, MD, MPH, FAAN, FAHA

President, American Academy of Neurology

Practicing in Boston / AAN Headquarters in Minneapolis, MN

LEARNING OBJECTIVES (3 required)

1. Describe core principles of AAN Brain Health Initiative and its relevance to neuro-ophthalmology.
2. Explain how interdisciplinary collaboration across neurology subspecialties enhances brain health outcomes.
3. Evaluate role of scientific research in shaping evidence-based strategies for neurologic disease prevention and treatment.

CME QUESTIONS AND MULTIPLE CHOICE ANSWERS (3 required)

1. What are the core principles of the AAN Brain Health Initiative, and why are they relevant to neuro-ophthalmology?
 - A) Focus on acute intervention and isolated treatment of neurological symptoms.
 - B) Emphasize prevention, early intervention, and holistic care for neurological health; relevant to neuro-ophthalmology by encouraging integration of preventive strategies and collaboration across subspecialties.
 - C) Prioritize only genetic research in neuro-ophthalmology.
 - D) Limit care to traditional neurology practices without interdisciplinary input.
2. How does interdisciplinary collaboration across neurology subspecialties enhance brain health outcomes?
 - A) It creates competition between subspecialties, reducing overall care quality.
 - B) It enables shared approaches, data-driven insights, and comprehensive care models, improving prevention, diagnosis, and treatment of brain health conditions.
 - C) It restricts innovation by enforcing rigid protocols.
 - D) It focuses solely on administrative efficiency rather than patient outcomes.
3. What is the role of scientific research in shaping evidence-based strategies for neurologic disease prevention and treatment?
 - A) It provides anecdotal evidence for clinical decisions.
 - B) It supports only theoretical models without practical application.
 - C) It provides the foundation for identifying effective prevention and treatment strategies, informs evidence-based practices, guides policy-driven access, and supports health equity.
 - D) It is not necessary for developing neurologic disease prevention strategies.

KEYWORDS (5 max)

1. Brain health
2. Preventive neurology
3. Cross-disciplinary collaboration
4. Policy-driven access
5. Health equity

HIGHLIGHTS

- The presentation positions brain health as a central, unifying concept across neurology subspecialties. Through neuro-ophthalmology examples, the session illustrates how these principles can be applied to broader neurological care.
- Attendees provided a comprehensive overview of the AAN Brain Health Initiative, including its strategic goals and pillars. The discussion emphasizes the relevance of these principles to neuro-ophthalmology, particularly in the context of visual biomarkers and pathways that inform neurologic disease management.
- Lecture underscores critical role of scientific research in advancing prevention and treatment strategies for neurological diseases. Evidence-based approaches are highlighted as essential for guiding clinical practice and improving patient outcomes.

- Examples of successful collaboration across neurology subspecialties are highlighted, demonstrating how shared approaches and data-driven insights can enhance neuro-ophthalmic care and foster innovation.
- Attendees will be encouraged to explore cross-disciplinary partnerships, to leverage collective expertise, to advance patient care, and to promote health equity.

SUMMARY

The presentation, “Bridging Subspecialties: A Unified Approach to Brain Health,” led by Dr. Natalia S. Rost, President of the American Academy of Neurology, explores how brain health serves as a unifying concept across neurology subspecialties, with a particular focus on neuro-ophthalmology.

CME KEY

What are the core principles of the AAN Brain Health Initiative, and why are they relevant to neuro-ophthalmology?

B) Emphasize prevention, early intervention, and holistic care for neurological health; relevant to neuro-ophthalmology by encouraging integration of preventive strategies and collaboration across subspecialties.

How does interdisciplinary collaboration across neurology subspecialties enhance brain health outcomes?

B) It enables shared approaches, data-driven insights, and comprehensive care models, improving prevention, diagnosis, and treatment of brain health conditions.

What is the role of scientific research in shaping evidence-based strategies for neurologic disease prevention and treatment?

C) It provides the foundation for identifying effective prevention and treatment strategies, informs evidence-based practices, guides policy-driven access, and supports health equity.

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Member Initiated Symposium: Negotiation Skills Workshop [1.5 CME]

Directors: Sangeeta Khanna, MD; Catherine Soehner, BSN, MLS; Leanne Stunkel, MD

Approaching Difficult Conversations, *Catherine Soehner, BSN, MLS*

Principles of Negotiation, *Barbara Yates, MD; Nurhan Torun, MD, FRCSC, MCSO; Andrew Melson, MD*

Scenario-Based Teaching, *Kimberly Wings, MD; Rashmi Verman, MD; Victoria Pelak, MD*

Skills Workshop, *Sangeeta Khanna, MD; Leanne Stunkel, MD; Catherine Soehner, BSN, MLS; Andrew Melson, MD; Nailyn Rasool, MD; Barbara Yates, MD; Kimberly Wings, MD; Victoria Pelak, MD; Nurhan Torun, MD, FRCSC, MCSO; Amanda Henderson, MD; Rashmi Verman, MD; Negar Moheb, MD*

In this symposium, we aim to provide participants with skills to approach difficult conversations and negotiations, to empower them in advocating for their needs in neuro-ophthalmic practice. Our expert panel includes providers who have experience in neuro-ophthalmic practice and in formal negotiation training, and Catherine Soehner, MLS, BSN, is the Associate Dean and Executive Director of the Eccles Health Sciences Library (home to NOVEL) and the author of *Effective Difficult Conversations*. The panel will provide didactic teaching on the principles of negotiation and illustrative role-playing scenarios. Afterward, participants will have the opportunity to practice techniques in one-on-one structured role playing. This symposium is co-sponsored by the Women in Neuro-ophthalmology (WIN) Committee and the Young Neuro-ophthalmologist (YONO) Committee.

Upon completion of this session, participants should be able to:

- (1) Understand how to plan for successful difficult conversations
- (2) Understand the principles of negotiation techniques
- (3) Improve communication and negotiation skills through role playing and practice at the symposium

Member Initiated Symposium: OCT Odyssey [1.5 CME]

Directors: Susan P. Mollan, MBChB, PhD & Clare L. Fraser, FRANZCO

OCT Imaging Features of Ischemic Optic Neuropathy, *Steffen Hamann, MD, PhD*

Systematic review of OCT in Papilledema, What Did We Learn? *Fiona Chan*

OCT in concussion and neurodegeneration that you can use in clinic, *Clare L. Fraser, FRANZCO*

Can You Interchange Values from OCT Cirrus (Zeiss) and Spectralis (Heidelberg Engineering)

in Papilledema? *Gabriele Berman, MD*

A trip to White Mars, tips for working with OCT angiography data, *Susan P. Mollan, MBChB, PhD*

Seeing the Unseen: OCT in Acute Retrobulbar Optic Neuritis, *Ana Banc, MD, PhD*

AI-Based Optimization of OCT findings in Neuro-Ophthalmology, *Dan Milea, MD, PhD*

Optical Coherence Tomography (OCT) is a non-invasive, light-based imaging technique which enables in vivo, high-resolution, cross-sectional imaging of structures, including human tissues. Current OCT devices can now accurately resolve the individual retinal layers and provide automated measures estimated to the nearest micron. OCT imaging has become important in the routine management of optic neuropathies (including papilledema) and a variety of related central nervous system disorders including multiple sclerosis, brain tumors, neurodegeneration and syndromes of raised intracranial pressure. Understanding the different device measures is helpful when trying to compare research to your clinical practice, where you might have a different machine. There are key quantitative and qualitative features that have been established in neuro-ophthalmology to aid clinical practice. This session will bring wide ranging expertise across devices to highlight areas of growth for our subspecialty. The speakers will share the latest in artificial intelligence and OCT imaging research. Importantly this session will bring the research findings back to real world clinical practice. Be ready for the OCT Odyssey!

Upon completion of this session, participants should be able to:

- (1) Summarize the differences between the main OCT devices
- (2) Describe the OCT imaging findings of ischemic optic neuropathy, optic neuritis, papilledema and neurodegeneration
- (3) Gain knowledge of the use of artificial intelligence in OCT imaging

Member Initiated Symposium: Advances in Mitochondrial Genetics and Relevance to Neuro-Ophthalmology Practice [1.5 CME]

Directors: Patrick Yu-Wai-Man, MD, PhD & Nancy J. Newman, MD

When Should I Suspect That Someone Has a Mitochondrial Disease? *Chiara La Morgia, MD*

The expanding genetic landscape of inherited optic neuropathies, *Neringa Jurkute, MD, PhD, FEBO*

My practical approach to genetic testing for suspected mitochondrial disease – Optic neuropathy and/or retinopathy, *Eric D. Gaier, MD, PhD*

Ophthalmoplegia, *Michael J. Gilhooley, MD, PhD, FRCOphth*

Panel Discussion - Genetics, *Chiara La Morgia, MD; Neringa Jurkute, MD, PhD, FEBO; Eric D. Gaier, MD, PhD; Michael J. Gilhooley, MD, PhD, FRCOphth*

Case 1: Unilateral/Asymmetrical CPEO, *Rustum Karanjia, MD, PhD*

Case 2: LHON-MS Overlap Syndrome, *Benson S. Chen, MBChB, PhD, FRACP*

Case 3: Syndromic Dominant Optic Atrophy, *Jing Liang Loo, MD*

Mitochondrial diseases affect ~ 1 in 4,300 people in the general population with over half of them developing prominent ocular manifestations. There are often significant diagnostic delays due to the variable clinical presentations and the rapidly expanding list of disease-causing variants within the mitochondrial and nuclear genomes. This symposium will provide a state-of-art review of the evolving genetic landscape of mitochondrial diseases, focusing on involvement of the optic nerve, outer retina and extraocular muscles. Genetic diagnostic pathways will be discussed, in particular, which tests would be more appropriate based on the clinical features and family history. The application of next-generation sequencing will be described together with the challenges of genetic counselling when a variant of unknown significance (VUS) is identified.

Upon completion of this session, participants should be able to:

- (1) Appreciate the variable and expanding clinical manifestations of mitochondrial disease and potential diagnostic clues
- (2) List the investigations that can be used to diagnose mitochondrial disease depending on the clinical presentation
- (3) Understand the genetic tests that are currently available and their advantages and disadvantages

Member Initiated Symposium: Update on Neurovascular Interventions [1.5 CME]

Directors: Laurel N. Vuong, MD; Thomas R. Hedges, MD; Yosbelkys Martin Paez, MD; Adel Malek, MD, PhD

Case: Ophthalmic Artery Aneurysm

Intracranial Aneurysm Management and Arterial Flow Dynamics, Adel Malek, MD, PhD

Case: Long Standing Dural AVM

Classification and treatment of Dural AVMS and CCFs, Timo Krings, MD, PhD, FRCPC

Case: Post-Stent Stenosis

Venous Stenting for IIH, Mohamad Abdalkader, MD

Case: Subdural Hematoma

Endovascular Treatment of Chronic Subdural Hematoma, Christopher S. Ogilvy, MD

Case: Intracranial Hypotension

Intracranial Hypotension Treatment, M. Ali Aziz-Sultan, MD

This symposium is designed to discuss neurovascular conditions diagnosed and followed in neuro-ophthalmology, as well different neurosurgical management available. The case examples will be provided, and local neurosurgeons will discuss their experiences with them and the outcomes of different interventions. By the end of the symposium, the audience should know when to refer to neurosurgery and the surgical options available to better advise their patients on management options, outcomes, and prognoses.

Upon completion of this session, participants should be able to:

- (1) Know common neurovascular conditions seen in neuro-ophthalmology and co-managed with neurosurgeons
- (2) Identify most up-to-date treatment options for each neurovascular process
- (3) Advise patients accordingly regarding treatment options, outcomes, and prognosis

New Eyes on NAION: Revisiting Risk in a Changing Medical Landscape [2.0 CME]

Moderators: Kenneth Shindler, MD, PhD & Amanda Henderson, MD

How Do We Identify Risk Factors? *Beau B. Bruce, MD, PhD*

GLP1 Medications as a Possible Risk Factor, *Lindsey De Lott, MD, MS*

Systemic Conditions as Possible Risk Factors, *Anthony Arnold, MD*

Anatomical Factors as Possible Risk Factors, *Steffen Hamann, MD, PhD*

Iatrogenic Possible Risk Factors, *Clare L. Fraser, FRANZCO*

NAION Risk Factors Discussion, *Beau B. Bruce, MD, PhD; Lindsey De Lott, MD, MS; Anthony Arnold, MD; Steffen Hamann, MD, PhD; Clare L. Fraser, FRANZCO*

What is Actionable, *Julie Falardeau, MD*

Panel Discussion, *Beau B. Bruce, MD, PhD; Lindsey De Lott, MD, MS; Anthony Arnold, MD; Steffen Hamann, MD, PhD; Clare L. Fraser, FRANZCO; Julie Falardeau, MD*

This session will highlight potential risk factors for non-arteritic anterior ischemic optic neuropathy, focusing on systemic, anatomical, and iatrogenic factors. By reviewing and discussing the available evidence, we aim to equip neuro-ophthalmologists to provide their patients with evidence-based clinical recommendations.

Upon completion of this session, participants should be able to:

- (1) Name potential risk factors for NAION.
- (2) Discuss the available evidence for each risk factor.
- (3) Apply this evidence to the counseling of patients.

HOW DO WE IDENTIFY RISK FACTORS

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LEARNING OBJECTIVES

1. Explain the counterfactual ideal
2. Describe bias and confounding and list ways to address them
3. Explain why the pyramid of evidence has the hierarchy it does

CME QUESTIONS

1. Based on the counterfactual ideal, the perfect comparison/control group for research purposes would be:
 - A. the exposed patients in your study
 - B. the unexposed patients in your study
 - C. the general population
 - D. unexposed patients exactly like your exposed patients in every way except the exposure of interest
 - E. unexposed patients mostly like your exposed patients
2. You generally do NOT want to control for the following in your analyses:
 - A. Intermediates on the causal pathway
 - B. Confounders
 - C. Common effects of exposure and outcome
 - D. A & B
 - E. A & C
3. The key advantage of randomized controlled trials over other study designs is that:
 - A. the patients and physicians do not know the treatment
 - B. they can easily be done with just a few patients
 - C. they balance known factors that could be related to outcome
 - D. they balance unknown factors that could be related to outcome
 - E. they allow the investigator to calculate the underlying risk of disease

KEYWORDS

26. epidemiology
27. confounding
28. bias
29. statistics
30. risk factors

HIGHLIGHTS

- Epidemiology provides the scientific foundation for determining whether observed associations reflect true causal effects on health outcomes.
- Causal inference relies on approximating the counterfactual through rigorous study design and analysis.
- Statistical significance alone is insufficient; valid research conclusions require careful consideration of bias, confounding, and the limitations of the study design and analysis.

SUMMARY

Epidemiology is “the study of the distribution and determinants of health-related states or events in specified populations, and the application of this study to the prevention and control of health problems.”¹ While many fields study the determinants of disease (e.g., basic and clinical medicine), epidemiology’s additional focus on the distribution of disease determinants and disease itself links it analytically with statistics.

When an association between two factors is observed, the statement that “correlation is not causation” is worthwhile remembering. Correlation or association simply means that two factors tend to occur together; causation, in contrast, means that one factor actually causes the other factor to occur. Indeed, the question of when correlation is causation with respect to diseases and their proposed determinants is precisely the domain of epidemiology. When an association is observed between two things, say a medication and a disease, four possibilities can account for it:

1. The association occurred by chance (this highlights the close relationship of analytical epidemiology with statistics);
2. The association is the result of a bias (this is the major focus of epidemiologic analysis);
3. The “disease” causes the “exposure”, e.g., the disease leads people to more often be taking the medication; or
4. The “exposure” causes the “disease”, e.g., the medication causes the illness.

The determination of causality in modern epidemiology relies on the “counterfactual ideal.” Consider, for example, Mr. Jones, a 67-year-old man who experiences a heart attack. He smokes, is overweight, and does not exercise. How could we determine with certainty whether smoking caused Mr. Jones’s heart attack? The only way would be in a hypothetical, counterfactual scenario in which we could observe Mr. Jones who, at the very moment he chose to begin smoking in his actual life, instead chose never to smoke, while all other factors unrelated to that decision remained identical. If, in that alternative world, Mr. Jones did not experience a heart attack or experienced it later, then we could conclude that smoking caused the heart attack in his case.

Such a counterfactual universe is obviously not observable in the real world, so we must instead infer what would have happened by using different people who are ideally just like Mr. Jones in every way except that they did not smoke. When the counterfactual ideal is not achieved, bias is present. When bias is present, the observed association may be entirely spurious (creating an association that does not exist), or it may over- or underestimate the true association.

CHANCE

Statistics deals with the role of chance in explaining an observed association—the first of the four possibilities highlighted above. As noted previously, epidemiology is the study of the *distribution* of disease determinants which means that statistics plays a key role in epidemiologic science. In general, statistics tend to use a sample from a larger population to describe, summarize, or compare one group to another in that population. Properly used and respecting the necessary assumptions, statistics can allow one to infer information about the larger population. However, all statistics are based on mathematical models which means that they only reflect the real world to the extent that reality is accurately described by the model. Most basic statistics assume the sample is random, independent, and identically distributed. In many real-world situations, these assumptions do not fully apply. Furthermore, statistical inference about the population (i.e., point estimates, confidence limits, statistical significance) all require that bias and confounding have been addressed, if it has not, then statistical significance is meaningless. A significant statistical result in a study does not necessarily mean that there is a real difference between the groups, e.g., uncontrolled confounding, bias, or even residual random error (usually allowed to happen 5% of the time or a failure to follow the underlying assumptions of the test).

BIAS

Epidemiologic researchers can classify biases into one of three all-inclusive categories: information bias, selection bias, or confounding. Information bias is a distortion that results from the mismeasurement or misclassification of the disease or its potential determinants. Selection biases are distortions that result from the procedures used to select subjects and from

factors that influence study participation. Confounding is the third type of bias and the most complex to describe and understand. Confounding is a distortion that results from a common cause (direct or indirect) of both the exposure and the disease. For a factor to confound an association, it must be either an actual cause of the disease or a surrogate marker for an actual cause of disease other than the exposure, it must be associated with the exposure under study in the source population (i.e., the population at risk from which the cases of disease are derived), and must not be caused by the exposure or the disease. This last criterion is automatically satisfied when the factor precedes the exposure or disease. However, these three characteristics of confounding are an oversimplification since a factor can still be a confounder and not fully meet the third criterion in all circumstances (e.g., it may be that in some instances the exposure also contributes to the potentially confounding variable despite the confounder already being present prior to exposure and disease development), and this leads to analytical difficulties in fully disentangling the effects of the confounder and the exposure and outcome so that a fully unbiased assessment of the association can be achieved. The degree of confounding matters more than its mere presence or absence.²

STUDY DESIGNS & LEVELS OF EVIDENCE

Bias is addressed in two ways: (1) by sound study design and (2) by the correct application of analytical techniques to produce unbiased estimates from the data collected. Unfortunately, not all bias can be removed through analysis, and achieving an unbiased (i.e., true and correct) result is dependent upon the underlying study design. There are several primary study designs to discuss from the highest to lowest level of evidence.

Randomized controlled trials. Well-conducted, randomized placebo-controlled trials (RCTs) are the pinnacle of medical evidence because they, at least ideally, provide everything needed to support a causal relationship between an exposure and a disease state while excluding the other three possibilities that can account for an association as described above. First, through randomization of subjects, RCTs achieve what is called the counterfactual ideal by balancing the exposed and unexposed groups for not only the factors we know or suspect as confounders of the relationship between exposure and disease but all the things we do not know about or even suspect may be related to that relationship. This converts confounding from a systematic error (one that does not improve with sample size) to a random error (an error that is minimized by including more subjects in the study). Second, a sufficiently large, randomized study with no or minimal loss to follow-up of the outcome (a possible source of selection bias in RCTs) and well-characterized exposure and outcome measurement (excluding information bias) minimizes the chance that random error or other biases account for the observed association. Finally, because the treatment is assigned by the investigators prior to assessment of the outcome, if the study shows an association the only tenable conclusion is that the exposure results in the change in disease state observed rather than the other way around. However, even RCTs are not infallible: false conclusions can be reached by, for example, a failure to mask subjects or researchers to the exposure, failure to follow an intention to treat analysis, or simply the failure to be “lucky” (since a random process is involved, imbalances of confounders are still possible). In addition, RCTs are not always feasible, e.g., where exposure would potentially expose subjects to unnecessary risk, where there is no anticipated clinical benefit, or where the outcome is so rare that untenably large sample sizes or study durations would be required to detect a significant difference between two groups.

Cohort studies. Next in the hierarchy of study designs are cohort studies. Cohort studies are an observational study involving a group of subjects who are outcome-free at the start of follow-up with a non-randomized exposure distribution (an RCT is a cohort study where the exposure is randomized). When exposure is measured prior to the outcome assessment, as is true of a well-designed cohort study, such a study can potentially substantiate causality (since the exposure must by definition occur before the outcome to have caused the outcome). However, cohort studies are subject to sources of bias that are not relevant in randomized controlled studies. Selection biases can occur not only from differential dropout but also by poor subject selection or a difference in willingness to participate between exposed and unexposed subjects. Incorrect assumptions about the timing of exposure and disease can cause information biases particularly for chronic exposures and diseases where it is possible the disease onset precedes exposure but is subclinical when assessed. Finally, all non-randomized studies are subject to known unmeasured confounders and more importantly to unknown confounders, for which there is no way to adjust the analysis to adequately control for them.

Case-control studies. In a case-control study, the outcome or disease has already occurred, and this group of cases is compared to a group of disease-free “controls.” While a case-control study may simply appear to be a cohort study in reverse, treating a case-control study as a reverse cohort study can lead to some important errors in design and interpretation, the so-called “trohoc fallacy” (trohoc is cohort spelled in reverse).³ Instead of thinking of a case-control study as a comparison between diseased and disease-free subjects, it should still be thought of as a comparison between exposed and unexposed groups. Indeed, the most valid view of a case-control study is as a sampling of cases and a sampling of controls from the cohort study one would like to have done if one could have done the prospective study.

The chief advantage of case-control studies is that they, unlike RCTs and cohort studies, are much easier to apply to rare diseases (and luckily most disease is rare). However, case-control studies also have substantial disadvantages, including many that go beyond those seen in cohort studies. Those disadvantages include: first, case-control studies can only estimate relative differences and not the underlying absolute risks of disease based on exposure. Second, a failure to understand that the only purpose of the control group is to determine the controls’ distribution of exposure can lead to substantial biases if one fails to account for possible selection biases or confounding. And third, because of their design, certain biases are more common, or more commonly differential, in case-control studies, such as recall bias and proxy bias.

Meta-analysis. A meta-analysis typically combines results, such as measures of association, from multiple previously performed studies and allows some evaluation and quantification of the differences between studies. While meta-analyses may carry an aura of greater authority because they combine the results of several other studies, they are subject to all the biases and limitations of their component studies. Combining multiple, poorly designed or inadequately controlled studies does not lead to an improved or more reliable result. Furthermore, the components of meta-analyses frequently use different definitions of exposure and outcome and have different degrees and types of bias. Difference in the designs of the component studies is sometimes referred to as “heterogeneity.” Even a single poorly conducted or biased study can inappropriately influence the overall result of a meta-analysis. This is why the Cochrane Collaboration generally only allows meta-analyses of RCTs. Meta-analyses, especially those composed of observational studies, tend to give results that present a more precise and conclusive picture than the data actually warrant. They offer increased statistical power without addressing any underlying biases in study design. As a result, many meta-analyses do not adequately account for the average bias across studies. When uncertainty is included about sources of bias, confidence intervals will “expand dramatically.”^{2,4}

Other sources of evidence. Other types of evidence include anecdotal human studies, large database analyses, ecological study designs, animal experiments, and mechanistic studies. Although they may be useful for generating hypotheses, none of these study designs allow one to conclude whether exposure causes a particular outcome in humans. As a result, such studies are generally afforded less weight. In recent years, the availability of large claims and electronic medical record databases has led to a great number of studies using them. However, these studies are subject to a variety of additional limitations. For example, even where apparently precise estimates are derived from large databases, these precise estimates are frequently wrong due to unaccounted for biases. In other words, the investigators have likely very precisely estimated an incorrect estimate. Sample size cannot overcome systematic error, i.e., bias by another name, because by definition it is an error that cannot be minimized by larger sample sizes.

Controlling for confounding in epidemiologic research. From a design perspective, known confounders can be dealt with through randomization (i.e., an RCT), restriction (i.e., limiting subjects to all be the same or similar with respect to the known or suspected confounder), or by matching exposed and unexposed subjects by their status with respect to the known or suspected confounder. From an analysis perspective, measured confounders can be “controlled for” via several techniques such as stratification or multivariate modeling, and sensitivity analyses can be used in an attempt to determine the potential effects of unmeasured confounders on the observed associations. In general, observational studies, because of confounding and bias considerations, can only identify associations, not establish causal relationships. Methodologies to perform sensitivity analyses for unknown confounders exist but make a great number of assumptions about the strength and direction of potential unknown confounders. However, even when thoughtfully designed and competently executed,

such analyses may fail to identify causal relationships or may misidentify relationships as causal that randomized trials subsequently demonstrate or debunk conclusively.

CME ANSWERS

- 19. D
- 20. E
- 21. D

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GLP1 MEDICATIONS AS A POSSIBLE RISK FACTOR FOR NAION

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LEARNING OBJECTIVES

1. Describe the important benefits of specific Glucagon-Like Peptide-1 receptor agonist (GLP-1 RA) medications.
2. Summarize the evidence linking GLP-1 RA to non-arteritic ischemic optic neuropathy (NAION).
3. Identify key knowledge gaps in GLP-1 RA medication-related NAION research.

CME QUESTIONS

1. GLP-1 RA have United States Food And Drug Administration and European Medicines Agency approval for all of the following adult indications except:
 - A. Alzheimer's disease
 - B. Chronic weight management
 - C. Glycemic control in type 2 diabetes
 - D. Reduction of major adverse cardiovascular events in type 2 diabetes with established heart disease
2. Which of the following best summarizes the benefit of semaglutide in the reduction of major adverse cardiovascular events (MACEs) based on recent large randomized controlled clinical trials?
 - A. Semaglutide has not demonstrated any significant reduction in MACEs among individuals with type 2 diabetes or obesity.
 - B. Semaglutide significantly reduces the risk of MACEs in adults with established cardiovascular disease or risk factors.
 - C. Semaglutide increases the incidence of MACEs in treated patients compared to placebo.
 - D. Semaglutide reduces MACE in individuals with type 2 diabetes and cardiovascular disease or cardiovascular risk factors, but not overweight/obese individuals with cardiovascular disease.
3. Which of the following best summarizes the potential risk of NAION with GLP-1 RA use?
 - A. GLP-1 RAs are associated with a high risk of NAION, and routine ophthalmologic screening is recommended for all patients using these medications.
 - B. GLP-1 RAs decrease the risk of NAION through improved glycemic control.
 - C. GLP-1 RAs have no reported association with NAION.
 - D. Current evidence suggests a small but possibly increased risk of NAION with GLP-1 RA, particularly semaglutide.

KEY WORDS

1. Glucagon-Like Peptide-1 Receptor Agonist
2. Non-arteritic ischemic optic neuropathy
3. Pharmacovigilance
4. Bias
5. Confounding

SUMMARY

- I. What are GLP-1 receptor agonists?
 - A. Background

1. Incretin concept: refers to the observation that oral glucose provokes a greater insulin response than intravenous glucose, suggesting gut-derived factors stimulate insulin. In the 1980s, researchers identified two key incretin hormones: glucose-dependent insulintropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1).
2. Mechanism of action of GLP-1: GLP-1 is produced by intestinal L-cells in response to food intake. It enhances glucose-dependent insulin secretion, suppresses glucagon release, slows gastric emptying, and promotes satiety among many other things. Endogenous GLP-1 is rapidly degraded in minutes by dipeptidyl peptidase-4 (DPP-4).
3. GLP-1 receptor agonist discovery: In the 1990s, scientists identified a GLP-1-like peptide (exendin-4) in the saliva of the *Heloderma suspectum* lizard (i.e., Gila monster), which showed high affinity for the human GLP-1 receptor and a longer duration of action. Exenatide (synthetic exendin-4) became the first FDA-approved GLP-1 RA in 2005. After exenatide, researchers developed human GLP-1 RA analogs with structural modifications for longer action. Next-generation GLP-1 RA are exemplified by semaglutide and tirzepatide with enhanced receptor engagement and pharmacokinetics.

Table 1. United States Food and Drug Administration (FDA)-Approved Indications for GLP-1RA

Drug (Brand)	Year FDA Approved	Type 2 Diabetes (Adult)	Weight Management	Cardiovascular Risk Reduction
Semaglutide (Ozempic®)	2017	✓		✓
Semaglutide (Wegovy®)	2021		✓	
Semaglutide (Rybelsus®)	2019	✓		
Liraglutide (Victoza®)	2010	✓		✓
Liraglutide (Saxenda®)	2014		✓	
Dulaglutide (Trulicity®)	2014	✓		✓
Exenatide (Byetta®/Bydureon®)	2005/2012†	✓		
Tirzepatide (Mounjaro®)	2022	✓		Awaiting FDA review
Tirzepatide (Zepbound®)	2023		✓	

✓ = FDA-approved indication. Note: European Medicines Agency (EMA) approvals (and year of approval) are similar, except tirzepatide which is only approved for type 2 diabetes.

† Byetta® approved 2005; Bydureon® (once weekly) approved 2012

Tirzepatide's cardiovascular trials have reported positive results, but formal FDA indication is still pending review.

Tirzepatide is a dual GIP/GLP-1 agonist.

- B. Current United States Food & Drug Administration (FDA) indications for GLP-1 RA in adults (**Table 1**)
1. Chronic weight management in adults with obesity (Body Mass Index [BMI] ≥ 30) or overweight (BMI ≥ 27 with weight-related comorbidity). Weight-related conditions include hypertension, type 2 diabetes (T2D), dyslipidemia, obstructive sleep apnea, etc.
 2. Glycemic control in T2D: Indicated as adjuncts to diet and exercise to improve glycemic control in adults with T2D.
 3. Cardiovascular disease reduction in overweight or obese adults: Approved for reducing major adverse cardiovascular events (MACE: cardiovascular death, non-fatal myocardial infarction, non-fatal stroke) in adults with T2DM and established CVD
 4. PENDING: Chronic kidney disease (CKD) progression in adults with T2D
 - a. Semaglutide: Recently demonstrated to slow CKD progression in adults with T2DM (FLOW trial, 2024); full FDA indication pending.
 5. Investigational and emerging: Alzheimer's disease, substance use disorder/addiction, steatotic liver disease, polycystic ovarian syndrome, osteoarthritis, inflammatory conditions.¹
- C. Medication pipeline
1. Oral drugs and small molecules

- Combination drugs: In addition to single agents and dual agents, other combination drugs (e.g., combined with glucagon, amylin) are in development and trials (e.g., triple agonist, retatrutide).

D. Major side effects

- Very Common/Common: GI issues, reduced appetite, hypoglycemia (higher risk if combined with insulin or sulfonylurea), site reactions
- Less Common (<1%): cholelithiasis/cholecystitis
- Rare/Very Rare (<0.1%): pancreatitis, allergic reactions (rash, angioedema, anaphylaxis)

II. What do we know about the major benefits of GLP-1 RA (focused on semaglutide)?

- A. Clinical trial data (**Table 2**): Semaglutide significantly decreased risk of major cardiovascular events (MACE composite outcome including non-fatal MI, non-fatal stroke, and cardiovascular death) in both obese/overweight participants (SELECT Trial²) and in participants with T2D mellitus (SUSTAIN-6,³ PIONEER-6 Trial⁴) with CV disease or risk factors

Table 2. Major adverse cardiac events (MACE)* in semaglutide clinical trials

Trial and key criteria	Treatment arms and median follow-up	Semaglutide MACE, % (n)	Placebo MACE, % (n)	Hazard Ratio (95% CI)	ARR (%)	RRR (%)	MACE prevented per 100,000 treated	NNT; Annualized NNT
SELECT² BMI≥27 & CV disease	Sema=8803 Placebo=8801 ~3.3 years	6.5% (569)	8.0% (701)	0.80 (0.72–0.90)	1.5	18.8	1500	67; 207
SUSTAIN-6³ T2D HbA1c≥7% & CV disease or CKD or CV risk factors	Sema=1,648 Placebo=1,649 ~2.1 years	6.6% (108)	8.9% (146)	0.74 (0.58–0.95)	2.3	25.8	2300	44; 91
PIONEER-6⁴ T2D & CV disease if >50 or CV risk factors if >60	Sema=1591 Placebo=1592 ~1.3 years	3.8% (61)	4.8% (76)	0.79 (0.57–1.11)	1.0	20.8	1000	10; 131

*MACE was the primary outcome for each trial. **Sema**, semaglutide. **ARR**, Absolute risk reduction. **RRR**, Relative Risk Reduction. **NNT**, Number needed to treat. **CV**, cardiovascular. **T2D**, type 2 diabetes. **CKD**, chronic kidney disease.

B. Key Secondary Analyses

- Across SELECT, SUSTAIN-6 and PIONEER-6, the published subgroup and pooled/post-hoc analyses to date *generally* show consistent semaglutide effects across most clinically relevant subgroups (age, sex, BMI, baseline therapies, eGFR strata)
- In a prespecified analysis of the SELECT trial: cardioprotective effects of semaglutide were independent of baseline weight and weight loss and had only a small association with waist circumference, suggesting benefit beyond weight reduction (i.e., it may have CV disease modifying effects)⁵
- In 2 post hoc pooled analysis of the SUSTAIN-6 and PIONEER-6:
 - No heterogeneity of treatment effect observed in MACE reduction in those with HgbA_{1c} <8% vs. ≥ 8%.⁶
 - Reduced incidence of any stroke (hazard ratio [HR], 0.68 [95% CI, 0.46–1.00]; P=0.048) was driven by significant reductions in risk of small-vessel occlusion (0.3 versus 0.7 events/100 PYO; HR 0.51 [95% CI, 0.29–0.89]; P=0.017). The risk was lower irrespective of prior stroke.⁷

C. Important practice guidelines including GLP-1 RA

- Stroke (American Heart Association/American Stroke Association):

- a. Primary Prevention 2024⁸: In patients with diabetes and high cardiovascular risk or established CVD and hemoglobin A1c $\geq 7\%$, treatment with a glucagon-like protein-1 (GLP-1) receptor agonist is effective to reduce the risk of stroke (Class 1 recommendation, level A evidence)
- b. Secondary Prevention 2021⁹: In stroke patients with diabetes, a glucagon-like protein 1 agonist or sodium glucose co-transporter 2 (SGLT2) inhibitor can be added to metformin
2. Chronic Coronary Disease Management 2023 (American Heart Association Guideline)¹⁰:
 - a. In patients with CCD who have T2D, the use of either an SGLT2 inhibitor or a GLP-1 receptor agonist with proven cardiovascular benefit is recommended to reduce the risk of MACE (Class 1, level A).
 - b. In patients with CCD and T2D, addition of a GLP-1 receptor agonist at US prices is projected to be of high value compared with standard of care (level B, non-randomized)
 - c. For patients with CCD and overweight or obesity in whom pharmacologic therapy is warranted for further weight reduction, a GLP-1 receptor agonist can be beneficial (Class 2a, level B)
3. Diabetes management (American Diabetes Association 2025)¹¹: In adults with T2D and
 - a. In people with diabetes and overweight or obesity, the preferred pharmacotherapy should be a GLP-1 RA or dual glucose-dependent insulinotropic polypeptide and glucagon-like peptide 1 receptor agonist with greater weight loss efficacy (i.e., semaglutide or tirzepatide), especially considering their added weight-independent benefits (e.g., glycemic and cardiometabolic) (level B)
 - b. Established or high risk of atherosclerotic cardiovascular disease, the treatment plan should include medications with demonstrated benefits to reduce cardiovascular events (e.g., glucagon-like peptide 1 receptor agonist [GLP-1 RA] (irrespective of A1C) (level A)
 - c. symptomatic heart failure with preserved ejection fraction (HFpEF) and obesity, a GLP-1 RA is recommended (irrespective of A1C) (level A)
 - d. CKD (with confirmed estimated glomerular filtration rate [eGFR] 20–60 mL/min/1.73 m² and/or albuminuria), an SGLT2 inhibitor or GLP-1 RA with demonstrated benefit in this population should be used for both glycemic management (irrespective of A1C) and for slowing progression of CKD and reduction in cardiovascular events. (level A)
 - e. advanced CKD (eGFR <30 mL/min/1.73 m²), a GLP-1 RA is preferred for glycemic management due to lower risk of hypoglycemia and for cardiovascular event reduction. (level B)
 - f. metabolic dysfunction–associated steatotic liver disease (MASLD), and overweight or obesity, consider using a GLP-1 RA or a GIP and GLP-1 RA (level B)
- D. Utilization of GLP 1 RA
 1. Diabetes: 26.5% used a GLP-1 RA in 2024 (Centers for Disease Control, Data Brief No. 537, August 2025)
 2. Obesity/overweight: 11.8% in 2025 (RAND research report, August 2025)

III. What do we know about the risk of NAION with GLP-1 RA?

- A. Baseline population risk of NAION compared to MACEs in people over 50
 1. NAION: Annual incidence rates in adults over 50 years old range from ~2.5 to 12 per 100,000 individuals globally. In the most recent US data from Foster *et al.* (Rochester Epidemiology Project) overall age and sex adjusted incidence was 3.89 per 100,000 individuals (95% confidence interval [CI]: 3.14-4.65).¹² The incidence was 7.73 (CI: 6.24-9.22) in patients aged 40 years or older and 10.19 (CI: 8.15-12.23) in patients aged 50 years or older.

2. MACEs: Annual incidence rates among adults over 50 with T2D are approximately 2000 to 2500 per 100,000 per year) and those with obesity are about 600 to 2000 per 100,000 per year. These rates are consistently lowest in parts of Asia and highest in the USA and Europe.
3. Summary: MACE incidence is ~200–500 time higher than NAION in adults over 50.

B. Overview of the important studies (as of December 2025)

1. Background: Hathaway *et al.*¹³ was the first study to raise a safety signal about semaglutide and NAION risk leading to additional retrospective observational studies, pharmacovigilance studies, and meta-analyses of clinical trial data. Notable studies are listed in **Table 3**.
2. Observational study results and notable limitations
 - a. Results of individual studies have been conflicting. However, a recent meta-analysis of observational studies to date by Goldenberg *et al.* indicated an increased hazard of NAION particularly among those individuals using semaglutide vs control (HR 1.60 [1.12, 2.31]) but there was a significant amount of statistical heterogeneity and low certainty of evidence.¹⁴
 - b. Notable limitations
 - i. Misclassification of the outcome, exposure, and covariates:
 - How is the outcome defined (and covariates)? All studies to date, except Hathaway *et al.*, use ischemic optic neuropathy ICD10 codes alone to define NAION leading to possible misclassification bias. Multiple studies attempted to address this by requiring specific numbers of codes (e.g., Cai *et al.*) leading to differences in their results, excluding participants with specific diagnoses (e.g., giant cell arteritis and optic neuritis, Hsu *et al.*¹⁵), or requiring at least 1 code from an ophthalmologist or neurologist at some point in time (i.e., a proxy of access to care, Abbass *et al.*¹⁶). Just as the presence of a code does not mean that a condition is present, the absence of a code does not mean that the condition of interest, whether outcome or covariate, is not present (e.g., obesity is poorly coded in EHR and administrative data).
 - How is exposure defined (and covariates)? Most studies to date rely on prescribing data and we cannot know that individuals actually filled the prescription *and* took the drug *and/or* for what period of time. Dose is also often unknown.
 - ii. Unmeasured confounding/residual confounding: Despite attempts to control confounders and confounding by indication with matching strategies (e.g., propensity score matching), important risk factors, such as cup-to-disc, are missing across the current studies, which may impact baseline risk. Other residual confounders, such as severity and duration of diabetes, are also missing across numerous studies. Additionally, much remains unknown about the risk of NAION and how risk factors interact within a single individual modifying their baseline risk. We cannot adjust for unmeasured factors.
 - iii. Selection bias and generalizability: This was the primary methodological concern with Hathaway *et al.*, which was conducted at a single center. However, this can also be problematic in studies using multi-center US data (or even US predominant data as in TriNetX) which only captures events in people that actually access health care, have insurance (note: people also repeatedly enter and leave plans), and/or have access to eye care providers. Only a two studies have used nationally representative data to date (Danish and Norwegian Registries) which demonstrated an increased hazard of NAION in individuals with T2D and in pooled analyses of both Danish and Norwegian data.^{17,18} However, the Danish data is limited to people admitted to hospitals, which the authors report is common practice, but the Norwegian data also includes outpatient visits.
3. Pharmacovigilance studies
 - a. Multiple studies to date use FDA Adverse Event Reporting System (FAERS) data and global WHO Vigibase data. All studies have reported a disproportionality signal suggesting more NAION in

Table 3.
Notable
studies of
semaglutide
and NAION
risk to date.



individuals treated with semaglutide.^{19,20} Notable limitations: FAERS data are voluntarily reported data and diagnoses cannot be confirmed.

- b. An additional study using the FDA Sentinel program (data: commercial insurance, Medicare with 65 million unique patients) compared new users of semaglutide to new users of sitagliptin (T2D only). The primary pharmacovigilance analysis observed 17 and 13 new cases of NAION (code H47.01*) in the ambulatory care setting among semaglutide and sitagliptin users, respectively within the first 6 months of use.^{21,22} The high dimension propensity score sensitivity analysis yielded 15 and 12 cases, respectively. The incidence among semaglutide users: 12.7 (95% CI: 7.9-20.4) cases/100,000 persons vs. sitagliptin users: 9.7 (95%CI: 5.6-21.8) cases/100,000 persons.

4. Clinical trials

- a. Meta-analyses have assessed NAION events within clinical trials for GLP1-RA and arrived at different conclusions.^{23,24} Note, however, that the trial sequential analysis in Natividade *et al* indicated that the included number of trials (5) was insufficient to definitively determine whether semaglutide affects the risk of NAION, mainly due to its very low incidence. Also note that Silverii *et al* study included a study with liraglutide in which 3 events occurred in the control group and 1 in the active treatment arm.
- b. Notable limitations: NAION was not a pre-specified adverse event and could have been overlooked. NAION was not an adjudicated outcome in most of the trials.

C. Plausible mechanism(s) and timing

- 1. Exact mechanisms are unknown. Most discussed mechanisms involve changes in glycemia in T2D and obesity. This may have to do with the rate of change and/or changes in the vasculature. Direct tissue toxicity unlikely.
- 2. GLP-1 RA have been reported as a possible risk factor in other conditions
 - a. Eye-related example: transient worsening of diabetic retinopathy during tight glycemic control has been known since the 1980s. The exact mechanism is unknown, but thought to be related to rapid glycemic, vascular, and cardiometabolic changes. A meta-analysis of 23 T2D RCTs indicated no overall increased risk (RR 1.14 [0.98-1.33]), but a subgroup analysis of semaglutide showed higher risk compared to placebo (RR 1.24 [1.03-1.50]).²⁵ No increased risk in Natividade *et al* (OR 1.04 [0.92-1.17]).²⁴
 - b. Non-eye related example: Increased odds of diabetic lumbosacral neuropathies and common fibular neuropathy in a retrospective case control study of individuals with T2D using any GLP-1 RA (lumbosacral neuropathies: OR 1.5 [1.2-1.9; p<0.001] and fibular neuropathy: OR 1.3 [1.0-1.5]; p=0.018).²⁶
- 3. Timing unclear. Hathaway *et al* noted a median time of 14 months, but other studies have found an increased risk out to approximately 3 years.

D. Putting it all together under the assumption that there is an increased risk . . .

- 1. Incidence rates: based on meta-analysis by Goldenberg *et al*, the incidence rates of NAION in the non-GLP-1 RA cohorts ranged from 4.0 to 13.7 per 100,000 person-years. If we apply the HR = 1.60 observed, this translates to an estimated absolute increased risk of NAION between 6.4 and 21.9 per 100,000 person-years in semaglutide treated individuals.
- 2. Based on definitions used by the European Medicines Agency (FDA follows similar cut-offs, but no published definitions), these are still considered *very rare events* (i.e., <0.01% incidence rate).
- 3. Comparing the benefits and risks
 - a. See Table 1 regarding MACEs prevented with semaglutide and annualized NNT ~ 90-200
 - b. Assuming a baseline risk of NAION of 10 per 100,000 and a HR 1.6, you would need to treat over 16,000 people for one additional person to develop NAION (i.e., number needed to harm). With a HR 2, NNT~10,000

IV. What are the major gaps in our knowledge about NAION risk with GLP-1 RA?

- A. Does semaglutide (or other GLP-1 RA) cause NAION or clearly increase risk of NAION?
- B. If so,
 - a. by what mechanism(s)?
 - b. over what period of time?
 - c. which risk factors are important?
 - d. are there ways to mitigate/modify the risk?
 - e. is risk different globally or in specific populations?
 - f. is the risk of NAION in the setting of GLP-1 RA different among individuals that have experienced a single event whether or not they were using a GLP-1RA?
 - g. is there an increased risk of a second NAION event among individuals that have already experienced a single event in one or both eyes?

V. Conclusion

The existing studies indicate a possible small increased risk of NAION in patients taking semaglutide, but the overall risk remains very low, is yet to be confirmed, and causation has not been shown. The implications for other GLP-1 RAs have not been adequately studied; therefore, whether the possible increased risk found for semaglutide extends to other drugs in this class remains to be determined.

CME ANSWERS

1. A
2. B
3. D

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NANOS 2026 SESSION: NEW EYES ON NAION: REVISITING RISK IN A CHANGING MEDICAL LANDSCAPE: SYSTEMIC RISK FACTORS

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LEARNING OBJECTIVES

The attendee will be able to:

1. List three commonly cited systemic risk factors for the development of NAION
2. Describe the proposed pathogenetic mechanism for increased risk of NAION related to obstructive sleep apnea
3. Summarize the Quark207 study conclusions regarding the prevalence of systemic risk factors in patients with NAION

CME QUESTIONS

1. Which of the following conditions has been reported to increase the risk of NAION?
 - a. Thrombocytopenia
 - b. Diabetes mellitus
 - c. Fibromuscular dysplasia
 - d. Atrial fibrillation
2. Obstructive sleep apnea is proposed to increase the risk of NAION by which of the following mechanisms?
 - a. Obesity-related insulin resistance
 - b. Periodic hypoxemia
 - c. Chronic hypoxemia
 - d. Nocturnal hypotension
3. The Quark207 study data confirmed which of the following risk factors to be more prevalent in patients with NAION than in controls?
 - a. Hypertension
 - b. Diabetes
 - c. None
 - d. Smoking

KEYWORDS

NAION; systemic risk factors; diabetes, hypertension; hyperlipidemia; obstructive sleep apnea.

INTRODUCTION

The pathogenetic mechanisms behind the development of optic disc ischemia in NAION are unclear¹. Aside from a “crowded” optic disc structure, characterized by small diameter, and small optic cup (which will be discussed elsewhere), vascular insufficiency of the optic nerve head is most frequently attributed to

1. Compromise of the microcirculation by various abnormalities within the optic disc, including arteriosclerosis, thrombosis, embolization, vasospasm, and failure of autoregulation; and
2. Reduced perfusion pressure.

A number of systemic factors which might contribute to these components have been implicated for the risk of development of NAION. The most commonly listed are blood pressure abnormalities including both hypertension and hypotension, diabetes, hyperlipidemia, obstructive sleep apnea (OSA), smoking, and hypercoagulable state. The literature is difficult to analyze due to the varying methodologies utilized and the lack of high quality epidemiologic data.

THE ROLE OF BLOOD PRESSURE

Both hypotension and hypertension have been implicated in the development of NAION.

Acute systemic hypotension, blood loss, and anemia may produce optic nerve ischemia^{2,3}. The most commonly reported causes of blood loss associated with ION (anterior or posterior ION) are spontaneous gastrointestinal or uterine bleeding and surgically induced hemorrhage, such as cardiac bypass or lumbar spine procedures^{4,6}. The ischemic event may be delayed up to weeks following the blood loss. Hayreh² postulated that this may be caused by vasoconstriction in the posterior ciliary artery system secondary to activation of the renin-angiotensin pathway as a late response to blood loss. These uncommon cases with specific acute inciting events do not fit the common clinical scenario for NAION, but the development of optic nerve ischemia in the face of hypotensive events does support reduced perfusion pressure as a pathogenetic component in NAION.

Systemic hypotension has been suggested as a factor in the development of NAION in patients with chronic renal failure (CRF) and dialysis^{7,8}. The hypotension may be acute, temporally associated with the dialysis procedure, or chronic. Most patients also are chronically anemic. The accelerated diffuse vasculopathy that occurs with CRF may predispose to the development of NAION, as may previous chronic hypertension, with possible arteriosclerosis and impaired autoregulation of the optic disc vascular supply. This scenario is the cause for a high percentage of cases of NAION in patients under the age of 30⁸. The term “uremic optic neuropathy” has been applied to cases in this category, but the role of uremia is unclear^{9,10}.

Nocturnal systemic hypotension has been proposed to play a role in the development of NAION. The relative hypotension that normally occurs with sleep has been postulated to chronically compromise optic disc circulation, particularly in patients with an exaggerated nocturnal “dip” in pressure or in patients, such as those with systemic hypertension, in whom optic disc circulation autoregulatory mechanisms are impaired. This effect could be worsened with aggressive antihypertensive therapy, particularly if administered at night, by exacerbating the nocturnal pressure drop. The data related to this theory are controversial, with Hayreh’s large study (without controls)¹¹ supporting it and Landau’s study (with controls)¹² refuting it. The conflicting data from these two groups leave the role of nocturnal hypotension in NAION unresolved. The possible accentuation of nocturnal hypotension by nighttime use of antihypertension medications has prompted consideration of dosing other than at bedtime. However, studies in recent years have suggested a cardiovascular benefit to the nocturnal dip in reducing the risk of stroke, and recommendations against reducing this dip have been proposed¹³.

Systemic hypertension has been documented to increase risk of arteriolar sclerosis on the basis of lipohyalinosis and impaired autoregulation. The risk of stroke and heart disease is well documented. The link of hypertension to NAION has been based on this information and the fact that a large percentage of NAION patients suffer hypertension. However, whether this is increased over the population in general has not been clearly established.

VASCULOPATHIC RISK FACTORS

NAION has been reported in association with a number of conditions that may predispose to decreased optic nerve head perfusion via microvascular insufficiency. Multiple cross-sectional case series in past decades have estimated the prevalence of such systemic diseases in patients with NAION^{14,22}. Systemic hypertension was documented in 34–57% of patients (47% in the IONDT)¹⁷. Diabetes was reported in 5–34% (24% in the IONDT)¹⁷. Hypercholesterolemia was reported in up to 49–69%^{18,19,22}, smoking in 23–51%^{8,20}. An uncontrolled study by Chung et al²¹ concluded that smoking was a significant risk factor on the basis that smokers developed NAION at a significantly younger age than nonsmokers. In many of the studies, however, comparisons with either population studies or with control groups have been limited, resulting in strikingly disparate conclusions regarding significance of the findings. In 2 major studies, hypertension was considered significantly more frequent in NAION than in non-NAION groups only in the subpopulation aged 45–64^{14,16}; however, in Hayreh’s large study¹⁸, it was more frequent in all age groups. Diabetes, in contrast, was consistently more prevalent in NAION than non-NAION patients across all ages¹⁹. Hyperlipidemia was reported as a significantly associated

risk in 2 studies^{20,22}, but not in others¹⁹. Similarly, smoking was reported as a significant factor in Hayreh's series¹⁸ but not in others^{19,20}.

In 2016, Cestari, et al²³ analyzed a large US managed care network database for associations between factors including vasculopathic conditions and the development of NAION. Among those commonly studied as above, significant associations were found only in hypertension (HR = 1.62) and hypercoagulable state (HR = 2.46), with diabetes only demonstrating a significant association in patients with documented end-organ disease (HR = 1.27). In 2020, the Mayo group analyzed 104 cases of incident NAION versus 104 controls from the Rochester database, with baseline figures for the most commonly reported risk factors similar to previous studies (hypertension 79.8%, diabetes 39.4%, hyperlipidemia 74.0%, OSA 23.1%) but not statistically significantly different from controls²⁴.

In 2021, a meta-analysis of 49 original studies of risk factors in NAION reported significant associations with male gender, hypertension, diabetes, hyperlipidemia, coronary heart disease, obstructive sleep apnea, factor V Leiden, and medication history of cardiovascular drugs, but not with smoking²⁵. The analysis of these prior studies incorporated some of the limitations of the original studies but did corroborate the conclusions of the large body of prior data regarding vasculopathic risk factors.

In 2024, in contrast, the Quark207 Study, a large-scale clinical trial of a neuroprotective agent for treatment of NAION (the largest prospectively studied cohort to date) revealed data markedly divergent from prior studies^{26,27}. Hypertension was present in 30.3% of patients, diabetes in 15.1%, hyperlipidemia in 15.2%, obstructive sleep apnea in 10.1%, smoking in 10.2%; 10% had none of the commonly associated risk factors present. None of the previously reported vasculopathic risk factors for NAION were significantly more frequent in NAION patients than in the general population. Further, the prevalence levels were substantially lower than the large majority of prior studies. The reasons for these disparities are as yet unexplained. Interestingly, obesity was frequent at 35.6% and overweight at 41.7%, a factor not previously studied in depth.

OBSTRUCTIVE SLEEP APNEA (OSA)

OSA is associated with increased risk of hypertension, stroke, and heart disease, possibly related to chronic hypoxia occurring with repeated apneic episodes and stimulation of C-reactive protein (CRP), which is increasingly implicated as a predictor for cardiovascular disease²⁸. OSA has also been linked to elevation of intracranial pressure and chronic disc edema related to hypoxemia and hypercapnia²⁹.

In 2002, Mojon et al³⁰ reported evidence of OSA in 71% of 17 consecutively seen NAION patients versus 18% of 17 age- and sex-matched controls with similar vasculopathic risk factors. Bilgin et al³¹ reported similar findings, with OSA in 56% of 27 NAION patients versus 22% of 27 age and sex-match controls with similar vasculopathic risk factors. Palombi et al³² studied 27 consecutive, newly diagnosed NAION patients for evidence of OSA, finding 24 of 27 (89%) positive on polysomnography, with a risk ratio comparison to prior general population data for prevalence of OSA of 4.9. The lack of appropriate control groups and other methodological variances, including criteria for OSA diagnosis, limit the usefulness of this and other early studies³³⁻³⁴, including the study of Bandi et al, with OSA in 95% of 19 NAION patients versus 41.9% of 31 controls³⁵.

Viewed from a different perspective, the risk of NAION developing in patients with OSA is also increased. Yang, et al in 2019³⁶ utilized a Korean National Health database to assess risk of NAION development in newly diagnosed OSA patients, finding a 10-year incidence probability of 0.92% in OSA versus 0.44% in non-OSA ($p = 0.002$).

Risk of fellow eye NAION involvement in patients with OSA has been studied by Aptel et al³⁷ who found development by 3 years in 15.4% of 52 patients with OSA versus 9.5% of 21 patients without OSA ($p = 0.04$). Behbehani et al³⁸ suggested a lack of benefit for continuous positive airway pressure (CPAP) therapy in reducing risk of NAION, reporting its development in 3 patients while on chronic CPAP therapy for OSA. In contrast, Aptel et al³⁷ found that nonadherence to CPAP in patients with severe OSA significantly increased 2nd eye involvement risk (HR = 5.54). Chang et al³⁹ found

similar results in a study of 119 patients, with noncompliance with CPAP therapy in moderate-to-severe OSA associated with increased risk (HR = 4.50) for 2nd eye involvement.

HYPERCOAGULABLE STATE

NAION in most cases is not felt to be a thromboembolic disease. While venous congestion has been proposed as a pathogenetic feature of NAION⁴⁰, there is no clear clinical or histologic evidence for the role of thrombus in the disorder. However, a hypercoagulable state, with its many contributing components, has been proposed as a risk factor in younger (< 50 years) patients, based on its association with premature ischemic events.

Elevated plasma homocysteine levels, whether or not associated with C677T methylenetetrahydrofolate reductase (MTHFR) polymorphism, have been shown to be atherogenic and thrombogenic, based on the damaging effect on endothelial structures. They have been associated with an increased risk of ischemic events (peripheral vascular disease, stroke, myocardial infarction) in patients younger than 50⁴¹. Hyperhomocysteinemia is an attractive therapeutic study target, as blood levels are readily reduced with folate and B-vitamin supplementation, although the benefits for treatment have been limited in multiple clinical trials⁴². The relation of hyperhomocysteinemia to NAION remains unclear. Case series are small, with conflicting conclusions. Only one series studied patients under 50 years: Kawasaki et al⁴³ found 17% of 12 patients under 50 years with NAION had hyperhomocysteinemia. Biousse et al⁴⁴ found 0 of 14 NAION patients with hyperhomocysteinemia, even though the MTHFR mutation was present in 5. On the other hand, two controlled studies suggested an association. Pianka et al⁴⁵ found 45% of 40 NAION patients with hyperhomocysteinemia versus 9.8% of 81 controls. Weger et al⁴⁶ found 23.7% of 59 NAION patients with hyperhomocysteinemia versus 5% of controls.

In addition to interest in hyperhomocysteinemia, consideration has been given to a number of additional prothrombotic risk factors, with mixed results. A study by Salomon et al⁴⁷ has not confirmed an association between NAION and multiple prothrombotic risk factors, including lupus anticoagulants, anticardiolipin antibodies, prothrombotic polymorphisms (factor V Leiden), and deficiencies of protein C and S and antithrombin III. The same group, however⁴⁸, found a statistically significant association with the single copy of the VNTR B allele of the GPIIb gene in NAION versus controls; second eye involvement was more frequent and earlier in onset in those with the polymorphism. The clinical significance of this finding remains unclear, although a second report in 2019 described a 52 year old man with sequential bilateral NAION who had both copies of VNTR B alleles of the GPIIb gene⁴⁹.

These issues for hypercoagulability and NAION are summarized clearly in a 2019 review in the Journal of Neuro-Ophthalmology⁵⁰.

SUMMARY AND RECOMMENDATIONS

NAION occurs in a population commonly afflicted with one or more systemic risk factors for cardiovascular disease. A consensus has not been reached as to whether they are present with a higher frequency in NAION patients than in population samples and are causative for the disorder; the specific pathogenetic mechanism for NAION remains unclear. This does not detract from the value of screening for these systemic disorders in NAION patients, as this may be the stimulus for detection of significant medical conditions requiring treatment. In NAION patients under age 50 or with an atypical presentation, such as prior history of thrombotic disease, screening for hypercoagulability may be considered.

CME ANSWERS

1. b
2. c
3. c

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ANATOMICAL RISK FACTORS FOR NAION

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LEARNING OBJECTIVES

The attendee will be able to:

1. Appreciate the importance of having an anatomical risk factor for NAION in a clinical setting
2. Know the approach to assess the optic nerve head anatomy via a dense optic nerve head OCT scan
3. Know what constitutes a disc-at-risk for NAION
4. Know the importance of optic disc drusen for the risk of NAION
5. Know the importance of vitreopapillary traction for the risk of NAION

CME Questions

1. Which of the following is true?
 - a. NAION sometimes occur in completely healthy young adults
 - b. Optic disc drusen are rarely seen together with NAION
 - c. Vitreopapillary traction is the main cause of NAION
 - d. Patients with glaucoma are at risk of NAION
2. Which of the following is true?
 - a. Small optic disc drusen are unlikely to cause NAION
 - b. Large optic disc drusen are unlikely to cause NAION
 - c. Optic disc drusen associated NAION is most common in deep optic disc drusen, irrespective of drusen size
 - d. Optic disc drusen associated NAION is most common in superficial optic disc drusen, irrespective of drusen size
3. Which of the following is true?
 - a. NAION in an anatomically normal optic disc is a rare occurrence
 - b. A PHOMS is sometimes seen in NAION and is probably a sign of axoplasmic stasis
 - c. Bruch's membrane opening is a well-established surrogate marker of the scleral canal
 - d. The diameter of Bruch's membrane opening is usually smaller in NAION eyes compared to normal eyes
 - e. All of the above

KEYWORDS

1. Nonarteritic anterior ischemic optic neuropathy
2. Optical coherence tomography
3. Anatomical predisposition for NAION
4. Axonal crowding

CME Answers

1. a
2. c
3. e

PROPOSED OUTLINE (10 minutes total)

1. What constitutes a disc-at-risk for NAION?
 - a. Disc-at-risk assessed using fundus photo

- b. Disc-at-risk assessed using OCT
2. Use of the dense optic nerve head OCT scan in the assessment of NAION
3. The relative role and importance of optic disc drusen and vitreopapillary traction for the occurrence of NAION
4. Incipient NAION – what is it?

HIGHLIGHTS

Nonarteritic anterior ischemic optic neuropathy (NAION) is the most frequent cause of acute optic neuropathy in individuals over 50 years of age, with an estimated annual incidence of 2.3-10.2 cases per 100,000 people [1, 2]. However, in contrast to arteritic AION (AAION), NAION is not seen exclusively in older individuals and can occur at any age. Clinically, NAION is characterized by the abrupt onset of typically unilateral, painless visual loss, varying in severity from mild to profound, disc edema and an afferent pupillary defect [3, 4].

The prevailing model of NAION pathogenesis is a multifactorial process involving both local anatomical susceptibilities of the optic nerve head and systemic vascular risk factors. Short posterior ciliary artery hypoperfusion results in microvascular ischemia followed by axoplasmic stasis within the restricted confines of the anterior optic nerve head, ultimately producing a compartment syndrome [5, 6].

The ‘disc at risk’

In the ophthalmic literature, the term ‘disc at risk’ stems from landmark studies of optic disc anatomy in ischemic optic neuropathy from the 1980s and onwards, mainly from Dr. Hayreh and colleagues. It derives conceptually from work consistently showing that a small, crowded optic disc with a minimal or absent cup – identified on funduscopy examination – confers an increased susceptibility to NAION [7, 8]. Although a small or absent cup has traditionally been regarded as essentially synonymous with a ‘disc at risk’, advances in high-resolution optical coherence tomography (OCT) of the optic nerve head have refined this concept. Modern OCT scanning, especially involving enhanced depth imaging (EDI-OCT) has provided new insights into the structural features that truly define a ‘disc at risk’ and underlie an increased susceptibility to NAION.

Anatomical points of interest revealed using OCT

The use of optic nerve head OCT has opened up for a clearer identification, phenotyping and sometimes even quantification of the constituents of what used to be the black box of anatomical NAION risk factors. Individuals with a funduscopy disc at risk, indicative of axonal crowding, will on OCT of the optic nerve head often display a peripapillary hyperreflective ovoid mass-like structure (PHOMS). An additional anatomical point of interest is the Bruch’s membrane opening (BMO), signifying the anatomical edge of the optic nerve head, and thus the true clinical optic disc margin on OCT, as well as the inner aspect of the scleral canal opening.

Peripapillary hyperreflective ovoid mass-like structure (PHOMS)

A PHOMS is the OCT-specific equivalent of the peripapillary axonal distension (PAD) often seen in histologic specimens from patients with axoplasmic stasis in the optic nerve head [9-11]. It is thus seen in optic disc edema from whatever reason, in optic disc drusen (ODD), and in patients with anomalous, often tilted optic discs [12]. In young (<50 years) individuals with NAION, a PHOMS has been observed in the NAION eye in more than 50% of cases [13, 14]. The prevalence of PHOMS in fellow eyes in patients with NAION has not been specifically reported, but it is the clear clinical impression of this author that it is elevated compared to the background population.

Bruch’s membrane opening (BMO) diameter

The literature on the diameter of BMO in NAION patients is ambiguous. An early study using fundus photo-based, morphometric analysis of the optic disc size, showed that NAION occurred preferentially in eyes with small optic disc diameter and small cup/disc ratio, but that there was no significant difference between affected eyes and fellow, normal eyes in patients with unilateral NAION [15]. An OCT-based study including 23 NAION eyes, 17 fellow unaffected eyes, and 23 age-matched control eyes, showed no difference in BMO diameter between the three groups [16]. A study by

Martín-Moro et al., comparing 40 patients with NAION and 120 controls, integrated the BMO diameter in a so-called crowding index (CI) defined as the retinal nerve fiber layer thickness divided by the Bruch's membrane opening area [17]. The authors of the study found that the CI was similar in NAION patients and controls.

There are indications, that NAION under specific circumstances may be associated with smaller BMO diameters. In a study comparing 34 patients with ODD-associated NAION (ODD-AION) to 34 NAION patients without ODD, ODD-AION patients had a significantly smaller BMO diameter compared with eyes with NAION without ODD [18]. A recent case series of 4 NAION patients who were all treated with semaglutide showed an unusually small (< 1.4 mm) BMO diameter in the affected eye in three out of the four patients [19]. It remains to be established whether a small BMO diameter in itself is an independent risk factor for acquiring NAION.

Specific anatomical risk factors for NAION

Optic disc drusen

Retrospective studies in NAION patients below the age of 50 years using EDI-OCT scanning of the optic nerve head have documented ODD as an independent anatomical risk factor, with a prevalence of ODD of more than 50% [13, 20] compared to 2% in the background population [21]. It is conceivable that ODD play a role in the development of NAION by further occupying space within an already narrow 'disc at risk', thereby increasing the vulnerability of the optic nerve head to a compartment syndrome.

One study comparing ODD-AION patients to NAION patients without ODD, found ODD-AION patients to be significantly younger at the time of diagnosis and with fewer vascular risk factors [18]. In patients with ODD-AION, the ODD were predominantly (82% of cases) deeply located, i.e. below BMO, while the size of the ODD was found to be unimportant (52% large, 48% small) [18].

Vitreopapillary traction

The anatomical apposition and adherence of the posterior vitreous body with the optic disc has led to a theory of a role of vitreous separation or traction in the pathogenesis of NAION. Some studies have argued *for* such a role [22, 23] while others have argued *against* [24, 25]. Recently, a study comparing NAION patients around the age of 64 with healthy age, sex, and refraction-matched non-NAION patients with and without optic disc crowding, found a higher rate of focal vitreopapillary attachments on crowded discs than on noncrowded discs, and a closer relationship between these attachments and optic nerve vessels in eyes with NAION compared to eyes without [26]. It was speculated, that such attachments could lead to the transmission of strong mechanical, tractional forces by a synergetic vitreous gel, ultimately resulting in NAION [26]. Further studies using imaging of the vitreoretinal interface in crowded optic discs may provide greater insight into the significance of this finding for the pathogenesis of NAION. However, this hypothesis does not account for the occurrence of NAION in younger patients who show no evidence of vitreous syneresis.

Clinical and subclinical axoplasmic stasis

From a clinical standpoint it is well established, that papilledema in itself poses a risk of superimposed NAION due to the axonal crowding caused by the axoplasmic stasis. In fulminant cases of idiopathic intracranial hypertension (IIH), where the risk of visual loss is imminent, it can be hard to differentiate vision loss from the IIH from vision loss from superimposed NAION. In these cases, one can benefit from magnetic resonance imaging (MRI), which will often show diffusion weighted imaging (DWI) restriction in the optic nerve as a result of the infarction [27].

It is conceivable, that axoplasmic stasis does not need to be symptomatic in order for it to constitute a risk of NAION. The so-called *incipient NAION* is most likely a condition of subclinical axoplasmic stasis, seen in the fellow eye of patients with unilateral NAION, where progression to NAION is more or less likely to happen [17, 28, 29]. Recently it has been suggested, that a widefield swept source OCT, employing a larger 12 x 12 mm scan compared to the usual 6 x 6 mm scan, thereby capturing both the macula and the optic disc instead of just the former, allows for earlier detection of incipient NAION – and thus potentially visual loss – when coupled with a semi-automated algorithm for quantifying retinal and disc thickness changes over time [30]. Advanced imaging techniques integrated with semi-automated algorithms provide promise for the future in order to prevent an incipient NAION to progress to an ischemic event.

SUMMARY

- NAION is a multifactorial optic neuropathy characterized by acute, painless visual loss and optic disc edema, arising from the interplay between systemic vascular risk factors and local anatomical susceptibility of the optic nerve head
- The concept of the ‘disc at risk’ has evolved from a funduscopy description of a small cup/disc ratio to a more refined OCT-based understanding that includes specific structural features detectable with high-resolution EDI-OCT
- OCT has identified key anatomical markers associated with NAION, including PHOMS, BMO characteristics, ODD, and vitreopapillary interface abnormalities, which may contribute to the axonal crowding and compartment syndrome
- ODD constitute a particularly important and independent risk factor, especially in younger NAION patients, where deeply located ODD may predispose to ischemia even in the absence of traditional vascular risk factors
- Emerging imaging techniques enable detection of incipient NAION and may allow earlier identification of eyes at risk and future strategies aimed at preventing progression to overt NAION

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IATROGENIC CAUSES AND RISK FACTORS IN NAION

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LEARNING OBJECTIVES (3 required)

1. Understand the risks of NAION with intra-ocular surgery
2. Breakdown the risks of surgery leading to NAION
3. Name the drugs associated with NAION risk

CME QUESTIONS (3 required)

1. At which time point post-cataract surgery does the literature point to a drop in the risk of NAION back to baseline?
 - a) 6 days
 - b) 6 weeks
 - c) 6 months
 - d) 18 months
2. Which surgical procedure has the highest risk of peri-operative vision loss from NAION?
 - a) glaucoma surgery
 - b) cardiac surgery
 - c) spinal surgery
 - d) abdominal surgery
3. True or false? There is no definitive proof of a causal relationship between PDE-5 inhibitors (Viagra/Cialis) but there is enough concern that regulators and guidelines include precautionary warnings.

KEYWORDS (5 Max)

1. Peri-anaesthetic
2. Cardiac
3. Spinal
4. PDE5 inhibitor drugs
5. Amiodarone

HIGHLIGHTS

Management of iatrogenic NAION focuses on urgent evaluation to exclude arteritic causes (especially giant cell arteritis), review precipitating factors, and optimize systemic vascular status, as no therapy has convincingly reversed established NAION. Any potentially causative medication such as amiodarone, PDE-5 inhibitors, or aggressively dosed nocturnal antihypertensives should be reassessed, often with dose adjustment or discontinuation. After surgery-related NAION, perioperative contributors such as hypotension, anaemia, hypoxia, large fluid shifts, or uncontrolled IOP should be corrected promptly. Longer term, management includes controlling systemic risk factors, counselling about fellow-eye risk and medication precautions, and arranging low-vision support where needed. Fortunately, anaesthetic guidelines have reduced the rates of peri-operative vision loss.

SUMMARY

Iatrogenic refers to any injury or adverse event that is caused unintentionally by medical care, including diagnostic or therapeutic interventions such as a drug, a surgical procedure.

1 Intra-ocular surgery

Non-arteritic anterior ischemic optic neuropathy (NAION) can occur after ophthalmic surgery, most notably cataract extraction. In patients with prior NAION in one eye, ophthalmic surgery on the fellow eye may raise the risk of a second NAION episode, so specific counselling about this complication is recommended. (1)

1.1 Cataract

Reported absolute risks of NAION after cataract surgery vary by study design and population, but most large series place the risk in the range of ~1 per 1000-3000 surgeries, with higher reported rates in patients who have had NAION in the fellow eye. (2)

The direct mechanism for NAION evolving post cataract surgery is debated. Local vasoactive peptide release during and after uncomplicated cataract surgery may be responsible for the development of postoperative cystoid macular oedema and possibly the progression of ischaemic diabetic intraocular complications. However, it seems unlikely that such peptides could affect posterior ciliary artery function, but they could conceivably influence optic nerve head perfusion by an effect on intravascular resistance in a predisposed individual. (1) It is certainly difficult to ascribe the occurrence of NAION more than a few weeks after a cataract surgery to the operation itself.

Population-based and cohort studies

A cohort study found an incidence of post-ataract surgery NAION of 1 per 1,000 to 1,500 cataract operations within one year, representing roughly a fourfold increase over background risk in that population. (3) Other retrospective and database studies have reported similar absolute risks, often between approximately 0.03% and 0.1%, with most confined to the first several months after surgery. Beyond 6 months the risk fell to baseline. (4) Reviews done only within the era of modern phacoemulsification cataract surgery did not replicate the findings of increased risk compared to the population. (5)

A large meta-analysis published in 2023 concluded that the risk of NAION after cataract surgery is four times greater within the first year and usually occurs within 6 months. The peak of events occurred within 72 hours (21%) and at 6 weeks (12%) post-surgery. However, the absolute risk remains low at 1 in 1,000-3,100 surgeries. (4)

Patients with prior NAION

In eyes where the fellow eye already had NAION, small series suggest the absolute risk of NAION in the operated eye to be in the order of 3–10%. However, exact percentages differ between reports because of small sample sizes and referral bias. (2) Because of this elevated fellow-eye risk, most authors consistently recommend explicit risk counselling and careful perioperative management in patients with a history of NAION.

1.2 Other intraocular surgery

NAION can follow other intraocular surgeries, but reported cases are far fewer than after cataract extraction, so the absolute risk appears very low and is not well quantified.

A large retrospective cohort series describes ocular ischaemic events after pars plana vitrectomy. (6) The authors conclude that vitrectomy is correlated with significantly increased risk of NAION particularly within the first month following surgery, with an incident rate ratio of 8.75. This risk gradually declines but remains elevated up to 6 months postoperatively. For other procedures there may be case reports only, but numbers are too small to estimate a precise incidence for any given non-cataract procedure. Given the nature of glaucoma surgery being done at a time when there is already significant optic disc cupping, it would not be anticipated to be an issue in these cases.

Local or orbital anaesthesia complications such as retrobulbar haemorrhage, severe orbital pressure rise and excessive external ocular compression from positioning devices or dressings may also play a role in NAION from ophthalmic surgery.

1.3 Preventative measures

The recently published meta-analysis found that pooled baseline risk factors not associated with post-surgical NAION included: hypertension, dyslipidaemia, diabetes, ischemic heart disease, obstructive sleep apnea, previous stroke or transient ischemic attack, smoking, and use of PDE5 inhibitors. (4) Despite this most surgeons would still focus on preventive measures to reduce NAION risk during ophthalmic surgery, with a focus on minimizing perioperative vascular compromise, avoiding large intraocular pressure (IOP) swings, and optimizing systemic risk factors, especially in patients with prior NAION.

Preoperative measures

Identify high-risk patients particularly in the fellow eye if one eye already has NAION, and coordinate with the primary physician to optimize blood pressure, glycaemic control, and sleep apnoea treatment, and avoid aggressive nocturnal antihypertensive regimens around the time of surgery. Low blood pressure was found to be linked to vision loss within the first 72 hours. (4)

Intraoperative measures

The use of modern, small-incision phacoemulsification with minimal surgical time is already best practice. Care should be taken to avoid prolonged, very high IOP from the fluid dynamics or ocular compression. Thorough removal of viscoelastic will reduce IOP spikes in the immediate post-op period.

In conjunction with the anaesthetic team, maintain stable systemic blood pressure and oxygenation, avoiding hypotension, or excessive sedation that could lower perfusion pressure to the optic nerve. Regional anaesthesia, as opposed to topical anaesthesia, also increases risk of NAION within the first 72 hours. (4)

Early postoperative measures

Advise patients to report sudden vision loss, field defects, or dyschromatopsia immediately, since early recognition allows exclusion of arteritic causes and management of modifiable systemic factors. Monitor and promptly treat large IOP spikes with acetazolamide and topical aqueous suppressants.

Early NAION outside of the first 72 hours is thought to be triggered by postoperative inflammation resulting in vasogenic disc edema in a similar fashion to post cataract surgery cystoid macular edema. (4) Prophylactic topical NSAIDs in the postoperative period to reduce posterior pole edema, is probably the least harmful intervention. No studies have assessed the effect of any of these interventions.

2 Non-ophthalmic surgery

Post-operative vision loss (POVL) after non-ocular general surgery, occurs predominantly after long, complex operations such as cardiac bypass and spine fusion, where reported incidences are roughly 0.06–0.11% for cardiac surgery (7) and about 0.03–0.2% for spine surgery (8), with additional scattered cases after head and neck, vascular, abdominal, joint replacement, and other major procedures. (9) Cardiac surgery is associated with anterior ischaemic optic neuropathy. Spinal surgery is more commonly linked with posterior ischaemic events, 67% posterior versus 23% anterior. (10) Most cases are bilateral simultaneous severe vision loss to worse than count fingers. (8)

The proposed mechanisms for NAION as a cause of the POVL focus on perioperative hypotension, anaemia, massive blood loss and fluid shifts, prolonged procedures with > 6 hours under general anaesthesia, prone or head-down positioning, and patient vascular risk factors. The exact causal pathway is probably multi-factorial, and there is no specific preventive strategy that has proven efficacy beyond meticulous maintenance of hemodynamic stability, blood counts, and avoidance of external ocular compression.

2.1 Cardiac surgery

Cardiac surgery (especially with cardiopulmonary bypass) carries the highest well-documented risk of perioperative ischemic optic neuropathy, with reported incidences in the range of roughly 0.03–0.11%, much higher than background population risk. A case-control review of POVl in cardiac surgery found the risk factors to be a lower post-operative haemoglobin and the presence of atherosclerotic disease. A pre-operative angiogram was also associated with increased risk. (7) Most cases are discovered on the patient regaining consciousness, but a definite onset of visual loss days after the surgery, particularly after CABG, is reminiscent of the delay in AION onset which has been classically reported in patients with massive blood loss. (8)

2.2 Spinal surgery

Major spine surgery in the prone position has a risk on the order of about 0.03–0.2%, with most cases reported as posterior ION rather than classic anterior NAION. (8) In a review of perioperative ischemic optic neuropathy among spine surgery patients, nearly half of the patients had no vascular risk factors. (11) Visual loss was frequently bilateral (40% of AION, 47% of PION cases). In one review of spinal surgery vision loss the mean operative time was over 450 minutes, with the lowest average intraoperative mean arterial blood pressure 64 mm Hg. The mean lowest intraoperative haematocrit was 27%, and the average blood loss was 1.7 L for AION (and 5 L for PION patients). This suggested that decreased ocular perfusion pressure, blood loss and anaemia/hemodilution, and infusion of large quantities of intravenous fluids are some of the potential factors involved in the aetiology of postoperative ION. However, the authors concluded that these levels of blood pressure and anaemia intraoperatively were frequently at levels considered acceptable in anaesthesia practice. (11)

89% of the spine cases with ischemic optic neuropathy involved fusion and/or instrumentation on more than one vertebral level in the thoracic, lumbar or sacral spine, with 39% of patients having had previous spine surgery. (11) The mean prone position duration was 7.7 hours.

2.3 Risk factors

Although, intuitively, the presence of vascular risk factors would seem to be a logical predisposing risk factor for perioperative ischemic optic neuropathy, the occurrence of this complication in children, teenagers and in relatively healthy young adults weakens this proposed association, at least in some cases. (8) In the American Society of Anaesthesiology registry of POVl, although at least one vascular risk factor, including obesity, was noted in 82% of the patients in the ASA Registry, 64% of these patients were relatively healthy. (10)

There is no published estimate that specifically quantifies the incremental risk of second-eye NAION triggered by non-ophthalmic surgery.

2.4 Preventative measures

“One notable clinical fact is that perioperative ischemic optic neuropathy almost without exception occurs without any other accompanying evidence of vascular injury in other critical organs, including the brain, even in patients with preexisting atherosclerosis, diabetes and hypertension. This again emphasizes that the optic nerve of some patients, and particularly aspects of its vasculature, may be uniquely vulnerable to hemodynamic perturbations in the prone position. Since the pathogenesis of this disorder remains unclear, preventive measures remain elusive. Given the rarity of the complication, global recommendations to alter hemodynamic parameters in all patients have the potential to cause more harm than good.” (8)

Reducing NAION and other perioperative ischemic optic neuropathy risks in non-ocular surgery relies on optimizing vascular health before surgery.

Preoperative measures

Optimize systemic risk factors such as hypertension, diabetes, hyperlipidemia, anemia, and obstructive sleep apnea; encourage smoking cessation. Identify very high-risk procedures (major cardiac or long prone spine surgery) and counsel patients about the very low but serious risk of postoperative visual loss, particularly if multiple vascular comorbidities are present. (9)

Consideration should be given to the use of staged spine procedures in high-risk patients. (12)

Intraoperative strategies

These are some guidelines from the American Society of Anaesthesiologists Perioperative Visual Loss Task Force (12):

- Colloids should be used along with crystalloids to maintain intravascular volume in patients who have substantial blood loss.
- The use of deliberate hypotensive techniques during spine surgery has not been shown to be associated with the development of perioperative visual loss.
- At this time, there is no apparent transfusion threshold that would eliminate the risk of perioperative visual loss related to anemia.
- High-risk patients should be positioned so that their heads are level with or higher than the heart when possible. In addition, their heads should be maintained in a neutral forward position (e.g., without significant neck flexion, extension, lateral flexion, or rotation) when possible.

The rates of POVL in spinal surgery are reducing, showing that some of these measures are having an impact. (9)

Postoperative care

Monitor hemodynamics closely in the early postoperative period, avoiding prolonged hypotension or large swings in blood pressure and ensuring adequate oxygenation and hemoglobin levels. Educate staff and patients to report any sudden visual changes immediately so that arteritic causes are excluded quickly and modifiable systemic factors can be corrected without delay. If there is concern regarding potential visual loss, an urgent ophthalmologic consultation should be obtained to determine its cause. If an obvious ocular cause is not apparent, then urgent neuroimaging should be obtained, to assess for intracranial pathology such as pituitary apoplexy or occipital infarction.

3 Medications associated with NAION

Multiple medications have been linked to NAION in observational studies and case reports, including phosphodiesterase-5 inhibitors, nocturnal antihypertensives, amiodarone, and some other vasoactive or anticoagulant drugs, but for most agents the evidence is associative and confounded by underlying vascular risk rather than clearly causal. Current guidance is to exercise caution and review the risk–benefit balance when these drugs are used in patients with prior NAION or multiple vasculopathic comorbidities.

3.1 Nocturnal anti-hypertensives (to be covered in more detail by Dr A Arnold)

Evidence linking nocturnal antihypertensive medication to NAION is suggestive but not definitive, coming mainly from observational and pathophysiologic studies rather than randomized trials. Several case series and reviews describe many NAION patients reporting visual loss on waking and propose that excessive nocturnal blood pressure dips, sometimes accentuated by bedtime antihypertensives, may increase risk. Some authors therefore caution against aggressive night-time blood pressure lowering, particularly in patients with prior NAION or multiple vascular risk factors and recommend discussing dosing schedules with the treating physician. Larger epidemiologic studies have not conclusively demonstrated that evening or nocturnal antihypertensive use independently increases NAION incidence once overall hypertension and vascular comorbidity are accounted for, so the association remains biologically plausible but unproven. This needs to be weighed up against statistically significant beneficial effect of nocturnal antihypertensive dosing on cardiovascular outcomes and mortality. (13)

3.2 PDE-5 Inhibitors

Evidence for an association between phosphodiesterase-5 inhibitors (PDE-5I) and NAION is mixed, with no definitive proof of a causal relationship but enough concern that regulators and guidelines include precautionary warnings.

A 2018 meta-analysis and subsequent systematic review found no significant overall increase in NAION risk within one month of PDE-5I use. (14) However, exploratory subgroup analyses suggested possible higher relative risks for sildenafil and tadalafil based on a small number of studies and limited events, so these findings were considered hypothesis-generating rather than conclusive.

Large pharmaco-epidemiologic studies and one case-control analysis generally did not show a clear independent association between PDE-5I exposure and NAION once vascular comorbidities were accounted for, but numerous case reports continue to describe NAION occurring soon after sildenafil, tadalafil, or other PDE-5I use, particularly in older men with typical NAION risk factors. However, because some studies have shown a 2-fold increase in the risk of NAION the FDA, WHO, and national safety bulletins classify the link as “possibly” causal and advise that patients who have had NAION in one eye should avoid PDE-5Is, and that anyone taking these drugs who develops sudden visual loss should stop them and seek urgent assessment, while clinicians are encouraged to weigh visual risk especially in those with prior NAION or high vascular risk. (15)

“Because the neuro-ophthalmologists have accepted that there is a potential relationship between ingestion of the PDE-5I class of medications and NAION, the neuro-ophthalmologist should inquire about PDE-5I use when evaluating a patient with a new diagnosis of NAION, and counsel patients regarding the implication of continued use of PDE-5I.” (16)

3.3 Amiodarone

Evidence indicates that amiodarone can cause its own toxic optic neuropathy that often mimics NAION, but whether it truly increases NAION incidence remains debated. Amiodarone-associated optic neuropathy typically presents with insidious, often bilateral visual loss and prolonged disc swelling over months, features that differ from classic unilateral, acute NAION, and large case series and reviews suggest patients on amiodarone have about a twofold higher risk of optic neuropathy overall, leading regulators and authors to recommend careful monitoring and considering discontinuation or dose reduction if optic neuropathy develops, while acknowledging that distinguishing drug toxicity from coincidental NAION in vasculopathic patients can be challenging, and definitive causal data are limited. (17)

Case series and reviews report that visual function and optic disc swelling often stabilize or partially improve after amiodarone is stopped, but recovery is typically slow and incomplete. In many published series, disc edema may take several months (often 3–15 months) to resolve and visual acuity or fields can improve gradually over a similar timeframe, though some patients have persistent deficits despite drug cessation. (17)

4. Conclusion

Management of iatrogenic NAION focuses on urgent evaluation to exclude arteritic causes (especially giant cell arteritis), review precipitating factors, and optimize systemic vascular status, as no therapy has convincingly reversed established NAION. Any potentially causative medication (such as amiodarone, PDE-5 inhibitors, or aggressively dosed nocturnal antihypertensives) should be reassessed, often with dose adjustment or discontinuation. After surgery-related NAION, perioperative contributors such as hypotension, anaemia, hypoxia, large fluid shifts, or uncontrolled IOP should be corrected promptly. Longer term, management includes controlling systemic risk factors (blood pressure, diabetes, lipids, sleep apnea, smoking), counselling about fellow-eye risk and medication precautions, and arranging low-vision support where needed.

CME ANSWERS

- 22. c
- 23. b
- 24. True

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WHAT IS ACTIONABLE

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LEARNING OBJECTIVES

1. Identify key screening steps for NAION, including assessment of systemic contributors and medication-related risk factors
2. Discuss evidence-informed approaches to optimize modifiable risk factors
3. Review management recommendations, including targeted strategies for special scenarios

CME QUESTIONS

1. Which of the following findings *most strongly* warrants urgent evaluation for giant cell arteritis in a patient diagnosed with anterior ischemic optic neuropathy?
 - A. Female gender and age >70
 - B. Mild anemia noted on recent labs
 - C. Paracentral acute middle maculopathy on macular OCT
 - D. Severe disc edema associated with flame hemorrhages
2. In the management of systemic vascular risk factors for NAION, which specific condition is the STOP-BANG questionnaire recommended for screening?
 - A. Chronic kidney disease
 - B. Diabetes mellitus
 - C. Nocturnal hypotension
 - D. Obstructive sleep apnea
3. A patient with prior dialysis-associated unilateral NAION is preparing for upcoming sessions. Which modification aligns with recommended strategies to reduce the risk of fellow-eye NAION?
 - A. Encourage eating during dialysis to maintain energy levels
 - B. Increase ultrafiltration volume to improve fluid balance
 - C. Lower the dialysate temperature
 - D. Reduce the duration of dialysis sessions to minimize hypotension

KEYWORDS

1. NAION (nonarteritic anterior ischemic optic neuropathy)
2. Vascular risk factors
3. Obstructive sleep apnea
4. Medication modification
5. Nocturnal hypotension

HIGHLIGHTS

Nonarteritic anterior ischemic optic neuropathy (NAION) is the most common acute optic neuropathy in individuals over 50. While there is no proven therapy to reverse vision loss, a structured, action-oriented approach can help clinicians reduce the likelihood of misdiagnosis, identify modifiable contributors, and guide meaningful counseling.

Screening and Initial Evaluation

Individuals over age 50 with suspected anterior ischemic optic neuropathy (AION) require prompt evaluation to exclude giant cell arteritis (GCA), particularly if they are reporting new headaches, scalp tenderness, jaw claudication, fatigue, or polymyalgia rheumatica symptoms. Erythrocyte sedimentation rate, C-reactive protein, and platelet count serve as initial laboratory screening tools and, if warranted, temporal artery biopsy and/or ultrasound. For challenging cases, additional imaging studies may include MR vessel wall imaging as well as ^{18}F -FDGPET/CT. Adjunctive in-office tests may aid in the assessment for GCA. Fluorescein angiography may demonstrate delayed choroidal filling, a finding strongly suggestive of GCA. Macular OCT has emerged as a valuable screening tool, as acute middle maculopathy (PAMM) is strongly associated with GCA, particularly in patients presenting with AION.¹ Consideration of MRI of the brain and orbits is appropriate to exclude alternative diagnoses, particularly those associated with inflammatory optic neuropathies, such as myelin oligodendrocyte glycoprotein (MOG) antibody-associated optic neuritis.²

A recent prospective, randomized controlled trial found that cardiovascular risk factors in patients with NAION were not significantly more prevalent than in the general population.³ Despite this, a comprehensive assessment of systemic vascular risk factors, particularly diabetes mellitus, hypertension, hyperlipidemia, kidney disease, and anemia, remains an important component of clinical evaluation. Patients must be specifically questioned about symptoms of obstructive sleep apnea (OSA), including snoring, daytime somnolence, and observed apneas.⁴ Validated screening tools such as the STOP-BANG questionnaire may assist in risk stratification and guide referral for polysomnography.⁵

Medication review should focus on agents associated with hypotension or NAION risk, including bedtime antihypertensives, phosphodiesterase-5 inhibitors, interferon- α , amiodarone, and glucagon-like peptide-1 receptor agonists (GLP-1 RAs).

Risk-Factor Modification and Counseling

The principal aim of intervention is prevention of a fellow-eye event, though NAION can occur in the second eye despite efforts to optimize systemic risk factors. Primary care engagement is critical for optimizing systemic vascular risk factors and treating anemia when present. Smoking cessation remains a priority due to its strong association with cardiovascular disease. Patients at risk for OSA should be referred for polysomnography, and those with diagnosed OSA should be counseled on the importance of adherence to therapy.

Eliminating potentially high-risk medications or modifying dosing strategies may be helpful. Patients should be advised to discontinue phosphodiesterase-5 inhibitors, particularly when NAION occurs shortly after drug exposure. Decisions regarding discontinuation of interferon- α or amiodarone should be made in collaboration with the prescribing clinician. For patients using GLP-1 RAs, it should be explained that the current literature suggests a possible small increased risk of NAION with semaglutide; however, the absolute risk appears low, causality has not been established, and findings remain unconfirmed.⁶ Shared decision-making between the patient and the care team is recommended when considering continuation, or discontinuation of GLP-1 RA therapy, taking into account individual risk factors, overall health status, and available alternative treatments.

Observational data have linked nocturnal hypotension to NAION although causality remains unproven. It should be noted that some landmark studies have shown a statistically significant benefit of bedtime antihypertensive dosing on overall cardiovascular outcomes and mortality.⁷ However, other recent large-scale studies have not replicated this cardiovascular benefit.⁸ Collaboration with the primary care provider or cardiologist is essential to balance ophthalmic risk reduction against overall cardiovascular protection.

For dialysis-associated NAION, coordination with nephrology is important to minimize intradialytic hypotension. Actionable steps to be considered include increasing the frequency and/or duration of dialysis sessions, reducing the dialysate temperature, individualizing the dialysate composition, and discouraging/prohibiting the patient from eating during the session.⁹

Several strategies have been proposed to reduce the risk of NAION in the perioperative setting of cataract surgery, including the use of topical anesthesia, clear corneal incision phacoemulsification, careful intra- and postoperative IOP control, thorough removal of viscoelastic, and avoidance of posterior capsule violation. Adjunctive measures such as intravitreal anti-VEGF or corticosteroid and postoperative prophylactic topical NSAIDs have also been suggested. Although no controlled studies have confirmed the efficacy of these interventions, their use may be considered in patients who experienced perioperative NAION following prior cataract surgery and are now undergoing evaluation for fellow-eye surgery.¹⁰

While evidence-based strategies to mitigate the risk of perioperative ischemic optic neuropathy in non-ophthalmic surgery are lacking, several recommendations have been suggested because of their plausible physiologic rationale. These recommendations should especially be considered in high-risk patients, i.e., patients undergoing procedures that are prolonged, have substantial blood loss, and performed with the patient in prone position.¹¹

- Avoid prolonged hypotension
- Limit anemia
- Colloids could be considered along with crystalloids to maintain intravascular volume in patients who have substantial blood loss
- When possible, patient's head should be level with or higher than the heart and maintained in a neutral forward position
- Staged spine procedures

Given the absence of proven therapies for NAION, clinicians should avoid interventions that lack evidence of benefit and may introduce unnecessary risk. Such treatments include systemic steroids, aspirin solely for NAION prevention, brimonidine, pentoxifylline, levodopa, and hyperbaric oxygen.

Finally, a referral to low vision services should be offered, particularly for individuals with sequential NAION, to optimize functional vision and quality of life.

SUMMARY

Nonarteritic anterior ischemic optic neuropathy is the leading acute optic neuropathy in individuals over 50, and although no therapy reverses vision loss, a structured approach can minimize misdiagnosis, identify modifiable contributors, and guide preventive counseling. Clinicians should avoid ineffective treatments that introduce unnecessary risk and ensure referral to low-vision services to maximize functional outcomes.

CME ANSWERS

1. C
2. D
3. C

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Neuro-Ophthalmology in the Age of AI: Insights, Innovations, and Implementation [2.0 CME]

Moderators: Kevin E. Lai, MD & Meagan Seay, DO

Definitions: What is AI? *Kelvin Z. Li, MTech, MMed*

Getting Ophthalmic Imaging AI in the Clinic, *Aaron Y. Lee, MD, MSCI*

Will AI be Helpful for Ocular Motility? *Kemar E. Green, DO*

How Can AI Help Us Today: Education, *Sachin Kedar, MBBS, MD*

How Can AI Help Us Today: Clinical Activities With PHI, *Shannon Beres, MD*

How Can AI Help Us Today: Clinical Activities Without PHI, *Devin D. Mackay, MD*

Panel Discussion, *Aaron Y. Lee, MD, MSCI; Shannon Beres, MD; Kemar E. Green, DO; Devin D. Mackay, MD; Kelvin Z. Li, MTech, MMed; Sachin Kedar, MBBS, MD*

Artificial intelligence (AI) has rapidly transformed society. In medicine, AI-based developments impact multiple domains, including image analysis, education, clinical documentation, and research. This session will introduce key AI concepts, including machine learning and deep learning, foundation models, large language models (LLMs), and vision-language models (VLMs), and discuss how these technologies intersect with neuro-ophthalmic care. Participants will explore practical considerations for bringing AI into clinical practice, including data ethics, defining appropriate clinical applications and limitations, system integration, regulation, and liability. The session will also demonstrate practical applications of AI in ocular motility assessment, medical education, EMR integration, and academic writing and research. Attendees will leave with a framework for critically evaluating and responsibly implementing AI tools in both clinical and academic settings.

Upon completion of this session, participants should be able to:

- (1) Define and describe the terms artificial intelligence (AI), machine learning (ML), deep learning (DL), foundation models, large language models (LLMs), and vision-language models (VLMs).
- (2) Identify and explain the ethical, technical, logistic, regulatory, and legal factors involved in deploying ophthalmic imaging AI in clinical settings.
- (3) Evaluate emerging applications of artificial intelligence in ocular motility, education, electronic medical record systems (EMR), and research, and apply this understanding to improve clinical workflows and academic output.

DEFINITIONS: WHAT IS AI?

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LEARNING OBJECTIVES

1. Analyze the hierarchical relationship between Artificial Intelligence (AI), Machine Learning (ML), and Deep Learning (DL), contrasting rule-based clinical scoring systems (classical ML) versus the automatic feature learning used for complex analysis of high-dimensional clinical data (DL).
2. Differentiate between Foundation Models, Large Language Models (LLMs), and Vision-Language Models (VLMs) based on their application in processing diverse clinical data modalities (unstructured clinical notes, high-resolution imaging, or video).
3. Explain the importance of Responsible AI principles to patient care by linking data bias, model limitations (like hallucinations), and the necessity of human clinical validation of AI diagnostic output.

CME QUESTIONS

16. Which of the following statements most accurately represents the hierarchical relationship between Artificial Intelligence (AI), Machine Learning (ML), and Deep Learning (DL)?
 - A. DL is a broad field that encompasses ML, while AI is a specialized subset of ML used for neural networks.
 - B. AI is the overarching discipline; ML is a subset of AI that includes algorithms which learn from data; and DL is a specialized subset of ML capable of automatic feature learning.
 - C. AI, ML, and DL are distinct, non-overlapping fields: AI focuses on robotics, ML on statistics, and DL on image processing.
 - D. ML and DL are synonyms for the same process, while AI refers strictly to rule-based expert systems that do not learn from data.
17. Which category of models is characterized explicitly by being pre-trained on vast amounts of medical and genomic literature to serve as a base for other applications?
 - A. Supervised Learning Models
 - B. Large Language Models (LLMs)
 - C. Vision-Language Models (VLMs)
 - D. Foundation Models (FMs)
18. You are using an LLM to summarize a complex consultation note for a patient presenting with acute retrobulbar pain and vision loss. Your raw clinical notes explicitly state "Pupils equal and reactive, NO Relative Afferent Pupillary Defect (RAPD) detected". However, because the model statistically associates these symptoms with optic neuritis, the generated summary reads "Examination revealed a left relative afferent pupillary defect (RAPD)". The model has fabricated a clinical sign that aligns with the likely diagnosis but contradicts the actual exam findings. This is an example of:
 - A. Hallucination
 - B. Automation Bias
 - C. Data Leakage
 - D. Algorithmic Drift

KEYWORDS

1. Artificial Intelligence
2. Deep Learning
3. Medical Imaging
4. Diagnostic Bias
5. Clinical Data

HIGHLIGHTS

- Artificial Intelligence is the overarching discipline of mimicking human intelligence, while Machine Learning is the specific subset that empowers systems to predict disease progression by learning directly from historical data.
- Medical AI architecture has advanced from unimodal Large Language Models (LLMs) to multimodal models (e.g. Vision-Language Models, Foundational Models), which can simultaneously process text, images, and video to handle complex diagnostic tasks.
- We must mitigate risks like hallucination by adhering to Responsible AI principles—such as transparency, equity, and human autonomy—to ensure algorithms serve as probability-based augmentation tools rather than replacements for medical expertise.

SUMMARY

From Classical Machine Learning to Deep Learning

To understand the current landscape of medical artificial intelligence, we must first establish the hierarchy of the technology. Artificial Intelligence (AI) is the broadest concept—the overarching discipline of creating machines that mimic human intelligence. **Machine Learning (ML)** is a subset of AI that focuses specifically on the ability to learn from data, such as predicting disease progression based on historical trends.¹

Within this framework, we distinguish between **Classical ML** and **Deep Learning (DL)**. Classical ML typically relies on "manual feature engineering". In this approach, human experts must explicitly tell the model which variables matter—extracting specific data points like age, blood pressure, or lab values. This method excels with structured, tabular data and is the engine behind many traditional risk calculators and logistic regression models.

In contrast, **Deep Learning**²—the technology driving the current AI boom—utilizes neural networks and transformers to perform "automatic feature extraction." Instead of requiring a human to define the features, the model learns directly from raw, high-dimensional data. In neuro-ophthalmology, for example, deep learning models can analyze raw optical coherence tomography (OCT) scans to detect subtle optic disc changes³ or process fundus photos to identify papilledema⁴, identifying patterns that may be invisible to the human eye⁵ or too complex for classical algorithms.

Data Structure and Learning

The fuel for these models is data, but not all data is created equal. A significant limitation of this "engine" is **Data Bias**.⁶ If models are trained primarily on one demographic, they often fail to generalize when deployed in a diverse real-world setting, potentially exacerbating healthcare disparities.⁷

Medical data generally falls into three categories:

- **Structured Data:** Highly organized information like lab results, International Classification of Disease (ICD) billing codes, and standardized test scores.

- **Semi-structured Data:** Information with some organizational framework, such as Fast Healthcare Interoperability Resources (FHIR) or diagnostic machine outputs.
- **Unstructured Data:** This represents the majority of high-value clinical data, including narrative clinical notes, raw magnetic resonance imaging (MRI) image stacks, and genetic sequences.

To process this data, we employ different learning styles. **Supervised Learning** involves training a model with labelled examples—for instance, showing the AI thousands of MRIs explicitly marked as "stroke" or "normal".⁸ **Unsupervised Learning**, conversely, involves feeding the model unlabelled data and allowing it to discover hidden patterns and clusters on its own, which is particularly useful for identifying novel disease subtypes.

Modern Model Architectures

The architecture of AI models has evolved significantly with the advent of **Foundation Models (FMs)**.⁹ These are massive models pre-trained on vast repositories of medical and genomic literature, serving as a base upon which more specific tools can be built.

Two key derivatives of this architecture are:

1. **Large Language Models (LLMs)**¹⁰: These are unimodal systems designed to process and generate text. They are powerful tools for summarizing notes or drafting letters but are limited to the text modality.
2. **Vision-Language Models (VLMs)**^{11,12}: These represent a leap forward in multimodal capability. VLMs can process text, images, and video simultaneously, allowing for complex tasks like generating a text report directly from a surgical video feed or an imaging study.

Deploying these tools in clinical practice requires a keen awareness of their limitations. A primary risk is **Hallucination**—a phenomenon where the AI generates clinically false but highly plausible outputs.¹³ This might manifest as the fabrication of non-existent drug interactions, the citation of phantom pathologies, or the invention of clinical signs that were never documented.

To mitigate these risks, we must adhere to **Responsible AI (RAI) Principles**^{14,15}:

1. **Protect autonomy:** Humans must remain in full control of health care systems and medical decisions. AI should be designed to assist humans, not replace human judgment. This includes ensuring patients give valid informed consent and maintain privacy over their data.
2. **Promote human well-being, human safety, and the public interest:** AI technologies must not harm people. Developers must ensure regulatory quality control, safety, and accuracy to prevent errors. The deployment of AI should serve the broader public health good rather than just commercial interests.
3. **Ensure transparency, explainability, and intelligibility:** "Black box" algorithms should be avoided in high-stakes health contexts. There must be transparency regarding how an AI system is developed and tested. Explainability ensures that the logic behind an AI's decision can be understood by clinicians and patients.
4. **Foster responsibility and accountability:** Clear lines of liability must be established. If an AI system makes an error or causes harm, there must be mechanisms to determine who is responsible (e.g., the vendor, the developer, or the clinician) to ensure appropriate redress.
5. **Ensure inclusiveness and equity:** AI for health must be accessible to as many people as possible, regardless of age, sex, gender, income, or ethnicity. This principle also specifically warns against training AI on biased datasets that could deepen existing health disparities.

6. **Promote AI that is responsive and sustainable:** AI systems should be designed to be responsive to the actual needs of the health system and capable of adapting as those needs change. Furthermore, "sustainability" refers to minimizing the environmental impact (carbon footprint) of computing power and ensuring the infrastructure can be maintained over the long term.

CONCLUSION

Ultimately, **AI should be viewed as a probability-based augmentation tool, not a replacement for medical expertise.** While algorithms can process data at a scale humans cannot, they lack context and judgment. Human clinical judgment remains the indispensable final layer for ensuring patient safety and validating the insights provided by these powerful machines.

CME ANSWERS

25. B
26. D
27. A

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GETTING OPHTHALMIC IMAGING AI IN THE CLINIC

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LEARNING OBJECTIVES

16. Understand the complexity and barriers of AI integration
17. Learn about ophthalmic standards and their role in AI deployment
18. Discuss clear cut pathways to successful AI deployment

CME QUESTIONS

19. Which factor most commonly limits the translation of ophthalmic imaging AI models from research settings into routine clinical practice?
 - a. Insufficient algorithmic performance on benchmark datasets
 - b. Lack of clinician interest in AI-assisted diagnosis
 - c. Inadequate data interoperability and integration with clinical systems
 - d. Regulatory prohibition of AI use in ophthalmology
20. What role has the DICOM standard come to play in the development and deployment of ophthalmic imaging AI?
 - a. It primarily standardizes billing and reimbursement for imaging procedures
 - b. It has become essential for assembling large, structured imaging datasets required for AI development
 - c. It replaces the need for electronic health record integration
 - d. It is used only for regulatory submissions and not clinical workflows
21. Why has ophthalmology historically faced greater challenges than some other specialties in integrating AI into enterprise health data ecosystems?
 - a. Ophthalmic imaging data are too small to benefit from AI
 - b. Ophthalmology has limited participation in cross-specialty data standards and common data models
 - c. Ophthalmic AI models require proprietary hardware unavailable in health systems
 - d. Regulatory agencies restrict ophthalmic AI more than other medical fields

KEYWORDS (5 Max)

31. Artificial Intelligence
32. Deep Learning
33. Computer Vision
34. Standards
35. Interoperability

HIGHLIGHTS

- Modern ophthalmic AI succeeds because it is built for imaging—not retrofitted onto it. Deep learning approaches such as convolutional neural networks and representation learning are uniquely suited to high-dimensional ophthalmic data like OCT, enabling clinically meaningful pattern recognition that traditional image processing cannot achieve.
- Standards and infrastructure—not algorithms—are the primary barriers to clinical AI adoption. The lack of consistent use of DICOM, FHIR, and enterprise data models in ophthalmology has been a larger impediment to deployment than model performance, making data governance, interoperability, and scale essential prerequisites for success.

- Clinically viable AI requires system-level integration, not standalone models. Reliable deployment depends on automated, HIPAA-compliant pipelines that ingest imaging data, run inference, and return results directly into the EHR, allowing AI to operate as part of routine clinical workflows rather than as isolated research tools.

SUMMARY

The lecture opens with a focused introduction to modern artificial intelligence and deep learning as they apply to ophthalmic imaging. Rather than providing a broad or abstract overview of AI, the discussion centers on the classes of models that have driven recent advances in ophthalmology, particularly convolutional neural networks and representation learning approaches designed for high-dimensional image data. Attention is given to how these methods differ from traditional image processing techniques and why they are particularly well suited to imaging modalities such as optical coherence tomography.

To ground these concepts in practical examples, the presentation begins with representative research applications drawn from contemporary ophthalmic AI work. An optical coherence tomography–based age-related macular degeneration classification task is used to demonstrate how deep learning models can identify clinically relevant patterns directly from volumetric imaging data. Additional examples involving eyelid and ocular movement segmentation illustrate how AI applications in ophthalmology are expanding beyond retinal disease into periocular anatomy and functional assessment. Together, these examples highlight both the technical maturity of current research and the gap that often exists between algorithm development and clinical use.

The discussion then broadens to examine the current landscape of ophthalmic devices and electronic health record systems, with a focus on the data and interoperability challenges that complicate clinical AI deployment. The presentation introduces key healthcare standards commonly encountered in this space, including DICOM and FHIR, and explains their intended roles in enabling structured data exchange between imaging devices, analytic systems, and the electronic health record. Despite their importance, ophthalmology has historically had limited participation in the development and adoption of these standards, creating downstream challenges for AI integration.

The consequences of this limited engagement are explored through practical examples, including inconsistent imaging metadata, fragmented device ecosystems, and difficulty aligning ophthalmic data with enterprise-wide data models such as OMOP. The evolution of DICOM within ophthalmology serves as a particularly illustrative case. Once viewed as optional or overly burdensome, DICOM has become essential for assembling large, longitudinal datasets that support modern AI development and validation. The growing demand for data collation, harmonization, and scale has fundamentally changed how ophthalmic imaging data must be managed to support AI at an institutional level.

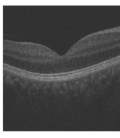
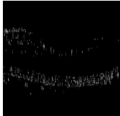
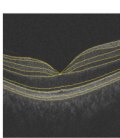
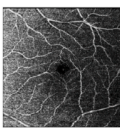
The narrative also addresses the concerns and resistance that have accompanied standardization efforts, including vendor pushback, fears of workflow disruption, and skepticism regarding the clinical value of evolving standards. These tensions are framed as practical realities that must be navigated thoughtfully rather than obstacles that preclude innovation.

The lecture concludes with a real-world case study drawn from Washington University’s approach to developing and deploying ophthalmic AI infrastructure. The discussion describes the creation of a fully HIPAA-compliant, on-premise research computing environment equipped with GPU resources and integrated with the Epic electronic health record through supported application programming interfaces. This infrastructure supports both research and clinical use while maintaining appropriate governance and security.

A central component of this approach is a dedicated DICOM endpoint that automatically receives all clinical ophthalmic imaging. This imaging stream is routed directly into an inference environment where AI models can be executed in a reliable and reproducible manner. The resulting outputs are then delivered back to the electronic health record through secure APIs, enabling AI-derived insights to be presented within existing clinical workflows. Emphasis is placed on

architectural principles such as automation, standardization, auditability, and scalability, demonstrating how AI systems can function as part of routine clinical care rather than as isolated research tools. The overall framework offers a reproducible pathway for academic medical centers seeking to move ophthalmic imaging AI from promising research to dependable clinical implementation.

Table 1
Retinal Imaging Information Object Definitions (IODs), references to their standards, and characteristics.

Information Object Definition (IOD)	Example DICOM image	SOP Class UID	PS3.3 DICOM Standards reference	IOD Characteristics
Ophthalmic Photography 8-Bit Image Storage		1.2.840.10008.5.1.4.1.1.77.1.5.1	A.41	● 2D (row, columns) ● No references to other images ● Information on image types (e.g., color, infrared, autofluorescence)
Ophthalmic Tomography Image Storage		1.2.840.10008.5.1.4.1.1.77.1.5.4	A.52	● 3D (row, columns, number of slices) ● References to ophthalmic photography
Ophthalmic Optical Coherence Tomography B-Scan Volume Analysis Storage		1.2.840.10008.5.1.4.1.1.77.1.5.8	A.84	● 3D (row, columns, number of slices) ● References to ophthalmic photography, OCT (Optical Coherence Tomography) ● Information on acquisition algorithm
Height Map Segmentation Storage		1.2.840.10008.5.1.4.1.1.66.8	A.91	● 3D (row, columns, number of slices) ● References to OCT ● Information on segmentation algorithm
Ophthalmic Optical Coherence Tomography En Face Image Storage		1.2.840.10008.5.1.4.1.1.77.1.5.7	A.83	● 2D (row, columns) ● References to OCT B-scan volume analysis storage, segmentation storage ● Information on derivation algorithm

CME ANSWERS

28. C
29. B
30. B

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WILL AI BE HELPFUL FOR OCULAR MOTILITY?

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LEARNING OBJECTIVES (3 required)

19. Summarize core ocular motility systems (saccades, pursuits, VOR, fixation) and how they map to brain, brainstem, cerebellar, and NMJ function.
20. Describe how AI models quantify eye-movement abnormalities across neuro-ophthalmic and neurologic diseases.
21. Critically evaluate the evidence, advantages, and limitations of AI-based ocular motility tools for diagnosis and remote neurologic screening.

CME QUESTIONS (3 required)

22. Which ocular motility subsystem most commonly reveals cerebellar dysfunction through hypometric or hypermetric movements?
 - a. Smooth pursuit
 - b. Saccades
 - c. VOR
 - d. Fixation
23. A major benefit of deep-learning models applied to ocular motility is:
 - a. They do not require high frame-rate video
 - b. They can extract diagnostic features directly from raw video without hand-engineered measurements
 - c. They eliminate inter-individual variability
 - d. They remove the need for clinical examination
24. In Myasthenia Gravis, which digital biomarker has reached reported sensitivity/specificity approaching 100% at optimized thresholds?
 - a. Saccadic latency
 - b. Smooth pursuit gain
 - c. OKN slow-phase velocity decrement
 - d. Torsion amplitude

KEYWORDS (5 Max)

1. Ocular Motility
2. Artificial Intelligence
3. Digital Biomarkers
4. Eye Tracking
5. Precision Neurology

HIGHLIGHTS

- Ocular motility provides a fast, high-resolution window into neurological and neuromuscular physiology.
- AI enables automated detection of abnormalities in saccades, pursuits, VOR, fixation, and nystagmus directly from raw video.
- Myasthenia Gravis and cerebellar ataxias exhibit quantifiable eye-movement signatures suitable for digital diagnostics.
- Synthetic eye-movement datasets overcome scarcity and privacy barriers in rare neurologic diseases.
- AR/VR-based autonomous eye-tracking may bring expert neuro-ophthalmic evaluation to remote and acute settings.

SUMMARY

This presentation explores whether artificial intelligence can meaningfully improve the assessment of ocular motility. Eye movements offer a precise, noninvasive indicator of neurologic function, reflecting physiology from the extraocular muscles and neuromuscular junction to the brainstem, cerebellum, and cortex. Key motility systems, saccades, smooth pursuit, VOR, and fixation, each have characteristic failure modes that help localize disease.

Modern AI approaches now analyze raw eye-movement video without requiring manually derived waveforms, enabling scalable, quantitative detection of abnormalities. We review evidence supporting AI applications in Myasthenia Gravis, where OKN slow-phase decrement has emerged as a robust digital biomarker, and cerebellar ataxias, where saccadic dysmetria and accuracy errors are early, sensitive markers. The role of synthetic “digital twin” datasets in improving model robustness, addressing privacy constraints, and enabling rare-disease training is also discussed.

Finally, we examine future directions, including AR/VR-based autonomous neurologic examinations, remote TeleAutoHINTS systems for acute dizziness, and wearable digital neuro-diagnostics. Together, these tools represent a pathway toward device-agnostic, AI-augmented neuro-ophthalmology accessible anywhere.

CME ANSWERS

- 31. (b). Saccades
- 32. (b). Direct raw-video feature learning
- 33. (c). OKN slow-phase velocity decrement

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NEURO-OPHTHALMOLOGY IN THE AGE OF AI: INSIGHTS, INNOVATIONS, AND IMPLEMENTATION!

How Can It Help Us Today: Education

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LEARNING OBJECTIVES (3 required)

22. Review our current state of preparedness for incorporating digital health and AI in clinical practice
23. Propose a curriculum to improve digital health and AI literacy
24. Discuss practical uses of AI tools to enhance medical education

Disclosure: The CME questions were prepared with a commercially available LLM tool for illustrative purposes. LLM was not used in any other part of the syllabus.

CME QUESTIONS (3 required)

25. A neuro-ophthalmology fellow uses an AI-based clinical decision support tool integrated into the EMR to assist with the evaluation of a patient with acute diplopia and suspected cranial nerve palsy. The fellow is uncertain how the tool generated its output and worries about relying on it for clinical decisions. Which educational intervention would best address this concern while supporting safe AI adoption in neuro-ophthalmology training?
 - a. Restrict AI use to attending physicians only
 - b. Provide training focused on foundational AI concepts, limitations, and ethical considerations
 - c. Emphasize board-style memorization of neuro-ophthalmic syndromes
 - d. Require fellows to learn computer programming before using AI tools
26. A faculty member develops an AI-powered virtual patient to teach residents about pupillary diseases. The chatbot presents cases of normal and abnormal pupils, adapts questioning based on learner responses, and provides feedback on localization and differential diagnosis. Which educational outcome is most directly enhanced by this AI application?
 - a. Replacement of bedside teaching
 - b. Improved experiential learning and clinical reasoning in neuro-ophthalmic localization
 - c. Automated assessment of surgical skills
 - d. Elimination of inter-faculty variability in teaching
27. A neuro-ophthalmology fellowship incorporates an AI tool that summarizes recent literature and suggests diagnostic pathways. Over time, faculty notice that some trainees increasingly accept AI outputs without independently verifying sources or considering alternative diagnoses. This scenario best illustrates which risk associated with AI use in medical education?
 - a. Digital divide limiting access among learners
 - b. Algorithmic transparency improving decision-making
 - c. Automation bias leading to de-skilling in clinical reasoning
 - d. Enhanced efficiency in evidence-based practice

KEYWORDS (5 Max)

36. Artificial intelligence
37. Medical Education
38. Digital health
39. Curriculum
40. Precision education

HIGHLIGHTS

A. Data explosion

Digital health refers to the use of information and communications technology in healthcare to improve patient outcomes and promote wellness. The US Food and Drug Administration (FDA) defines digital health to include a broad scope of categories such as mobile health (mHealth), health information technology (HIT), wearable devices, telehealth and telemedicine, and personalized medicine (1).

With near universal adoption of electronic medical records (EMR) and imaging technologies, there has been an exponential increase in the generation of health care data. The World Economic Forum estimates that by year 2020, the global healthcare sector had generated 2.3 zettabytes (10^{21}) of data with a predicted annual growth rate of 10-30% (2). A single patient is estimated to generate 80 megabytes/year in imaging and EMR data. Medical knowledge from new research and literature will challenge decision-making in patient care. Peter Densen, a renowned medical educator estimates that the doubling time for medical knowledge will have decreased from 50 years in 1950 to about 0.2 years in 2020 (3). This explosive growth of healthcare data as well as medical research could soon overwhelm human cognitive capacity for decision-making in patient care. The incorporation of data and information management tools such as predictive analytics - Artificial Intelligence and Machine Learning, are inevitable in healthcare.

B. Current state of preparedness

Artificial intelligence tools have increasingly percolated through our daily lives, including healthcare. In most surveys, stakeholders- physicians, patients, trainees, educators and administrators, have an overall positive perception for the use of AI in healthcare, but remain anxious about a perceived lack of understanding of these technologies (4). Clinicians worry about ethical usage, breach of privacy and personal liability. Patients are concerned about changed physician-patient relationships, threats to shared decision-making and privacy, and feel most comfortable with hybrid models where a physician remains involved in the decision-making process. Medical educators caution against erosion of clinical skills, depersonalization and a move away from holistic care as potential negative outcomes from digital technology (5). Despite increased visibility of these tools in daily life, medical trainees and practitioners feel unprepared and anxious about digital technologies, where it relates to healthcare. The ACGME, in a scenario planning exercise “Medicine in 2035” identified technology and data-driven changes to the medical profession to be a significant challenge to future providers. Such changes would result in escalating complexity of patient care delivery, ‘commoditization’ of healthcare services, increased transparency of data sharing and analyses, and disruption of current concepts of physician specialty distribution” (6). Undergraduate (UME) and Graduate Medical Education (GME) curricula have struggled to keep pace with the rapidly evolving landscape of medical education. Tradition, accreditation concerns, a focus on passing national board exams, faculty resistance to change, and perhaps lack of competence in the newer technologies present barriers to reforming the curriculum (7). Recognizing the need for urgent action, the American Medical Association (AMA) in 2018, adopted the AI policy “Augmented Intelligence in Health Care H-480-940” to enhance AI literacy across the continuum of medical education (8). As a result, 77% of USA medical school reported integration of AI into their medical school curriculum by academic year 2024 (9).

C. Curriculum for literacy in Artificial Intelligence for neuro-ophthalmologists

Despite increasing awareness, most practicing clinicians as well as medical trainees, lack basic understanding of AI (10). The AMA recommends creation of curricula designed to address needs of professionals across the health care spectra from medical school to current practitioners. At a minimum, the curriculum should include foundational concepts of AI and data science, the array of AI tools and their terminology, their application in medicine, critical appraisal of literature, and barriers including legal and ethical constraints (11). Table 1 provides a sample AI literacy curriculum which will be used to build an AI literacy collection within NOVEL.

D. Artificial Intelligence applications in Medical Education

About 5300 manuscripts related to medical education and artificial intelligence were published in 2025 compared to 646 in 2020. AI enabled tools are being tested for various aspects of medical education such as administration, curriculum development, clinical teaching, assessments and evaluation

1. Applications for education administration: Utilization of AI tools to evaluate various aspects of medical school and residency program applications such as prediction of selection, ranking and match were noted to have variable degrees of success compared to traditional methods. While AI applications could be feasibly used in the early screening processes,

they were limited in the evaluation of nuanced or inferred qualities such as resilience, passion, commitment, where human judgement was essential (12-14)

2. Applications to augment classroom teaching: Large Language Model (LLM) based tools can be trained to prepare representative patient cases can provide experiential learning to enhance clinical reasoning and apply concepts learnt through classroom teaching material. These AI chatbots can be used as standardized patients and trained to replicate classical and atypical presentations, mimic human communications, collect data about learning gaps, provide feedback, assess learner needs, and help create individualized learning plans (15-16). Machine Learning (ML) algorithms applied to surgical simulators can be used to assess, provide feedback and coaching in a stress-free and safe environment to medical students and residents to reduce the time to competency in the clinical setting (17-19).

3. Application for teachers: LLM algorithms can assist teachers in creating curriculum, lesson plans, presentation/lecture outlines and assessments, using the course guidelines, goals and objectives. Lecture contents can be enriched with image generators which allows for multimodal delivery of content through text-to-image and text-to-video formats. Learning can also be optimized by recording and summarizing lectures, monographs, videos and podcasts, with information that is relevant to the learner's context (20).

E. Artificial Intelligence in Patient Education

The ability of LLM to generate text adaptable to any necessary context, sophistication or learning level and in multiple languages, make it suitable for preparing patient education material, including the ability to create easily understandable figures (21-23). LLMs could improve readability of peer-reviewed scientific publications, allowing the general population access to highly technical medical literature (24). However, human review remains important to assure accuracy due to variability in model performance and output (25). Inability to access digital material particularly among older adults may present additional barriers to utilizing patient education chatbots (26).

F. Pitfalls and barriers

By creating a technology that is closer to human intelligence, AI has the capacity to fundamentally alter medical education and clinical practice. The speed with which this technology has developed in the past decade has outpaced AI literacy for most individuals. Thus, most medical educators are either slow or unable to utilize these tools of learning.

Increasing reliance on AI tools may not just result in off-loading of rote-tasks, but complex and critical tasks such as clinical reasoning and decision making resulting in automation bias and “de-skilling”, “never-skilling” or “mis-skilling” from erroneous outputs from these tools over time (27). AI models operate as “black box” and are subject to “hallucinations” resulting in variable and inaccurate output. Most of these tools have not undergone the rigorous field testing that most drugs and devices are subject to. Most of these tools are created using non-representative population data resulting in biased outputs and perpetuating inequities through the learning process. The world of Artificial Intelligence applications is currently a “wild west” with most governments and regulatory bodies struggling to come up with rules and regulations for safe and equitable implementation in the modern society.

SUMMARY

Explosive growth of medical knowledge and healthcare data makes AI tools inevitable in healthcare and medical education. In the realm of medical education, these tools can reduce administrative burden, augment classroom teaching, promote experiential learning and creates a plausible path to individualized “precision” education. However, these promises should be tempered by challenges that are both intrinsic to the tools such as inaccuracies, hallucinations and bias, clinical challenges such as loss of clinical skills, depersonalisation and conflicts with humanistic values.

CME ANSWERS

- 34. b
- 35. b
- 36. c

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Table 1: Draft of proposed curriculum in artificial intelligence (AI)/machine learning (ML) for clinicians (Adopted from Kedar S, Khazanchi D. Curr Opin Neurol. 2023 Feb 1;36(1):51-58)

Topic	Learning Outcomes
Conceptual foundations of AI - What is digital health - What is AI - Big data and AI - Computer Imaging - Machine learning - Deep Learning - Large language models	• List various sources and types of data which can be used for clinical research and practice • Define basic AI/ML concepts • Describe differences between traditional statistical models (automation) and ML • Differentiate between different types of AI techniques (ML, Deep ML, Computer Imaging) • Create a framework for the broad categories that comprise Artificial Intelligence
AI/ML in clinical practice - Digital revolution - Research applications - Clinical applications	• Analyse current examples of AI/ML applications in neuro-ophthalmology • Examine how ML could work with evidence-based medicine • Explain the process for evaluation of ML Applications and Research
Ethical and Social impacts of AI in healthcare - Ethics - Legal and regulatory concerns - Financial drivers - Medical education	• Describe ethical and medicolegal pitfalls of incorporating AI/ML technology in current clinical practice • Determine the financial drivers of data based technological applications in clinical practice

Table 2: Applications of AI/ML tools in medical education

Education administration	• Use of Machine Learning algorithms to predict residency applicants likely to be screened, interviewed, ranked and matched (12, 13). • Systematic review of MSPE, personal statements and recommendation letters including extraction and annotation of specific text snippets (14)
Augment classroom teaching	• Create personalized curriculum and outcome assessment • Use of AI chatbots as standardized patients and virtual “clinical learning coaches” (15) • Narrow focused LLM models (RAG models) such as Open Evidence can be used to retrieve and synthesize information in specific context and enhance bedside learning. • ML tools can augment surgical and procedural simulation to provide personalized feedback and coaching for procedures (17-19) • Use of image generator to enrich lecture experience through multimodal content delivery
Health literacy	• Generate text and figures adaptable to any context, learning level and language for patient education material • Enhance readability highly technical scientific publications for the general population

MSPE- Medical student performance evaluation

LLM- Large language models

RAG- Retrieval augmented generation

ML- Machine Learning

HOW CAN IT HELP US TODAY: CLINICAL-PHI

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LEARNING OBJECTIVES (3 required)

25. Identify what AI assistant programs are available for HIPAA protected patient care.
26. Describe the capabilities and shortcomings of the AI assistant programs.
1. Recognize how AI assistants can be customized to fit your clinical practice.

CME QUESTIONS (3 required)

1. AI assistant programs have been shown to reduce physician burn out. (True/False)
2. Patient safety and privacy is protected during use of AI assisted programs under this type of agreement between the business and medical practice.
 - a. HIPAA Agreement
 - b. Purchase Product Safety Agreement
 - c. Business Associate Agreement
 - d. Medical Facility Agreement
3. The AI scribes currently on the market are cleared through the FDA approval process. (True/False)

KEYWORDS (5 Max)

1. AI Assistant Programs
2. HIPAA
3. customizable
4. hallucinations

HIGHLIGHTS

- AI scribes can save hours of typing and lead to improvement in physician burnout.
- Companies sign Business Associate Agreements with healthcare practices who employ the AI assisted programs to protect patient safety and privacy.
- Most states mandate that all patients consent to use of AI assistant programs that are used during the patient interaction.
- AI assisted programs are customizable and helpful in saving time in clinic and patient documentation; however, they have common errors that providers need to be aware of, such as AI hallucinations, misinterpretation of information, omission of information, and speaker attribution errors.

SUMMARY

AI assistant programs have been quickly adopted into the everyday medical clinical practice with the promise of improving patient care and reducing physician burn out.^{1,2} AI assistance capabilities have advanced and is now integrated with our electronic medical record to help with chart review and documentation, specifically AI scribes.³

How AI Scribes Work

AI scribes use large language models to generate output while listening through an audio device during a patient-physician encounter. At the end of the recording, text is generated and incorporated into the note through templated commands (ie. Smartphrases) within a few minutes. This text can be edited by the physician. The text can be structured based on customizable preferences by each physician to appear and read like notes authored without AI assistance.

Safety and Privacy

Patient safety and privacy is protected under a Business Associate Agreement with the AI assistant program companies and the medical practice, which mandates the AI assistance follows HIPAA security requirements. Documentation must include the verbal or written consent from the patient which can be done easily using a templated statement in the note (ie. Smartphrase)

Limitations and Potential Pitfalls

The same concerns of AI hallucinations or fabrications and misinterpretation of information that AI-generated information has sparked in other platforms apply to the use in medicine, but there can be a high safety risk when this occurs with patient information raising significant concerns with each patient safety violation.

Other AI scribe shortcomings also include:

- Omission of information: the ophthalmic exam may not integrate into the electronic medical record-specified exam format
- Speech recognition limitations: there can be difficulty understanding which speaker is who, especially with specific linguistic patterns and accents.⁴
- Ability to synthesize complex Assessment & Plan discussions.

These shortcomings can be corrected with physician oversight and editing; however, this process is time-consuming and increases cognitive load, which detracts from the net benefit an AI scribe can have on physician well-being.

Suggested Utility for the Neuro-Ophthalmologist

Patients in the neuro-ophthalmology clinic are often complex, with extensive history taking and can lead to lengthy meaningful discussions where face-to-face conversations are imperative. AI Scribes can be very helpful in a neuro-ophthalmology practice especially during the history taking portion of the exam and help with:

- reducing fatigue during the clinic day with less time charting while in the room with the patient.
- fostering a less distractible environment without computers and typing conducive to difficult or sensitive conversations.
- Reduce length of visit as exam and history taking can occur simultaneously for a portion of the visit as history questions can occur during examination while the AI scribe is recording the patient responses.

Practitioners who do not have time/interest in editing or those who have a current practice with brief encounters or documentation may find the AI Scribe more wordy in the output and could take more time to complete notes.

Getting started using an AI Scribe:

- Large medical centers, university settings: inquire if there is access to an AI Scribe. If available, take a short course on practical implementation of synchronizing the AI scribe output with the electronic medical documentation.
- Private practice: There are many AI companies offering AI scribes on the market and it is important to find one that synchronizes with your current electronic medical documentation software. A Business Associate Agreement will be needed to proceed with use of product.
- Best practice is notifying the patient everytime an AI scribe is recording in the background and have a templated notation in the clinic note that the listening device was consented to by the patient and used during portions or the entirety of the visit.
- Recommend starting off using the AI Scribe for the entire visit and then reviewing the output for the history, physical exam, and assessment and plan to see if these are accurate and helpful for your practice. If you find that you only need the history or the plan then you can modify the template for the future encounters to only synchronize output from the AI scribe for those sections of the note.
- Toggle with the customizable features to see what works best for you and look for software updates as this is rapidly evolving technology

Future Developments and Conclusions

Because the field of AI assistance is rapidly changing, there are adaptations ahead that are purported to help with chart review, referral triage and better customization and synchrony with established exam documentation practices. With the complex patients seen in neuro-ophthalmology clinics, the use of an AI scribe can be most helpful in synthesizing the patient history and allows for multi-tasking during the visit so that some of the history can continue during the physical exam portion of the visit. The provider is less distracted by typing and can be more engaged face-to-face with the patients which may increase patient satisfaction and protect against provider burnout.

CME ANSWERS

1. True
2. C
3. False

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ARTIFICIAL INTELLIGENCE, HOW IT CAN HELP US TODAY: NON-PHI

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LEARNING OBJECTIVES

1. Describe at least two non-PHI applications of artificial intelligence (AI) relevant to neuro-ophthalmology.
2. Identify barriers to implementation of AI in non-PHI applications and strategies to overcome them.
3. Apply a practical framework to implement an AI tool in a non-PHI neuro-ophthalmology task.

CME QUESTIONS

1. Which of the following is a non-PHI application of AI that can immediately assist neuro-ophthalmologists?
 - A. Automated visual field interpretation using protected patient data
 - B. Generating plain-language summaries of journal articles for patient education
 - C. Predicting optic neuritis recurrence using hospital imaging archives
 - D. Integrating AI directly into electronic health records
 - E. Automated fundus photography analysis to distinguish papilledema from pseudopapilledema
2. Which of the following is an ethical consideration when implementing AI in non-PHI domains?
 - A. Ensuring transparency and validation of AI-generated content
 - B. Removing patient identifiers prior to data upload
 - C. Increasing the number of PHI datasets used for training
 - D. Replacing all human educational material with AI-generated text
 - E. Using chatbots to respond to patient inquiries
3. In a five-step implementation framework for AI tools in neuro-ophthalmology, which step comes first?
 - A. Evaluate the output
 - B. Identify the problem or workflow gap
 - C. Select the AI tool
 - D. Share results publicly
 - E. Brainstorm potential solutions

KEYWORDS

1. Artificial Intelligence (AI)
2. Neuro-Ophthalmology
3. Education
4. Research Analytics
5. Technology Tools

HIGHLIGHTS

- Artificial intelligence (AI) can streamline non-PHI tasks across research, education, communication, and workflow management in neuro-ophthalmology.
- AI tools help clinicians overcome information overload, improve productivity, and expand creative capacity for teaching and outreach.
- Common use-cases include:
 - Summarizing research evidence

- Drafting or revising professional communications
- Brainstorming ideas for research or curricula
- Generating patient-facing messages or educational materials
- Creating presentation graphics
- Producing first drafts of insurance appeals
- Major barriers include accuracy concerns (hallucinations), data bias, limited transparency, misinformation risk, and workflow integration challenges.
- Over-reliance on AI may lead to “cognitive off-loading,” reducing critical evaluation skills—verification remains essential.
- AI behaves like a “book-smart trainee”: productive and capable but requiring supervision proportional to task importance.
- A 5-step implementation strategy enables safe adoption: identify a problem → select a tool → pilot → critically evaluate → refine/iterate.
- Beginning with one tool and applying it to a low-risk task helps clinicians gain familiarity and confidence.
- Strategic use of AI can free time for patient care, research, education, and wellness, while broadening a clinician’s impact.

SUMMARY

Artificial intelligence (AI) is rapidly transforming how clinicians process information and communicate and its value extends beyond patient-specific data. The array of available AI tools is rapidly expanding, each with a unique combination of strengths and weaknesses to tackle problems that regularly face neuro-ophthalmologists. AI can enhance efficiency and creativity in non-PHI domains such as research support, public and professional education, task automation, and digital communication.

Benefits to AI use include time savings, enhanced productivity, and expansion of ideas. AI tools help clinicians manage information overload and focus attention on higher-level judgment and decision making.

Common practical-use scenarios:

- Summarizing research evidence to answer clinical questions
- Revising professional correspondence including emails and academic manuscripts
- Brainstorming ideas for research projects, curriculum design, or solving problems
- Generating responses to patient communications (e.g., patient portal messages)
- Generating first draft of insurance coverage denial appeal letters
- Creating presentation graphics
- Generation of lay-language educational materials for patients

A variety of barriers remain to the more widespread implementation of AI-powered tools. Technical concerns include uncertainty regarding the accuracy of AI tool output, including hallucinations (fabrication of ideas that may seem real but are not) and data bias. Whether an AI model exhibits data bias depends on how fully its training datasets represent the range of contexts in which it will be applied. Limited or biased training data leads to biased output. Ethical considerations include transparency, equity, and misinformation. The opacity of many complex deep learning algorithms undermines trust in them. Practical barriers include awareness of available tools, willingness to try new things, ease of workflow integration, and cost (financial and opportunity). Because AI can tempt users toward “cognitive off-loading” (delegating the cognitive effort of a task to AI), it can also limit the development and retention of critical evaluation skills. Verification of AI-generated output is essential prior to dissemination.

Like supervising a “book-smart” trainee, the more one works with AI tools, the more they learn where the AI tool can be trusted and where it cannot. Like all trainees, AI tools require supervision. The more critical the task, the closer the supervision should be.

As with any new technology or even medical treatment, there are early and late adopters, and the personal decision to integrate AI tools into one's workflow depends on exposure to and familiarity with the technology and its strengths and limitations. For those interested in adopting AI tools that do not know where to begin, I offer this five-step implementation strategy:

1. Identify a specific problem or workflow gap in your career or practice.
2. Select an appropriate non-PHI AI tool (text, data, or image) and learn about it. See table for some examples.
3. Pilot tool use and critically evaluate output quality.
4. Refine and iterate based on feedback.
5. Share results and lessons learned with colleagues.

Clinicians are encouraged to experiment safely with AI by first identifying a problem to be addressed, selecting a relevant AI tool, applying it to a low-risk task related to the problem, and critically evaluating its utility. Repeatedly using a tool increases one's familiarity with it and how to use the tool in a way that leverages its strengths while allowing the user to mitigate its weaknesses. Through careful use, neuro-ophthalmologists can leverage AI to extend their educational reach, foster collaboration, and reclaim time for patient care, scholarship, and personal care.

Below is a table containing a compilation of popular AI tools in alphabetical order with a brief description of their strengths and access considerations.

Tool / Platform	Primary Use or Strength	Access / Cost
General AI Tools		
ChatGPT / GPT-4 / GPT-5 (OpenAI)	General-purpose LLM for summarizing research, drafting text, and generating educational material.	Free tier; paid Plus / Pro plans for advanced models.
Claude.ai (Anthropic)	Structured summarization and drafting, AI assistant; excels in readability.	Free limited; paid Pro.
Gemini	General-purpose LLM that integrates with other Google apps and handles text, images, audio, and video.	Free basic; paid Pro.
Hugging Face	Repository of open-source models for NLP and imaging tasks, has AI app directory.	Free / open source.
Microsoft Copilot / 365 Copilot	AI assistant with Office suite integration for writing and data tasks.	Free Copilot; paid plans with Office integration and unlimited usage.
Research and Writing AI Tools		
ChatPDF / Humata.ai	Summarize and query PDFs (e.g., articles or guidelines).	Free limited; paid for long documents.
Consensus.app	Synthesizes findings from peer-reviewed papers with citations.	Free limited; paid Pro.
Elicit.org	AI assistant for systematic literature reviews.	Free academic use.
NotebookLM (Google)	Organize and summarize uploaded PDFs and notes for literature review or topic exploration.	Free (beta).
OpenEvidence	Evidence-based summaries from biomedical literature for clinical and research questions.	Free academic; subscription for analytics.
Perplexity.ai	Research-focused conversational search with citations.	Free basic; Pro tier available.
QuillBot / GrammarlyGO	Grammar checking and professional writing assistance.	Free basic; paid Pro.
Scite.ai	Evaluates citation reliability; ideal for vetting literature quality.	Free limited; paid institutional plans.

AI Tools for Visual Design and Education		
Bing Image Creator / DALL·E	Generates images and videos without PHI.	Free with Microsoft account.
Gamma.app	Creates AI-assisted slide decks and visuals for lectures, documents, websites.	Free limited; paid Pro.
Khanmigo (Khan Academy)	Educational AI for teaching and learner engagement, like a tutor	Free for educators; paid for learners.
Canva Magic Studio	Generates visuals and infographics for education, social media, and web design.	Free basic; Pro plan available.

Abbreviations: AI (artificial intelligence), LLM (large language model), PHI (protected health information), NLP (natural language processing)

CME ANSWERS

1. B
2. A
3. B

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