Neuro-Ophthalmology 2017
When Should I Worry?
Dangerous Signs, Symptoms, and Findings in Neuro-Ophthalmology

Program Directors
Michael S Lee MD and Prem S Subramanian MD PhD

In conjunction with the North American Neuro-Ophthalmology Society

Ernest N Morial Convention Center
New Orleans, Louisiana
Saturday, Nov. 11, 2017

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The American Academy of Ophthalmology

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CME Credit

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The purpose of the American Academy of Ophthalmology's Continuing Medical Education (CME) program is to present ophthalmologists with the highest quality lifelong learning opportunities that promote improvement and change in physician practices, performance, or competence, thus enabling such physicians to maintain or improve the competence and professional performance needed to provide the best possible eye care for their patients.

2017 Neuro-Ophthalmology Subspecialty Day
Meeting Learning Objectives
Upon completion of this activity, participants should be able to:

■ Recognize urgent signs and symptoms in the evaluation of adults with diplopia
■ Direct the initial workup of a patient with visual loss from optic neuropathy
■ Distinguish the key neuro-ophthalmic manifestations of systemic diseases affecting visual function
■ Determine when and how to order and interpret diagnostic testing studies for ophthalmic conditions

2017 Neuro-Ophthalmology Subspecialty Day
Meeting Target Audience
The intended audience for this program is comprehensive ophthalmologists.

2017 Neuro-Ophthalmology Subspecialty Day
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The Academy designates this live activity for a maximum of 7 AMA PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

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■ Register in advance and pick up your badge onsite if materials did not arrive before you traveled to the meeting;
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- CME credit reporting/proof-of-attendance letters
- Onsite registration receipt
- Instruction course and session verification

Visit www.aao.org/cme for detailed CME reporting information.
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Livingston, NJ

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Kimberly M Winges MD
Portland, OR

Michael S Vaphiades DO
Birmingham, AL

No photo available

Zoe R Williams MD
Rochester, NY
How to Use the Audience Interaction Application

Pull Out Your Mobile Device or Laptop and go to:
join.fxptouch.com/neuro

- Respond to polls
- Submit questions to the moderators
- Take and save digital notes
- Follow along with the content on screen via your tablet, smartphone or laptop

In conjunction with the North American Neuro-Ophthalmology Society (NANOS)

**SATURDAY, NOV. 11**

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<td>CONTINENTAL BREAKFAST</td>
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<tr>
<td>8:00 AM</td>
<td>Introduction</td>
<td>Prem S Subramanian MD PhD*</td>
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## Section I: Help, My Patient Can't See!
Moderators: Sarita B Dave MD and Julie Falardeau MD
Panelists: Lanning B Kline MD, Mark J Kupersmith MD*, Leah Levi MD, and Neil R Miller MD*

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<td>Lulu L Bursztyn MD</td>
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<td>Transient Vision Loss in an Older Patient</td>
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<td>Vision Loss after Non-ophthalmic Surgery</td>
<td>Kaitlyn W Nolan MD</td>
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<td>Michael S Lee MD*</td>
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## Section II: Could Systemic Disease Cause This Problem?
Moderators: Anne S Abel MD and Rudrani Banik MD*
Panelists: Larry P Frohman MD*, Jacqueline A Leavitt MD, Andrew G Lee MD, Jeffrey G Odel MD*, and Valerie A Purvin MD

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<td>Sidney K Gicheru MD</td>
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<td>Vision/Visual Field Loss with Disc Swelling</td>
<td>Michael S Vaphiades DO</td>
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<td>Progressive Orbital Swelling and Pain</td>
<td>Roger E Turbin MD*</td>
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<td>11:05 AM</td>
<td>Visual Field Loss and Normal Fundus</td>
<td>Mark L Moster MD*</td>
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<td>An Elderly Patient Who Can't Read</td>
<td>Victoria Pelak MD*</td>
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* Indicates that the presenter has financial interest. No asterisk indicates that the presenter has no financial interest.
## Program Schedule

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<td>Transient Bilateral Vision Loss</td>
<td>Fiona E Costello MD*</td>
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<td>Double Vision and Dizziness</td>
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<td>Diplopia after Concussion</td>
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<td>2:20 PM</td>
<td>My Eyes Are Not Moving!</td>
<td>M Tariq Bhatti MD*</td>
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<td>New Double Vision in the Young</td>
<td>Valerie I Elmalem MD</td>
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<td>Blurred Vision with Reading</td>
<td>Paul H Phillips MD</td>
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<td>Marie D Acierno MD</td>
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<td>Abnormal OCT in a Patient with a Normal Exam</td>
<td>Kimberly M Winges MD</td>
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<td>Abnormal Visual Field Defects with Normal Optic Nerves</td>
<td>Y Joyce Liao MD PhD</td>
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<td>Panel Debate: Obese Female with Bilateral Disc Swelling—Do You Need Magnetic Resonance Venography? Lumbar Puncture?</td>
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<td>Conclusion/Wrap-up</td>
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* Indicates that the presenter has financial interest. No asterisk indicates that the presenter has no financial interest.
Case Presentations
Section I: Help, My Patient Can’t See!

Painful Vision Loss

Lulu Bursztyn MD

CASE

History and Exam

A 27-year-old female is referred by her optometrist for right eye pain and blurred vision. Five days ago, she developed pain in the right eye, exacerbated by eye movement. Two days later, she felt like there was a “thumbprint” blocking the vision in that eye. The pain is resolving, but the vision is becoming increasingly blurry. She was evaluated by her optometrist, who noted decreased visual acuity and right optic disc edema.

Her past medical history is unremarkable, and she takes no prescription medications. She is a half-pack/day smoker and drinks alcohol rarely. Family history is positive for diabetes mellitus and heart attack in her father.

On examination, her BCVA is count fingers right eye and 20/20 left eye. Pupils are equal and reactive, with a right relative afferent pupillary defect (RAPD). Color vision is full in the left and untestable in the right by Ishihara color plates. Extraocular movements are full. Alignment is orthophoric. Anterior segment examination is normal. Fundus examination shows diffuse optic disc edema on the right and a normal optic disc, with cup-to-disc ratio of 0.5 on the left. Visual field testing shows diffuse depression in the right eye and is normal in the left.

An MRI of the head and orbits demonstrates gross abnormality of the right optic nerve, with enlargement and enhancement extending from the optic foramen into the intraorbital component. Protrusion of the optic nerve head into the globe is easily visible. There are also 2 small, nonspecific, white matter hyperintensities that do not enhance.

Clinical Course and Outcome

This patient has new-onset painful vision loss in the right eye associated with marked optic disc edema. Although significant disc edema is unusual, this presentation is highly suspicious for optic neuritis. Standard protocol for assessing suspected optic neuritis should include a careful history, measurement of BCVA, assessment for a RAPD, ophthalmoscopy, and visual field testing. All patients should undergo a contrast enhanced MRI of the brain to assess for future risk of developing MS.

Atypical features of optic neuritis that should prompt further workup are lack of pain or protracted pain, significant optic disc edema, bilateral vision loss, retinal exudates, lack of visual recovery after 3 months, worsening after withdrawal of steroids, or past medical history of cancer. It is particularly important to make the diagnosis of neuromyelitis optica spectrum disorder, as patients must be treated early and aggressively to minimize permanent disability.

Although the MRI appearance is consistent with a demyelinating optic neuritis, bloodwork for idiopathic optic neuritis mimics is warranted due to the atypical features of significant swelling and the extent of optic nerve involvement. Bloodwork was negative for aquaporin-4 antibodies, anti-thyroid peroxidase, anti-thyroglobulin antibody, rheumatoid factor, anti-double stranded DNA, anti-nuclear antibody, extractable nuclear antigen, angiotensin-converting enzyme, and syphilis serology.

The patient was treated with 1250 mg oral prednisone daily for 3 days. At her 6-week follow-up visit, visual acuity was unchanged at count fingers, but the optic disc was hyperemic and only slightly elevated. The dense RAPD was still present. On further questioning, she complained of new-onset paresthesias in both arms. Spinal MRI demonstrated longitudinally extensive transverse myelitis. She was ultimately diagnosed with neuromyelitis optica spectrum disorder and started on immunosuppressive therapy. At 6 months, the visual acuity was 20/400 with a residual inferior arcuate visual field defect and optic disc pallor.

Unilateral Painless Vision Loss

“My vision went bad sometime last year”

Shakthi Kanagalingam MD

CASE

History and Exam

A 64-year-old right-handed white male is referred by his primary care physician for vision loss in the right eye. He is a poor historian. He thinks that the vision loss in the right eye may have occurred approximately 6 months prior. The vision in the right eye has been blurry for this period of time, with no fluctuations. He denies any headaches or ocular pain. He feels the vision in the right eye has been stable, without any progressive decline since the onset of his symptoms. Review of systems is otherwise negative.

His past medical history is significant for hypertension, hyperlipidemia, non-insulin dependent diabetes mellitus, and sleep apnea. He was diagnosed with sleep apnea a year ago, but has not obtained a sleep machine as yet. He is a current every day smoker. His current medications include amlodipine-atorvastatin, metoprolol, baby aspirin, and metformin.

On examination, the patient’s BCVA was 20/70 in the right eye, and 20/25 in the left eye. IOPs by applanation were 15 in the right, and 16 in the left. Color vision with HRR plates revealed a slow 5/10 in the right eye, and a brisk 10/10 in the left eye. A relative afferent pupillary defect was present in the right eye. Ocular motility was full bilaterally. Static visual fields demonstrated an inferior altitudinal defect in the right eye, and...
full visual field in the left eye. Examination of the optic nerves revealed small cup-to-disc ratios bilaterally, with pallor of the right optic nerve. The maculae and peripheral retina were normal bilaterally.

**Clinical Course and Outcome**

At his last physical examination a month ago, he informed his primary care physician about his vision loss. Lab work was subsequently drawn, including a complete blood count, platelets, erythrocytes sedimentation rate, C-reactive protein, and HbA1C. The HbA1C was found to be elevated, at 7.5. All other labs were normal.

MRI of the brain and orbits with gadolinium was obtained, and found to be normal.

Differential diagnosis of an optic neuropathy includes compressive or infiltrative optic nerve lesion, ischemic (arteritic anterior ischemic optic neuropathy [AAION]), nonarteritic ischemic optic neuropathy (NAION), post-traumatic, demyelinating, hereditary, or toxic.

Hereditary causes of optic neuropathy are typically bilateral, although they can present sequentially. Toxic etiologies also have bilateral presentation. Both hereditary and toxic optic neuropathies typically demonstrate central visual field defects. There was no history of trauma preceding this patient’s vision loss, ruling out post-traumatic optic neuropathy.

In this case, the AAION is unlikely given his normal inflammatory markers and the absence of systemic symptoms of giant cell arteritis (ie, headache, jaw claudication, fever, weight loss, anorexia, tongue pain). Vision loss is typically severe (<20/200) in AAION, with a normal or large optic disc cup in the fellow eye.

In our case, examination of the patient’s optic nerves revealed a disc-at-risk appearance bilaterally, with pallor of the right optic nerve. The presence of structural crowding of the optic disc and multiple vasculopathic risk factors favor NAION as the likely diagnosis. Risk factors associated with NAION are small cup-to-disc ratio, diabetes mellitus, systemic hypertension, and hyperlipidemia. Other associations are sleep apnea, generalized hypoperfusion, nocturnal hypotension, anemia, and medications such as amiodarone, and phosphodiesterase inhibitors (eg, sildenafil).

In the absence of documented optic disc swelling at the time of vision loss, neuro-imaging should be obtained to rule out a compressive lesion causing optic atrophy.

In this case, his neuroimaging was normal. The patient returned to have a repeat visual field 6 weeks later, which revealed a stable, unchanged inferior altitudinal defect in the right eye.

He followed up with his primary care physician for long-term control of his vasculopathic conditions. He was referred to the sleep clinic to obtain a CPAP machine.

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**Bilateral Painless Vision Loss**

*Raghu Mudumbai MD*

### CASE

#### History and Exam

Sixty-four-year-old African immigrant male presents with 6-week history of a “shadow in his vision” in the right eye, referred after initially seeing his primary care physician. It occurred during the day, while he was watching soccer. It has not progressed or improved over the last 1 month. He also endorses having numbness/tingling in his left lateral foot about 1.5 months ago; his right foot had similar sensations a few days later. For both, the sensation lasted only a few days and is now much improved and completely resolved. On review of symptoms, he states that about 1 week ago he had sharp pain in his left chest while resting. It lasted for about 15 minutes, then resolved spontaneously. Did not radiate to his left arm or neck. Denies dyspnea, pain. No changes since then. No changes to the left eye. He denies any current numbness, tingling, weakness, headache, jaw claudication, scalp tenderness.

The patient carries a diagnosis of myopia and ocular hypertension for which he is being monitored. His past medical history is significant for hypertension, hyperlipidemia, chronic obstructive asthma, *H. pylori* infection, renal insufficiency/renal cyst, and positive PPD. His medications include albuterol, amlodipine, atorvastatin, nitroglycerin, ranitidine, and tamsulosin. The patient is originally from Nigeria, having come to the United States in 1970s. He is currently living in Seattle by himself. No pets at home; has allergies. Never tobacco, no alcohol, no illicit drugs. There is no known family history.

Examination shows BP 120/80, height 5’10” weight 205 lb. His BCVA is 20/600 O.D., 20/25 O.S. A relative afferent pupilary defect (RAPD) is present O.D. Ocular motility is full. Color vision is 0/11 O.D. and 11/11 O.S. on Ishihara plates. IOP in mmHg is 24 O.D., 19 O.S. Pachymetry in microns is 590 O.D. and 610 O.S. Anterior segment exam is normal for 2+ nuclear sclerotic cataracts O.U. Gonioscopy reveals open angles in both eyes. Optic nerves and retina are shown below.

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*Figure 1. Right fundus.*
Clinical Course and Outcome
The optic nerves had a suggestion of mild temporal pallor, in addition to moderate cupping and peripapillary atrophy. Humphrey visual field testing was highly suggestive of a bitemporal hemianopia.

OCT optic nerves indicated severe superior quadrant thinning O.D. and mild thinning inferiorly, temporally, and nasally O.S.

MRI scan of brain and orbits indicated a large 2.6x2.5x3.8 cm sellar / suprasellar, heterogenous, enhancing mass with internal pockets of acute / subacute hemorrhage, most consistent with hemorrhagic pituitary macroadenoma. The suprasellar extension results in severe mass effect and superior displacement of the optic chiasm and cisternal segments of the optic nerves, bilaterally.

Patient had urgent trans-sphenoidal decompression of the macroadenoma. He was noted to have panhypopituitarism. Approximately 1 month following surgery, his vision improved to 20/30 O.D. and 20/20 O.S., with significant reduction in the size of the RAPD. His Ishihara color plates measured 9/11 O.D. and 11/11 O.S.

Although the broad differential included glaucomatous optic neuropathy (prior history of ocular hypertension and moderate cupping) and ischemic optic neuropathy (multiple cardiovascular risk factors and acute, painless loss of vision), several features of the clinical exam led to concern for a compressive lesion of the anterior visual pathway. While the optic nerve did demonstrate cupping, central visual acuity was disproportionately affected, along with loss of color vision, which is not typical for glaucoma. The optic nerve was not swollen, which would be expected with acute anterior ischemic optic neuropathy. Additionally, the optic nerve did not demonstrate the typical small cup-to-disc ratio (“disk at risk”) found in nonarteritic anterior ischemic optic neuropathy.

Features suggestive of a compressive process include loss of central vision, loss of color plates, and pallor of the optic nerve (diffuse or in the temporal rim).
Transient Vision Loss in an Older Patient

Kenneth S Shindler MD PhD

CASE

History and Exam

A 65-year-old white woman presents to the emergency department complaining of episodes of loss of vision in the right eye and is seen in consultation by ophthalmology.

The patient reports 5 episodes of darkening of her vision, right eye only, over the past 2 months. Vision loss is described as being like a curtain coming down across her vision. Vision improves after several minutes. She brings a written list of the dates/times of each episode and the activities she was involved in when the vision loss began. There is no pain or headache associated with these episodes, but she does have a long history of classic migraines with a scintillating scotoma visual aura, which have occurred several times a year since she was a young adult. Her classic scintillating scotomas can occur without headache, but they often are followed by throbbing headache with nausea and photophobia. She denies any other related symptoms, including no jaw claudication, scalp tenderness, weight loss, fever, or fatigue.

Her past medical history is significant for hypertension, hyperlipidemia, and migraines. Her medications include lisinopril and atorvastatin, and she takes a daily multivitamin with calcium. She does not smoke and only drinks alcohol on rare occasions. Her family history is significant for migraine headaches.

On examination, her BCVA is 20/20 O.D. and 20/25 O.S. Pupils are equal and briskly reactive to light without an afferent pupillary defect. Visual fields are full to confrontation. Ocular motility is full. IOP is 14 in each eye. Slitlamp examination is normal except for trace blepharitis and mild nuclear sclerosis in both eyes. Gonioscopy reveals open angles in both eyes. Dilated fundus examination shows normal optic nerves and macula and peripheral retina are normal in both eyes. No emboli are visible in retinal vessels in either eye. Sedimentation rate (ESR) drawn in the emergency department is 31 mm/h, and C-reactive protein is 0.2 mg/dL.

What are your next steps?
1. Recommend artificial tears and warm compresses with lid scrubs
2. Start high-dose steroids and obtain temporal artery biopsy
3. Obtain imaging of the carotid arteries and start daily aspirin
4. Reassure the patient that this is just a variation in her migraine aura

Clinical Course and Outcome

Further evaluation by the emergency department included MRA of the carotid arteries, which showed minimal stenosis, 0%-30%, bilaterally, and MRI brain, which was unremarkable. Pulse was normal, and no cardiac murmur was heard. The patient was given aspirin in the emergency department and sent home, instructed to take aspirin daily and to follow-up with her primary care physician to further assess her cardiovascular risk factors. Follow-up outpatient echocardiogram the next day was unremarkable. The patient reported 1 additional episode of vision loss a few days after presentation, but has had no further episodes since then.

The transient darkening of the vision in one eye experienced by this patient is consistent with a diagnosis of amaurosis fugax (“fleeting blindness”) or transient monocular ischemic attack. Ischemia is the most common etiology for transient monocular blindness, and the source of such ischemia is most commonly from stenosis of the carotid arteries. As in this case, however, critical stenosis of the carotid artery is not always found, and further investigation for a source of emboli and other sequelae of embolic disease, as well as consideration for other etiologies, needs to be considered.

Absence of visible emboli in the retina does not exclude an embolic etiology, as emboli clear after transient occlusion, and it is not uncommon that no vessels retain any visible emboli; the presence of a retinal embolus on examination is thus very helpful in diagnosis, but absence is not. When transient ischemia is suspected clinically, consideration of other sources of emboli need to be considered if carotid studies fail to identify a source. Cardiac evaluation for calcification of heart valves or for thrombus from atrial fibrillation or other abnormalities may identify a source, but emboli can also arise from other proximal vessels such as the aorta and thus may not be found even after carotid and cardiac studies are performed, as in the current case. With a high index of suspicion, aspirin therapy should still be considered, and while the resolution of the episodes of vision loss in the current case after initiation of aspirin therapy does not prove there was indeed an embolic etiology, it is at least consistent with that diagnosis.

Giant cell arteritis (GCA) can also present with amaurosis, and given the potential serious consequences of this disease, GCA must be considered in all older patients presenting with amaurosis. In the current case, the patient was perhaps on the younger end of the age range for GCA, but certainly well within its limits. Clinical suspicion for GCA was significantly reduced by a careful, negative review of symptoms, and further reduced by normal inflammatory blood markers. It is helpful to note that some blood laboratories will flag an ESR of 31 as high, using a single average “normal” test range for all samples regardless of age; however, ESR is known to increase with age, and 31 is not outside the normal range for a 65-year-old woman. As a general rule, the upper limit of the normal ESR range for a woman is approximately her age plus 10, then divided in half, or for our patient (65 + 10) / 2 = 37.5. Her low C-reactive protein provides further comfort in concluding low suspicion for GCA.

Visual aura of migraine is also a consideration in the current case. Negative visual phenomena, such as the darkening of the vision described in the current case, is uncommon in migraine, but not unheard of. The fact that the patient has a long-standing history of classic visual migraine auras with scintillating scotomas may actually increase suspicion that her current episodes could be migraine phenomena, as the pattern and type of migraine symptoms that one patient experiences can change as the patient ages; whereas new-onset migraines at age 65 is much less common. Nonetheless, migraine as an etiology for transient monocular vision loss should remain a diagnosis of exclusion,
and with darkening of the vision it is much less common than ischemic etiologies.

Other causes of transient vision loss can be considered but are unlikely in this case. Intermittent angle closure can present with transient visual disturbance, although not typically a dark curtain crossing the vision as in this case. Visual symptoms from intermittent angle closure are also often accompanied by pain or discomfort in or around the eyes. Gonioscopy reassuringly did not identify narrow, occludable angles. Ocular surface disease causing intermittent drying or irritation of the ocular surface can also lead to transient visual disturbances, although typically these include blurring or distortion, not a darkening of the vision as in this case. Such phenomena would also typically be less distinct and more frequent, and the fact that the patient was able to record a list of times when her vision loss episodes occurred suggests a more acute onset and distinct features than would be expected with ocular surface irritation.

Vision Loss after Non-ophthalmic Surgery
Kaitlyn Nolan MD

CASE

History and Exam
An 84-year-old man with no past ocular history presents to the hospital for admission to undergo scheduled triple coronary artery bypass graft. He has a past medical history significant for coronary artery disease, atrial fibrillation, congestive heart failure, hypercholesterolemia, obesity, and hypertension. His medications include isosorbide mononitrate, metoprolol, warfarin, furosemide, nitroglycerin, simvastatin, terazosin, and aspirin. His cardiac catheterization 2 months prior demonstrated significant stenosis of 3 coronary arteries, and a transesophageal echocardiogram showed a dilated ascending aorta, mild aortic regurgitation, and mild tricuspid regurgitation with an ejection fraction of 45%. His warfarin and aspirin were discontinued 1 week prior to the admission.

During the operation, the patient was placed on cardiopulmonary bypass, and the 3 coronary arteries were bypassed successfully. The patient’s heart then distended and he went into ventricular fibrillation. Multiple attempts at decompressing the heart and cardioversion were made without success. At this point, the surgeon decided to proceed with aortic valve replacement on bypass. It was noted that the valve was not positioned well, and the decision was made to replace the ascending aorta. At this point, the heart was functioning well and the patient was weaned from cardiopulmonary bypass. The chest was left open due to bleeding and edema of the heart. The procedure took 12 hours, and the estimated blood loss was 1 liter; he received 7 units packed red blood cells.

Postoperative course was tenuous, with prolonged cardiogenic shock requiring multiple vasopressors. The lowest blood pressure measured 80/40 mmHg, hemoglobin 6.5 g/dL, and the hematocrit 22.9. The patient’s clinical condition improved over the next 3 days, and his sternum was closed. The patient was extubated and awoke 3 days after the sternal closure. The patient immediately complained “I cannot see anything.” He had a mild headache.

An ophthalmology consultation was obtained. His visual acuity was light perception only in the right eye and hand motions only in the left eye. The examiner was unable to elicit confrontation visual fields due to poor vision. His pupils were symmetric and sluggishly, with a right relative afferent defect. The extraocular movements were full, and there was 2 mm of ptosis on the left. Cranial nerves were otherwise normal, and the rest of the neurological exam was intact. His IOP was 14 mmHg in the right eye and 12 mmHg in the left eye. Anterior and posterior segment examinations were unremarkable. Both optic nerves had 0.5 cup-to-disc ratios and appeared normal.

Clinical Course and Outcome
This is a patient with bilateral visual loss after prolonged cardiac surgery. We do not know what the visual field looks like, but the pupils are sluggish, suggesting involvement of the optic nerves or chiasm. There are multiple potential causes of postoperative visual loss (POVL): anterior or posterior ischemic optic neuropathy (ION), central retinal artery occlusion (CRAO), cortical visual loss, posterior reversible encephalopathy (PRES), and pituitary apoplexy. ION and CRAO (either by embolus or increased IOP) may be unilateral or bilateral, whereas cortical visual loss, PRES, and pituitary apoplexy most of the time have bilateral findings.

Cortical visual loss and PRES are unlikely in this case due to the pupil abnormality. Pituitary apoplexy, especially in a bilateral case such as this, must be ruled out. We are told there is 2 mm of ptosis in the left eye; this is a very small finding in the absence of paralytic strabismus or anisocoria and may have been present prior to surgery. However, given the severe nature of his presentation, a CT was ordered, which showed only chronic microvascular changes. There was no pituitary adenoma or hemorrhage.

Bilateral CRAOs, while rare, can occur. However, we would expect to see whitening and edema of the retina, and possibly a plaque in an arteriole. This patient’s dilated fundus exam was normal. Similarly, we would expect to see optic nerve edema in a case of bilateral anterior ION. Thus, the correct diagnosis is bilateral posterior ION (PION).

The patient was monitored but did not recover any additional visual function. After 6 weeks, he was noted to have global pallor of the optic nerve bilaterally. He was referred to low vision services.

PION is a known, albeit rare, complication of cardiac and spinal surgery. While the exact mechanism is unknown, this may be related to increased venous pressure and interstitial edema, resulting in damage to the optic nerve by compression of the vascular supply, infarction, or direct mechanical compression.1 It is bilateral in 66% of cases.2 According to a recent study using data from the National Inpatient Sample (NIS), the risk of ION after coronary artery bypass grafting (CABG), valve replacement, or left ventricular assist device placement is 0.014%.3 Risk factors include carotid artery stenosis, stroke, and degenerative eye diseases (diabetic retinopathy, hypertensive retinopathy, cataract, glaucoma, and macular degeneration).1 In a series of 1442 patients undergoing “off-pump” CABG over a 10-month period, PION occurred in 4 patients (0.28%).4 The incidence of ION following spinal fusion (thoracic, lumbar, or sacral) between 1998 and 2012 was 1.02 per 10,000 cases in the NIS.5 Risk factors include increased age,
male sex, obesity, and blood transfusion.5 The American Society of Anesthesiologists also cites longer anesthetic duration, greater blood volume loss, and insufficient colloid administration.1 Hypothermia and hypotension (MAP < 70 mmHg, systolic pressure < 90 mmHg) are additional risk factors.6 PION is typically a clinical diagnosis, but in some cases restricted diffusion on diffusion-weighted imaging or gadolinium enhancement of the nerve may be seen.7,8

There are no established treatments available for PION. Some have reported an improvement in visual acuity after adequate blood transfusion for anemia, the use of vasopressors for hypotension, or the use of corticosteroids; however, these reports did not include controls.6

The most important diagnosis to keep on the differential of POVL is pituitary apoplexy, as this can be life threatening and is also the only cause of POVL that may be treatable. Bilateral vision loss, bitemporal field defects, cranial nerve palsies, altered consciousness, and headache should raise high concern. Suspicion should be roused even in cases of isolated blindness.9 These patients should be imaged emergently, and consultations should be obtained from neurosurgery and endocrinology. Similarly, cortical stroke needs to be ruled out swiftly, either clinically or by neuroimaging.

References

Vision Loss with a Normal Exam
Peter A Quiros MD

CASE

History and Exam
A 24-year-old white male is examined in neuro-ophthalmology clinic 2 months after a motor vehicle accident (MVA) with loss of consciousness for 20 minutes. Two months prior to neuro-ophthalmic consultation, the patient had been involved in a motor vehicle accident in which the car collided with a tree. The patient was pulled, unconscious, from the wreckage and taken to the emergency department at Harbor-UCLA Medical Center. He underwent a complete trauma evaluation. He had regained consciousness shortly after arriving in the ED. At that time he underwent CT scanning of the head, spine, thorax, and abdomen. He was noted to have a fractured humerus and multiple contusions to his body, including the face. Both eyes were swollen shut. He was admitted for observation. Three days later, as the lid swelling subsided, the patient complained that he was “blind” in his left eye and could not see well from his right eye. An ophthalmology consult was called.

The ophthalmology consult resident found the patient to have 20/200 vision in the right eye and NLP vision in the left eye. The pupils were both sluggishly reactive to light, but no relative afferent pupillary defect (RAPD) was noted. Intraocular pressures were 20 and 21. Portable slitlamp exam did not reveal any iridodialysis or lens subluxation. Media were clear. Funduscopic examination revealed a normal fundus, there was no optic nerve edema or pallor, and the retina was flat and free of hemorrhage or chemotio.

A presumptive diagnosis of traumatic optic neuropathy (TON) was made, and a high-resolution CT scan of the orbits was obtained. The scan was normal and did not reveal any optic canal fractures or sheath hemorrhages. Megadose steroid therapy was not given. The patient was asked to follow up with neuro-ophthalmology within 1-2 weeks after discharge.

The patient missed 3 outpatient appointments and finally came to neuro-ophthalmology 2 months after the accident.

The examination was unchanged from that conducted as an inpatient. The patient claimed NLP vision O.S. and 20/200 vision O.D. Both pupils remained sluggishly reactive to light, but no RAPD was elicited. The remainder of the examination was normal, and there was no pallor of the optic nerves.

Visual field testing O.D. was unreliable. Retinal nerve fiber layer OCT and ganglion cell complex (GCC) analysis were both full and normal.

An MRI scan was performed and found to be normal, without any visual pathway disruption.

Clinical Course and Outcomes

Given the circumstances preceding the vision loss (MVA) and the paucity of findings on examination, the diagnosis of TON was reasonable. However, the lack of an RAPD in the initial setting would not be consistent with a TON resulting in NLP vision.

Given the natural history of TON, optic nerve atrophy should have developed in one or both eyes within several weeks.
Even though the RNFL thinning may lag behind an event by several months, disruption of the GCC is usually fairly immediate, especially in injury of the retrobulbar optic nerve. The normal OCT examinations are also not in keeping with the visual acuities.

In this case, it is reasonable to obtain an MRI to ensure that there is no disruption of the anterior or posterior visual pathway. Stroke of the posterior pole could potentially cause this clinical picture, but it would be unusual for such severe vision loss to occur without a significant change in the posterior pole. Therefore, the MRI findings cannot explain the vision loss either.

At this point, additional office testing should be performed. Optokinetic nystagmus (OKN) testing can be helpful in cases of NLP vision. Computerized OKN can be correlated with visual acuity and can serve as an objective means of assessing visual acuity. It is not readily available outside the research lab; nonetheless, manual OKN is useful in assessing NLP in vision, as the OKN response will be suppressed in the NLP eye. In our case, the OKN response was equivocal in the NLP eye and normal in the 20/200 eye.

Stereo testing with the use of polarized lenses can also be of use. These tests are readily available in most offices in the form of Titmus fly testing (see Figure 1). In patients with NLP vision there should be no stereopsis. If stereopsis is detected, the level of stereopsis correlates with Snellen visual acuity, as the degree of stereopsis is only as good as the vision in the worse eye.

In our case there did not appear to be stereopsis, even at the level of the Titmus fly. However, our patient was able to discern the right and left designators on the bottom of the Titmus page. These are consistent with 20/100 acuity at minimum, and the left-hand letter can only be seen by the O.S., while the right-hand letter can only be seen by the O.D. This finding is not consistent with NLP vision in the O.S.

Visual evoked potentials (VEP) can also be of use. However, these tests are not as readily available as the in-office tests, and whereas a normal VEP will effectively rule out NLP vision it is possible to produce an abnormal VEP in normal individuals through “defocusing” and “inattentiveness.”
2017 Advocating for Patients
Sidney K Gicheru MD

Ophthalmology’s goal to protect sight and empower lives requires active participation in and commitment to advocacy from every ophthalmologist. Contributions to the following three critical funds are a part of that commitment:

- OPHTHPAC® Fund
- Surgical Scope Fund (SSF)
- State Eye PAC

Please join the dedicated community of ophthalmologists who are contributing to protect quality patient eye care for everybody. The OPHTHPAC Committee is identifying Congressional Advocates in each state to maintain close relationships with federal legislators in order to advance ophthalmology and patient causes. At Mid-Year Forum 2017, we honored nine of those legislators with the Academy’s Visionary Award. This served to recognize them for addressing issues important to us and to our patients. The Secretariat for State Affairs is collaborating closely with state ophthalmology society leaders to protect Surgery by Surgeons at the state level. This year has seen an unprecedented effort by optometry to advance its scope of practice via legislation rather than education. Our mission of protecting sight and empowering lives requires robust funding of both the Surgical Scope Fund and the OPHTHPAC Fund. Each of us has a responsibility to ensure that these funds are strong.

**OPHTHPAC® Fund**

OPHTHPAC is a crucial part of the Academy’s strategy to protect and advance ophthalmology’s interests in key areas, including physician payments from Medicare and protecting ophthalmology from federal scope of practice threats. Established in 1985, OPHTHPAC is one of the oldest, largest, and most successful political action committees in the physician community. We are very successful in representing your profession to the U.S. Congress.

As one election cycle ends, a new one starts, yet the pressure to remain vocal on our issues remains. Advocating for our congressional issues is a continuous battle, and OPHTHPAC is always under financial pressure to support our incumbent friends as well as to make new friends with candidates. These relationships allow us to have a seat at the table with legislators willing to work on issues important to us and our patients.

The relationships OPHTHPAC builds with members of Congress is contingent on the financial support we receive from Academy members. Academy member support of OPHTHPAC allows us to advance ophthalmology’s federal issues. We need to increase the number of our colleagues who contribute to OPHTHPAC and the other funds. Right now, major transformations are taking place in health care. To ensure that our federal efforts and our PAC remain strong, we need the support of every ophthalmologist to better our profession and ensure quality eye care for our patients.

The significant impacts that OPHTHPAC has made include the following:

- Derailed the onerous global surgery data collection proposal
- Preserved global surgical payments
- Halted the Part B Drug Demonstration
- Continued efforts in collaboration with subspecialty societies to preserve access to compounded and repackaged drugs such as Avastin

Contributions to OPHTHPAC can be made here at AAO 2017 or online at www.aao.org/ophthpac by clicking “Join.”

Leaders of the North American Neuro-Ophthalmology Society (NANOS) are part of the Academy’s Ophthalmic Advocacy Leadership Group (OALG), which meets every January in the Washington, D.C., area to provide critical input and to discuss and collaborate on the Academy’s advocacy agenda. The topics discussed at the 2017 OALG agenda included panel discussions on the Merit Based Incentive Payment System (MIPS) and APM implementation, as well as Academy analysis initiatives related to the IRIS® registry. In addition, meeting participants discussed the changing paradigm for optometric scope battles, held a roundtable to discuss challenges for surgical subspecialties, and considered opportunities to ensure physician and patient choice regarding access to pharmaceuticals.

At Mid-Year Forum 2017, the Academy and the NANOS ensured a strong presence of neuro-ophthalmologists to support ophthalmology’s priorities, and a record number of ophthalmologists visited members of Congress and their key health staff to discuss ophthalmology priorities as part of Congressional Advocacy Day. The NANOS remains a crucial partner with the Academy in its ongoing federal and state advocacy initiatives.

**Surgical Scope Fund**

The Surgical Scope Fund (SSF) provides grants to state ophthalmology societies to support their efforts to derail optometric surgery proposals that pose a threat to patient safety. Since its inception, the Surgery by Surgeons campaign and the SSF, in partnership with state ophthalmology societies, has helped 32 state/territorial ophthalmology societies reject optometric scope of practice expansion into surgery.

In 2017, your colleagues serving on the Academy’s Secretariat for State Affairs, along with State Governmental Affairs staff and the leaders of state ophthalmology societies, have been put to the task while dealing with an unprecedented number of simultaneous legislative battles. Eleven states have been affected so far this year:

- Alaska
- California
- Florida
- Georgia
- Illinois
- Iowa
- Maryland
- Massachusetts
- Nebraska
- North Carolina
- Pennsylvania
Patient safety setbacks as well as victories will be reviewed during the presentation, but do know that in each of these legislative battles, the benefits from SSF distributions are abundantly clear. The best lobbyists and public relations consultants are contracted as necessary, and media campaigns (including TV, radio, and social media) to educate the voting public are launched when needed to secure success and stop optometry from expanding its scope of practice to include surgery. Each of these endeavors is very expensive, and no one state has the resources to wage one of these battles on its own. Ophthalmologists must join together and donate to the SSF to fight for patient safety when a state faces a scope battle over optometric surgery.

The Academy relies not only on the financial contributions to the SSF from individual ophthalmologists and their practices, but also on the contributions made by ophthalmic state, subspecialty, and specialized interest societies. The NANOS contributed to the SSF in 2016, and we thank them and look forward to their contribution in 2017. Contributions to the SSF can be made here at AAO 2017 or online at www.aao.org/ssf.

**State Eye PAC**

It is also extremely important for all ophthalmologists to support their respective State Eye PACs because campaign contributions to legislators at the state level must come from individual ophthalmologists and cannot come from the Academy, OPHTHPAC, or the SSF. The presence of a strong State Eye PAC providing financial support for campaign contributions and legislative education to elect ophthalmology-friendly candidates to the state legislature is critical, as scope of practice battles and many regulatory issues are all fought on the state level.

**Action Requested: ADVOCATE FOR YOUR PATIENTS**

Academy SSF contributions are used to support the infrastructure necessary in state legislative/regulatory battles and for public education. PAC contributions are necessary at the state and federal level to help elect officials who will support the interests of our patients. Contributions to *each* of these three funds are necessary and help us protect sight and empower lives. SSF contributions are completely confidential and may be made with corporate checks or credit cards, unlike PAC contributions, which must be made by individuals and are subject to reporting requirements.

Please respond to your Academy colleagues and be part of the community that contributes to OPHTHPAC, the SSF, and your State Eye PAC. Please be part of the community advocating for your patients now.

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Section II: Could Systemic Disease Cause This Problem?

Vision/Visual Field Loss with Disc Swelling

Michael Vaphiades DO

CASE

History and Exam

A 51-year-old white man reported a 3-week history of painless visual loss in both eyes. The vision loss was gradual, and he did not awaken with it. He denied giant cell arteritis symptoms, pain with eye movement, and other neurologic symptoms. He has no past medical history and is not taking prescription medications. He does not smoke or drink alcohol, and he works as a flight attendant. Upon examination, blood pressure was 125/80. Visual acuity was 20/60 right eye (O.D.), 20/30 left eye (O.S.). Color vision was 3/8 O.D. and 6/8 O.S. using the Ishihara pseudo isochromatic plates. Automated visual fields showed a central scotoma O.D. and nonspecific pattern deviation changes O.S. Pupils measured 5 mm O.U. with a 0.3 log unit relative afferent pupillary defect (RAPD) O.D. The ocular motility was normal. Slitlamp examination was unremarkable aside from vitreous cells O.D. more than O.S. Fundus exam showed disc edema O.U.

What is the most likely diagnosis?
1. Nonarteritic anterior ischemic optic neuropathy
2. Demyelinating optic neuritis
3. Sarcoïd optic neuropathy
4. Neumyelitis optica
5. Syphilitic optic neuropathy

Clinical Course and Outcome

Upon additional review of symptoms, the patient described a recent rash with painless brownish-red spots that were rough to the touch on the palms of his hands and soles of his feet. Laboratory workup included a complete blood count, electrolytes, glucose, serum angiotensin converting enzyme (ACE), and HIV, which were all normal. Chest radiograph was also normal. A rapid plasma reagim (RPR) and fluorescent treponemal antibody absorption (FTA-ABS) were positive. T1-weighted orbital fat-suppressed gadolinium-enhanced MRI of the brain and orbits was normal. Lumbar puncture had an opening pressure of 17 cm H2O, 100 mononuclear cells/UL, protein 55 mg/dL (20-40), and glucose 46 mg/dL (45-80). Serum glucose was 100 mg/dL. Cerebrospinal fluid (CSF) Venereal Disease Research Laboratory test (VDRL) was positive.

Discussion

This patient’s diagnosis becomes clear in light of the characteristic rash and the laboratory results. However, the differential diagnosis of bilateral disc edema must be considered. Malignant hypertension must be considered, but his blood pressure was normal. Nonarteritic anterior ischemic optic neuropathy is unlikely as it is usually nonsimultaneous, most common upon waking, usually associated with vascular risk factors, and not associated with rash or uveitis. Demyelinating optic neuritis is higher in the differential because uveitis, while uncommon, can certainly occur.1 However, the bilateral presentation, the lack of pain with eye movement (present in 92% of demyelinating optic neuritis), the normal orbital MRI (enhancement of the orbital optic nerve on gadolinium-enhanced T1-weighted fat-suppressed MRI occurs in roughly 94% of cases), and the skin rash make demyelinating optic neuritis unlikely.2 Another consideration higher in the differential would be sarcoidosis. Ocular involvement in sarcoidosis occurs in approximately 25% of patients affected by the disease, and sarcoid uveitis comprises 3%-10% of all cases of uveitis.3 Sarcoidosis is associated with a rash, yet the maculopapular rash of sarcoidosis typically appears on the face, and rarely, trunk and extremities.4 Syphillis is a curable, multiorgan, acute and chronic infection caused by the bacteria Treponema pallidum (T. pallidum).56 Neurosyphilis can occur any time after infection and has been referred to as “the great mimicker” of other diseases.57 There are 5 stages of the disease: incubation, primary, secondary (where the dermatologic, neurologic, and ocular manifestations commonly occur), latent, and tertiary (late). The ocular manifestations of neurosyphilis may occur in any stage of the disease and include uveitis (the most common manifestation), interstitial keratitis, chorioretinitis, retinal vasculitis, papilledema, anterior optic neuritis (as in our patient), retrobulbar optic neuritis, periopitc neuritis, and pupillary and ocular motor dysfunction.589 Syphilitic uveitis is the most common ocular manifestation in syphillis, occurring early or late in the disease and, in some cases, as the only manifestation.5 The syphilitic rash is typically on the hands and feet and in one study was the most common dermal manifestation of syphilis.10 The skin lesions are often surrounded by hyperkeratosis and thin white rings or a collar of scales. Some patients also may have a faint macular and papular eruptions diffusely disseminated over the trunk and upper and lower extremities.10 Syphilis testing includes nontreponemal reagin tests (VDRL and RPR) and specific treponemal tests (T. pallidum particle agglutination [TPPA] and FTA-ABS).3 Ocular involvement implies neurosyphilis, and a lumbar puncture should be performed in all such patients. The CSF analysis usually reveals a mononuclear pleocytosis between 2 and 200 cells/UL and an elevated protein.56 The CSF VDRL is 99.8% specific and 50% sensitive, and CSF FTA-ABS is 94% specific and 100% sensitive.5 In patients with suspected syphilis, one should always test for HIV because syphilis and HIV seem to have a unique clinical interaction, both are sexually transmitted, and the genital ulcers of syphilis tend to increase the risk of HIV infection.5 In turn, HIV infection tends to accelerate the course of ocular and central nervous system syphilis.5
Treatment of neurosyphilis includes aqueous crystalline penicillin 18-24 million units per day IV, administered as 3 to 4 million units every 4 hours, or 24 million units daily as a continuous infusion for 10-14 days. Alternatively, procaine penicillin 2.4 million units IM daily plus probenecid 500 mg orally 4 times daily may be administered, both for 10-14 days. Probenecid inhibits tubular secretion of penicillin and usually increases penicillin plasma levels. If the patient is allergic to penicillin, consider ceftriaxone 2 g IV or IM daily for 10 to 14 days. Alternatively, doxycycline 200 mg orally twice a day for 21 to 28 days may be given, but is not recommended by the CDC or European guidelines.6

References

Progressive Orbital Swelling and Pain
Roger E Turbin MD

CASE

History and Exam
A 42-year-old male of African American descent complained of painless left visual loss of 10 days duration, preceded by bilateral orbital swelling with mild painful discomfort and tearing of 3 months duration. He was unaware of double vision. Friends had been telling him his cheeks looked swollen for some time.

His past medical history is notable only for hypertension, treated with metoprolol and hydrochlorothiazide. He had not been exposed to tuberculosis. He is a nonsmoker, nondrinker, and has used no recreational drugs.

A review of systems elicited xerostomia and 20 lbs. of weight loss over the last few months.

At examination, BCVA is 20/20 O.D. and 20/150 O.S. A 1.2 log unit left relative afferent pupillary defect (RAPD) is present. Color vision is decreased in the left eye (6/6 HHR plates O.D., 0/6 O.S.). IOPs are symmetric at 11 mmHg. Ocular motility is abnormal on the right, with mild, diffuse limitation of ductions, although a poor left visual acuity precluded accurate alternate cover testing prism measurements. A visual field measured by confrontation is normal in the right and diffusely depressed in the left eye field.

Slitlamp biomicroscopic evaluation is unremarkable, with no evidence of intraocular inflammation, past or present, except the eyelid and facial findings displayed in Figures 1 and 2—namely, bilateral lacrimal gland enlargement with “S” shaped eyelid ptosis.

![Figure 1. Parotid enlargement.](image1)

![Figure 2. Lacrimal gland enlargement.](image2)
Evaluation of the optic nerves, macula, and retina is normal, except the left optic disc is subtly elevated with trace peripapillary nerve fiber edema, no hemorrhages, and no vitritis.

**Clinical Course and Outcome**

The patient’s initial evaluation included normal CMP (comprehensive metabolic panel), CBC, ANA, RPR, ANCA, and chest X-ray. Serum ACE (angiotensin converting enzyme), SSA, and SSB were ordered, but results returned “sample not received.” An ESR was 32 mm/hr. His PPD (purified protein derivative) was negative, but anergy panel was not placed.

In the emergency room the patient underwent contrast-enhanced orbital CT scan, which showed infiltration with mild bilateral enhancement of lacrimal glands, periorbital tissue, and orbital fat. The right inferior and medial recti were thickened, including tendinous insertions.

Subsequent contrast-enhanced MRI imaging revealed a plaque of left frontal pachymenigeal thickening, and a segment of left optic perineural intracanalicular enhancement.

Preoperative differential diagnosis included sarcoid (neuro/systemic), lymphoma/chloroma, IG4-related disease, orbital pseudotumor, Sjögren disease, Mikulicz syndrome, and tuberculosis. Body gallium scan and PET scanning, pulmonary function testing, anergy panel, and 24-hour urinary calcium excretion were considered but deferred after left lacrimal and concurrent lower lip incisional salivary biopsies each confirmed noncaseating granulomas. Tissue AFB cultures remained negative for organisms.

The patient began treatment with 100 mg oral prednisone (1 mg/kg), and his visual acuity, parotid, and lacrimal enlargement had nearly normalized by his second postoperative visit.
organic visual loss is a diagnosis of exclusion; in addition, this patient had vitreous cells which suggest underlying ocular pathology. A diffuse outer retinopathy was the suspected site of visual loss. A full-field electroretinogram was performed and showed severe reduction of the scotopic and photopic responses, consistent with generalized photoreceptor dysfunction. In the same week, the patient was found to have a mass in the right lung. Biopsy of the mass revealed a small cell carcinoma.

Cancer-associated retinopathy (CAR) is one of the visual paraneoplastic syndromes. It is mediated by autoantibodies directed against retinal specific antigens. Small cell carcinoma of the lung is the malignancy most commonly associated with CAR, and in women there is high association with gynecologic tumors (ovarian, endometrial, and cervical) and breast cancer as well. Growing recognition of the syndrome has led to recognition of a variety of other solid tumors and hematologic malignancies associated with paraneoplastic visual loss.

It is important to know that visual loss due to CAR precedes the cancer diagnosis in nearly half of patients. The average age of patients with CAR is 65 years. The classic presentation is a painless bilateral visual loss that progresses fairly rapidly over several weeks to months. Photopsias and photosensitivity are common accompanying symptoms. When significant rod dysfunction intervenes, impaired dark adaptation and night blindness occur. In the early stage, the fundus may be normal. Later, attenuation of retinal arterioles, thinning and mottling of the pigment epithelium, and disc pallor can be observed. Some patients may have vitritis and/or anterior uveitis. Full-field electroretinography (ERG) is extremely helpful in suspected cases of CAR. ERG is already abnormal in the early stage, with global reduction in a- and b-wave amplitudes of scotopic and photopic responses. Quickly, the ERG becomes extinguished (unrecordable).

The pathophysiology of CAR is an autoimmune-based retinopathy. In response to the primary tumor, the immune system generates antibodies against various tumor-based antigens. However, antigenic similarity to certain retinal antigens leads to cross-reaction by these antibodies and unintentional retinal cell dysfunction and death. The first autoantigen to be identified in patients with cancer and retinopathy was a 23 kD calcium-binding protein called recoverin, now called the CAR antigen. Since then, many retinal antigens have been identified. In a cohort of 209 patients with cancer and retinopathy, about 65% were seropositive for antiretinal autoantibodies. The most common autoantibody was directed against a 46 kD glycolytic enzyme, α-enolase. Interestingly, antirecoverin CAR autoantibodies were found in only 10% of seropositive patients. However, the antirecoverin antibodies are specific. The presence of these antibodies in a patient with unexplained visual loss is associated with an underlying cancer in almost 100% of cases, and a thorough investigation for cancer should be undertaken without delay.

The patient in this case had CAR due to a small cell carcinoma of the lung. He was treated with chemotherapy and radiotherapy for the cancer. Oral steroids were given for the retinopathy, but he continued to have visual loss. Four weeks after presentation, his vision was hand motion in both eyes. Treatment with more aggressive immunosuppression was under consideration.
Transient Bilateral Vision Loss
Fiona E Costello MD

CASE

History and Exam

A 23-year-old woman presents with painless onset vision loss in the right and left eyes, which she noted after awakening from a nap. In retrospect, she reports that she has been experiencing recurrent bilateral episodes of transient vision loss lasting minutes in duration for the past 3 weeks. These visual disturbances have been painless, and she describes them as “dark patches” in her vision without positive visual phenomena. She denies any clear provocative or palliative factors with respect to her episodic vision loss. During events, her symptoms of vision loss have affected either one eye or the other, but she denies simultaneous vision loss in both eyes until now.

Her past medical history is noteworthy for 3 prior first-trimester miscarriages.

On examination visual acuity is hand motions in the right eye and count fingers in the left eye, with a mild right relative afferent pupillary defect. Visual acuity testing to confrontation reveals dense central scotomas. Dilated fundus exam demonstrates bilateral optic disc pallor, arterial attenuation, arterial “box-carrying,” and bilateral cherry red spots. Fluorescein angiography shows extensive retinal nonperfusion in both eyes.

Cranial MRI shows multiple hyperintense fluid-attenuated inversion recovery (FLAIR) and T2 lesions in the subcortical white matter, with no gadolinium enhancement. MR-venography is normal. Blood work reveals normal cell count with differential, electrolytes, rheumatoid factor (RF), antinuclear antibody (ANA), anti-double-stranded DNA, and antineutrophil cytoplasmic antibody (ANCA) testing. Serum protein C, protein S, and homocysteine concentrations are within the normal range. No mutation of the allele of the gene factor V 1691 G-A (V Leiden) or prothrombin gene allele is found. The patient is negative for antithrombin III deficiency.

ARS Question: The most likely diagnosis in this case is:

1. Bilateral optic neuritis
2. Cerebral venous sinus thrombosis
3. Posterior reversible encephalopathy
4. Antiphospholipid antibody syndrome

Clinical Course and Outcome

Antiphospholipid antibodies including lupus anticoagulant and antibodies against cardiolipin and β2-glycoprotein 1 are positive. The patient is diagnosed with antiphospholipid antibody syndrome with bilateral central retinal artery occlusions. She is anticoagulated with intravenous heparin and treated with high-dose corticosteroids, but after 3 months her visual function remains unchanged.

Discussion

The differential for transient episodes of vision loss in a young person is broad and includes manifestations of Uhthoff phenomenon (worsening vision with increased body temperature due to central nervous system demyelination), raised intracra-
nial pressure with transient visual obscurations, retinal vasospasm, migraine equivalent, and pre-syncope (see Table 1). In the case presented, the symptoms were presumed referable to retinal arterial ischemia, which preceded bilateral central retinal artery occlusions (CRAO). This finding prompted concern for underlying stroke risk factors, including a cardioembolic source, a connective tissue disorder / systemic illness, or a thrombophilia causing a hypercoaguable state.

Table 1. Approach to Transient Vision Loss

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monocular</td>
<td></td>
</tr>
<tr>
<td>Vascular</td>
<td>Cardioembolic</td>
</tr>
<tr>
<td>Vascular</td>
<td>Thrombotic (giant cell arteritis)</td>
</tr>
<tr>
<td>Vascular</td>
<td>Stenotic</td>
</tr>
<tr>
<td>Vasospasm</td>
<td></td>
</tr>
<tr>
<td>Retinal migraine</td>
<td></td>
</tr>
<tr>
<td>Ocular</td>
<td>Closed angles, hyphema</td>
</tr>
<tr>
<td>Binocular</td>
<td></td>
</tr>
<tr>
<td>Thromboembolic</td>
<td></td>
</tr>
<tr>
<td>Occipital epilepsy</td>
<td></td>
</tr>
<tr>
<td>Complex migraine</td>
<td></td>
</tr>
<tr>
<td>Monocular or Binocular</td>
<td></td>
</tr>
<tr>
<td>Papilledema or optic nerve disease</td>
<td></td>
</tr>
<tr>
<td>Uhthoff phenomenon</td>
<td></td>
</tr>
</tbody>
</table>

CRAO should be viewed as a version of stroke. Notably, transient vision loss can be a precursor to branch retinal artery occlusions (BRAO) and CRAO. In fact, transient vision loss has been reported in 12% of CRAO cases and 15% of BRAOs. The general approach in this context is to perform echocardiography (transthoracic / transesophageal) and holter monitoring (atrial fibrillation) testing to investigate for sources of cardioembolism due to valvular disease (prior rheumatic fever or endocarditis).

An evaluation for underlying systemic illnesses that can be associated with a prothrombotic state is necessary, including systemic lupus, sarcoidosis, granulomatosis with polyangiitis (formerly known as Wegener granulomatosis), microangiopathy of brain, ear, and retina (also known as Susac syndrome), sickle cell disease, Behçet, and syphilis. Specific studies to check for a thrombophilia, including prothrombin G20210, antithrombin III deficiency, factor V Leiden mutation, and protein C/S deficiency, are also integral to the evaluative approach. Notably, most of the hereditary thrombophilias are associated with increased risk of venous thromboembolism (deep vein thrombosis and/or pulmonary embolism), not arterial occlusions. The presence of a hereditary thrombophilia does not necessarily imply that the patient will definitely develop venous occlusions, as each thrombophilia is associated with a variable degree of risk for developing a first lifetime and recurrent venous event (see Table 2).

The investigations in this case eventually rendered the diagnosis of bilateral CRAO caused by antiphospholipid antibody syndrome.

Antiphospholipid syndrome (APS) is an autoimmune disease characterized by arterial and venous occlusions due to antiphospholipid antibodies. The disorder is referred to as primary when it occurs in the absence of another autoimmune disease. In contrast, secondary APS occurs in association with other autoimmune disorders, such as systemic lupus erythematosus. Notably, APS must be distinguished from other forms of thrombotic microangiopathies such as hemolytic-uremic syndrome, thrombotic thrombocytopenic purpura, disseminated intravascular coagulation, and heparin-induced thrombocytopenia.

References


Table 2. Hereditary Thrombophilia and Relative Risks for Venous Thromboembolism

<table>
<thead>
<tr>
<th></th>
<th>Relative Risk Incident Venous Thromboembolism (95% CI)</th>
<th>Relative Risk Recurrent Venous Thromboembolism (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Activated protein C resistance (factor V Leiden)</td>
<td>4.3 (1.9-9.7)</td>
<td>1.3 (1.0-3.3)</td>
</tr>
<tr>
<td>Prothrombin G20210A</td>
<td>1.9 (0.9-4.1)</td>
<td>1.4 (0.9-2.0)</td>
</tr>
<tr>
<td>Protein C deficiency</td>
<td>11.3 (5.7-22.3)</td>
<td>2.5</td>
</tr>
<tr>
<td>Antithrombin deficiency</td>
<td>17.5 (9.1-33.8)</td>
<td>2.5</td>
</tr>
<tr>
<td>Protein S deficiency</td>
<td>32.4 (16.7-62.9)</td>
<td>2.5</td>
</tr>
<tr>
<td>Elevated factor VIII activity</td>
<td>...</td>
<td>1.8 (1.0-3.3)</td>
</tr>
<tr>
<td>Hyperhomocysteinemia</td>
<td>...</td>
<td>2.5</td>
</tr>
<tr>
<td>Non-O blood group</td>
<td>1.79 (1.56-2.05)</td>
<td>2.0 (1.2-3.8)</td>
</tr>
</tbody>
</table>

Section III: Don’t Tell Me You’re Seeing Double?!

Diabetic Patient with New Diplopia

Madhura A Tamhankar MD

CASE

History and Exam
A 65-year-old woman presented with a sudden-onset diplopia for the past 3 weeks. She notes that the double vision is binocular and horizontal and resolves with closing either eye. She notices the diplopia only at a distance and not up close. She notes intermittent flashes of light but no floaters. She denies any prior episodes of diplopia. She denies any other neurological symptoms. She has no generalized weakness, no difficulty swallowing or breathing. She denies recent headaches, weight loss, or jaw claudication.

The patient’s past medical history is significant for diabetes, hyperlipidemia, shoulder arthritis, fibrocystic breast disease, and anxiety. Her past surgeries include benign breast biopsies, endometrial ablation, cesarean section, and removal of ovarian cyst. She has never smoked, drinks alcohol socially, and denies recreational drug use. Her family history includes diabetes in her mother and father, who had heart failure. She is currently on aspirin, metformin, sertraline, and simvastatin. Her last HbA1C was 6, about 2 months ago.

On examination her BCVA was 20/25 in the right eye and 20/20 in the left eye. Color vision was full in both eyes. Pupils were equal and briskly reactive to light, with no afferent pupillary defect. Confrontational visual fields were normal. External examination was normal, with no evidence of ptosis or lid retraction. Ocular ductions demonstrated a right abduction deficit of −0.5. Cover testing revealed 10 PD of esotropia in primary gaze, 14 PD in right gaze, and 2 PD in left gaze. Anterior segment and ophthalmoscopic examination were normal in both eyes, including optic nerves and maculae.

Clinical Course and Outcome
The patient underwent MRI of the brain with and without gadolinium. There was an enhancing mass measuring 24x18x26 mm involving the skull base with posterior epidural extension to the right greater than the left prepontine cistern, also involving the Dorello canal. There was involvement of the pituitary gland with right greater than left elevation of the superior margin and leftward deviation of the pituitary stalk. There was no associated mass effect on optic chiasm. The lesion abutted the right greater than left posterior aspect of the cavernous carotid artery and posterior cavernous sinus. There was also involvement of the superior aspect of right Meckel’s cave. The mass did not demonstrate restricted diffusion. Differential considerations included invasive macroadenoma, metastasis, plasmacytoma lymphoma, or chordoma. A transnasal biopsy was planned.

Double Vision and Dizziness

Janet C Rucker MD

CASE

History and Exam
A 29-year-old woman presented to her ophthalmologist reporting 1 day of double vision and vertigo. When specifically asked, she also reported nausea with 2 episodes of vomiting and endorsed a mild posterior headache. She was not certain, but also felt that she might not be hearing as well as usual in her right ear. She reported that she felt less steady while walking than usual and attributed this to the vertigo. She had seen her primary care doctor the day it started and was sent for a head CT, which was unremarkable.

The patient’s medical history was remarkable for migraine, with which she occasionally experienced vertigo—though the current headache was different than her migraines in location and was less severe. She had no history of hypertension, diabetes, or head trauma. She exercised regularly at a gym and had started a cardio-kickboxing class within the last week.

On exam, acuity was 20/20 O.U. Color vision, pupils, visual fields, and fundus were normal. Eye movement range was full. She had a comitant left hypertropia. There was left-beating horizontal nystagmus in central position that increased when she looked to the left, and in right gaze the nystagmus changed to right-beating horizontal nystagmus.

What would be the next step?

Clinical Course and Outcome
The patient was sent immediately to the emergency room and emergent neurology consultation was obtained. Neurological exam again revealed the same ocular misalignment and nystagmus, but also revealed ataxia of the right arm and difficulty with tandem walking, supporting the presence of gait ataxia.

An emergent brain MRI was obtained. T2 and diffusion-weighted imaging (which will reveal an infarction as a bright signal within the first week of infarction and which is a standard component of brain MRI at most facilities) revealed restricted diffusion diagnostic of acute infarction in the right cerebellar hemisphere and right inferolateral pons and middle cerebellar peduncle. Given her young age, lack of vascular risk factors, and recent history of initiation of new kickboxing class, vertebral artery dissection was highly suspect and was confirmed with vascular imaging. She was treated with warfarin.
Diplopia after Concussion

“I see double and can’t focus when reading”

Veeral Shah MD PhD

CASE

History and Exam

A 13-year-old girl is referred by her family physician after experiencing double vision and focusing issues for the past 4 months. The patient complains of intermittent double vision that is described as binocular, horizontal, and occurring sporadically. Notably, she has difficulty with focusing while reading or using her iPhone. She occasionally feels “dizziness” with these episodes of double vision. These episodes started 4 months ago, after a gymnastic practice in which an abrupt landing caused her to fall and hit the back of her head on the ground. There was no loss of consciousness. With ongoing symptoms, she followed up with her family physician, who ordered a CT-scan that revealed no intracranial abnormalities. Her family physician recommended she see an ophthalmologist.

Her past medical history is significant for a previous history of head trauma from gymnastic practice 8 months prior to current presentation. She has no history of medication or allergies. She is an active ninth grader in high school. She has been practicing gymnastics for the past 5 years. Her family history is noncontributory.

On examination, her BCVA was 20/20 O.D. and 20/20 O.S., with normal pupillary exam, normal color vision, and full fields by confrontational visual field testing. Ocular motility testing demonstrated full versions and ductions. Alignment demonstrated small exophoria flick at distance, and larger intermittent exotropia of X(T) = 16 at near fixation on alternate cover testing. External and anterior segment exam were normal. Dilated fundus examination showed normal appearing optic nerves, macula, vessels, and peripheral retina in both eyes. Her subjective and cycloplegic refractions were similar.

Extended ocular efferent examination was performed. She had a near point convergence of 16 cm. Fusional convergence were measured, with a break point of 16 PD and recovery point of 4 PD. Accommodative facility on monocular testing was normal (6 cm) for both eyes. On Randot stereo vision testing she demonstrated 9/9 on graded circle testing. She demonstrated normal saccades, smooth pursuit, and vestibular ocular reflex.

Clinical Course and Outcome

Visual complaints of diplopia demand a thorough clinical history and require a comprehensive ocular exam. Upon further questioning, this patient’s diplopia can be defined as binocular, horizontal, intermittent, and worse at near fixation. With her clinical history of a mild head trauma or concussion, the initial differential diagnosis for trauma-related diplopia includes cranial nerve palsies, skew deviation, and decompensated phoria, as well as anterior segment (ie, ocular surface issues, decentered lens, traumatic mydriasis) and retinal pathologies (commotio retinae, retinal hemorrhage, retinal detachment). Her slitlamp and dilated fundus exams ruled out anterior and posterior segment pathologies, and her CT-scan, obtained by the family physician, was normal.

The ocular motility and alignment examination is paramount in delineating the diagnosis. Recently acquired cranial nerve palsies will have inconstant deviations depending on the cranial nerve(s) involved. Checking alignment in all cardinal gazes as well as with head tilts may show an alignment pattern that could distinguish a cranial nerve palsy from a skew deviation (important since our patient had dizziness symptoms). Our patient had full ocular motilities, and her alignment at distance had minimal exophoria in all 9 cardinal gazes and with head tilts. The diagnosis of cranial nerve palsy and skew deviation was unlikely.

The key clinical finding of intermittent exotropia greater at near fixation raises the strong suspicion of postconcussive convergence insufficiency (CI) and, additionally, rules out a subtle VI nerve palsy. This finding strongly supports performing an extended ocular efferent examination to confirm suspicion of CI and identify other impairments of the ocular motor system. The examination should include convergence amplitude, fusional vergences, accommodative function, stereovision, motility (saccade / smooth pursuits / VOR), and refraction, as mentioned in this case. Her near point of convergence (NPC) was measured at 16 cm (normal, 4-10 cm; abnormal, > 10 cm). Her fusional amplitudes demonstrated a fusional breakpoint of 16 PD and recovery point of 4 PD (both values are normally 30-35 PD). The increased near point convergence and decreased fusional amplitudes confirmed her diagnosis of CI. Her efferent ocular exam was otherwise unremarkable.

Our patient was started on orthoptic convergence exercises, which typically involve near point (pencil push-ups and computer-based orthoptic exercises) or prism convergence exercises. We conservatively recommended 3-4 pencil push-ups sessions daily, with each session consisting of 20-25 repeats of convergence eye movements. Since starting the orthoptic exercises, she noted gradual resolution of symptoms and was asymptomatic at 6 weeks follow-up. At that time her NPC was 8 cm, and fusional version improved 30/25. With the recovery of her CI and resolution of postconcussive symptoms, she was cleared to resume gymnastics activity. The possibility of recurrences, necessary precautions, warning signs, and future outlook were extensively discussed the patient.
My Eyes Are Not Moving!

M Tariq Bhatti MD

CASE

History and Exam

Three years prior to presentation at our institution, a 49-year-old man with a history of arterial hypertension, morbid obesity, pre-diabetes mellitus, and anxiety experienced binocular double vision. A local ophthalmologist diagnosed a left III nerve palsy and had him see a neuro-ophthalmologist, who noted bilateral ptosis, limited adduction of the left eye with a 40 PD exotropia (XT) and 6 PD left hypertropia (HT). Thyroid-stimulating hormone and acetylcholine receptor (AChR) antibody were normal / negative. An edrophonium test was negative, and forcedduction testing was noted to be “likely positive.” Computed tomography (CT) of the orbits with contrast was reportedly normal. The patient was referred to a pediatric ophthalmologist, who noted a large angle incomitant XT with a left HT and underacting left medial rectus muscle. He was given a diagnosis of a partial left III nerve palsy (medial rectus and inferior rectus involvement) with a plan to wait 1 year prior to considering strabismus surgery. Approximately 1 year later the patient was seen by another pediatric ophthalmologist, who noted a large angle left XT with a left HT with limitation of adduction and infrafduction of the left eye. MRI of the brain with contrast was reportedly normal. It was felt that he most likely had a left microvascular ischemic inferior divisional III nerve palsy and IV nerve palsy. Three months later, a general ophthalmologist noted bilateral ptosis, with no movement of the left eye, and the patient was referred to our institution with the working diagnosis of progressive external ophthalmoplegia.

On examination, visual acuity was 20/20 O.U. with normal pupillary reflexes. Slitlamp examination was normal with IOPs of 10 mmHg O.U. Dilated fundus examination was normal O.U. There was upper eyelid ptosis O.U., with a compensatory brow hike and orbicularis oculi muscle weakness. Eye movements were abnormal O.U., with limitation in all directions of gaze (see Figure 1). In primary gaze, there was a 30 PD XT and 7 PD LHT. The patient declined forcedduction testing.

Figure 1. There is limitation of eye movements in all directions. Note the large angle exotropia in primary gaze. The eyelids are being held up manually because of the bilateral upper eyelid ptosis. The pupils are pharmacologically dilated. (Printed with patient permission, consent form on file.)

Ice pack test was negative. AChR binding antibody was negative, AChR modulating antibody was 20% loss of function (normal, < 20% loss of function), and striational antibody was < 1:120 (normal, < 1:120).

A procedure was performed.

Clinical Course and Outcome

A single fiber electromyogram demonstrated an abnormality of neuromuscular transmission with increased jitter and blocking. The MRI showed enlargement of the midportions of the medial recti and inferior recti muscles bilaterally. Thyroid function tests, including thyroid-stimulating immunoglobulin, were negative / normal. Chest CT was negative for a thymic gland abnormality. The patient was referred to neurology for treatment of myasthenia gravis.
New Double Vision in the Young
Valerie I Elmalem MD

C A S E

History and Exam
A 29-year-old woman complains that her vision seems off when she looks to the side. She is having difficulty driving because she sees double when she checks her blind spot on the right.Reading has also become challenging. Past medical history includes occasional headaches and 4 uncomplicated pregnancies. She does not take any medications.

Clinical Course and Outcome
On physical examination, visual acuity is 20/20 O.U. and confrontation visual fields are full. Pupils are equally reactive with no relative afferent pupillary defect. Ocular motility shows full versions and ductions but slow adducting saccades in the left eye. There is horizontal jerk nystagmus of the right eye in right gaze. Slitlamp and dilated funduscopic examination are normal in both eyes.

Blurred Vision with Reading
Paul H Phillips MD

C A S E

History and Exam
A 26-year-old woman was referred for a cataract extraction O.D. She described episodes of intermittent decreased vision associated with “twitching” of the right eye for the past year that occurred after downgaze and lasted about a minute. Her past medical history was significant for asthma frequently treated with systemic steroids. She had cataracts attributed to systemic steroids O.U. She was currently taking no medications.

Physical examination showed a visual acuity of 20/30 O.U. with full confrontation visual fields. Pupils were equal, reactive, with no relative afferent pupillary defect. She had full ductions and versions and was orthotropic in all fields of gaze. Slitlamp examination showed mild posterior subcapsular cataracts O.U. Funduscopic examination was normal.

She was told that cataracts are responsible for her decreased vision and that surgery would improve her symptoms.

Clinical Course and Outcome
Downgaze elicited episodes of torsional eye movements O.D. that were most apparent when focusing on a conjunctival vessel during slitlamp examination. Treatment with topical B-blockers did not improve her symptoms. Surgery consisting of right superior oblique tenectomy and inferior oblique myectomy resolved her symptoms. However, she now had vertical diplopia in downgaze that was treated with Fresnel prisms.
Section IV: Abnormal Test Result—Panic, or Repeat It?

Abnormal MRI, Headache, and Normal Fundus

Marie D Acierno MD

CASE

History and Exam

A 24-year-old female is referred from her primary care provider for an abnormal MRI. She complained of a new-onset daily headache for the past 4 months. The pain was described as beginning at the base of her neck and radiating to the top of her head, associated with photophobia, and relieved with rest. Review of systems is unremarkable except for increased anxiety as a new graduate student. Past medical history is non-contributory. Vital signs and physical examination are normal. A contrasted brain MRI was ordered, and it showed a pituitary tumor.

On neuro-ophthalmic examination, her visual acuity is 20/20 in each eye. There is no dyschromatopsia or metamorphopsia in either eye. The pupillary examination is normal, with no relative afferent pupillary defect in either eye. The ocular motility examination is normal. The funduscopic examination reveals a normal appearing optic disc in each eye with a small cup-to-disc ratio. There are no macular lesions, and the vitreous is clear in either eye.

Clinical Course and Outcome

The patient had formal perimetry by Humphrey visual field 24-2 testing, which did not reveal any specific defect in either eye. OCT of the retinal nerve fiber layer was bilaterally symmetric without evidence of thinning. The patient was referred to an endocrinologist and scheduled for yearly ophthalmic examinations.

Abnormal OCT in a Patient with a Normal Exam

Kimberly M Winges MD

CASE

Clinical History and Exam

A 60-year-old man was referred by optometry for abnormal retinal nerve fiber layer (RNFL) thickness and macular ganglion–inner plexiform layer (GC-IPL) on OCT, which was performed originally for a glaucoma suspect exam. He had no visual complaints. Past ocular history included myopia with astigmatism and presbyopia O.U. Past medical history was remarkable for hyperlipidemia and osteoarthritis. There was no family history of glaucoma or neurologic disease. Eye exam revealed 20/20 BCVA with manifest refraction of −4.25 sphere O.D. and −4.75 +1.50 x 096 O.S. IOP was 16 O.U. by applanation. Patient had full confrontation visual fields, no relative afferent pupillary defect, and normal color vision O.U. Slitlamp biomicroscopy was normal O.U. Dilated fundus exam showed a normal optic nerve O.D. with 0.4 cup-to-disc, and an inferiorly tilted optic nerve O.S. with 0.1 cup-to-disc and peripapillary atrophy inferiorly. No optic nerve pallor, notching, disc hemorrhages, or edema was appreciated. Peripheral exam was normal O.U. Humphrey visual fields were full O.U., apart from a mild enlarged blind spot O.S. consistent with his peripapillary atrophy.

OCT of the RNFL and macular ganglion cell layer were inspected and showed thinning of the superior RNFL quadrant in both eyes, with polygonal areas of black on the thickness maps. Macular GC-IPL scan showed nasal thinning O.S. and significant disruption of the thickness map.

What would be your next step?
1. Provide reassurance that there is no optic neuropathy
2. Repeat the OCT after instilling artificial tears, instructing the patient to blink, and rechecking positioning
3. Obtain OCT at a different visit for comparison
4. Throw out the OCT and follow visual fields only
5. Order MRI orbit with/without contrast

Clinical Course and Outcome

In summary, this is a case of abnormal OCT scan in a patient with a healthy-appearing eye exam, raising the question of whether abnormal OCT measurements are due to artifact or represent subclinical disease that must be further investigated. In this case, there are several examples of artifact demonstrated in the RNFL and GC-IPL analysis printouts, which arise from poor scan signal, misalignment, poor retinal layer segmentation, and optic nerve tilt in a myopic patient.

The patient was rechecked with eye exam and OCT testing on the same day after instillation of artificial tears, which improved some of the signal strength and uniformity. At follow-up visit 3 months later, dilated exam including visual fields were stable, and the RNFL/GC-IPL thickness values in each eye were compared to their prior values, with stable findings. The patient was reassured and followed clinically.
Abnormal Visual Field Defects with Normal Optic Nerves
“Doctor, now my other eye is bad!”
Y Joyce Liao MD PhD

CASE

History and Exam
A 43-year-old white man was referred for new blurry vision in the right eye. He had a history of blurry vision in the left eye a few months prior, which improved. He also felt some left eye soreness and had episodic, mild, nonspecific headaches. His past medical history was otherwise unremarkable. He had not been on any medications until his left eye vision event, at which point he was started on aspirin (ASA). He had no known medication allergies. He lived with his family and is a nonsmoker. His family history was significant for no history of glaucoma, other optic neuropathies, or macular degeneration.

On examination, his BCVA was 20/20 bilaterally. On confrontation visual field testing, the patient had subjective inferior visual field constriction in the left eye. His color vision with HRR plates was normal in both eyes.

His IOP was 16 mmHg in the right eye and 17 mmHg in the left eye. He had a left relative afferent pupillary defect. Ocular motility and eye alignment were normal. Anterior segment examination was normal. His optic nerve examination revealed no evidence of optic disc edema. His cup-to-disc ratio was 0.4 in both eyes.

His automated perimetry with Humphrey visual field 24-2 test was reliable per reliability indices, but there were a lot of eye movements throughout testing O.U. In the right eye, there was an inferior nasal peripheral visual field defect, with mean deviation of −6.9 dB. In the left eye, there was a dense superior > inferior nasal visual field defect, with mean deviation of −16.6 dB.

Goldman visual field testing showed inferior nasal > temporal visual field constriction in the right eye and a nasal hemifields defect in the left eye.

Clinical Course and Outcome
The optic nerve color was relatively normal in the right eye, and there was subtle left temporal pallor in the left. There was also some nonspecific, mild retinal arteriolar narrowing in the left eye. Retinal vessels were normal in the right. We obtained outside retinal photography at the onset of left eye vision loss, which showed evidence of acute branch retinal artery occlusion (BRAO) superiorly and inferiorly in the left eye. Outside OCT at that time also showed diffuse retinal swelling consistent with BRAO.

Optic nerve OCT showed thinning of the retinal nerve fiber layer in the left eye and normal measurements in the right eye. The macular ganglion cell complex and volume scan revealed inferior thinning in the left eye consistent with prior BRAO.

In young-onset BRAO or in those without known vascular risk factors, hypercoagulable and stroke workup should be performed. Other evaluations include workup for infections and to rule out drug use.

The patient’s hypercoagulable blood tests were negative. Transthoracic echocardiogram did not show a thrombus or patent foramen ovale. MRI of the brain and orbits with and without gadolinium revealed no significant enhancement. There were scattered T2/FLAIR cerebral white matter hyperintensities in the right frontal subcortical and periventricular white matter that were thought to be nonspecific but may represent chronic ischemic microvascular disease.

Because of recurrent BRAO while on ASA, the patient was also started on clopidogrel. In anticipation of lumbar puncture, he was off ASA and clopidogrel for a short time. He developed a new-onset migraine aura-like episode while reading to his son. This was described as an arc of black and white stripes that started in the left lower corner of his visual field (present even with eyes closed), elongated over minutes, and then gradually resolved over 15-20 minutes. There was no headache, photophobia, phonophobia, confusion, neurological symptoms, or other issues. This never recurred after he resumed ASA and clopidogrel.

His lumbar puncture revealed normal intracranial pressure and normal CSF studies other than for elevated protein of 73 mg/dL (normal < 45). Oligoclonal banding was negative.

While on ASA and clopidogrel, the patient developed an episode of decreased hearing. Hearing test was normal in the right ear, but there was mild high-frequency sensorineural hearing loss at 6000-8000 Hz in the left ear. He was diagnosed with Meniere disease and treated with a 12-day course of prednisone. The hearing loss improved rapidly.

Fluorescein angiography revealed evidence of prior left BRAO and no significant optic disc staining O.U. In the right eye peripheral retina, there was segmental hyperfluorescence of the vessel wall along one arteriole but no evidence of BRAO.

Repeat orbit and brain MRI revealed T2 hyperintense lesion in the corpus callosum and no enhancement.

Based on recurrent, bilateral BRAOs, an episode of hearing loss, asymptomatic retinal arteritis, and corpus callosum lesion, the diagnosis of Susac syndrome was made. Patient was treated with high-dose IV methylprednisolone and has not had recurrent events.
Abnormal Electrophysiology with a Normal Exam

Vivek R Patel MD

CASE

History and Exam

A 43-year-old woman was referred to us by her pulmonologist for painless, rapidly declining vision in both eyes over the past 1 month. Her past medical history was significant for systemic lupus erythematosus, and she was on BiPAP therapy for advanced cystic fibrosis and awaiting lung transplantation. She had no history of known malignancy.

She denied any fevers, chills, or new constitutional symptoms. She saw an eye care provider 1 week after noticing a change in her vision and was told she has bilateral cataracts. Given continued decline in her vision over the next 2 weeks, she continued to seek further care. She described diffuse progressive blurring and desaturation of her vision, with central field predominance; however, no metamorphopsia, micropsia, or macropsia. She denied any recent change or addition of medications and had not taken ethambutol or isoniazid. She has taken hydroxychloroquine (Plaquenil) 400 mg daily (6.3 mg/kg/day) for the past 2 years, with normal renal function. She has no known history of hereditary vision loss.

On examination, vision was counting fingers at 2 feet O.D. and counting fingers at 3 feet O.S. without improvement with pinhole. She could not identify any of the Ishihara color plates and endorsed central scotomas bilaterally amid diffuse blurring, supported by tangent screen testing and Goldmann visual fields. IOPs were 14 O.D. and 16 O.S. Pupils were equal and mildly sluggish to react to light, but with no relative afferent papillary defect. Orbital and adnexal examinations were normal. Slitlamp examination revealed mild cataracts and clear corneas bilaterally, with no evidence of new or resolving intraocular inflammation. Dilated posterior segment examination revealed a clear view without vitritis, optic disc edema, or atrophy, as well as essentially normal appearing retinal architecture, with the exception of mild arteriolar narrowing bilaterally. OCT retinal nerve fiber layer and macula, as well as fundus autofluorescence, were normal. MRI orbits and brain with and without gadolinium were unremarkable, with notable absence of optic nerve enhancement or thickening.

Given the above picture we decided to pursue electrophysiological testing. Multifocal electroretinography (ERG) (mfERG) and full-field ERGs (ffERG) were performed, revealing significant scotopic and photopic dysfunction bilaterally, with a predominance of central retinal abnormalities, corroborated by the mfERG.

What would you do next? (More than one answer may apply.)
1. Stop the hydroxychloroquine: this is classic macular toxicity.
2. Perform a lumbar puncture due to suspicion of an infectious process.
3. Order spinal cord imaging due to suspicion of neuromyelitis optica (NMO).
4. Repeat the ERG and mfERG.
5. Order lots of bloodwork.
6. Order imaging of the chest, abdomen, and pelvis.

Clinical Course and Outcome

We felt a broad investigative approach was certainly necessary here, given the lack of objective findings on routine examination and fundus imaging techniques, but abnormal electrophysiology. The lack of systemic features to suggest meningocencephalitis, negative MRI brain (no retrochiasmal abnormalities) and orbits (no enhancement or thickening), made the possibility of NMO or primary CNS process extremely unlikely. Hence further imaging of the neuraxis and lumbar puncture were not pursued. Although hydroxychloroquine toxicity is a very important consideration in an individual on chronic therapy presenting with predominantly central loss of vision in both eyes, there were several features here that suggested that hydroxychloroquine toxicity alone was unlikely to be responsible for our patient’s precipitous presentation. In addition, typical perifoveal thinning on macular OCT (“flying saucer” sign) was absent, and there was electrophysiological evidence of significant involvement of the cone system inside (mfERG) and outside (photopic ffERG) the macula as well the rod photoreceptor system, assayed under scotopic conditions. We had a full discussion with our patient regarding the various possibilities, and she chose to stop the hydroxychloroquine.

We opted to send her blood for a number of tests. Given her metabolic condition and presentation of bilateral severe vision loss, we sent for vitamin A, RBC folate, vitamin B12, B6, B1, zinc, and copper levels; all were within normal limits, as was a toxic screen (lead, arsenic, cadmium). The same day, her blood was sent to the Oregon Ocular Immunology Laboratory at Oregon Health & Science University for antiretinal antibody testing. Notably, antirecoverin antibodies were not detected; however, 9 other antiretinal antibodies were reported as positive, and we had a full discussion with our patient regarding the various possibilities, and she chose to stop the hydroxychloroquine.

We initiated aggressive immunosuppressive therapy, including 5 days of 1 g of solumedrol, subsequent oral prednisone for 6 weeks, intravenous immunoglobulin therapy, followed by rituximab (induction dosing x 2 then a third dose 6 months later). Although her retina continued to thin over the next several months on objective testing, with relatively greater inner retinal involvement, her vision improved to 20/200 O.D. and 20/300 O.S., and she regained the ability to see 5/8 and 4/8 color plates, respectively, with slightly eccentric viewing. Our patient remarked that the central scotomas had definitely “lightened up” in comparison to at presentation. With low vision aids she could read relatively large print (20/70 near vision O.U.). This improvement was corroborated on repeat mfERG and ffERG testing, 2 months after the first set of tests.

All waveforms were still markedly abnormal but revealed better amplitudes.
White Matter Lesions on Brain MRI Disease or Artifact?

Zoë R Williams MD

CASE

History and Exam

A 46-year-old male is referred by neuro-oncology for evaluation of diplopia. His prior workup includes a contrast MRI brain, which demonstrates an enhancing 1.3x0.7-cm lesion of the right side of his medulla extending into the pons, of uncertain etiology. The lesion is heterogeneous and irregular, with mainly peripheral contrast enhancement. Per radiology, differential considerations include neoplasm, demyelination, or inflammatory process. Additional nonspecific white matter lesions are present, with differential including chronic small vessel ischemic changes, post-traumatic, or inflammatory process. The patient is seen by neurosurgery, and a CT chest, abdomen, and pelvis is ordered to assess for a possible primary tumor. His CT studies demonstrate a mildly enlarged right hilar lymph node and an enlarged right lower cervical lymph node. In addition, there are a few scattered pulmonary nodules (largest = 5 mm). He is referred to neurology and is noted to have a right horizontal gaze palsy but otherwise normal neurologic exam. Serology shows a positive ANA (1:320) with speckled pattern, normal ESR, normal ACE, and negative syphilis screen. MRI cervical, thoracic, and lumbar spine with contrast is unremarkable. Lumbar puncture shows normal CSF studies, including cell count and total protein. There are no oligoclonal bands. Neuromyelitis optica antibody, CSF ACE, cytology, and flow cytometry are all negative. He is treated with dexamethasone (Decadron) 2 mg t.i.d. for 1 week without improvement. Dexamethasone is tapered and he reports resolution of his diplopia after 2 weeks. He is subsequently referred to neuro-ophthalmology.

Patient is no longer symptomatic but reports gradual onset of constant binocular horizontal diplopia 8 weeks prior to referral. He denies worsening of his diplopia in any direction of gaze or for distance vs. near. He denies any history of a “lazy eye,” patching for ambylopia, or strabismus surgery. He denies any oscillopsia, ataxia, weakness, numbness, tingling, imbalance, or headaches. He denies any other visual concerns, including blurred vision, loss of color vision, dimming of his vision, decrease in his peripheral vision, or transient obstructions of vision.

His past medical history is significant for hypertension. His only medications are lisinopril and carvedilol. His steroid taper was completed 2 days prior to neuro-ophthalmology evaluation. He is a former smoker with a 5 pack-year history.

On examination, his BCVA is 20/20 in each eye. His color vision is full by HRR plates. His pupils are brisk, with no afferent papillary defect. Tangent screen is full bilaterally. His extraocular motility is full with brisk saccades. There is no internuclear ophthalmoplegia. Pursuit is smooth without nystagmus. Ocular alignment testing by cover / alternate cover method reveals a mild comitant left hyperphoria (2 PD). His external exam is unremarkable. There is no induced ptosis with sustained upgaze or contralateral lid elevation. There is mild orbicularis oculi weakness bilaterally. His facial sensation is intact and symmetric. There is no facial weakness or asymmetry. Slitlamp exam is unremarkable. Dilated funduscopic exam reveals no optic disc pallor or edema. The retinal nerve fiber layer is intact bilaterally. There is a < 1 DD flat choroidal nevus inferotemporally in the left macula. There is no vascular sheathing. The retinal periphery is normal.

Clinical Course and Outcome

Repeat contrast MRI brain demonstrates an interval decrease in the size of the right lateral medullary lesion. There is complete regression of enhancement. No new lesion or enhancement is seen. One month after discontinuation of corticosteroids, he denies any recurrent diplopia. There is no interval change in exam. Based on his repeat neuroimaging, serology, and CSF results and resolution of his diplopia with corticosteroid treatment, his medullary lesion is suspected to be due to an inflammatory or demyelinating etiology rather than a neoplasm. Referral to neuroimmunology is recommended, but the patient declines and is subsequently lost to follow-up.

Eighteen months later the patient is seen by neuro-oncology. He is asymptomatic. His neurologic exam remains normal. Repeat contrast MRI brain demonstrates mild interval decrease in the T2 FLAIR signal abnormality in the right medulla. There is no enhancement or new lesions. Two and a half years after initial presentation, he returns to the neuro-ophthalmology clinic. He denies any visual concerns. He is orthophoric with an otherwise unchanged exam.

He is seen 8 months later for urgent evaluation of dimming of his vision in the right eye and pain with extraocular movement. He reports “splotchy vision” in his right eye. He denies any transient weakness, numbness, tingling, or imbalance. Exam reveals BCVA of 20/30-2 in the right eye and 20/20 in the left eye. His color vision (HRR) is 10/14 in the right eye and is normal in the left eye. His right pupil is 2-3+ reactive and his left pupil is brisk with a 1+ right afferent papillary defect. Humphrey 24-2 visual field testing shows a central scotoma extending inferonasally in the right eye and is normal in the left eye. His ocular motility is full with brisk saccades and smooth pursuit. He is orthophoric. His anterior segment exam is normal. Dilated funduscopic exam shows mild diffuse right optic disc edema without peripapillary hemorrhage, cotton wool spots, or pallor. The left optic disc is normal. There is no vascular sheathing, macular exudate, or hemorrhage.

He is diagnosed with right anterior optic neuritis. MRI brain and orbits without and with gadolinium show enlargement of the entire right optic nerve with associated enhancement. Residual T2 hyperintense signal change in the right lateral medulla are concerning for a prior focus of demyelination. There are small foci of T2 hyperintensity in the subcortical white matter of the bilateral frontal lobes. Repeat contrast MRI cervical and thoracic spine shows no spinal cord lesions. Serum neuromyelitis optica antibody is negative. Repeat ANA is weakly positive at 1:80 titer with a speckled pattern. ACE, anti-RO, anti-LA, and RF are negative. Lumbar puncture shows normal CSF studies with no oligoclonal bands and immunoglobulin G synthesis rate of 0.0. He is treated with a 3-day course of IV methylprednisolone 1000 mg daily, followed by prednisone taper with improvement in his vision.

He is diagnosed with relapsing-remitting MS and started on glatiramer acetate (Copaxone). Six weeks later, his visual acuity improves to 20/25 in the right eye. His color vision (HRR)
is full. There is resolution of his prior right afferent pupillary defect. His HVF 24-2 is normal bilaterally. He has mild temporal optic disc pallor in the right eye. There is mildly subnormal average retinal nerve fiber layer thickness in the right eye by OCT at the 6-month follow-up. His visual acuity improves to 20/20. Contrast MRI brain shows slight residual increased T2 signal in the right optic nerve and is otherwise stable, with no new or enhancing abnormalities.

The differential diagnosis of white matter lesions is broad and includes infectious, inflammatory, ischemic, neoplastic, and demyelinating etiologies. Our patient’s nonspecific cerebral white matter lesions seen on initial MRI were attributed to incidental chronic small vessel ischemic disease in the setting of hypertension. His diagnosis of MS was made 3 years later, when he had a second clinical event suggestive of demyelination. Distinguishing between the various etiologies causing white matter lesions can be difficult, especially in the setting of a clinically isolated syndrome. In our patient, neuromyelitis optica (NMO) was on the differential diagnosis both for his initial presentation with an enhancing medullary lesion (although posterior fossa lesion location is more typical for MS), and for his subsequent optic neuritis, especially in the setting of diffuse enlargement and enhancement of the optic nerve. However, optic neuritis secondary to NMO tends to be more severe, with worse visual prognosis than in MS. In addition, there is usually more substantial loss of retinal nerve fiber layer after a single episode of optic neuritis in NMO than in MS. Although brain T2 FLAIR hyperintensities can be seen in NMO, the location (predominantly in the diencephalon adjacent to the ventricles) and appearance (usually not ovoid) differs from lesions typically seen in MS (predominantly periventricular, juxtacortical, or located in posterior fossa and classically > 5 mm and ovoid). Brain stem neoplasm was also considered as a potential cause of patient’s medullary lesion, but biopsy was deferred based on his excellent steroid response and no recurrence on serial neuroimaging after steroid taper. Neurosarcoidosis can also present with periventricular white matter lesions that are hypointense on T1 and hyperintense on T2. Clinical and MRI signs distinguishing neurosarcoidosis from MS include peripheral CN VII palsy and presence of leptomeningeal enhancement. Neurosarcoidosis was also considered less likely based on his sustained improvement after discontinuation of immunosuppressive therapy.
Diagnosis and Teaching Points
Section I: Help, My Patient Can’t See!

Painful Vision Loss

Lulu Bursztyn MD

Final Diagnosis

Neuromyelitis optica spectrum disorder

Teaching Points

1. Workup of optic neuritis should include brain MRI to prognosticate future risk of developing MS, but in typical cases no further investigations are required. Atypical features of optic neuritis include lack of pain or protracted pain, significant optic disc edema, bilateral vision loss, retinal exudates, lack of visual recovery after 3 months, worsening after withdrawal of steroids, and past medical history of cancer.
2. When atypical features are present, further workup to look for MS mimics should include orbital imaging, aquaporin-4 antibodies, anti-thyroid antibodies, anti-ENA, ANA, ACE, dsDNA, and serology for syphilis and/or Lyme in endemic areas.
3. Bioequivalent doses of oral corticosteroids (1250 mg daily) or IV corticosteroids (1000 mg daily) can be used in the acute treatment of optic neuritis. High-dose oral prednisone has been shown to be noninferior to IV methylprednisolone for typical optic neuritis. Oral prednisone is less expensive and more convenient to access and administer. Extended oral taper is not necessary after a pulse of high-dose oral or IV corticosteroids in typical optic neuritis. When NMO is suspected, patients should be maintained on oral steroids until evaluated by a neurologist or neuro-ophthalmologist familiar with treatment of NMO.

Selected Reading


Unilateral Painless Vision Loss

“My vision went bad sometime last year”

Shakthi Kanagalingam MD

Final Diagnosis

Optic atrophy secondary to prior nonarteritic ischemic optic neuropathy (NAION)

Teaching Points

1. NAION is thought to be the result of vascular insufficiency in the posterior ciliary circulation to the optic nerve. Risk factors include small cup-to-disc ratio of the optic nerve, diabetes mellitus, systemic hypertension, and hyperlipidemia. Other associations are sleep apnea, generalized hypoperfusion, nocturnal hypotension, anemia, medications such as amiodarone, and phosphodiesterase inhibitors (eg, sildenafil). Patients typically present with painless, unilateral vision loss. The most common pattern of visual field loss is an altitudinal defect. The optic disc edema on presentation can be segmental or diffuse. Frequently a disc hemorrhage is present as well. The optic nerve in the contralateral eye characteristically has a small diameter with a small or absent cup-to-disc ratio. The affected optic disc becomes atrophic within 6-8 weeks.
2. If an ophthalmic examination was performed at the time of the vision loss, efforts should be made to obtain and review those records. Confirming the presence of acute initial optic nerve edema at the time of vision loss can help establish the diagnosis of NAION. In the absence of documented initial disc edema, neuro-imaging should be obtained to rule out compressive causes of optic atrophy.
3. No proven treatment currently exists for NAION. The 5-year risk of contralateral eye involvement is 15%. For this reason, these patients should follow up with their primary care physician to ensure that their vasculopathic risk factors are under good control.

Suggested Readings

Bilateral Painless Vision Loss

Raghu Mudumbai MD

Final Diagnosis
This patient had vision loss from compressive optic neuropathy related to a hemorrhagic pituitary adenoma.

Teaching Points
1. Clinical characteristics of compressive lesions of the optic nerve include painless loss of central visual acuity. Depending on the timing of detection, the optic nerves may look normal without disc swelling but will eventually exhibit optic nerve pallor, which may be more prominent in the temporal optic nerve (see figures).
2. Patients may have cupping that is physiologic or related to other risk factors, such as African ancestry or myopia. Correlation with other elements of the clinical exam (vision, color plates, presence of pallor of the optic nerve temporally or diffusely) is paramount in distinguishing optic neuropathies, including compressive, from glaucoma.
3. Although cupping may be associated with optic neuropathies aside from glaucoma, these other pathologies will usually have associated pallor of the optic nerve, which may be more detectable in the temporal optic nerve.
4. Ancillary testing with automated visual field can be helpful in identifying the etiology. Visual field defects that respect the vertical midline (compressive) or are central or cecocentral (metabolic/toxic) or altitudinal in the setting of small cups (NAION) are suggestive of pathology that is not glaucoma.

Progression of optic nerve pallor

Selected Readings
Transient Vision Loss in an Older Patient

*Kenneth S Shindler MD PhD*

**Final Diagnosis**
Amaurosis fugax from unidentified embolic etiology causing transient retinal ischemia

**Teaching Points**
1. While carotid etiology is most common, retinal emboli can arise from cardiac sources or other proximal vessels, and a source may not be identified even when this etiology is strongly suspected clinically.
2. Visible retinal emboli are often not present at time of examination.
3. Aspirin therapy should be considered when embolic transient retinal ischemia is suspected, whether or not a specific embolic source is identified.
4. Brain imaging to look for other signs of embolic disease should be considered.
5. Giant cell arteritis must be considered in older patients with amaurosis, with clinical suspicion, careful review of symptoms, and laboratory testing serving as guidance for whether further workup is needed.
6. Migraine as a cause of transient darkening of the vision in one eye is atypical and should be considered a diagnosis of exclusion even when clinically suspected.

Vision Loss after Non-ophthalmic Surgery

*Kaitlyn Nolan MD*

**Final Diagnosis**
This is a case of bilateral postoperative visual loss caused by posterior ischemic optic neuropathy (PION).

**Teaching Points**
1. There are multiple potential causes of postoperative visual loss: anterior or posterior ischemic optic neuropathy, central retinal artery occlusion, cortical visual loss, posterior reversible encephalopathy, and pituitary apoplexy.
2. There are no established treatments available for postoperative PION. Some have reported an improvement in visual acuity after adequate blood transfusion for anemia, the use of vasopressors for hypotension, or the use of corticosteroids; however, these reports did not include controls.
3. Longer anesthetic duration, greater blood volume loss, insufficient colloid administration, hypothermia, and hypotension (MAP < 70 mmHg, systolic pressure < 90 mmHg) are risk factors for perioperative/postoperative ischemic optic neuropathy.
4. Postoperative PION is a diagnosis of exclusion, as life-threatening emergencies (pituitary apoplexy, stroke) must be ruled out first, either clinically or with neuro-imaging.

Vision Loss with a Normal Exam

*Peter A Quiros MD*

**Final Diagnosis**
Functional vision loss

**Teaching Points**
1. The lack of an relative afferent pupillary defect (RAPD), particularly in the setting of NLP vision in one eye, should bring into question the visual acuity. Similarly, an RAPD should always be present when there are 2 or more lines of difference in visual acuity, even in cases of bilateral traumatic optic neuropathy (TON).
2. Whereas the funduscopic appearance of the eye is normal in TON initially, that should not be the case after several months, especially in the setting of profound vision loss.
3. OCT ganglion cell complex (GCC) analysis can be useful early on to detect optic nerve damage; OCT RNFL thickness analysis should corroborate the GCC analysis findings after several months.
4. The use of simple in-office tests is often all that is needed to disprove a questionable visual acuity. Stereo tests are particularly useful, as patients do not often equate these with visual acuity.
Section II: Could Systemic Disease Cause This Problem?

Vision/Visual Field Loss with Disc Swelling
Neurosyphilis Presenting as Subacute Vision Loss with Optic Disc Edema and a Visual Field Defect
Michael Vaphiades DO

Final Diagnosis
Neurosyphilis

Teaching Points
1. When comparing syphilitic optic neuritis and demyelinating optic neuritis, remember that uveitis is common in syphilitic optic neuritis and uncommon in demyelinating optic neuritis. Demyelinating optic neuritis is usually painful, and the T1-weighted orbital fat-suppressed gadolinium-enhanced MRI usually shows optic nerve enhancement.
2. Both syphilis and sarcoidosis may present with uveitis and a rash. The syphilitic rash occurs on the palms of the hands and soles of the feet; the rash of sarcoidosis typically appears on the face and rarely involves the trunk and extremities.
3. In evaluating a patient with suspected syphilis, ocular involvement implies neurosyphilis and a lumbar puncture should be performed in all such patients. The CSF typically shows a mononuclear pleocytosis and an elevated protein. The CSF VDRL is 99.8% specific and 50% sensitive. The CSF FTA-ABS is 94% specific and 100% sensitive.
4. Always check an HIV test because HIV has a unique clinical interaction with syphilis.
5. Penicillin is the mainstay of therapy.

Progressive Orbital Swelling and Pain
Roger E Turbin MD

Final Diagnosis
Multifocal neurosarcoid, with bilateral orbital, parotid and salivary gland, optic perineural, and pachymeningeal involvement

Teaching Points
Neurosarcoid is an inflammatory disease of the central nervous system and has an estimated prevalence of 5% in patients with sarcoid. It may affect the meninges (46%); cranial nerves (55%); especially facial nerve (24%); brain parenchyma (51%); and spinal cord. Neurosarcoid may occur in isolation or in association with systemic sarcoid. Common locations of involvement include the eye (21%), optic nerve (21%), lymphoreticular and/or pulmonary (60%), and cardiac systems. Authors frequently refer to “Zajicek’s criteria,” which stratify the diagnosis of neurosarcoid into “definite, probable, and possible.” Diagnostic criteria include histologic identification of noncaseating granuloma, supportive laboratory and imaging studies, and compatible clinical course. Corticosteroid therapy remains first-line therapy, but immunosuppressive and corticosteroid-sparing agents may be necessary and commonly include methotrexate, azathioprine, mycophenolate mofetil, cyclosporine A, hydroxychloroquine, targeted and TNF alpha or B-cell agents, and occasionally cyclophosphamide.

A recent meta-analysis (2016) described features of neurosarcoid in 1088 patients classified as neurosarcoid; however, this did not include a series of 24 patients with neurosarcoid of the anterior visual pathway, which may be of particular interest to ophthalmologists. Eighty-one percent of the latter cases were biopsy confirmed and therefore meet Zajicek’s “definite criteria.”

Table 1 presents data on abnormal ancillary testing comparing Fritz’s meta-analysis with the anterior visual pathway paper (Frohman).
It is important to recognize, as in our case, that retrobulbar optic neuropathy is not always synonymous with demyelinating optic neuritis or its association with multiple sclerosis. Neurosarcoid commonly mimics the visual loss of optic neuritis or optic nerve sheath meningioma, but other clues supporting orbital and systemic involvement direct diagnostic ancillary testing that would not otherwise be warranted in “run of the mill” demyelinating optic neuritis. The ophthalmologist may play a key role in establishing histologic evidence to support the diagnosis of neurosarcoid by providing biopsy of lacrimal, orbital, and salivary tissue.

References

Visual Field Loss and Normal Fundus
Mark L Moster MD, Aki Kawasaki MD

Final Diagnosis
Cancer-associated retinopathy

Teaching Points
The combination of unexplained visual loss in a patient with cancer should raise suspicion for a paraneoplastic syndrome. Paraneoplastic syndromes involving the eye include cancer-associated retinopathy (CAR), melanoma-associated retinopathy, paraneoplastic vitelliform maculopathy, paraneoplastic optic neuropathy, and diffuse uveal melanocytic proliferation.

In this patient with newly diagnosed lung cancer, the severe bilateral visual loss with nearly extinguished ERG in the absence of a normal fundus points to a clinical diagnosis of CAR. The diagnosis was serologically confirmed by finding antiretinal antibodies to a 23 kD antigen, known as the CAR antigen. Because visual loss from CAR can precede the cancer diagnosis, the finding of positive CAR antibodies should direct immediate and appropriate investigations for an underlying cancer.

Selected Readings
An Elderly Patient Who Can’t Read

Victoria Pelak MD

Final Diagnosis

Posterior cortical atrophy, which is a neurodegenerative condition most commonly associated with Alzheimer disease (AD) pathology and presents with prominent visual dysfunction (previously referred to as the visual variant of AD)

Teaching Points

1. Visual dysfunction, particularly reading impairment, can be the initial presentation of AD. Alzheimer disease is the most common form of dementia, affecting over 5.4 million Americans. Prominent visual symptoms with relative sparing of memory loss can be the initial presentation of AD, just as is noted in this patient. In these instances, there is often a disproportionate degree of posterior cortical atrophy involving the occipital and parietal lobes on neuroimaging, and this syndrome is referred to as posterior cortical atrophy (PCA).1 People with PCA are younger than typical AD, with symptoms that usually begin in the sixth decade of life, and PCA could be responsible for as many as 5% of cases of AD.2 Rarely, pathological entities other than AD are noted on autopsy, such as Lewy body dementia and prion disease.1

2. A disconnection between visual complaints and ophthalmologic examination findings in an older patient should raise the suspicion for a neurodegenerative disorder. A significant difference between patient-reported visual function and ophthalmologic examination in the appropriate setting (patients older than 45-50 years) should raise the suspicion for cortical visual dysfunction. Impairment of activities of daily living (reading, working, driving) without explanation is a common presenting feature of PCA. Subtle problems on examination, such as the inability to read all of the Ishihara color plates (linked to simultanagnosia) or difficulty with the use of a pinhole device (linked to apraxia) are clues to underlying posterior cortical dysfunction. Causes of central nervous system disease other than degenerative disease should also be considered, and further workup and a neurologic evaluation are warranted.

3. Homonymous visual field loss with a report of a normal brain imaging. Many patients with PCA develop homonymous visual field defects.2 Thus, when homonymous visual field pattern occurs in the setting of a reportedly normal brain scan or a brain scan described as having cortical atrophy only, then neurodegenerative disease should be suspected and further evaluation for such should be sought. Fluorodeoxyglucose-positron emission tomography (or FDG-PET) of the brain can also be useful in identifying hypometabolism in posterior cortical visual regions when a concern regarding the diagnosis of PCA arises.4 Ultimately, neurologic evaluation and formal cognitive testing is necessary to identify the degree of cognitive impairment and to determine the appropriate diagnosis and/or diagnostic workup that is necessary.2

References


Transient Bilateral Vision Loss

Fiona E Costello MD

Final Diagnosis and Teaching Points

The fundus examination in this case was essential in directing the diagnostic process toward an underlying source of arterial occlusion, and in this respect the approach mirrors the evaluation required in the young stroke patient. Young patients, with no prior vascular risk factors, may present with conditions such as antiphospholipid antibody syndrome that predispose them toward unexpected thrombotic events which can in turn result in arterial and venous occlusive causes of vision loss. Retinal vascular occlusions are analogous to cerebral infarction and require emergent evaluation by a stroke specialist.1

Reference

Section III: Don’t Tell Me You’re Seeing Double?!

Diabetic Patient with New Diplopia

Madhura A Tamhankar MD

Final Diagnosis

Right VI nerve palsy secondary to skull-based tumor

Teaching Points

Abducens nerve palsy is the most common acquired ocular motor cranial mononeuropathy to occur in isolation. The causes of the abducens nerve palsy are diverse, and diagnostic decisions can be challenging and sometimes controversial. The causes of VI nerve palsies include neoplastic, traumatic, microvascular, and aneurysmal causes, giant cell arteritis, conditions causing raised intracranial pressure, and demyelinating diseases. Likewise myasthenia gravis and thyroid eye disease can mimic abducens palsy. In some patients the etiology may be undetermined.

The initial step in the evaluation of VI nerve palsy is to determine if it is truly neurologically isolated. Accompanying signs and symptoms of facial weakness, hemiparesis, ataxia, and vertigo may indicate brain stem injury. Papilledema can be seen in those with raised intracranial pressure from any cause, and in such patients the VI nerve palsy may be falsely localizing. Involvement of oculomotor, trochlear, trigeminal nerve, and ipsilateral Horner syndrome localizes to the cavernous sinus and orbital apex from infections such as mucormycosis in immunosuppressed patients, infiltrative lesions, or idiopathic inflammatory pathologies such as Tolosa-Hunt syndrome.

Hearing loss and facial palsy indicates involvement of the petrous bone. A history of head trauma, vascular risk factors, systemic malignancy, and giant cell arteritis should be sought. In younger patients with pseudotumor cerebri, VI nerve palsy can be a false localizing sign. MRI of the brain with and without contrast is the initial neuroimaging modality of choice in affected patients with VI nerve palsy. Based on the clinical scenario a lumbar puncture with cytology should be undertaken.

Many other conditions can mimic an isolated abduction deficit and should be considered in the differential diagnosis of VI nerve palsy. Myasthenia gravis, a disorder of the neuromuscular junction, should be considered in any patient presenting with unexplained ocular motility deficit. Presence of accompanying ptosis is a valuable clue. Patients may describe variability of their symptoms, including worsening at the end of the day. Acetylcholine receptor antibody testing and/or electromyography testing should be undertaken if the index of suspicion is high.

Other conditions such as thyroid orbitopathy and idiopathic orbital myositis can mimic lateral rectus palsy, especially when it involves the medial rectus muscle causing a restrictive deviation or the lateral rectus muscle if it causes a paretic deviation. Thyroid orbitopathy, however, is more insidious in onset and is often associated with proptosis and eyelid retraction. In the majority of patients there is associated thyroid dysfunction, although some may be euthyroid. In orbital myositis the presentation is more acute, with pain, diplopia, and proptosis. There is often eyelid swelling, conjunctival injection, and chemosis. Imaging of the orbit may reveal the enlargement of one or more muscles (in both conditions) and fat stranding in those with orbital myositis.

The most common cause of isolated VI nerve palsy in patients over the age of 50 years is presumed microvascular ischemia. Neuroimaging is normal in such individuals, and the palsy typically resolves within 10-12 weeks. The decision to observe patients clinically and image those with nonresolution or progression, rather than performing an immediate brain MRI at presentation, is controversial. While there are studies that recommend clinical observation and monitoring without neuroimaging,1,2 other studies have reported an alternative diagnosis such as neoplasm, brain stem infarction, demyelinating disease, or pituitary apoplexy—all of which would have altered management with early neuroimaging.3,4 In all patients who present with VI nerve palsy along with other neurological signs and symptoms, those younger than 50 years of age, those with prior history of cancer, and those with immunosuppressed status should obtain neuroimaging early. For older adults with microvascular risk factors, the pretest probability, cost-effectiveness, and patient preferences should be taken into consideration. If initial imaging is not obtained then close follow-up is important. Laboratory evaluation should include Lyme disease testing if clinical suspicion is high and checking erythrocyte sedimentation rate and c-reactive protein in older patients with suspected giant cell arteritis.

The diagnostic modality of choice for evaluation of VI nerve palsy is a brain MRI with and without gadolinium. In the absence of contrast, small structural lesions involving the VI nerve, cavernous sinus, and leptomeningeal enhancement may be missed. If orbital lesions are suspected, fat-suppressed thin coronal and axial cuts through the orbit should be obtained. It is important to note that small skull-based tumors such as choromas and invasive nasopharyngeal cancers can be overlooked on neuroimaging if they are small. High-resolution MRI scans may be helpful in such cases if the index of suspicion is high.5 Alternatively, if the initial MRI is nonrevealing, repeating the MRI scan should be considered.

References

Double Vision and Dizziness

Janet C Rucker MD

Final Diagnosis
Vertebral artery dissection with brainstem and cerebellar infarction causing acute-onset vertigo with direction-changing nystagmus, vertigo, double vision from skew deviation, and ataxia

Teaching Points

1. Assessment of vertigo
The main challenge when faced with a patient experiencing acute-onset vertigo is to determine if the vertigo has a peripheral origin from such conditions as peripheral vestibular neuritis, benign paroxysmal positional vertigo, and Meniere disease, or if the vertigo may represent a more ominous condition, such as a brainstem stroke. Vertigo is common with brainstem strokes, but of all causes of vertigo, central brainstem lesions, including stroke, represent only approximately 5% of cases. The vast majority of cases of vertigo have a peripheral inner ear origin.

Age and medical history are often (but not always, as seen in this case) helpful features in assessing the risk of brainstem stroke in a patient with vertigo. The risk is much higher in older patients with classic vascular risk factors, such as hypertension and diabetes. It should be kept in mind that younger patients may also have infarction and that vascular dissections are a common cause in this younger age group.

2. “The company it keeps”
As always in neurological disorders, diagnosis is heavily dependent on whether or not additional symptoms and signs are present. In other words, a symptom must be interpreted in terms of the neurological “company it keeps.” Vertigo as a completely isolated symptom is less worrisome, in general. Accompanying symptoms and signs highly suggestive of brainstem infarction include changes in facial or body sensation or strength, double vision, changes in swallowing, hiccups, sudden hearing loss, limb or gait ataxia, and Horner syndrome. Nausea and vomiting may occur with either brainstem or inner ear causes of vertigo. Headache is common with migraine, with which vertigo can be associated. Headache is also common with vascular dissections.

3. Nystagmus patterns
The presence of vertigo with left-beating horizontal nystagmus in a young, healthy patient might give an initial impression of a benign inner ear problem, such as acute peripheral vestibular neuritis on the right side (with the nystagmus beating away from the affected side). However, the gaze direction–changing nature of the nystagmus, with left-beating in central gaze and left gaze and right-beating in right gaze, was very suggestive of a central cause for vertigo, rather than a “benign” peripheral one. Furthermore, the presence of double vision, report of a possible hearing change in one ear, and gait instability also raised concern for a central process.

4. Skew deviation
With regard to the vertical double vision, examination features did not support an extraocular muscle process or IV nerve palsy, given that the range of ocular motility was full and the vertical misalignment was comitant. A hyper-deviation from IV nerve weakness would be worse in downgaze, in contralateral gaze, and upon ipsilateral head tilt. Vertical diplopia with full ocular motility range and a comitant deviation is highly suggestive of a skew deviation from asymmetry of vestibular circuits ascending through the brainstem. It is important to recognize that ocular misalignment from skew deviation is not always comitant. There are other features to assist in identifying it as a skew deviation. Most notably, the eye that is higher will exhibit incyclotorsion rather than the excyclotorsion characteristic of a IV nerve palsy.

5. Head CT does not rule out acute stroke.
The day this patient’s symptoms started, she had a head CT that was read as normal. This is not reassuring and does not rule out infarction. Emergent head CT is sensitive for intracranial hemorrhage, but acute infarction is often not seen, especially in the brainstem and cerebellum, where CT is very insensitive for detecting pathology.

Diplopia after Concussion
“I see double and can’t focus when reading”

Veeal Shah MD PhD

Final Diagnosis
Decompensated phoria (convergence insufficiency) secondary to concussion

Discussion
The fusional vergence system serves to align the eyes in order to establish and maintain binocular fixation and vision. Heterophoria is the natural deviation of the eyes to a rest position without these underlying fusional mechanisms. Clinically, disruption or deficiencies in the vergence system can result in decompensated heterophorias that presents with visual symptoms. Multiple etiologies can cause decompensated heterophorias, including abnormal anatomy, fatigue, medications, and refractive error.1 The most prevalent cause of decompensated phorias is head trauma. This case illustrates a patient with a decompensated phoria secondary to a concussion.

Concussion is defined as mild traumatic brain injury (mTBI) from a biomechanical or impulsive force transmitted to the head, resulting in cognitive and neurologic alterations in an awake individual.2 According to the CDC, 1.6-3.8 million sport
and recreational injuries resulting in concussion occur annually in the United States, and there is a growing public awareness of the long-term consequences of multiple or repetitive concussions on brain physiology. The lack of radiographic findings on conventional neuroimaging has left physicians and health-care professionals to search for objective clinical exam findings to diagnose, monitor, and manage patients with concussion.

Visual symptoms and signs are quite commonplace in concussion and may include blurred / distorted vision, diplopia, asthenopia, headache, poor depth perception, and/or ocular discomfort. There is a growing body of literature on ophthalmologic evaluation as a reliable test to assess postconcussive brain dysfunction. The afferent visual pathway and ocular motor function have broad-reaching neural circuits that involve multiple cortical and subcortical structures. In particular, the assessment of ocular motor function has emerged as a sensitive test for underlying brain function.

Evaluation of the postconcussive or mTBI patient in the clinic include standard afferent exam, with a more focused ocular motor function examination. The evaluations in Table 1 are recommended.

Neuroimaging evaluations for concussion and mTBI are typically unrevealing, and a vast number of medical consensus statements report that conventional CT and MRI scans are not needed or recommended. Criteria for red flags and when imaging is indicated are found in Table 2.

Management of postconcussive symptoms should be formulated to return the individual back to their baseline level of activity. In the presented case, the patient’s clinical exam is consistent with convergence insufficiency (CI) with symptoms of intermittent diplopia at near, asthenopia, and headaches. CI has high prevalence among those with concussion and mTBIs. Treatment for CI includes pencil push-ups, prism recession exercises, base-in prism, and computer-based orthoptic therapy. Postconcussive individuals with persistent vestibular-ocular symptoms have also shown improvement from vestibular rehabilitation exercises with physical therapy.

Table 1. Recommended Evaluation of the Postconcussive or mTBI Patient

<table>
<thead>
<tr>
<th>Ocular Motor Function</th>
<th>Examination Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eye alignment</td>
<td>Cover test and alternating / cover test at near and distance</td>
</tr>
<tr>
<td>Convergence amplitude</td>
<td>Near point convergence</td>
</tr>
<tr>
<td>Fusional vergence</td>
<td>Step vergence test</td>
</tr>
<tr>
<td>Accommodative function</td>
<td>Monocular accommodative facility / amplitudes</td>
</tr>
<tr>
<td>Binocular vision</td>
<td>Stereopsis (Randot, butterfly)</td>
</tr>
<tr>
<td>Motility</td>
<td>Saccades, smooth pursuits, vestibular-ocular reflex</td>
</tr>
<tr>
<td>Refraction</td>
<td>Subjective and cycloplegic refraction</td>
</tr>
</tbody>
</table>

Table 2. Guidelines from the American College of Emergency Physicians

Imaging is indicated in patients with a loss of consciousness or amnesia if at least one of the following is present:

- Headache (diffuse)
- Vomiting
- Age > 60 years
- Intoxication
- Deficits in short-term memory
- Evidence of trauma above the clavicle
- Seizures
- GCS score < 15
- Focal neurologic deficits
- Coagulopathy

Imaging is indicated in patients with no loss of consciousness or amnesia if at least one of the following is present:

- Focal neurologic deficit
- Vomiting
- Severe headache
- Age > 65 years
- Signs of basilar skull fracture
- GCS score < 15
- Coagulopathy
- Significant mechanism of injury (eg, ejection from vehicle, pedestrian struck by vehicle, fall from a height greater than 3 ft or 5 stairs)

Guidelines from the American Academy of Pediatrics and the American Academy of Family Physicians

Inclusion criteria: Presenting within 24 hours for isolated closed head injury

Imaging for any of criteria met below:

- Loss of consciousness > 60 seconds
- Consider CT head for even brief loss of consciousness.
Teaching Points

1. Disruption of vergence system (fatigue, medication, and trauma) will result in a decompensated heterophoria and visual symptoms.

2. Concussion is frequently associated with abnormalities in ocular motor function, including convergence, accommodation, saccades, smooth pursuits, and vestibular-ocular reflex, and necessitates a comprehensive efferent ocular exam for diagnosis and management.

3. Postconcussive patients frequently have CI, which is a type of decompensated exophoria that is worse at near than at distance fixation and characterized by a large near point of convergence and reduced fusional convergence amplitudes.

4. Management of CI includes pencil push-ups, base-in prism, and computer-based orthoptic therapy.

References


My Eyes Are Not Moving

M Tariq Bhatti MD

Final Diagnosis
Seronegative ocular myasthenia gravis (MG) and euthyroid eye disease

Teaching Points
1. The hallmark clinical manifestations of MG can be summed up in two words: variability and fatigability. Ocular MG should be considered in the differential diagnosis of any patient with a pupil-sparing ocular motility deficit or intermittent double vision. Common eyelid signs and symptoms include unilateral or bilateral ptosis (worse on prolonged upgaze or enhanced ptosis) and Cogan lid twitch sign. Orbicularis oculi muscle weakness often accompanies ocular MG. Clinical tests that can be performed in the office include the sleep-rest test, ice pack test, and Bienfang test. Pharmacological testing with edrophonium or neostigmine can be done in the clinic to see if there is improvement in ocular motility or ptosis. Serological testing for acetylcholine receptor binding antibodies are approximately 50%-75% sensitive in ocular MG. Electrophysiological testing with either repetitive nerve stimulation or single fiber EMG is often needed in cases of serologically negative cases.1

2. Thyroid eye disease (TED) is an inflammatory-mediated disorder associated with Graves disease (GD) and in a small percentage of cases (2%) with Hashimoto thyroiditis. Approximately 25% of patients with GD will manifest ophthalmic findings, usually within 18 months of the onset of the hyperthyroidism. The eye findings can proceed or follow the thyroid dysfunction, but most often they occur after the diagnosis of GD has been established. The majority of patients with TED are hyperthyroid, but some cases occur in the presence of hypothyroidism or euthyroidism (10%). Upper eyelid retraction (ie, Dalrymple sign) is the most common sign associated with TED. Another common eyelid finding is upper eyelid lag during downgaze (von Graefe sign). Periorbital fullness may be caused by edema / inflammation, increased orbital fat, or prolapsed orbital fat. Proptosis is present in 60% of patients. The proptosis is often bilateral and symmetric, but it can be unilateral. Conjunctival edema (chemosis) and injection overlaying the insertion of the horizontal extraocular muscles may be present. Transient or constant diplopia occurs from orbital congestion and infiltration of the extraocular muscles. The inferior rectus and medial rectus muscles are most frequently involved, leading to a limitation of elevation (hypotropia) and abduction (esotropia), respectively.2

3. Approximately 3%-10% of patients with MG have TED, and < 1% of patients with TED have MG.3 GD and MG are common autoimmune diseases and appear to share some similar pathogenetic mechanisms. T-helper 17 cells have been implicated in the development of both MG and GD.4 In addition, cross-reactivity of autoantibodies to acetylcholinesterase and thyroglobulin have been shown to occur in MG and GD.5 Other autoantibodies in patients with MG may target antigens on extraocular muscles associated with TED, explaining the overlap of MG and TED in some patients.6 From a clinical perspective, TED and MG often manifest differently. The symptoms of TED are worse upon waking in the morning, whereas MG symptoms are least upon waking and worsen as the day progresses.

Any patient with TED who develops an exotropia, ptosis, or weakness of orbicularis oculi muscle strength should be evaluated for MG. Conversely, TED should be considered in a patient with MG who develops proptosis, eyelid retraction, or signs of orbital congestion (eg, eyelid edema, conjunctival chemosis, or injection).

References
New Double Vision in the Young
MS and Double Vision
Valerie I Elmalem MD

Final Diagnosis
Left internuclear ophthalmoplegia as the first presenting sign of multiple sclerosis

Discussion
Typical causes of internuclear ophthalmoplegia include brainstem ischemia and demyelination. The latter cause is more common in patients under age 50, who are at higher risk for developing multiple sclerosis (MS). Demyelinating lesions in the brainstem or cerebellum can result in abnormalities of ocular motility, including ocular misalignment, causing diplopia; ocular instability, causing oscillopsia; or relatively asymptomatic abnormalities of ocular motor control. The most common ocular motility abnormality in MS is internuclear ophthalmoplegia (INO), characterized by ipsilateral adduction deficit and abducting nystagmus of the contralateral eye. Other findings in a unilateral INO can include a skew deviation, and in bilateral INO, gaze-evoked upbeat nystagmus in upgaze may be present. Occasionally, the adduction deficit can be subtle and detectable with slow ipsilateral adducting saccades in the absence of contralateral abducting nystagmus. This may be the only residual sign of an old INO.

In INO associated with MS, acute demyelinating lesions in the dorsal median midbrain and pons affect the medial longitudinal fasciculus (MLF). The MLF contains interneurons that transmit signals from the VI and III nerve nuclei for coordinating the medial and lateral rectus muscles in control of horizontal gaze. MLF fibers cross shortly after leaving the VI nerve nucleus, and thus dorsal pontine lesions involving the MLF will cause ipsilateral impairment of adduction. Demyelinating lesions that are small and cross the midline may cause bilateral INO, often referred to as “WEBINO” (wall eyed bilateral INO, due to the large exotropia from bilateral impaired adduction).

In initial evaluation, one should elicit a history of transient neurological symptoms in the past, suggestive of prior demyelinating events. Workup of initial neurologic presentation of MS includes brain MRI without and with contrast to detect old and active lesions, especially the T2 FLAIR sequence. At initial presentation, MRI of the entire spine can also be helpful in assessing for additional demyelinating lesion burden, but it is not necessary for routine monitoring subsequently. Lumbar puncture with cerebrospinal fluid studies may show myelin basic protein, oligoclonal bands, elevated IgG index, and mild pleocytosis, as well as other more recently described biomarkers; however, lumbar puncture is not routinely required for diagnosis of MS.

Treatment of acute neurologic impairment in MS may include pulse high-dose corticosteroids for 3-5 days, intravenous immunoglobulin, and even plasma exchange in severe refractory cases. Monocular occlusion for relief of diplopia may be performed. Often, the INO will improve and become asymptomatic within 4-6 weeks of onset. In some cases, strabismus surgery or botulinum toxin is used for persistent symptomatic exotropia.

Teaching Points
1. New horizontal binocular diplopia in young patients may be due to INO.
2. Careful observation of speed of adducting saccades may detect mild or healed cases.
3. INO is the most common eye movement finding in MS and may be the first presenting sign.
4. Workup of suspected MS requires MRI brain and spine initially. Analysis of cerebrospinal fluid may be supportive but is not necessary for diagnosis.
5. Generally, symptoms improve significantly without treatment over 4-6 weeks.

Selected Readings
Blurred Vision with Reading

Paul H Phillips MD

Final Diagnosis
Superior oblique myokymia

Summary
Superior oblique myokymia (SOM) occurs from episodic, monocular contractions of the superior oblique muscle resulting in high-frequency, low-amplitude torsional and vertical eye movements. Onset of episodes may be spontaneous or may be elicited by downgaze, ipsilateral head tilt, or blinking. Duration of episodes is typically seconds to minutes. SOM maybe difficult to detect on routine examination and is best observed by focusing on a conjunctival vessel at the slitlamp.

Symptoms include intermittent blurry vision, tremulous ocular sensations, oscillopsia, and diplopia. Although most patients are otherwise normal, SOM has been described after CN IV palsy, and in rare cases has been associated with trauma, stroke, compressive lesions, and multiple sclerosis. Vascular compression of the nerve root may be the most common etiology. MRI should be considered to detect associated conditions.

Patients may have spontaneous resolution. Treatment options include topical and systemic B-blockers, carbamazepine, phenytoin, baclofen, gabapentin, and memantine. Strabismus surgery is typically reserved for patients with severe symptoms and includes superior oblique tenectomy to eliminate the oscillations, and inferior oblique myectomy to treat the iatrogenic superior oblique palsy. Many patients will have diplopia in downgaze after surgery, which can be managed with prisms. Vascular decompression of CN IV at the nerve exit zone has been reported to alleviate symptoms, although most patients elect less invasive treatment options described above.

Teaching Points
1. SOM should be suspected from the characteristic history of episodic monocular oscillopsia, diplopia, and tremulous ocular sensations.
2. SOM may be difficult to detect on “routine” motility examination and is best observed by focusing on a conjunctival vessel during the slitlamp examination.
3. Although SOM is idiopathic in most patients, it is rarely associated with trauma, stroke, compressive lesions, and multiple sclerosis. It is therefore reasonable to obtain cranial MRI.
4. Topical or systemic B-blockers as well as other medications may improve symptoms.
5. Strabismus surgery is reserved for patients with severe symptoms.

Selected Readings
Section IV: Abnormal Test Result—Panic, or Repeat It?

Abnormal MRI, Headache, and Normal Fundus

Marie D Acierno MD

Diagnosis
Pituitary tumor

Teaching Points
In summary, this patient had a pituitary tumor. Due to its size, less than 1 cm, it is classified as a pituitary microadenoma. Patients with symptoms from pituitary tumors will frequently present with headache not alleviated with medication. The second most common presenting symptom of a pituitary tumor is visual disturbances. Thirdly, patients may have hormonal dysfunction, such as problems with their menstrual cycle or lactation without being pregnant. Basically, any hormonal regulation that the pituitary gland is involved with may be disrupted.

About 10% of pituitary tumors are only 2-3 mm in size. The patient is usually not even aware that they harbor such a tumor, and they often lack symptoms. The pituitary gland resides in the sella turcica, and the optic nerves and optic chiasm lie 1 cm above. The ocular motor nerves run laterally in the cavernous sinus. Pituitary tumors that alter vision result in symptoms of decreased central vision in one or both eyes, a change in peripheral vision, or diplopia. Many soft tissue pituitary tumors tend to grow upward and disrupt the body of the optic chiasm where nasal retina fibers cross, resulting in a bitemporal hemianopsia. The optic chiasm can be anatomically pre- or postfixed and cause a visual field defect, such as a junctional scotoma or homonymous hemianopsia, respectively. In some cases the pituitary tumor chronically compresses the optic nerves or optic chiasm, and therefore the patient may be unaware of their reduced vision or visual field loss.

Ophthalmologic examination with visual field analysis is necessary to assess visual function. Visual function determination is useful information for both the patient and the neurosurgeon. Retinal nerve fiber layer analysis, and especially ganglion cell layer measurements, via OCT, assists the ophthalmologist in delineating realistic expectations for visual prognosis.

Selected Readings

Abnormal OCT in a Patient with a Normal Exam

Kimberly M Winges MD

Final Diagnosis
Tilted optic nerve O.S., with multiple artifacts preventing accurate OCT interpretation

Teaching Points
OCT as a clinical tool
Fundus OCT is a powerful and easy-to-use tool that has become standard in the diagnosis and management of glaucoma, retinal, and optic nerve disease. It uses interference patterns of light to form a cross-sectional image of the optic disc and macula, quantifying the retinal nerve fiber layer (RNFL) and macular thicknesses in microns, including automated segmentation of retinal layers such as the ganglion cell–inner plexiform layer (GC-IPL). A high level of repeatability and reproducibility has been achieved with the newer spectral domain platforms, but values from individual platforms should not be cross compared (Cirrus to Spectralis, for example). Importantly, OCT should be interpreted in context of the clinical scenario and dilated fundus exam, because it is subject to multiple sources of artifact and misinterpretation. Especially when an unexpected result is produced, the scan should be manually inspected for errors in both software algorithms and patient factors, such as positioning, blinking, and concurrent ocular pathology that limits segmentation algorithms. Thickness values vary with age, and normative values are not provided on current platforms for patients under 18 years old.

Recognizing artifacts in optic disc and peripapillary RNFL analysis
Among artifacts that lead to misinterpretation of RNFL readings, low signal strength is common, affected by dry eye, media opacities, and cataract, producing a mild decrease in RNFL thickness that may lead the reader to a false-positive diagnosis...
of optic neuropathy. For example, with Stratus and Cirrus OCT platforms, the segmentation algorithm may fail below a signal strength of 7/10.2,3 Additionally, blinking causes linear black lines on the en-face OCT thickness maps. Eye motion may shift the disc border or vessels on the thickness maps and are improved with built-in eye tracking technology.4 Media opacities such as vitreous floaters create focal vertical shadows that interrupt scan signal. Decentering or misalignment of the OCT in the z-axis results in truncation of the scan, seen as rectangular areas of RNFL thickness on the probability plots that drop abruptly to 0.0 microns; this is nonphysiologic and should clue the reader to a false-positive result.5 Segmentation algorithm errors can occur in measuring the optic disc rim and rim area, causing small diameter nerves to falsely appear edematous and large optic nerve diameters to measure a larger cup-to-disc ratio than seen on exam. Long or short axial lengths cause similar problems in interpretation, as they both change the angle of insertion of RNFL fibers and cause a direct ocular magnification difference (ie, highly myopic eyes may measure smaller disc size and thinner RNFL). Focal gliosis and blood vessels can falsely elevate the RNFL reading. Finally, OCT directed at a focal area of RNFL fibers and cause a direct ocular magnification difference (ie, highly myopic eyes may measure smaller disc size and thinner RNFL). Focal gliosis and blood vessels can falsely elevate the RNFL reading. Finally, OCT directed at a nerve obliquely, such as that from poor patient positioning, fundus torsion, or a tilted nerve, is particularly subject to misalignment and segmentation error.

Recognizing artifacts in macular ganglion cell layer analysis When interpreting macular OCT for automated segmentation of the GC-IPL, artifact is also common and most likely due to segmentation error with misidentification of the retinal layers.5 One clue to this type of error is the “propeller sign” of blue diagonal lines on the probability plot in Cirrus OCT.2 GC-IPL values of less than 40 microns also likely result from segmentation error rather than true pathology, except in the most severe optic neuropathies.2 Low signal strength, media opacities, optic nerve edema, and outer retinal structural abnormalities such as retinal pigment epithelial layer atrophy from macular degeneration are potential sources of artificially thin readings. Epiretinal membranes, staphyloma, retinal edema, and vitreomacular traction also commonly cause segmentation error. In this case, it is helpful to inspect the high-definition B-scans for correct layer definition and total macular thickness maps for any corresponding artifact or retinal pathology.

Key principles for correct interpretation of OCT results

- Carefully inspect the scan printout for correct name and age of the patient.
- Check for adequate signal strength, specific to the manufacturer.
- Check for correct centration of scan over the optic disc or fovea and match these locations on follow-up scans.
- Inspect the B-scans for accurate layer identification and alignment, as well as en-face thickness maps for areas of RNFL or ganglion cell layer loss that do not correlate to anatomy, especially those producing regional thicknesses of less than 40 microns.
- Pay attention to coexisting disease or anatomical variation that may render the patient’s RNFL or GC-IPL outside the normal range determined by the manufacturer’s normative database; if found, compare inter-eye differences and follow longitudinally on the same OCT platform.
- Excellent examples of common OCT artifacts can be found in references 2 and 4.

References


Abnormal Visual Field Defects with Normal Optic Nerves

“Doctor, now my other eye is bad!”

Y Joyce Liao MD PhD

Final Diagnosis

Susac syndrome

Teaching Points

1. Bilateral visual field defects can localize to the retina, optic nerve head, and, rarely, brain. Sudden onset of nasal visual field defect is characteristic of branch retinal artery occlusion (BRAO) or anterior ischemic optic neuropathy and is not glaucomatous optic neuropathy.

2. Susac syndrome is a rare cause of BRAO and consists of the triad of BRAO, hearing loss, and brain involvement (see more below).

3. Characteristic retinal findings of Susac syndrome include BRAO, focal segmental staining of the arterial wall (arterial wall hyperfluorescence) on fluorescence angiography, and Gass plaques, which are yellow emboli located between arteriolar bifurcations that reflect endothelial damage.

4. Diagnostic criteria for definite Susac syndrome include MRI finding of characteristic T₂ hyperintense lesion in the corpus callosum.

Susac syndrome, first described by John Susac in 1979 and coined by William Hoyt in 1986, is a rare autoimmune microangiopathy syndrome due to occlusion of the precapillary arterioles.1 It presents as the triad of visual field loss from BRAO, hearing loss, and central nervous system involvement.2-4 The triad is complete in only a minority of patients. There are many recent papers that review 304 cases of Susac syndrome2 and delineate the retinal manifestations and characteristic MRI findings.3,5
Susac syndrome is more common in women (78%) and in people of European ancestry (81%). The mean age of onset is 31 (range: 8-65 years), with mean number of relapses at 2.4 (range: 1-10). Differential diagnoses of Susac syndrome include multiple sclerosis and other inflammatory demyelinating diseases affecting the brain, stroke, vasculitis, infections, MELAS (malignancy, migraine, encephalopathy, lactate acidosis, and stroke-like episodes), and isolated BRAO. Major organ involvement in Susac syndrome includes:

1. Retinal involvement: To meet the retinal criterion, there should be at least one acute BRAO in fluorescein angiography or fundoscopy, focal segmental staining of the arterial wall (arterial wall hyperfluorescence) near the site of obstruction in fluorescein angiography, or sectorial damage of the inner retinal layers from the retinal nerve fiber layer through to the outer plexiform layer in OCT. Periperal retinal arterial wall plaques or Gass plaques are typical for Susac syndrome, but they are often transient.

2. Vestibulocochlear involvement: To meet this criterion, there should be new tinnitus, hearing loss, or peripheral vertigo. Since these symptoms are relatively nonspecific, the patients should have comprehensive evaluation by ENT with hearing test, video nystagmography, or vestibular evoked myogenic potentials.

3. Brain involvement: To meet this criterion, patients should have at least 1 symptom that suggests brain involvement and characteristic brain MRI findings. Symptoms include new cognitive impairment, focal neurologic symptoms, new headache, or behavioral change. There have to be typical brain MRI findings, such as multifocal small, round lesions, at least one of which is centrally located in the corpus callosum (“snowball”) in T2 (or FLAIR) weighted sequences. Other typical brain MRI lesions include sharply confined T2-hypointense lesions with or without gadolinium enhancement, gray matter lesions, and leptomeningeal gadolinium enhancement.

Based on 32 patients with an unambiguous diagnosis of Susac syndrome, the European Susac Consortium (EuSaC) proposed in 2017 the following diagnostic criteria:

1. Definite Susac syndrome: Patients with unequivocal clinical involvement of all 3 main organs (ie, fulfilling the typical clinical triad)
2. Probable Susac syndrome: Patients with unequivocal clinical involvement of 2 of the 3 main organs
3. Possible Susac syndrome: Patients who have some of the typical features of Susac syndrome but only fulfill 1 of the criteria

Treatment of Susac syndrome targets the immune-mediated endotheliopathy, starting with high-dose corticosteroid treatment such as IV methylprednisolone 1000 mg/day for 3-5 days and antiplatelet agents. Other immunomodulatory therapies to consider include IV immunoglobulin (IVIg), plasmapheresis, azathioprine, mycophenolate mofetil, methotrexate, cyclosporine A, and cyclophosphamide. Treatment should be prompt and aggressive since new events are common and neurological symptoms may be irreversible.

References

Abnormal Electrophysiology with a Normal Exam
Vivek R Patel MD

Final Diagnosis
Autoimmune retinopathy

Teaching Points
We felt the constellation of findings in this case supported our clinical diagnosis of relatively early (preatrophic stage) autoimmune retinopathy. This case demonstrates that early on in the presumed autoimmune attack on various retinal tissues, typical atrophic features may not be seen on fundoscopy, OCT (optic nerve or macula), or autofluorescence imaging. Given the paucity of objective findings, attention to subtle features such as arteriolar attenuation may be very fruitful in early cases of autoimmune or paraneoplastic retinopathies, allowing for consideration of this diagnosis and initiation of therapy before destructive changes set in. Hence, the therapeutic window may be narrow if present at all.

Electroretinography (ERG) was essential in case this for a number of reasons. Such cases, without objective evidence of dysfunction, can often be mislabeled as non-organic vision loss. In addition, ERG testing revealed a much more widespread process than focal macular cone dysfunction. Demonstration of cone involvement throughout the retina (photopic full-field ERG) and locally within the macula (multifocal ERG), as well as rod photoreceptor involvement (under scotopic conditions),
was essential to help differentiate this presentation from that of hydroxychloroquine toxicity. Further, an OCT macula performed 2 months after the initial presentation also failed to demonstrate the typical perifoveal outer retinal atrophy seen in hydroxychloroquine toxicity.1 Although a visual evoked potential (VEP) would likely have also been abnormal in our case, this test is fairly nonspecific and nonlocalizing. The VEP can be abnormal if there is an abnormality anywhere along the visual pathway, and hence would not help reliably distinguish between a diffuse retinal and a macular process. Leber hereditary optic neuropathy (LHON) can affect women and present with simultaneous painless bilateral vision loss in a similar manner to our patient. However, in LHON one would not expect the ERG changes observed here, underscoring the clinical utility of ERG testing in such cases.

We have learned a great deal about paraneoplastic and autoimmune retinopathies from decades of pioneering work published by Drs. Keltner, Thirkell, and many others.2-3 Although there remain many yet-unanswered questions regarding the true pathogenicity of many of the discovered antibodies, we do know that consideration of a paraneoplastic entity is essential in clinical presentations such as these since many patients lack a diagnosis of malignancy at the time of visual presentation. In many cases where a systemic malignancy is not uncovered, patients often (but certainly not always) have a history of a systemic autoimmune condition, presumably inciting a similar process of molecular mimicry between systemic and retinal antigens.

There remains a lack of consensus regarding an optimal management protocol for cases of autoimmune or paraneoplastic retinopathy. Certainly, control of the underlying autoimmune condition or malignancy is paramount. In addition, steroids, IV immunoglobulin, and antibody-mediated immunomodulatory approaches are considered. Rituximab is a nonspecific yet logical choice.4 Reports of treatment response are extremely varied; major contributors to this inconsistency are likely the heterogeneity in clinical presentations, extent of atrophy at time of diagnosis, and control of the underlying process, to name a few. Nonetheless, a high index of suspicion is necessary when patients present with significant vision loss with seemingly normal objective examinations but abnormal electrophysiologic testing. Making the diagnosis could save your patient’s life, and maybe even restore some vision.

White Matter Lesions on Brain MRI Disease or Artifact?

Zoë R Williams MD

Final Diagnosis

Probable relapsing-remitting multiple sclerosis (MS)

Teaching Points

The diagnosis of MS relies on separation of lesions in time and space. Based on the revised McDonald criteria from 2010, prediction of conversion to clinically definite MS could not be made based on our patient’s initial MRI brain. Dissemination in space was not fulfilled by 1 periventricular lesion and 1 posterior fossa lesion, as all symptomatic lesions are excluded in brainstem syndromes. Dissemination in time was not fulfilled on initial MRI as this requires the simultaneous presence of asymptomatic gadolinium-enhancing and nonenhancing lesions.

The recent Magnetic Resonance Imaging in Multiple Sclerosis (MAGNIMS) consensus guidelines, published in 2015, suggest that patients with suspected MS who do not meet the revised 2010 McDonald diagnostic criteria but have a clinically isolated syndrome at baseline should have repeat neuroimaging within 3-6 months to assess for new T2 hyperintense lesions. In 2016, the MAGNIMS group proposed new diagnostic MRI criteria for MS. Dissemination in space can now be fulfilled regardless of whether the lesions are symptomatic or asymptomatic; the optic nerve was added as a lesion site; juxtacortical and cortical lesions were combined as a site; and 3 or more periventricular lesions are now needed to define periventricular involvement. Imaging of the entire spine is recommended for patients who do not meet brain criteria for dissemination in space. MRI criteria for dissemination in time were not modified, with the exception of the clarification that if a patient with a previously radiologically isolated finding has a subsequent clinical event, a diagnosis of MS can be made based on dissemination in time and space.

Recent expansion of the available disease-modifying therapy effective in early phases of MS makes timely and definitive diagnosis essential; however, it is also important not to "overcall" the diagnosis as numerous diagnoses can resemble MS radiographically, including autoimmune disease, such as neuromyelitis optica/neuromyelitis optica spectrum disorder; infectious disease, such as Lyme disease and HIV/JC virus–induced progressive multifocal leukoencephalopathy; migraine and chronic small vessel ischemia; and neoplasm (especially glioma and CNS lymphoma). Reports of development of “sentinel” demyelinating lesions prior to onset of CNS lymphoma and the potential for CNS lymphoma to improve with corticosteroid treatment further complicates the clinical picture. Appropriate ancillary studies and serial neuroimaging are imperative to ensure correct diagnosis. Identification of T2 hyperintense spinal cord lesions and the presence of oligoclonal bands or increased immunoglobulin G synthesis rate in cerebrospinal fluid can help establish a probable diagnosis of MS, although these findings are not 100% specific to MS.

References


Selected Readings


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