

Functional Ocular Complaints: Tips for the Ophthalmologist

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Identification of functional visual complaints is one of the more difficult areas of clinical diagnosis. Ocular complaint with no evident organic basis for the symptoms or signs is a relatively common presenting problem for the ophthalmologists and while the diagnosis of functional ophthalmic disorder requires exclusion of structural pathology, it should not be considered of diagnosis of exclusion. The ophthalmologist needs to document confirmatory findings and collect data supporting the diagnosis of functional ocular complaints. Early diagnosis is important to avoid prolonged or multiple unnecessary workups. Once a diagnosis of functional disorder is made, the ophthalmologist has the opportunity to play a key role in facilitating care within the broader health care system.

The objectives of this case-based interactive course are:

- To provide an overview of examination techniques used to support the diagnosis of functional disorder
- To discuss how to approach a patient with functional disorder

I. Monocular functional vision loss

- a. RAPD
- b. Vertical prism test
- c. Stereo test
- d. Optotype chart
- e. Confusion tests (e.g. fogging, duochrome, polarized lens test)
- f. Binocular visual field test for patients with monocular visual field defect

II. Bilateral functional vision loss

- a. Observing visual behavior
- b. Pupillary reaction
- c. Optotype chart
- d. OKN test
- e. Mirror test
- f. Proprioceptive test (e.g. finger-touching test)

III. Tunnel visual fields

- a. Observing visual behavior
- b. Tangent screen
- c. Testing saccades

- IV. Organic vision loss with functional overlay
- V. Importance of in-office ancillary tests
 - a. Visual fields
 - b. OCT (optic nerve and retina)
 - c. Fundus autofluorescence, FA
 - d. Full field and multifocal ERG
- VI. Functional eye movement disorders
 - a. Spasm of the near reflex
 - b. Gaze palsy
 - c. Voluntary nystagmus
- VII. Functional ptosis and blepharospasm
- VIII. How to approach the patient when a diagnosis of functional disorder is made
 - a. Displaying empathy, employing active listening, and carefully recording the patient's story help the clinician to ensure that the doctor-patient relationship remains productive and nonconfrontational.
 - b. Don't be afraid to use the term functional; SPIKES protocol can be a useful tool
 - c. Education of patients and families (many excellent on-line resources geared towards patients)
 - d. Referral to psychologist or psychiatrist, cognitive behavioral therapy

Title: Neuro-ophthalmological Immune Related Adverse Events of Targeted Cancer Therapy

Education Level: Intermediate/Advanced

Target Audience: Comprehensive Ophthalmologists/Subspecialists/Both

Hours Requested: All courses have been standardized to 75 minutes to allow for one hour of instruction time and 15 minutes of Q&A.

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Background:

Targeted cancer therapy (TCT), such as immune checkpoint inhibitors, is a major advancement in the field of oncology. Through the years, the number of FDA-approved and off-label indications has expanded with promising survival benefit in varieties of cancers e.g., metastatic melanoma, renal cell carcinoma (RCC), non-small cell lung cancer (NSCLC), Hodgkin lymphoma, and other malignancies. TCT is an exceptional cancer treatment that works by influencing the immune system, blocking various pathways involved in cancer cell development, and interfering with specific signaling and angiogenesis pathways. Although theoretically TCT are more tumor-targeted and less destructive than standard chemotherapy, some distinct TCT classes have been linked to several unfavorable side effects known as immune related adverse events (irAEs).

Ocular immune-related adverse events (irAEs) are one of the most common side effects of TCT and are becoming increasingly important to recognize in the management of patients on these medications as the eye has a unique microenvironment and is at risk of ocular irAEs.

The purpose of our course is to highlight the wide spectrum of ocular irAEs, including their type, frequency, severity, and recognizing class- specific TCT that can present with serious complications to provide a better understanding of these side effects. At the conclusion of this course, the attendee will be able to recognize class- specific irAEs and determine the next step in management.

State Society Presentation: Would you be willing to present the material at a state society meeting? (Yes) Are you a state society member? (Yes)

Special Audio-Visual Requirements: Will your course require any special AV support? Please list. No

Synopsis: These 4 cases highlight the large variety of ways that target cancer therapy can cause ocular immune-related adverse events.

Case 1:

A 78-year-old male had a history of recurrent chordoma of the sacrum that continued to grow despite multiple resections. He was treated with the immune checkpoint inhibitor, pembrolizumab, for x months. One week after his last dose, he started to have generalized body weakness, double vision, and difficulty swallowing foods. On examination he was found to have left lid ptosis, orbicularis weakness, Cogan lid twitch and limitations in eye movements. The work up was negative for acetylcholine receptors antibodies, though he was positive for striated muscle antibodies. He was found to have an elevated CPK of 8,451. The muscle biopsy was consistent with immune related myositis leading to the diagnosis of checkpoint inhibitor-induced myasthenia gravis and immune related myositis. He was started on a 5- day course of prednisone 40mg daily and pembrolizumab was discontinued. He reported improvement in his symptoms, but he currently needs assistant and a wheelchair for ambulation.

Final diagnosis: checkpoint inhibitor-induced myasthenia gravis and myositis

Case 2:

A 70-year-old male with a diagnosis of metastatic anaplastic thyroid cancer was treated with vemurafenib/cobimetinib/atezolizumab and received 17 cycles over 1.5 years. After his 17th treatment, he presented with painless decreased vision in the left eye. On examination he was found to have left optic nerve swelling. Work up was negative for metastasis or leptomeningeal disease. MRI showed sign of left optic neuritis and hypophysitis. Treatment was discontinued and he was treated with high dose steroids leading to improvement of visual acuity and visual fields. The optic nerve swelling resolved leaving mild post-swelling optic atrophy.

Final diagnosis: Immune related optic neuropathy and hypophysitis

Case 3:

A 36-year-old female with a diagnosis of stage IV M1C metastatic melanoma involving the liver, lung and peritoneum s/p post wide local excision was started on Ipilimumab plus Nivolumab, which led to resolution or reduction in all disease sites. After 6 months of treatment, she presented with progressive vision loss, double vision, and bilateral eye congestion. Exam showed bilateral periorbital edema, conjunctival congestion, and mild lid lag. Sensory motor exam showed bilateral abduction deficit consistent with restrictive motility. CAS score was 7. MRI of the brain showed diffuse symmetric enlargement of the extraocular muscles. Further work up revealed abnormal thyroid function. The patient was diagnosed with immune checkpoint inhibitor-related thyroid eye disease. Treatment was held and she was started on high dose steroids that led to some improvement of her symptoms.

Final diagnosis: Immune checkpoint inhibitor-related thyroid eye disease

Case 4:

A 52-year-old male with a diagnosis of metastatic adenocarcinoma of the lung with brain metastasis s/p whole-brain radiation treatment with pembrolizumab presented with bilateral vision loss. Examination revealed bilateral optic disc edema and retinal edema. Both eyes showed no choroidal metastases. MRI of the orbit showed subtle thickening and enhancement of bilateral choroidal and optic nerve enhancement. =The patient was diagnosed with immune checkpoint inhibitor-related bilateral optic neuropathy and choroiditis. Pembrolizumab was discontinued and he was treated with 5 doses of plasmapheresis and high dose of IV solumedrol. Further follow up showed improvement of optic disc edema and sign of bilateral optic atrophy.

Final diagnosis was immune checkpoint inhibitor-related bilateral optic neuropathy and choroiditis.

Proposal for Neuro-Ophthalmology Instruction Course AAO 2024

Title: Down the Rabbit Hole: Making Sense of Cortical Visual Disturbances

Audience: Comprehensive ophthalmologists

Senior instructor: Kimberly Winges

Other instructors: Nailyn Rasool, Sangeeta Khanna, Collin McClelland, Lauren Ditta (limit 5)

Abstract:

Synopsis: Cortical visual disorders present in complex ways and are often difficult for the general ophthalmologist to recognize and diagnose. However, diseases such as strokes, seizures, dementia, and neurologic infections result in significant morbidity and mortality and thus are vital to identify and manage appropriately. This course will introduce varied aspects of cortical visual pathology such as alexia without agraphia and hallucinations in an efficient, easy to understand, and entertaining manner to the general ophthalmology audience. Through a series of interactive case presentations, a panel of experts will provide tools to recognize such symptoms and signs in patients. Important pearls for examination and management will be shared, including how to distinguish harmful from benign conditions.

Objective: At the conclusion of this course, attendees will gain comfort with the presentation of key cortical visual disorders and be better equipped to evaluate and recognize neurologic emergencies and associated systemic diseases within their practices.

Background statement for application: Cortical visual disorders are increasingly common in our aging population, but their symptoms are often neglected or difficult to elucidate in the routine ophthalmology exam. This course will give Academy members necessary tools to address them.

Course Outline:

Introduction (instructor: Kimberly Winges)--5 min

1. Welcome
2. What we will cover: positive, negative visual phenomena, visual illusions/distortions
3. How we will cover it:
 - a. Background: How does the brain make vision from sight?
 - b. Cortical Visual Disorders and Their Syndromes: The patient sees things they can't make sense of
 - c. Positive Visual Phenomena / Hallucinations: The patient sees things that are not there, including lights, patterns, or something obstructing vision.

- d. Visual Distortions / Illusions: The patient's visual perception misrepresents reality.
- e. Conclude with tips on takeaway pearls

How the Brain Turns Sight into Vision (instructor: Nailyn Rasool)--10 min

Presentation of the basis for cognitive visual phenomena. Discussion about the factors important in visual interpretation. This includes how we read and understand the words on the page, see and recognize faces and scenes, and navigate through a visuospatial environment. There will be a brief discussion of the neuroanatomic basis for cortical visual processing including the ventral and dorsal streams. Lastly, positive visual phenomena such as visual hallucinations and illusions will be touched upon briefly with respect to neuroanatomic correlates.

Higher Order Visual Disorders (Nailyn Rasool and Lauren Ditta)--25 min

The first cases will focus upon re-iterating the symptoms and signs of individuals with cortical visual disorders. This will also assist in solidifying and repeating the neuroanatomy as well as the importance of recognizing these as they may result from life-threatening diseases. These cases will focus upon what patients are unable to 'see' or identify well.

1. Visual Agnosia Cases (5): Apperceptive / Associative Agnosias; Simultanagnosia (5)
 - a. Recognition deficits in each of these
 - b. Connect to the dorsal/ventral cortical stream
2. Alexia without Agraphia Case (5)
 - a. Anatomy of reading and writing
 - b. Neuroimaging and visual fields in Alexia without Agraphia
3. Hemineglect Case (5)
 - a. Differentiating neglect from hemianopia
 - b. Importance of neuroimaging
4. Audience Q+A/panel discussion (10)

Positive Visual Phenomena (Sangeeta Khanna and Collin McClelland)--20 min

This set of cases will address cases where the patient sees "too much", including formed and unformed hallucinations and visual auras.

1. Unformed hallucinations (5)
 - a. Patient Cases with discussion of differential diagnoses and workup, management, patient and family counseling
 - i. Visual Aura of Migraine
 - ii. Occipital Lobe Seizures
 - iii. Visual Snow
 - b. How to differentiate between retinal and cortical conditions, as well as serious and benign conditions
2. Formed hallucinations (5)
 - a. Patient Cases with discussion of differential diagnoses and workup, management, patient and family counseling

- i. Charles Bonnet Syndrome
 - ii. Sleep-Related Hallucinations: Peduncular, Hypnagogic/Hypnapompic
 - b. How to differentiate between benign conditions such as Charles Bonnet Syndrome and those requiring neurologic workup, such as neurodegenerative disease or stroke
3. Audience Q+A/panel discussion: (10)

Visual Illusions/Distortions (Kimberly Winges)--10 min

This set of cases will address visual perception that misrepresents reality, for example: metamorphopsia, micropsia or macropsia, haloes, kaleidoscopic or fractured scenes, sensation of looking through heat or water waves, persistence of visual imagery (palinopsia), or loss of color vision (achromatopsia).

- 1. Patient Cases with discussion of differential diagnoses and workup, management, patient and family counseling, neuro-psychology referral (5):
 - a. Palinopsia
 - b. Alice in Wonderland Syndrome
- 2. Audience Q+A/Panel Discussion: (5)

Conclusion/Wrap-Up (Sangeeta Khanna)--5 min

Share "Takeaway Pearls" from each section to reiterate importance diagnostic and management concepts

American Academy of Ophthalmology 2024

Course

Emergency Neuro-Ophthalmology: Diagnosis and Management

Nicholas J. Volpe, M.D.

Mark L. Moster, M.D.

I. Introduction

- A. Few true neuro-ophthalmic emergencies.
 - 1. life, sight or "brain" threatening catastrophe
 - 2. vision loss that if treated would be reversible
 - 3. Is the patient's presentation non organic?
 - 4. Pseudo emergencies more common.
- B. True emergencies:
 - 1. temporal arteritis
 - 2. acute/impending stroke
 - 3. carotid dissection
 - 4. intracranial hemorrhage
 - 5. aneurysm
 - 6. papilledema/intracranial mass
 - 7. meningitis
 - 8. infectious orbital cellulitis

II. Case 1: Ischemic Optic Neuropathy

- A. must rule out:
 - 1. temporal arteritis
 - 2. embolic vision loss (CRAO)
- B. Work up
 - 1. review of systemic GCA symptoms
 - 2. laboratory testing
- C. Clinical Distinction of Arteritic AION
- D. Treatment
 - 1. vision loss: high dose intravenous steroids.
 - 2. never delay treatment waiting for biopsy

III. Case 2: Monocular Blindness/Transient and Permanent

- A. Historical considerations

- 1. possible temporal arteritis
 - 2. other TIA symptoms
 - B. Acute Management of CRAO
 - 1. Paracentesis, carbogen, massage ?< 6 hours
 - 2. anticoagulation
 - 3. **Stroke team DWI MR imaging**
 - C. Work up of embolic disease
 - 1. carotid non invasive/MRA
 - 2. echocardiogram
 - D. Carotid disease
 - 1. 25% of ischemic strokes, 50% preceded by TIA
 - 2. surgical indications
 - 3. medical therapy - aspirin, ticlopidine
 - E. Other causes of sudden visual loss
 - 1. Pre-geniculate
 - a. pituitary apoplexy
 - b. intoxication
 - 2. Post-geniculate
 - a. cortical blindness
 - F. Causes of transient bilateral visual loss
 - 1. giant cell arteritis
 - 2. vertebrobasilar TIA
 - 3. migraine
 - 4. papilledema

IV. Case 4: Headache and Miosis

- A. Horner's syndrome
 - 1. ptosis, miosis, anhidrosis
 - 2. diagnosis (drop testing)
- B. Diagnosis/Work up.(painless)
 - 1. not an emergency
- C. Diagnosis/Work up (painful)
 - 1. carotid dissection (true emergency)
 - 2. cluster headache
 - 3. cavernous sinus lesion, inflammation

V. Case 5:. Fixed Dilated Pupil

- A. Differential Diagnosis
 - 1. Adie's tonic pupil
 - 2. pharmacologic
 - 3. local trauma
 - 4. third nerve palsy
- B. Considerations
 - 1. is it isolated (ptosis, diplopia EOM limitation).

2. if isolated 3rd nerve palsy extremely unlikely
3. no other diagnoses is emergent
4. pharmacologic agents causing anisocoria
5. pharmacologic testing
6. pharmacologically dilated pupils are large
7. Adie's Tonic Pupil-clinical features

VI. Case 6: Third Nerve Palsy with Pupil Involvement

- A. Three groups of cases:
 1. diabetic (usually over 40 yrs old)
 2. aneurysm (rare under age 15, rarely painless)
 3. idiopathic (all ages)
- B.. Pain can occur with any
- C. Work up
 1. emergency room except older and complete pupil sparing
 2. ALL MRI/MRA or CTA
- C. Third nerve palsies: Management
 - 1 Complete third nerve palsies
 - a. pupil sparing
 - b. pupil involved
 2. Partial

VII. Case 7: Painful ophthalmoplegia with Orbital Signs

- A. Differential diagnosis of painful ophthalmoplegia
 1. posterior communicating artery aneurysm
 2. ischemic mononeuropathy
 3. pituitary apoplexy
 4. mucocele
 5. herpes zoster
 6. migraine
 7. Tolosa-Hunt Syndrome
 8. metastases
 9. idiopathic orbital inflammation
 10. orbital cellulitis
 11. giant cell arteritis
 12. carotid-cavernous sinus fistula
- B. Mucocele, cellulitis, idiopathic orbital inflammation, metastases, fistula will have orbital signs

1. proptosis, chemosis and injection
 2. positive forced ductions
 3. thyroid orbitopathy is rarely painful
- C. Painful ophthalmoplegia and orbital signs
 1. IMAGE
 - D. Acute Orbital Inflammatory syndrome
 1. any age, pain on eye movements
 2. any of the orbital tissue involved
 3. normal sinuses on CT/MRI
 4. response to steroids can be a diagnostic test

VIII. Case 8: Painful ophthalmoplegia without orbital signs

- A. Pituitary Apoplexy
 1. history of endocrine dysfunction
 2. simultaneous chiasmal/optic nerve visual loss
 3. sudden onset of severe pain (bleeding in tumor)
 4. visual loss can be severe
 5. double vision from 3rd nerve palsy
 6. neurosurgical management
 7. Steroid deficiency can be life threatening

IX. Case 9: Double vision secondary to brainstem stroke

- A. Eye movement abnormalities seen with stroke
 1. internuclear ophthalmoplegia (WEBINO)
 2. Midbrain syndromes with third nerve palsy
 3. Pontine syndromes
 4. skew deviation
 5. dorsal midbrain syndrome
 6. Wallenberg's Syndrome
- B. Acute management
 1. consider inflammatory etiology
 2. image, DWI, stroke team
 3. consideration of anti-coagulation

X Case 10: Variable bilateral eye movement abnormality

- A. Historical features of myasthenia
 1. variable with diurnal variation
 2. difficulty swallowing change in voice
 3. reduced exercise tolerance/SOB

4. history of thyroid disease
- B. Examination features of myasthenia
 1. variable ptosis
 2. ANY pattern of EOM involvement
 3. orbicularis weakness

- C. Work up
 1. anti acetylcholine receptor antibodies
 2. Tensilon test
 3. refer ANY patients with bulbar or systemic symptoms emergently to neurology or ER

XI. Case 11: Head trauma with visual loss and normal fundus exam

- A. Posterior Indirect Traumatic Optic Neuropathy
 1. any level of vision loss
 - a. findings of optic neuropathy
 2. normal appearing fundus
 3. generally does not overlap with globe injury
 4. forehead blow injures optic nerve in the canal
 5. CT scan only demonstrates fracture in one third of patients
 - 6 treatment unproven
 6. avoid steroids in head injury patients
- (CRASH) study
 7. in rare circumstances, consider optic canal decompression

XIII Case 12: Bilateral disc swelling- Papilledema and Pseudo Papilledema

- A. papilledema secondary to increase ICP
 1. approach to patient with bilateral disc elevation-use of OCT
 2. must have careful neurologic exam and must have emergent neuro-imaging study to r/o mass or hydrocephalus
 3. must exclude venous sinus thrombosis
 4. most have pseudotumor cerebri (idiopathic intracranial hypertension) or pseudopap
 5. other symptoms include
 - a. transient visual obscurations
 - b. pulsatile tinnitus
 5. PTC patients most often are obese have recent weight gain

6. rare in men
7. LP after normal neuroimaging study
8. signs of "malignant" IIH with increased risk of vision loss

XIV. Case 13: The "urgent" management of optic neuritis

- A. The Optic Neuritis Treatment trial
 1. inform patients of ONTT results
 2. no treatment shown to alter the visual outcome
 3. IV steroids will accelerate visual recovery and now used commonly because of NMO and MOG
 4. MRI scan predicts MS risk
 6. steroids for severe vision loss bilateral and always for MOG and NMO
 7. oral steroids should not be used
 8. Keep LHON in mind as a mimicker