C23

The Six Neuro-ophthalmic Emergencies You Should Not Miss

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Papilledema is acquired elevation of the optic disc caused by increased intracranial pressure. Ophthalmologists encounter papilledema most commonly in idiopathic intracranial hypertension (IIH, pseudotumor cerebri) or medication-induced intracranial hypertension because patients with these conditions do not have neurologic manifestations apart from those attributable to increased intracranial pressure (headache, pulsatile tinnitus, transient vision loss, diplopia, neck or back ache). But there are important non-idiopathic causes of papilledema, some of which are life-threatening and require urgent management, such as brain tumor, intraventricular and extraventricular blockage of cerebrospinal fluid outflow, dural venous sinus thrombosis, dural arteriovenous fistula of the sagittal or transverse sinuses, cervical tumor, traumatic brain injury, meningoencephalitis, and spinal cord tumor.

The pathology of papilledema is believed to consist of axoplasmic stasis in front of the lamina cribrosa of the optic disc. How does increased intracranial pressure cause this axoplasmic stasis? Probably by distending the vaginal sheath at the circle of Zinn-Haller and causing chronic ischemia of the ciliary arteries that nourish the optic disc. Why does increased intracranial pressure by itself cause so much trouble for the optic nerves without causing much trouble to the rest of the brain? Perhaps because the choroidal arteries normally take most of the blood flow of the ophthalmic arteries, leaving the ciliary arteries with relatively low perfusion. When high intracranial pressure squeezes the ciliary arteries, their normally low perfusion becomes critically low and insufficient to maintain the metabolic energy required to sustain axoplasmic flow.

Can you reliably distinguish congenitally anomalous elevation of the optic discs from papilledema by ophthalmoscopy? Usually yes. But some cases have subtle abnormalities. In those few cases, fluorescein angiography, optic coherence tomography (OCT), computed tomography, and autofluorescence photography may help to discover buried drusen, but most congenitally anomalous elevated optic discs do not have drusen. Many investigators are claiming that OCT can distinguish any type of congenitally elevated optic disc from papilledema, but more experience is needed to judge the reliability of this ancillary test.

Can you reliably distinguish papilledema from other causes of ACQUIRED optic disc elevation? Ophthalmoscopy is not very good at this task. Many causes of acquired optic disc elevation look alike. After all, how many different optic disc appearances would you expect from ischemia, neoplastic infiltration, or inflammation? Therefore, look for two features of papilledema: 1) it is usually binocular (although often asymmetric) and 2) it relatively spares visual function unless the papilledema is extremely acute and severe or very chronic and atrophic.

Can you predict which patients will lose vision from papilledema? Somewhat. At least in IIH, the four best indicators are initial visual dysfunction, initial degree of papilledema, systemic hypertension, and poor compliance with pressure-lowering medication.

Unfortunately, most patients with IIH arrive with chronic papilledema that has caused considerable visual dysfunction. Patients arrive late because most have no non-visual symptoms (even no headache!). Alas, non-ophthalmologists are not often performing ophthalmoscopy, so they are unlikely to detect papilledema.

Therefore, ophthalmologists should apply routine surveillance of patient groups prone to papilledema, including young women who are rapidly becoming obese, who taking minocycline for acne, those with renal transplants, tuberous sclerosis, and children with ventriculoperitoneal shunts. A practical future alternative will be inexpensive and easy-to-use non-mydriatic fundus cameras.

Finally, when intracranial pressure-lowering medications fail in patients with advancing visual loss from papilledema, which surgical procedure should be considered: cerebrospinal fluid shunt or optic nerve sheath fenestration? No rigorous trials have compared these two surgical options because most patients recover with medical therapy or spontaneously. Both surgical procedures are reported to be effective, but I choose shunt for 4 reasons: 1) it always lowers intracranial pressure; 2) it does not risk vision loss; 3) it has few complications and very low need for revision; 4) it requires only one surgery.
Pituitary apoplexy is defined as hemorrhage or infarction within the pituitary gland. This is reported to be the first manifestation of a pituitary tumor in 2-7% of patients. Presentation typically consists of acute headache and often neuro-ophthalmological symptoms and signs such as visual loss and double vision. There may be photophobia, nausea, vomiting, and altered mental status. Mimics include migraine, meningitis, ruptured aneurysm, cavernous sinus thrombosis and even optic neuritis. Risk factors for pituitary apoplexy include coagulopathies, estrogen therapy, radiation treatment, hypertension, head trauma, dopamine receptor agonists, and post-cardiac surgery.

Pituitary apoplexy can be an emergence because of hypo-adrenalism which can lead to hypotension, hemodynamic shock and even death (8%). Neuro-ophthalmic findings are due to compression of the anterior visual system and cavernous sinus invasion. Findings can include almost any pattern of retrobulbar optic neuropathy, chiasmal or retrochiasmal visual loss. Thus, there may be unilateral or bilateral decrease in acuity, unilateral temporal or bitemporal visual field defects or homonymous hemianopsia. Any of the ocular motor cranial nerves can be involved unilaterally or bilaterally. For reasons that are unclear, the oculomotor nerve is most commonly involved.

MRI or CT scan will show hemorrhage in the pituitary gland and possible chiasmal or cavernous sinus compression (Fig 1).

Fig 1. Pituitary apoplexy. Yellow arrow – chiasmal compression, Red arrow – cavernous sinus invasion.

Management begins with a high level of suspicion leading to neuroimaging. Once diagnosed, endocrine, neurosurgery and ophthalmology teams should be involved. Fluid and electrolyte balance must be assessed and treated. Urgent endocrine assessment must be done. Hydrocortisone replacement if needed. There is some controversy regarding urgency of surgical treatment. Surgery is urgently indicated if vision is severely reduced and/or there is deteriorating level of consciousness. If not, then conservative management with close neurologic, visual and endocrine monitoring can be consid
Neuroimaging for third nerve palsy

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High Stakes Encounter

- Aneurysm = 30% of TNP
- Unruptured aneurysm SAH rate = 1-3%
- Mortality rate after rupture = 50%
- Symptomatic aneurysm rupture rate = 2.4X asymptomatic rate
- Treatment before rupture is superior

Objectives

- Review rule(s) of the pupil
- Define internal & external dysfunction
- When not to apply “rule of the pupil”
- Describe “pre-test” likelihood of disease
- Define how MRA/CTA can reduce “post-test” likelihood of aneurysm

Why Should You Care About Third Nerve Palsy (TNP)

- 50 y/o M with DMHTN presents with an acute isolated TNP
  - Possible etiologies:
    1. Vasculopathic TNP that will resolve in time
    2. Life threatening posterior communicating aneurysm that will rupture in time

Third nerve palsy: …and the MRI head was normal

- You need an “A” (angiogram) to find an “A” (aneurysm)
- There is no “A” in MRI or CT
- You need an angiogram of some kind
  - CTA
  - MRA
  - DSA (Digital Subtraction Angiography)

Summer: Exception to exception

- A standard catheter angiogram might still be necessary despite a negative CTA and MRI/MRA if you the clinician still believe that it is an aneurysm...
- Or you don’t trust the neuroimaging
- Or you don’t trust the neuroradiologist
Myasthenia Gravis
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Diplopia in Myasthenia Gravis
- May be no obvious strabismus
- Strabismus may mimic any monocular or binocular ocular motor disorder (except pupil-involved III NP)
  - Pupil-sparing III NP
  - Divisional III NP
  - IV NP (including exocyclotorsion)
  - VI NP
  - Gaze palsy (vertical or horizontal)
  - Internuclear ophthalmoplegia
  - May be variable (or not)

Neuromuscular Diplopia
- Should be considered in every patient with diplopia and/or ptosis
- Look for associated eyelid abnormalities
  - Cogan lid twitch (MG only)
  - Enhancement of ptosis
  - Fatigue
  - Other peek sign
  - Weak eyelid closure
- Perform appropriate tests (eg, Ice test, Tensilon test, Prostigmin test)

Cogan Lid Twitch
- Have patient look down for 5-15 seconds
- Have patient look back up rapidly
- Look for twitch of upper eyelid
  - Lid may only elevate and slowly become ptotic again
  - Lid may show rapid twitch

Enhancement of Ptosis
- Based on Hering’s law of equal innervation
- Manually elevate one eyelid
- Look for new or increased ptosis of contralateral eyelid

Conversion to GMG
- Varies by age and sex
  - Men, age > 60 at higher risk
  - Up to 75% of OMG may convert
- Severity of eye findings not predictive
- Majority of patients convert within 18-24 mos of eye symptom onset
- 80% of eventual GMG present for eye findings

Immunology
- Acetylcholine receptor antibodies
  - 3 classes (binding, blocking, modulating)
  - Positivity much higher in GMG than OMG
- MuSK antibodies
  - Distinct muscle antigen (tyrosine kinase)
  - Also located at post-synaptic membrane
  - Role in OMG still questionable

Gomez Autoimmunity 2010;43:353
Urgent Considerations

- Myasthenic crisis
- Respiratory failure requiring mechanical ventilation
- Any severe exacerbation requiring hospitalization
- Mortality of up to 75% without treatment
- May occur at any time in the disease course

Chaudhuri QJM 2009;102:97
Patients with Horner syndrome may present with a chief complaint of anisocoria, ptosis, pain, or they may have no complaints whatsoever. In many ophthalmology offices, a technician will dilate the pupils before the ophthalmologist ever sees the patient, which makes it impossible to determine if the patient had a Horner syndrome. Therefore, providers should carefully instruct ancillary staff how to assess pupils and eyelids and to hold off on dilation before seeing the ophthalmologist.

When a patient presents with anisocoria, one must pay careful attention to the reactivity and the size of the pupils in light and dark. A Horner pupil will have a normal brisk reactivity. It will also be smaller than the fellow pupil and this disparity will be greater in the dark. Note that the disparity in the dark will be greatest in the first 5 seconds after turning off the light and there will be less anisocoria after about 15 seconds. This is known as dilation lag. Testing can include cocaine 4-10% or apraclonidine 0.5 – 1%. A drop is placed in BOTH eyes and then reassessed in 30-60 minutes. With cocaine, the Horner pupil will not dilate as well as the fellow eye. The eyelid will not change. With apraclonidine the Horner pupil will become equal or bigger than the fellow eye and the eyelid will normalize or become retracted.

When a patient presents with ptosis, one must pay careful attention to the pupil and motility. Motility should be normal. With Horner syndrome, the ptosis can be anywhere from 0.5 mm to 2.5 mm. The lower eyelid may also be elevated compared to the fellow eye, known as reverse ptosis. Most patients either do not sweat or do not notice anhidrosis.

When a patient presents with pain, then one should look for a Horner syndrome (ipsilateral smaller pupil and ptosis). The greatest concern is that this represents a carotid artery dissection, which becomes an emergency or urgency. Carotid artery dissections, when severe, can lead to stroke or vision loss.

The oculosympathetic anatomy begins in the hypothalamus, descends in the brainstem to the upper spinal cord C8-T1, then traverses over the apex of the lung and travels along the common carotid. After synapsing near the carotid bulb, the sweat fibers travel with the external carotid and the pupil/eyelid fibers travel with the internal carotid into the cavernous sinus and then to the eye. Therefore, MR imaging should encompass the area between the hypothalamus to T1. It should definitely include the neck with fat suppressed axial images. An MRA of the neck is also recommended, if there is pain.

If the MRI and MRA are normal and read out by a neuroradiologist who is familiar with the patient’s story, then this may be an idiopathic Horner syndrome or part of a headache syndrome (see below). It is critical that the neuroradiologist is given an accurate history. Generally speaking the ptosis and anisocoria are permanent. The ptosis can be repaired surgically. The anisocoria can be managed with apraclonidine or tetrahydrozoline (over the counter).

Trigeminal autonomic cephalgias (TAC) are a group of unilateral headache disorders with autonomic features including ipsilateral ptosis, miosis, epiphora, injection, and nasal stuffiness or rhinorrhea. They can last seconds, minutes, hours, or days. They present with “painful Horner syndrome” and require imaging to rule out carotid dissection among others. Depending on the frequency, duration, and quality
of the pain, there may be treatment options for these patients. Sending the patient to a headache specialist is reasonable.

C23.6

Toxic optic neuropathy

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The optic nerves are exposed to a wide range of chemicals in the environment, some of which may be harmful, but proving a causal link between exposure and the development of an optic neuropathy is often difficult. Various diagnostic criteria have been proposed, including (i) temporal association, (ii) dose dependency, (iii) improvement on removing the substance, (iv) deterioration on re-challenge, (v) plausible mechanism, (vi) class effect and (vii) exclusion of all other causes. In practice these criteria are rarely if ever fulfilled and in most cases toxic optic neuropathy is a presumptive diagnosis.

Patients typically present with painless subacute bilateral visual failure and are found to have central or caecocentral scotomata and dyschromatopsia. The optic discs are often normal but may be hyperaemic, swollen, pale or cupped, and the pupillary light reflex is usually symmetric with no RAPD. In some exceptional cases the problem may be unilateral (eg demyelinating optic neuritis in patients on anti-TNF alpha drugs) or present with signs suggestive of a chiasmopathy (eg ethambutol). The rest of the ocular examination is usually unremarkable, but patients may have other additional symptoms and signs of neurotoxicity – for example hearing impairment or peripheral neuropathy. The main clues to the toxic aetiology are a history of recent exposure to a new drug or chemical (usually started a few weeks or months before symptom onset) and exclusion of all other causes of optic neuropathy.

Toxic optic neuropathy is most commonly associated with prescribed medications. The largest group of offenders are antibiotics (eg anti-tuberculous drugs, antiretroviral agents, aminoglycosides, linezolid) which can damage the mitochondria in retinal ganglion cells. It is likely that this susceptibility arises because mitochondria have themselves evolved from intracellular bacteria (the endosymbiosis hypothesis). In some cases there is also an underlying genetic susceptibility (the ‘double hit’ – eg patients harbouring LHON mutations whose visual loss is then triggered by exposure to certain drugs). Other putative mechanisms of optic nerve damage include ischaemia (eg oncology drugs such as the taxanes, interferons, 5-FU; sildenafil; amiodarone), demyelination (eg the anti-TNF alpha drugs, SSRIs), raised ICP (eg tetracyclines) and raised IOP (eg steroids). In addition, where there are no likely candidates for toxicity among the list of prescribed medications, patients should be asked about exposure to solvents (eg recreational glue-sniffing), heavy metals (eg mercury in pescatarians, cobalt from metal hip prostheses) and, in hyperacute cases, methanol intoxication.

There remain a number of challenges to making a diagnosis of toxic optic neuropathy. These include the rarity of this condition (although it is almost certainly under-recognised), the lack of any confirmatory tests and the diagnostic uncertainty arising because these patients often have underlying medical conditions that could also account for the optic neuropathy (eg when the drug is prescribed in the context of infectious, inflammatory or neoplastic disease). When toxicity is suspected the usual
advice is to remove the chemical or drug, and in many cases this will lead to stabilisation or even improvement in visual function. However in some cases it may be dangerous to stop a drug (eg amiodarone, chemotherapy) and so it is usually wise to first liaise closely with the prescriber to assess the risk-benefit ratio. Given the ever increasing range of potential toxins, particularly the newer drugs and biologicals, it is important that we all remain alert to the possibility of neurotoxicity in any patient presenting with an unexplained optic neuropathy.