Acute Visual Loss and Other Neuro-Ophthalmologic Emergencies: Management

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KEYWORDS

• Vision loss • Double vision • Papilledema • Optic neuropathy

Neuro-ophthalmologic findings have exquisite localizing value to clinicians. They can guide emergency room providers in the management of acute visual complaints and alert them to other neurologic emergencies, such as hydrocephalus and transtentorial herniation. This article outlines the symptoms and signs of specific neuro-ophthalmic disorders and their association with neurologic emergencies.

SYMPTOMS AND SIGNS OF NEURO-OPHTHALMOLOGIC DISORDERS

Acute Visual Loss

The most important first step in evaluating acute visual loss is to establish whether the underlying cause is neurologic or optic. A readily available test in the emergency room is the pinhole examination (**Fig. 1**). Visual acuity should be tested for each eye separately. If the acuity improves with pinhole, then it is likely that the symptoms are optic. Common causes for this include uncorrected refractive error, lens or corneal opacity, and vitreous disease. If the acuity does not improve with pinhole, then the symptoms may be from neurologic visual loss either from optic nerve or retinal disease.

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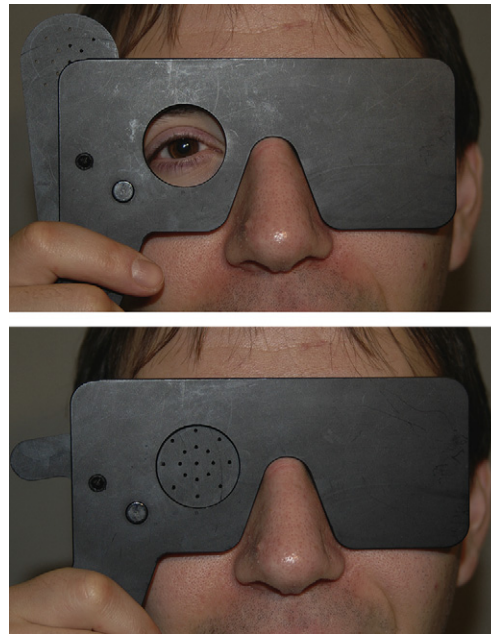

Fig. 1. Pinhole testing may help distinguish whether the visual loss is neurologic or optic. (*Top*) Occluder for testing vision one eye at a time. By convention the right eye is tested first. (*Bottom*) Occluder with pinholes. If the visual acuity is subnormal but can be improved with pinholes, refractive error or media opacities should be suspected. (*Adapted from* Liu GT, Volpe NJ, Galetta SL. Neuro-opthalmology: diagnosis and management. 2nd edition. Philadelphia: W. B. Saunders Company; 2010; Elsevier with permission.)

When there is suspicion for neurologic visual loss, localization may be provided by the swinging flashlight test, color vision evaluation, fundoscopic examination, and visual field testing. The swinging flash light test is used to determine the presence of a relative afferent pupillary defect (RAPD) and is performed by brisk and alternate stimulation of the eyes with a bright light source (**Fig. 2**). If there is pupillary dilatation in response to direct stimulation (the consensual response is greater than the direct response), then the patient has an RAPD. This finding is strongly suggestive of an optic neuropathy in the eye with the impaired direct response. Severe retinal disease may also produce an RAPD but it is less common and usually does produce the magnitude of the afferent pupillary defect (APD) that is associated with an optic neuropathy. Color vision loss further supports a diagnosis of optic nerve disease. This can be tested formally with a color plate book or by subjective comparison of colors, most commonly red, between the two eyes.

Funduscopic examination is helpful in identifying optic nerve and retinal disorders. Optic disc abnormalities can be seen in inflammatory, infiltrative, infectious, or ischemic disorders (discussed later). Although an MRI may demonstrate enhancement of the optic nerve in cases of acute idiopathic demyelinating optic neuritis, the fundoscopic examination is frequently unremarkable.[1] There is mild swelling in approximately one-third of patients. Conversely, the majority of patients with ischemic optic neuropathies have disc swelling and hemorrhages acutely. In ischemic optic neuropathy, the disc swelling may be segmental and this can be a clue to the mechanism of

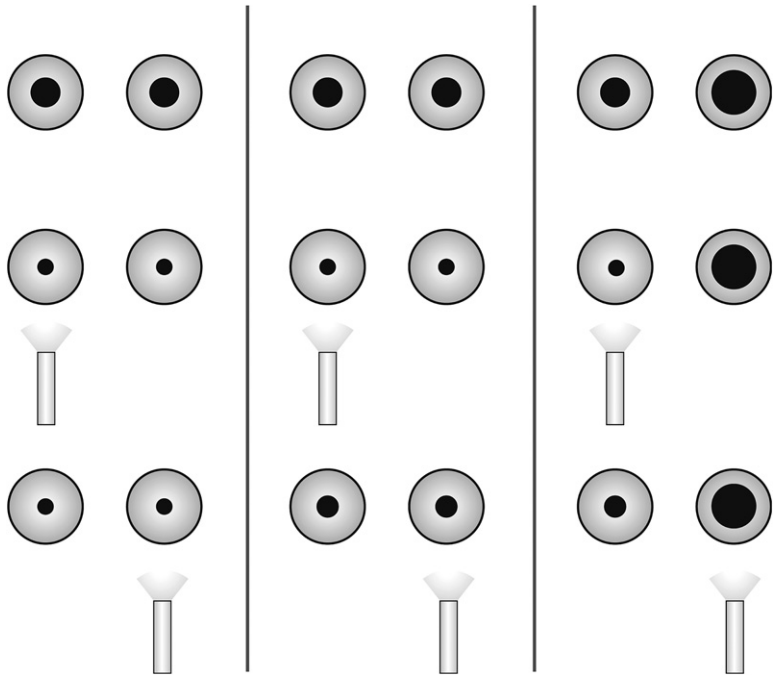

Fig. 2. Swinging flashlight test and the APD. (*Left panel*) Normal swinging flashlight test, in which light directed in either eye elicits the same amount of pupillary constriction. (*Middle panel*) Swinging flashlight test revealing a left RAPD in the hypothetical setting of visual loss in the left eye due to an optic neuropathy. Pupillary sizes are equal at rest in ambient lighting. Light stimulation of the good right eye results in brisk bilateral pupillary constriction. Light stimulation of the visually impaired left eye produces comparatively weaker pupillary constriction, and both pupils dilate. (*Right panel*) Left third nerve palsy and optic neuropathy. The left pupil is fixed and dilated. When the light is shone into the good right eye, the right pupil constricts normally. When the light is shone into the left eye, however, the right pupil dilates because of the left optic neuropathy. (*Adapted from* Liu GT, Volpe NJ, Galetta SL. Neuro-opthalmology: diagnosis and management. 2nd edition. Philadelphia: W.B. Saunders Company; 2010; Elsevier with permission.)

the visual loss. Infectious and infiltrative causes of optic neuropathy may also have significant optic disc elevation and edema. A chronic optic neuropathy may result in a pale appearance of the optic disc and the presence of shunt vessels on the disc may signify an underlying mass lesion compressing the optic nerve.

Visual field testing lends additional information to the localization of the visual loss (**Table 1**). Optic neuritis typically presents with central or centrocecal scotomas, although other patterns, such as generalized depression and altitudinal or arcuate defects, are seen.[1] Anterior ischemic optic neuropathy (AION) often presents with altitudinal defects. Abrupt onset of complete unilateral visual field loss is suggestive for a vascular process (central retinal artery or ophthalmic artery occlusion). Bitemporal field loss is characteristic of a compressive lesion in the region of the optic chiasm. Anterior chiasmal lesions may present with findings of an ipsilateral optic neuropathy and a temporal field deficit in the contralateral eye signifying injury to the junction of the optic nerve and the crossing fibers in the optic chiasm. Damage to the optic tract may manifest as an incongruous homonymous hemianopsia. Patients with an optic tract

Table 1
Causes of vision loss

Lesion	Cause	Findings
Optic	Refractive error, media opacities, vitreous abnormalities	No APD; usually unilateral; improvement with pinhole
Optic nerve	Inflammatory lesions (MS, sarcoid); ischemia (atherosclerotic, hypoperfusion, vasculitic); infiltrative/ infectious (neoplastic, cytomegalovirus, syphilis)	APD present; central, centrocecal, arcuate, or wedge field defect with apex at blind spot; disc swelling may be if papillitis is due to inflammatory, ischemic, or infiltrative lesion
Chiasm	Parasellar mass (pituitary adenoma, craniopharyngioma, meningioma, aneurysm); chiasmal neuritis	Bitemporal hemianopsia, may be asymmetric; junctional lesion may cause ipsilateral APD, central or centrocecal scotoma, and contralateral superior temporal defect
Optic tract	Neoplastic, inflammatory, ischemic, infectious	APD variable; incongruous hemianopsia; bow-tie disc atrophy if long standing
Lateral Geniculate	Infarction, arteriovenous malformation, neoplastic	Incongrous hemianopsia, optic atrophy late; horizontal sectoranopsia or quadruple quadrantanopia suggestive of infarction
Optic radiations (parietal)	Neoplastic, inflammatory, ischemic, infectious	No APD; inferior contralateral quadrantanopia; ipsilateral smooth pursuit abnormalities; spasticity of conjugate gaze
Optic radiations (temporal)	Neoplastic, inflammatory, ischemic, infectious	No APD; superior contralateral quadrantanopia, may be slightly incongruous
Occipital	Ischemic, neoplastic, infectious, inflammatory	No APD; congruous contralateral hemianopsia; macular sparing and Riddoch phenomena may be present

Data from Laskowitz D, Liu GT, Galetta SL. Acute visual loss and other disorders of the eyes. Neurol Clin 1998;16:323–53.

lesion frequently have an RAPD on the side with greater field loss. Moreover, optic atrophy associated with a homonymous field deficit indicates injury of the optic tract or the lateral geniculate body.

Homonymous quadrantanopsia is characteristic of lesions to the optic radiations. A superior quadrantanopsia results from damage to the temporal geniculocalcarine radiations (Meyer loop) and an inferior quadrantanopsia from injury to the parietal radiations. Often associated with parietal lesions are an ipsilateral disorder of smooth pursuit and spasticity of conjugate gaze. The latter refers to deviation of the eyes superiorly and away from the side of the lesion during eye closure as opposed to the normal Bell phenomenon (each eye typically deviates superiolaterally). Homonymous congruous lesions reflect occipital lobe disease. Common causes include ischemic, neoplastic, infectious, and inflammatory disorders. Due to a dual blood supply, the occipital poles are often spared in ischemic lesions and, therefore, macular (central) vision on the side of the hemianopsia may be preserved. Management of acute visual loss depends on the localization and cause of the disorder but most cases require neuroimaging and computerized visual field perimetry (**Fig. 3**).

Other causes of acute vision loss may need to be considered in the differential diagnosis of patients. Central serous retinopathy and other maculopathies may mimic optic neuropathy and present with edema of the macula and central vision loss. These patients typically do not have an APD unless the vision loss is severe and describe a distortion of images (metamorphopsia) not present in optic neuropathies. Retinal vascular insult or insufficiency causes acute vision loss. A central retinal artery occlusion is an emergency, although the efficacy of available treatments is debated ,with a recent prospective, randomized trial of thrombolytic therapy demonstrating poor efficacy and potential harm.[2,3] Patients present with sudden, typically unilateral vision loss with whitening of the retina, highlighting the cherry-red spot of the macula, which is devoid of overlying ganglion cells. Other associated findings may include optic nerve swelling or pallor, visible emboli, and boxcarring of vessels.[4] Visual outcome is often poor. A branch retinal artery occlusion is associated with less severe visual loss and whitening along a branch artery, most commonly a temporal branch. Etiologies for these vascular insufficiencies include various types of emboli, local thrombosis, underlying infectious or inflammatory disorder, vasospasm, or hypoperfusion. Venous vascular insufficiency may also occur. Central retinal venous occlusion classically presents with a dramatic "blood and thunder" appearance of the fundus with dilated tortuous retinal veins, extensive retinal edema, and intraretinal hemorrhages in all 4 quadrants. There may be optic nerve swelling. Complications of central retinal venous occlusion include macular edema and management may involve laser coagulation, intraocular steroid injection, and anti–vascular endothelial growth factor medications.[5]

Specific management of 2 common entities associated with acute vision loss is discussed.

Giant cell arteritis

Classically, giant cell arteritis (GCA) is strongly suggested when an older patient presents with headache, sudden visual loss, and jaw claudication. Unfortunately for diagnosticians, many patients present with occult signs of the disease, and vigilance must be maintained when considering this diagnosis. Patient demographics are an important factor in determining the level of clinical suspicion because the disease is rarely seen under age 60. GCA is more common in white patients and in women and may have both a genetic and environmental basis of pathogenesis.[6–8]

Depending on the extent of ophthalmic and retinal artery involvement, there may or may not be changes seen on the eye examination. The most common cause of

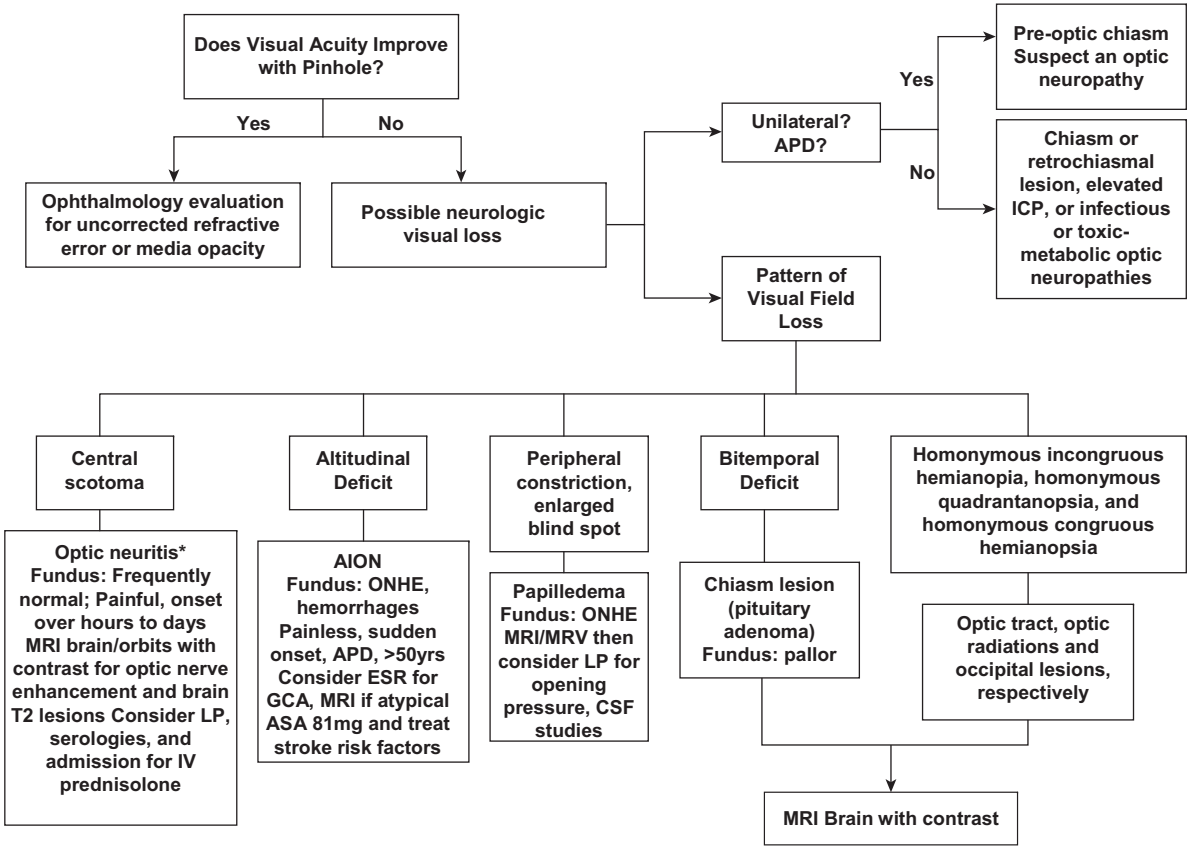

Fig. 3. Management of acute vision loss. he evaluation of acute vision loss that may present in the emergency room. Common causes are highlighted. ASA, aspirin; ICP, intracranial pressure; ONHE, optic nerve head edema. *Although central scotomas are the most common deficit seen in optic neuritis, other patterns may be seen as well.

GCA-related vision loss is arteritic AION. In this case, patients may have findings of decreased vision on examination consistent with an optic neuropathy, including an APD, and on fundus examination may have a chalky white optic disc with edema. Laboratory tests readily available in the emergency room that may aid in the diagnosis of GCA include an erythrocyte sedimentation rate (ESR) or C-reactive protein. Although nonspecific, elevation of either value may add to the clinical suspicion for GCA.[9–11] To make a definitive diagnosis, a biopsy is required.

The treatment of GCA is steroids and these should be initiated while awaiting an expeditious biopsy. Although the need for intravenous versus oral steroids remains controversial in the literature, the authors recommend for patients with visual symptoms that intravenous methylprednisolone (1 g total per day for 3 days) be given followed by prednisone (60 mg daily) until further follow-up.[11,12] **Box 1** summarizes the diagnostic features and acute management of GCA associated with visual complaints.

Acute demyelinating optic neuritis

Acute demyelinating optic neuritis is often associated with multiple sclerosis (MS) and presents with vision loss over hours to days (**Box 2**). Typically, retro-orbital pain worse with eye movements is present.[1] Patients may describe a central blur although any field loss may be observed. Patients usually complain of impaired color vision and images are described as dim or less bright. The most common demographic for this disorder is young women, but optic neuritis can be seen at any age, including children and older adults. If available, an MRI of the brain should be obtained to assess the risk of developing MS and an orbital MRI can be obtained to confirm the diagnosis. Orbital imaging should be strongly considered when the features of the event are atypical, including absence of pain, progressive visual loss, or failure to have some improvement in vision. Management in the emergency setting includes documentation of an eye examination with visualization of the fundus, initiation of intravenous steroids if appropriate, and ophthalmologic consultation or outpatient referral for computerized visual fields.

The Abnormal Optic Disc

Evaluation of neuro-ophthalmic complaints in the emergency room should always include a fundus examination. Direct visualization with an ophthalmoscope is the

Box 1
Evaluation and management of giant cell arteritis

Clinical Features

Sudden transient or persistent vision loss associated with headache or scalp tenderness in patients over age 50. Most prevalent in white women. History of jaw claudication and polymyalgia rheumatica strongly associated with GCA. May also more rarely present as an isolated third, fourth, or sixth nerve palsy or ocular muscle weakness.

Diagnostic Testing

ESR

C-reactive protein

Fluorescein angiography

Temporal artery biopsy

Treatment

Intravenous Solu-Medrol (1 g daily × 3 days) if visual symptoms present

Oral prednisone (60 mg daily) until follow-up

Box 2
Evaluation and management of acute demyelinating optic neuritis

Clinical Features

Onset over hours to days of vision loss

Retro-orbital pain worse with eye movements

Most common <50 years, women

Diagnostic Testing

MRI brain and orbits

Consider lumbar puncture, visual evoked potential

Computerized visual fields (outpatient)

Serologic studies if atypical

Treatment

Intravenous methylprednisolone (1 g daily × 3 days) if acute, followed by oral prednisone taper

Outpatient follow-up in 4 weeks; if no improvement, reconsider other diagnoses

Referal for consideration of disease-modifying therapy if high risk for MS[a]

[a] Patients with 2 or more lesions on their MRI of the brain have a high risk of conversion to clinically definite MS.

Data from Beck RW, Trobe JD, Moke PS, et al. High- and low-risk profiles for the development of multiple sclerosis within 10 years after optic neuritis: experience of the optic neuritis treatment trial. Arch Ophthalmol 2003;121:944–9.

most frequently used technique in this setting. A recently introduced supplementary tool is the nonmydriatic fundus camera, which allows a nonspecialist to have vivid views of the optic nerve and to provide a recording of the nerves' appearance for future follow-up with a neuro-ophthalmologist.[13] Disc swelling from elevated intracranial pressure, papilledema, indicates a medical emergency and requires immediate work-up and therapy. There are many other causes, however, of the abnormal-appearing optic disc (**Fig. 4**; **Table 2**).

Papilledema is a term often misapplied. This term should be used to describe swollen-appearing nerves associated with elevated intracranial pressure. A swollen appearance may also be caused by congenital anomalies, infection, inflammatory processes, and ischemia. In these cases (except congenital anomalies), *optic nerve head edema* is a better term to describe the swollen appearance. History is helpful in determining the likelihood for elevated intracranial pressure. The presence of headache, nausea, tinnitus, transient visual obscurations, double vision, or other neurologic deficits raises clinical suspicion. On examination, papilledema is typically bilateral. In the early stages, the swelling begins in the superior-inferior axis. The disc is hyperemic and there is obscuration of the retinal vessels as they leave the disc. The cup is preserved. As the papilledema progresses, exudates, cotton-wool spots, and hemorrhages often appear. Spontaneous venous pulsations are not typically present. Visual acuity and color vision are preserved until the late stage of papilledema. Mild swelling and decreased central vision should raise suspicion for a different cause of optic nerve head edema. The most common visual deficits associated with papilledema are an enlarged blind spot and peripheral field constriction.

Once suspected, papilledema requires immediate evaluation and neuroimaging. A mass lesion, severe cerebral edema, venous thrombosis, and hydrocephalus must

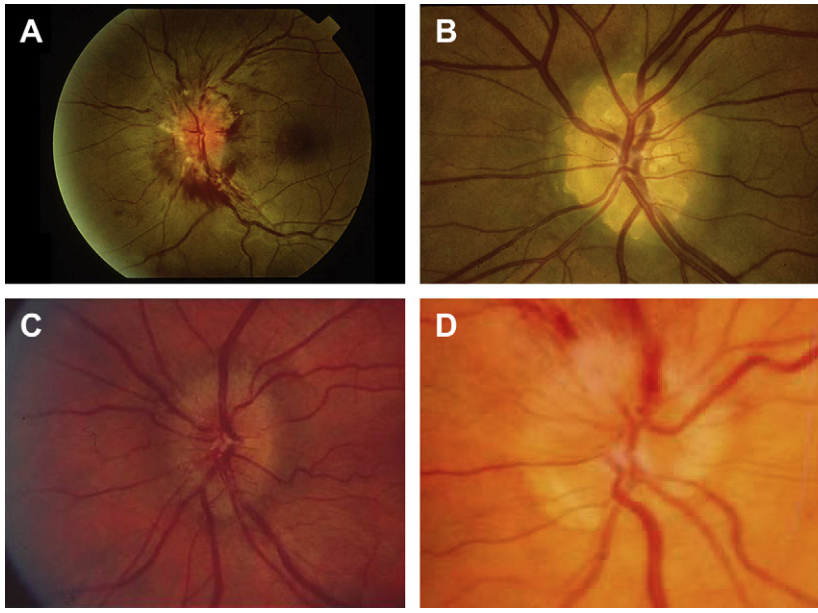

Fig. 4. Images of the abnormal optic disc. Fundus photos of the optic disc. (*A*) Acute papilledema with disc swelling, exudates, and hemorrhages. (*B*) Pseudopapilledema with optic nerve head drusen. (*C*) Acute optic neuritis with mild disc edema without hemorrhages. (*D*) Acute AION disc swelling with hemorrhages seen superiorly.

be ruled out. In the absence of lesions that might be associated with herniation, a lumbar puncture with opening pressure measurement should be performed. The diagnosis of pseudotumor cerebri (idiopathic intracranial hypertension) is suggested when neuroimaging studies and cerebrospinal fluid (CSF) examination are normal except for an elevated CSF opening pressure (**Box 3**). Pseudotumor cerebri is associated with obesity, anemia, and the prior use of glucocorticoids, vitamin A products, tetracycline derivatives, or synthetic growth hormones.[11,14–23] Often, patients report a recent weight gain. The disease is less common in thin men. Obstructive sleep apnea may be an important risk factor in men.[24] After diagnosis, baseline computerized visual fields should be performed. Treatment with acetazolamide may improve the papilledema, visual complaints, and headache.[25] If this medication is not successful, other diuretics and carbonic anhydrase inhibitors may be considered, such as furosemide and topiramate.[26] In obese patients, long-term therapy involves a weight loss program.[27,28] Progressive or severe vision loss, however, warrants more aggressive initial therapy. These patients may need to be hospitalized, administered glucocorticoids acutely, and evaluated for a surgical procedure, such as ventriculoperitoneal shunt or optic nerve fenestration.[29,30] The former is usually performed when the predominant complaint is headache.

A diagnosis frequently confused with papilledema, optic nerve drusen give the appearance of an elevated swollen nerve, though there is no acute edema. Termed *pseudopapilledema*, the appearance of this congenital abnormality is typified by glistening hyaline bodies, an absent cup, and anomalous but unobscured retinal vessels. These vessels seem to originate from the center of the disc and may have trifurcations. There are no cotton wool spots, exudates, or hemorrhages. The border of the disc may

Table 2
Differential diagnosis of the abnormal optic disc

Cause	History	Fundoscopic Appearance	Visual Examination	Ancillary Diagnostic Tests
Increased ICP (papilledema)	Morning headache, tranisent visual obscurations, double vision, tinnitus, nausea	Usually bilateral; disc hyperemia, cup preserved (early), cotton wool spots, exudates, obscuration of retinal vessels, absence of SVPs	No APD, central acuity spared, no color loss, enlarged blind spot, visual field constriction, and inferior nasal defect	MRI/MRV of head; lumbar puncture (document OP, rule out infection)
Drusen (pseudopapilledema)	Usually asymptomatic	Glistening hyaline bodies, absence of disc hyperemia, hemorrhage, or exudate; anomalous retinal vessels with central origination and trifurcations, irregular disc border, absent cup	Normal examination or irregular peripheral field constriction, enlarged blind spot; normal visual acuity	CT or orbital ultrasound may visualize calcified hyaline bodies
Optic neuritis	History of MS (or other inflammatory disorder); retro-orbital pain on eye movement, if demyelinating may worsen with heat (Uhthoff phenomenon)	Variable disc swelling, typically mild (retrobulbar involvement has normal disc appearance); unilateral in adults	APD; loss of central acuity and color discrimination; central or centrocecal scotoma	MRI for evidence of demyelination; CSF for pleocytosis and oligoclonal bands
Ischemia (AION)	Sudden painless loss of vision; >50 years of age; hypertension, diabetes, history of hypotensive episode	Usually unilateral; segmental disc edema; other eye may show absent cup	Variable field abnormality; often altitudinal; acuity variably affected; APD common	Work-up for hypertension, diabetes, vasculitis, GCA (glucose, BP, ESR, RPR)
Infection	History of known infection or compromised immune status, systemic symptoms, such as fever, meningismus, other focal neurologic deficits	May be bilateral or assymetric disc swelling with or without exudates, may also be associated with a macular star		Head CT or MRI, infectious work-up, including serologic and CSF studies (HIV, RPR, Lyme disease, cat scratch, and other as appropriate)
Infiltrative	History of neoplasm, sarcoid, or other infiltrative disease	Possible disc elevation and swelling; pallor	Variable field abnormality and acuity loss	MRI of the brain and orbits; CSF for pleocytosis and cytology

Abbreviations: BP, blood pressure; ICP, intracranial pressure; OP, opening pressure; RPR, rapid plasma reagin; SVPs, spontaneous venous pulsations.
Data from Laskowitz D, Liu GT, Galetta SL. Acute visual loss and other disorders of the eyes. Neurol Clin 1998;16:323–53.

Box 3
Evaluation and management of pseudotumor cerebri

Clinical Features

Headache, transient visual obscurations, double vision (if abducens affected), nausea, tinnitus. History of recent weight gain or obesity common. Typically bilateral papilledema. Central acuity preserved until late stages.

Diagnostic Testing

MRI and magnetic resonance venography (MRV) of the brain

Lumbar puncture with opening pressure recorded

Computerized perimetry

Treatment

Mild vision loss

Acetazolamide (furosemide, Topamax)

Weight loss

Severe or progressive vision loss

Prednisolone or prednisone

Ventriculoperitoneal shunt or optic nerve fenestration

be irregular due to the hyaline deposits. These patients rarely complain of visual symptoms. Pseudopapilledema is often observed in patients evaluated for other ocular or neurologic complaints. Computerized visual fields may reveal subtle deficits from the drusen, but significant visual loss is not seen. An orbital ultrasound can demonstrate the presence of the calcified drusen and establish the absence of true edema.[31] The drusen may also be seen on CT scan with cuts through the orbit.

There are several disease processes that can result in optic nerve head edema without elevated intracranial pressure. One-third of patients with acute demyelinating optic neuritis (discussed previously) demonstrate mild swelling (**Box 2**).[1] Hemorrhages in these patients are rare. They present with visual loss associated with retro-orbital pain with eye movements. In contrast, the majority of patients with AION present with acute optic nerve head edema, exudates, and hemorrhages. These patients tend to be over age 50, have painless sudden vision loss, and are less likely to recover their vision compared with those with optic neuritis.[32,33] Eyes at risk for AION are those with a small cup-to-disc ratio.[34] Often this finding is seen in the unaffected eye of patients suspected to have unilateral acute vision loss from AION. Due to the superior and inferior divisions of the retinal vasculature, the optic nerve swelling may be sectoral with corresponding altitudinal defects on visual field examination. Currently there are no approved therapies for AION. The use of steroids is controversial.[3] There is an approximately 15% risk of developing AION in the fellow eye.[35] Aggressive treatment of predisposing risk factors, diabetes, hypertension, and underlying collagen vascular disorders should be administered but it is unclear whether any measure affects the natural history of AION. Most patients with AION are given aspirin (81 mg daily) as a preventative agent. There is no long-term evidence that aspirin is effective in preventing fellow eye involvement. Owing to concern for nocturnal hypotension contributing to the ischemia, blood pressure medication dosing may need to be shifted to earlier times in the day.[36] GCA should be considered in all cases of AION (discussed

previously), in particular those older patients with scalp tenderness, headache, and jaw claudication (**Box 1**).

Infections or infiltrative processes may also cause optic disc swelling. Patients may or may not have prior history of systemic symptoms, or other neurologic findings. When presenting with only visual complaints, a thorough evaluation with neuroimaging, serologies, and CSF may be required. Possible infections include HIV, syphilis, or Lyme disease. Common infiltrative processes include sarcoid, lymphoma, and other cancers. Inflammatory disorders other than MS can be associated with optic neuritis, including neuromyelitis optica and systemic lupus erythematosis.

Optic neuritis, ischemic optic neuropathy, toxic metabolic disorders, and compressive and hereditary optic neuropathies may all cause optic nerve pallor or atrophy. Although less likely to present in an emergency room, compressive optic neuropathies should be considered if a patient's visual complaints are longstanding or progressive. A complete review of optic neuropathies and causes of optic nerve atrophy is beyond the scope of this article.

Double Vision

Double vision is a common complaint in neuro-ophthalmologic emergencies and there are many potential causes. It first should be established whether the double vision is monocular or binocular. This is most readily evaluated by asking a patient if the double vision resolves when he or she covers one eye. If it does not improve, then the origin of the visual defect is not in the binocular misalignment of the two eyes. Monocular double vision is rarely associated with neurologic disease. It is often secondary to refractive error or media opacity and in these settings improves when a pinhole is placed over the affected eye. If the double vision is binocular and improves with one eye covered, then it should be asked whether the images are deviated horizontally or vertically and in what direction of gaze the divergence is greatest. These details help to localize the nerve or muscle affected. History of timing of onset, association with pain or headache, and fluctuation of symptoms may also be critical in establishing the correct diagnosis. For example, painless diplopia worsened by fatigue raises the clinical suspicion for myasthenia gravis. Most cases of ocular misalignment are due to cranial nerve palsy, restriction of one or more of the extraocular muscles, or brainstem disease causing internuclear ophthalmoplegia or skew deviation. Forced duction testing, involving the direct pushing of an anesthetized eye with a cotton-tipped applicator, can help distinguish nerve palsy versus muscle restriction. Inability to move the eye manually indicates a restrictive process, such as thyroid eye disease or muscle entrapment. The presence of other brainstem neurologic findings supports the diagnosis of a supranuclear cause of diplopia.

The third cranial nerve innervates the superior, medial, and inferior recti and inferior oblique as well as the levator and pupil. A complete third nerve palsy presents with ptosis, pupillary dilation, and an eye positioned out and down. Many third nerve lesions, however, present with partial findings, with or without pupillary involvement. The third nerve may be damaged anywhere along its course from the nucleus through the cavernous sinus and superior orbital fissure. There are many causes of third nerve palsies (**Table 3**). Of most concern in the emergency room is the presence of an aneurysm compressing the nerve. Another common cause of third nerve dysfunction is microvascular ischemia. Care must be taken to complete a thorough evaluation of patients to determine if urgent imaging must be obtained to avoid a life-threatening complication.

Emergency room history and examination for a new-onset third nerve palsy aids in the localization and the differential diagnosis of the lesion. Special attention should be

Table 3
Differential diagnosis of third nerve palsy

Differential Diagnosis	History	Signs	Diagnostic Tests
Aeurysmal compression	Retro-orbital pain, headache, stiff neck	Pupillary involvement common; aberrant regeneration may be present	MRI and MRA of the head or CTA; if negative consider conventional angiogram
Uncal herniation	Trauma, intracranial hemorrhage, neoplasm	Altered mentation, pupillary involvement, ipsilateral hemiparesis	Neuroimaging (MRI, CT)
Vasculopathic	Over age 50; diabetes, hypertension, headache, retroorbital pain may be indistinguishable from aneurysm	No aberrant regeneration, pupil usually spared	ESR, RPR, BP glucose
Chronic meningitis	Immunocompromised, constitutional symptoms, meningismus	Other cranial nerves may be involved	Neuroimaging (CT or MRI), then lumbar puncture; MRI may show nerve or meningeal enhancement
Cavernous sinus neoplasm	Retro-orbital pain	Pupil may be spared; CSS	MRI
Cavernous-carotid fistula	Vasculopathy, trauma	Mastoid or orbital bruit, CSS, chemosis, exophthalmos	MRI, MRA
Cavernous aneurysm	Vasculopathy, trauma	Pupil may be spared; CSS	MRI, MRA
Cavernous sinus inflammation (Tolosa-Hunt syndrome)	Retro-orbital pain; may be associated with collagen-vascular disease	Pupil may be spared; CSS	MRI may document cavernous sinus enhancement
Pituitary apoplexy	Severe headache, meningismus, visual loss	CSS, ophthalmoparesis (may be bilateral), visual field loss	MRI (CT may miss apoplexy), lumbar puncture may document RBC, WBC
GBS (Miller Fisher variant)	Preceding viral illness; painless	Areflexia, ataxia, extremity numbness or weakness	Lumbar puncture may demonstrate cytoalbuminologic dissociation; electrodiagnostic studies; MRI to exclude other etiologies
Myasthenia gravis	Painless, fluctuates with fatigue; dysarthria or dysphagia	Pupil spared, ptosis, orbicularis weakness, fatigue with 1 min of upgaze, curtaining	Serum Ach-R antibody level, electrodiagnostic studies
Midbrain lesion (infarct, tumor, demyelination)	Hypertension, DM, cardiogenic emboli, MS	Contralareral hemiparesis, rubral tremor	MRI
Wernicke encephalopathy	Alcohol abuse, or other nutritional deficiency	Nystagmus, abduction deficit, ataxia, confusion	Improvement with thiamine (give before glucose)

Abbreviations: Ach-R, acetylcholine receptor; BP, blood pressure; CSS, cavernous sinus syndrome; DM, diabetes mellitus; RBC, red blood cell count; RPR, rapid plasma reagin; WBC, white blood cell count.

Data from Laskowitz D, Liu GT, Galetta SL. Acute visual loss and other disorders of the eyes. Neurol Clin 1998;16:323–53.

given to any additional neurologic deficits, status of the pupil, and presence or absence of aberrant regeneration. In third nerve nuclear lesions, for example, brainstem infarctions or masses, the contralateral superior rectus muscle is weak (innervation of the superior rectus is crossed) and there is bilateral ptosis (levator complex is midline). The third nerve fascicle travels ventrally and depending on its rostral-caudal position, lesions to the fascicle may also be associated with contralateral ataxia (Claude syndrome), contralateral rubral tremor (Benedikt syndrome), or contralateral hemiparesis (Weber syndrome). The nerve is susceptible to diseases of the subarachnoid space and in cases of CSF inflammation, infection, or malignancy, there may be other signs of neurologic imvolvement, such as other cranial nerve palsies or weakness. As the nerve passes freely in the subarachnoid space, it is subject to compression against the free tentorial edge, as in the case of impending uncal herniation. Context is important in evaluating the likelihood of herniation as a cause of third nerve dysfunction. An awake alert patient sitting upright in the emergency room is likely to have another cause for the palsy, whereas an intensive care unit patient who is obtunded or has a history of trauma or mass lesion is at much higher risk. Additional dysfunction of the fourth, sixth, or the first or second divisions of the fifth cranial nerve indicates the site of the lesion may be in the cavernous sinus (discussed later). Loss of vision or signs on examination of optic pallor or visual field deficits suggests involvement at the orbital apex or a rapidly expanding sellar lesion as may occur in pituitary apoplexy. The latter may also present as a cavernous sinus syndrome.

The presence or absence of pupillary dilation may help distinguish between aneurysmal compression and microvascular ischemia as causes of third nerve palsies. Aneurysms in the subarachnoid space compress the superficial parasympathetic fibers traveling along the third nerve and lead to early pupillary involvement. In contrast, ischemic palsies involve the pupillary fibers in approximately a third of patients.[37] These patients tend to have the risk factors of age over 50, diabetes, and hypertension. Patients with partial third nerve palsies, however, may initially present with pupil sparing but then develop pupil involvement as the lesion (ie, aneurysm) enlarges. Careful and expedient follow-up is required for these patients and they should undergo neuroimaging. The authors prefer CT angiography (CTA) imaging in evaluating patients with isolated third nerve palsies, but magnetic resonance angiography (MRA) imaging also has good sensitivity in detecting aneurysms.[38,39] Although the sensitivity of MRA and CTA for detecting aneurysms is in the 90% to 98% range (depending on the size of the aneurysm), these results are dependent on the skills of the neuroradiologist and the quality of the imaging.[39–41] Thus, if there is any doubt about the presence of an aneurysm, the authors suggest conventional angiography. A complete third nerve palsy without pupillary involvement is unlikely to be from a compressive aneurysm, but in the authors' experience it is prudent to consider imaging in any patient with an isolated ocular motor nerve palsy. Vascular palsies on average improve or resolve within 3 months.[42] In the absence of improvement, neuroimaging is required.

Aberrant regeneration refers to the chronic denervation and reinervation with misdirection of third nerve fibers. On adduction or depression of the eye there is often eyelid retraction. Alternatively, retraction of the globe may occur on attempted vertical gaze or pupillary constriction with adduction. Aberrant regeneration is a sign of a chronic compressive lesion, such as a slow growing aneurysm or tumor. It almost never occurs in ischemic lesions.

The fourth cranial nerve innervates the superior oblique muscle, responsible for intortion and depression of the eye in adduction. A patient with injury to this nerve has vertical double vision worse in contralateral gaze and ipsilateral head tilt

(**Box 4**). The most common reason for acute acquired fourth nerve palsy is trauma. Microvascular disease and inflammatory disease of the subarachnoid space may also cause fourth nerve injury. Neoplasm rarely affects the fourth nerve in isolation. Decompensation of a congenital fourth nerve palsy is typically insidious in onset and more frequently presents in the clinic than the emergency room. The 3-step test for diagnosing a fourth nerve palsy is as follows: identify the hypertropic (higher) eye, establish whether the hypertropia increases in right or left gaze, and similarly tilt the head to the right and left to determine if there is worsening of double vision and alignment (Bielschowsky test). A typical fourth nerve palsy worsens with contralateral gaze and ipsilateral head tilt but improves with contralateral head tilt. Patients may not be aware that are holding their head in a contralateral tilt as compensation for the nerve palsy.

The sixth cranial nerve innervates the lateral rectus. Palsies of the sixth nerve present with horizontal double vision that worsens when gazing in the ipsilateral direction. On examination, evaluation of a patient's eye movements reveals a deficit in abduction, unless the palsy is subtle, in which case measurements of eye alignment are required to localize the injury. Using alternate cover or Maddox rod testing, an esophoria, greater in the ipsilateral direction, defines an abduction deficit. Care must be taken, however, to differentiate between a sixth nerve palsy and a restrictive process, such as thyroid disease involvement of the medial rectus. The sixth nerves are vulnerable to compression in cases of increased intracranial pressure as they ascend and then bend along the clivus to enter the Dorello canal. Trauma, microvascular disease, and neoplasm may cause sixth nerve palsies (**Table 4**). The sixth nerve's prolonged course through the subarachnoid space makes it susceptible to traumatic injury. Ischemic injury is also common. Timely imaging is warranted, however, even in patients with isolated sixth nerve palsies and vascular risk factors, because brain lesions may present in this setting. As in suspected cases of vascular

Box 4
Fourth nerve palsy

Action of Fourth Nerve

Incyclotorsion

Depresses the eye in adducton

Clinical Presentation

Vertical diplopia

Posttrauma

Microvascular risk factors

Positional head tilt

Three-Step Test

Identify which eye is hypertropic

Determine if hypertropia is worse in right versus left gaze

Bielschowsky head tilt test—tilt head to right and left

Diagnosis

Hypertropia worse in contralateral gaze and ipsilateral head tilt; improved alignment and vision in contralateral head tilt

Table 4
Differential diagnosis of abduction deficits

Differential Diagnosis	History	Additional Signs	Diagnostic Tests
Brainstem disease (infarction, tumor, demyelination)	Vertigo, dysarthria, perioral numbness	Ipsilateral gaze paresis, INO, facial paresis, contralateral hemiparesis	MRI brain
Meningitis (carcinomatous, TB, fungal, sarcoid, Lyme disease, syphilis)	Systemic/constitutional symptoms, headache meningismus; history of TB, syphilis, or malignancy	Other cranial nerves involved	MRI brain may show leptomeningeal and nerve enhancement; lumbar puncture, including cytology and microbiology studies
Increased intracranial pressure	Headache, nausea, ataxia	Papilledema, enlarged blind spots; often bilateral	CT head, lumbar puncture
Trauma	History of trauma	Vision loss, other ocular motility abnormalities with orbital trauma, Battle sign, CSF otorrhea, hemotympanum, VII or VIII deficits with a fracture of middle cranial fossa (petrous apex)	CT head and orbits, consider angiogram if chemosis, exophthalmos to rule out a carotid-cavernous fistula
Microvascular	Over age 50, diabetes, hypertension, ± headache	Unilateral isolated	RPR, ESR (GCA can cause an isolated cranial nerve palsy), BP, glucose
Neoplasm	Progressive diplopia, facial weakness or numbness, hearing loss	Isolated abduction deficit or multiple cranial neuropathies, papilledema, ataxia	MRI brain
Thyroid eye disease	Progessive, may be worse in mornings, symptoms of hyperthyroidism	Proptosis, eyelid retraction and lag, restriction on forced duction	CT or MRI orbits to rule out entrapment or mass, orbital ultrasound, thyroid function tests
Cavernous sinus inflammation (Tolosa-Hunt syndrome)	Retro-orbital pain; may be associated with collagen-vascular disease	Cavernous sinus syndrome	MRI may document cavernous sinus enhancement
Convergence spasm	Report bilateral eye crossing	Symptoms improve when distracted, fluctuating esotropia, miosis	Oculocephalics
Myasthenia gravis	Fluctuates with fatigue; dysarthria or dysphagia	Ptosis, orbicularis weakness, fatigue with 1-min upgaze, curtaining	Serum Ach-R antibody level, Tensilon test, electrodiagnostic studies
Wernicke encephalopathy	Alcohol abuse or other nutritional deficiency	Nystagmus, bilateral abduction deficit, ataxia, confusion	Improvement with thiamine (give before glucose)

Abbreviations: Ach-R, acetylcholine receptor; BP, blood pressure; INO, internuclear ophthalmoplegia; RPR, rapid plasma reagin; TB, tuberculosis.

third nerve palsies, if there is no improvement in three months, neuroimaging is required.

Neoplasms of the skull base, such as meningiomas, nasopharyngeal carcinomas, chondromas, or cordomas, may compress the sixth nerve at the clivus, resulting in insidious onset of double vision and progressive esophoria and abduction deficit. Because it is the only cranial nerve not fixed to the wall of the cavernous sinus, it may be the first to be compressed by a cavernous sinus neoplasm or cavernous carotid aneurysm.

The presence of other findings on the examination aids to localize and differentiate the causes of sixth nerve palsies. An abduction deficit, ipsilateral facial weakness, and contralateral hemiparesis localizes to the ventral pons (Millard-Gubler syndrome).[43,44] A sixth nerve palsy associated with headache, nausea, fever, meningismus, and other cranial nerve involvement is concerning for basilar meningitis from tuberculosis, sarcoid, or fungal infections. Bilateral sixth nerve palsies must be imaged urgently to rule out states of elevated intracranial pressure or neoplasm. Other causes of bilateral sixth abduction deficits include ocular myasthenia, Miller Fisher variant of Guillain-Barré syndrome (GBS), and restrictive disease, such as thyroid eye disease or entrapment of the medial rectus.

Bilateral ophthalmoplegia involving any of the ocular motor nerves may indicate a condition requiring immediate work-up and treatment in the emergency room (**Box 5**). If there is a history of alcohol use, bariatic surgery, or other nutritional deficiency, Wernicke disease should be considered and thiamine given before any glucose solutions. A thiamine level before administration and response to the vitamin confirm the diagnosis. Typically, these patients also present with altered mental status, nystagmus, and ataxia. A brainstem stroke with bilateral ocular motor involvement is acute in onset and commonly associated with other localizing symptoms, such as loss of consciousness, other cranial nerve involvement, weakness, or ataxia. Pituitary apoplexy may result in blood or infarcted tissue expanding into unilateral or

Box 5
Causes of bilateral ophthalmoparesis

Wernicke encephalopathy

History of alcohol abuse or nutritional deficiency, confusion, ataxia; treat with thiamine

Brainstem stroke

Stroke risk factors, other brainstem symptoms; emergent MRI brain

Pituitary apoplexy

Severe headache, meningismus; cranial nerve III, IV, V1 or V2 involvement; emergent MRI

Botulism

Anorexia, vomiting, dilated unreactive pupils, bradycardia; electrodiagnostic studies and serum bioassay

Myasthenia gravis

Painless, fluctuates with fatigue, ptosis, orbicularis weakness, dysarthria, pupil spared; evaluate respiratory status, anti-acetylcholinereceptor antibody, electrodiagnostic tests, Tensilon test

GBS (Miller Fisher variant)

Preceding gastrointestinal or upper respiratory illness, areflexia, ataxia, extremity numbness or weakness; lumbar puncture, electromyogram/nerve conduction studies

bilateral cavernous sinuses. Botulism presents with bilateral duction deficits and must be managed urgently in the emergency room. Other neuromuscular diseases, myasthenia gravis, or less commonly Miller Fisher variant of GBS may also present acutely. In addition to neurologic evaluation, respiratory function must be evaluated in these conditions. Thyroid eye disease may produce bilateral ophthalmoplegia but the onset is typically more insidious.

Lastly, a skew deviation causes vertical misalignment of the eyes and double vision. Most commonly it occurs from acute brainstem dysfunction but can result from peripheral vestibular or cerebellar lesions. Other signs of brainstem injury help distinguish a skew deviation from a third or fourth nerve palsy. The examination also suggests a likely skew deviation when the eye movements and alignment do not support either of these cranial nerve palsies and there is no evidence for myasthenia gravis or thyroid disease.

The combination of a skew deviation with ocular torsion and a head tilt is referred to as the ocular tilt reaction. This triad of signs is typically observed with lesions of the lateral pontomedullary junction or the paramedian thalamic-mesencephalic region and results from dysfunction of the utricular pathways that begin in the labyrinths and terminate in the rostral brainstem.[45] The utricular pathway mediating vertical gaze synapses at the vestibular nuclei and crosses to ascend in the medial longitudinal fasciculus. In the rostral brainstem, it connects to the nuclei that activate the 4 vertically acting muscles: the superior rectus, superior oblique, inferior rectus, and inferior oblique. Although the exact pathways that mediate a skew deviation and ocular tilt reaction are unknown, clinical observation has demonstrated the localizing value of a skew deviation (**Table 5**).[46] Helpful in relating the site of the lesion and the neuro-ophthalmologic findings is remembering that the superior rectus subnucleus and trochlear nucleus control contralateral superior rectus and superior oblique muscles, respectively. This means that a lesion of the right utricular nerve or caudal brainstem causes left hypertropia from impaired left inferior rectus and right superior rectus function. In contrast, a rostral lesion after the crossing in the medial longitudinal fasciculus results in ipsilateral hypertropia.

The most common causes of a skew deviation are brainstem stroke and neoplasm, emphasizing the need for expedient imaging in these patients.

NEURO-OPHTHALMOLOGIC SIGNS OF NEUROLOGIC EMERGENCIES

Increased Intracranial Pressure

Neuro-ophthalmic findings alert an emergency room provider to increased intracranial pressure, even before ventricular changes are seen on neuroimaging (**Box 6**).[47,48]

Table 5
Localizing value of skew deviation

Lesion Location	Type of Skew	Associated Signs
Lateral pontomedullary	Contralateral hypertropia	Ipsilateral excyclotorsion; ipsilateral facial numbness; ipsilateral Horner; lateropulsion
Midline cervicomedullary junction	Bilateral inferior rectus	Downbeat nystagmus
Medial longitudinal fasciculus	Ipsilateral hypertropia	Internuclear ophthalmoplegia
Rostral midbrain	Ipsilateral hypertropia	Vertical gaze palsy; conjugate cyclotorsion, eyelid retraction

Box 6
Neuro-ophthalmic signs of increased intracranial pressure

Dorsal midbrain syndrome

Impaired upgaze, pupillary light-near dissociation, eyelid retraction, convergence retraction nystagmus

Ocular motility deficit

Bilateral abduction deficit or divergence insufficiency; rarely fourth nerve palsy

Papilledema

Bilateral, may be assymetric, optic nerve head edema; enlarged blind spot; peripheral constriction; late stage with central vision loss

Early hydrocephalus may present with a dorsal midbrain syndrome (Parinaud syndrome) or ocular motility abnormalities. In Parinaud syndrome, the dorsal midbrain is compressed by ventricular dilatation. It must be differentiated from other causes of midbrain compression, such as a tumor. Bilateral upgaze is impaired. A patient's eyes may drift downward after an initial attempt to look up or there may be complete paresis of upgaze. Commonly, light-near dissociation is observed, with poor pupillary response to light but an intact response to near. Other features of the dorsal midbrain syndrome are eyelid retraction and convergence retraction nystagmus (saccades). The eyelid retraction (Collier sign) may be subtle or prominent, and the nystagmus refers to the periodic retraction of the eyes back into the orbit with attempted upgaze. The latter can be elicited with a downward moving optokinetic strip or drum, driving the patient to attempt upward saccades.

In addition to the dorsal midbrain syndrome, bilateral abduction deficits may be seen in early hydrocephalus due to brainstem compression and stretching of the sixth cranial nerves. Patients complain of horizontal double vision and in early stages only at distance. Mild esotropias are well tolerated at near. Thus, early hydrocephalus can mimic divergence insufficiency and care must be taken to look for other signs and symptoms of elevated intracranial pressure. Fourth nerve dysfunction has been reported in hydrocephlus but is rare.[49,50] Third nerve palsy in this setting is uncommon and should raise suspicion for a cause other than hydrocephalus.

As discussed previously, papilledema is optic nerve head swelling in the setting of raised intracranial pressure. It is the most common cause of visual loss in hydrocephalus and spares central vision until the late stages. The first deficit is typically an enlarged blind spot, followed by peripheral visual field constriction. Patients often describe vague blurry vision, transient visual obscurations, or peripheral vision loss. Depending on the cause of the increased intracranial pressure, shunting or shunt repair may be necessary urgently to preserve vision.

Herniation Syndromes

A feared emergency in the ICU setting, brain herniation is catastrophic and, depending on the structures compressed, associated with specific neuro-ophthalmic signs. The most familiar to clinicians, uncal herniation results in compression against the free tentorial edge of the parasympathetic fibers traveling on the third nerve. In early stages there may be ipsilateral pupillary dilation with sluggish response to light and in later stages with further compression of the third nerve and midbrain and a complete third nerve palsy as well as ipsilateral or contralateral hemiparesis. Ultimately, the vestibular

ocular response disappears with worsening brainstem ischemia and the contralateral pupil also dilates.

Subfalcian herniation may compress the ipsilateral anterior cerebral artery causing frontal lobe ischemia with isilateral gaze deviation and leg weakness. Central transtentorial herniation compresses the diencephalon with resultant progressive lethargy. Initially the pupils are small and reactive. Roving eye movements and oculocephalic reflexes indicate the midbrain is intact. With continued compression, the pupils dilate to midposition and become fixed, the third nerve pressed against the clivus or petroclinoid ligament. With midbrain ischemia, the pupils may become irregular and the oculocephalic reflexes difficult to elicit. Patients may develop midbrain hyperventilation and decerebrate rigidity. Autonomic dysfunction and death occur when the compression reaches the caudal brainstem.

Occipital infarction and cortical vision loss occur in transtentorial herniation when the posterior cerebral artery is compressed against the free edge of the tentorium. Either right or left artery may be involved and the infarction may be unilateral or bilateral in this setting. Given the depressed mental status in this setting, the vision loss likely is undetected acutely.

Vascular Lesions

Carotid dissection

Patients with a carotid dissection typically have a history of trauma affecting the cervical region or a history of connective tissue disease making them susceptible to vessel wall tears. They present with unilateral neck pain and headache and half present with a Horner syndrome from damage to the sympathetic fibers traveling in the pericarotid plexus.[51] Horner syndrome consists of miosis, ptosis, and, depending on the location of the injury to the sympathetc fibers, ipsilateral anhidrosis. The ptosis of Horner syndrome tends to be mild. Patients may also describe tinnitus or a rushing sound in the ipsilateral ear. Of concern in a carotid dissection is embolization of clot to distal arteries and resultant ischemic stroke, amaurosis fugax, or central retinal or ophthalmic artery occlusion. Ischemic optic neuropathy and orbital ischemia are also reported.[52,53]

Cavernous sinus syndrome

The cavernous sinus is a collection of venous channels posterior to the orbit and lateral to the pituitary fossa. It is encapsulated by dura and not contiguous with the subarachnoid space. Through the right and left cavernous sinuses traverse the carotid siphons, oculosympathetic fibers, and cranial nerves III, IV, VI, V1, and V2. All of the cranial nerves except the sixth are fixed along the lateral wall of the sinus. Depending on the location of the lesion, any of these structures may be involved in a cavernous sinus syndrome. A complete syndrome would consist of ophthalmoplegia, ptosis, mydriasis, hypesthesia of V1 and V2, and orbital pain. Partial syndromes that can be seen include an isolated third or sixth nerve palsy or a combination of a sixth nerve palsy and Horner syndrome.

Mass lesions in the cavernous sinus may cause the insidious onset of diplopia and facial numbness. Meningiomas are the most common neoplasms arising from the cavernous sinus.[54,55] Metastases and contiguous head and neck cancers, such as nasopharyngeal carcinoma, also cause cavernous sinus syndromes. A slow-growing cavernous carorid aneurysm may present with compressive symptoms. These aneurysms are not typically life threatening because hemorrhages are contained within the sinus and dura. They are not causes of subarachnoid bleeding but are treated for their neuro-ophthalmic symptoms.

Acute causes of a cavernous sinus syndrome that require immediate recognition and treatment include a cavernous sinus thrombosis and high-flow carotid cavernous fistula. Septic cavernous sinus thrombosis typically involves extension of a facial or sinus infection into the cavernous sinus and if untreated may lead to meningitis and infarction. The most common organisms involved are staphylococcus and streptococcus and the mainstay of treatment is antibiotics.[56,57] Fungal infections are more rare but, when present, often require surgery in addition to amphotericin. The use of anticoagulants is controversial.[56,58] A carotid cavernous fistula may present with a triad of a painful red eye with chemosis, pulsatile exophthalmus, and an ocular bruit.[59] An examiner may note arteriolization of the episclerotic vessels. Double vision and motility deficits are not uncommon and vision loss may occur from elevated intraocular pressure, optic neuropathy, or retinopathy.[60]

An idiopathic granulomatous inflammatory reaction (Tolosa-Hunt syndrome) and pituitary apoplexy may also cause a cavernous sinus syndrome. The former is a diagnosis of exclusion and is treated acutely with corticosteroids. Orbital inflammation may be evident on MRI. Pituitary apoplexy is discussed below.

Pituitary Apoplexy

Pituitary apoplexy refers to the hemorrhagic infarction of the pituitary gland. It can be life threatening and must be recognized in the emergency room. Often it occurs in the setting of a previously undetected pituitary lesion. Patients present with headache and commonly neuro-ophthalmic signs. If there is an underlying large lesion or extension of the hemorrhage superiorly, bitemporal visual field loss or a junctional scotoma may be present from compression of the crossing nasal fibers in the chiasm and junction of the optic nerve and chiasm, respectively. Lateral extension may involve the cavernous sinus and cause a third nerve (located superiorly in the sinus) palsy or other variation of a cavernous sinus syndrome. These patients may have meningismus from subarachnoid blood and chemical meningitis. Red blood cells and polymorphonuclear cells may be present in the spinal fluid. Care must be taken to differentiate pituitary apoplexy from subarachnoid hemorrhage because CT scans of the head and vasculature may be unremarkable. Similarly, this dangerous condition may also be mistaken for viral or bacterial meningitis. Clinicians must have suspicion for this diagnosis, with the neuro-ophthalmic examination often providing important clues, and if the head CT is negative, pursue an MRI of the brain in the emergency setting. Treatment involves immediate supplementation with hydrocortisone to avoid life-threatening hemodynamic instability and neurosurgical consultation.[61]

Other Neurologic Emergencies with Neuro-ophthalmic Signs

Neuro-ophthalmic findings may provide localizing information for neurovascular injuries. Frontal lobe infarctions and hemorrhages are associated with a contralateral gaze palsy. An acute frontal hemorrhage, however, may cause wrong-way eyes or forced contralateral gaze from the irritating effects of the hemorrhage. Parietal damage may incur inferior field cuts and smooth pursuit abnormalities. There are multiple neuro-ophthalmic findings associated with thalamic hemorrhages. The most common is an esotropia caused by bilateral pseudo-sixth nerve palsies with downward gaze deviation, presumably due to the loss of projections that inhibit convergence. Pontine hemorrhages may cause pinpoint reactive pupils or ocular bobbing.

Ocular motility deficits are common in several neuromuscular emergencies. Almost all patients with myasthenia gravis have ptosis and extraocular motor palsies during the course of their disease. Evidence for myasthenia on examination should prompt

immediate assessment of breathing, swallowing, and weakness to determine if treatment should be pursued as inpatient or outpatient and whether immediate breathing support is required. The Miller Fisher variant of GBS, with features of ophthalmoplegia, areflexia, and ataxia, or typical GBS must also be considered in patients with bilateral ocular motility deficits.[62] Urgent evaluation of these patients also includes a respiratory and swallowing assessment. The most common neuro-ophthalmic finding is bilateral abduction deficits.[63] Botulism, another neuromuscular emergency, presents with extraocular muscle weakness, ptosis, and poorly reactive dilated pupils. Early on, the condition may be confused with myasthenia gravis, but the pupillary abnormalities are distinctive.

Trauma causes many neuro-ophthalmic disorders. Compression or severing of the optic nerve causes acute vision loss and treatment is controversial. The acute use of steroids has not been well supported by the literature.[64] Surgical intervention is also controversial and depends on the nature of the injury.[65] Orbital fractures may result in entrapment of the extraocular muscles and motility deficits. Forced ductions help distinguish entrapment from traumatic cranial nerve palsies. In the setting of trauma, fourth nerve palsies are the most common and when bilateral are usually accompanied by loss of consciousness.[66] Severe head trauma with neurologic injury may cause cortical blindness. The most common neuro-ophthalmic complaint after trauma is convergence insufficiency.[67] Patients report difficulty with seeing objects at near and on examination may have abnormal accommodation. This issue tends to improve over time without intervention, but orthoptic exercises, prisms, and surgery may be helpful in persistent cases.

REFERENCES

1. The clinical profile of optic neuritis. Experience of the Optic Neuritis Treatment Trial. Optic Neuritis Study Group. Arch Ophthalmol 1991;109:1673–8.
2. Schumacher M, Schmidt D, Jurklies B, et al. Central retinal artery occlusion: local intra-arterial fibrinolysis versus conservative treatment, a multicenter randomized trial. Ophthalmology 2010;117:1367–75, e1.
3. Hayreh SS. Vascular disorders in neuro-ophthalmology. Curr Opin Neurol 2011; 24:6–11.
4. Hayreh SS, Zimmerman MB. Fundus changes in central retinal artery occlusion. Retina 2007;27:276–89.
5. Wong TY, Scott IU. Clinical practice. Retinal-vein occlusion. N Engl J Med 2010; 363:2135–44.
6. Galetta SL, Raps EC, Wulc AE, et al. Conjugal temporal arteritis. Neurology 1990; 40:1839–42.
7. Gonzalez-Gay MA. Genetic epidemiology. Giant cell arteritis and polymyalgia rheumatica. Arthritis Res 2001;3:154–7.
8. Mitchell BM, Font RL. Detection of varicella zoster virus DNA in some patients with giant cell arteritis. Invest Ophthalmol Vis Sci 2001;42:2572–7.
9. Hunder GG, Bloch DA, Michel BA, et al. The American College of Rheumatology 1990 criteria for the classification of giant cell arteritis. Arthritis Rheum 1990;33: 1122–8.
10. Hayreh SS, Podhajsky PA, Raman R, et al. Giant cell arteritis: validity and reliability of various diagnostic criteria. Am J Ophthalmol 1997;123:285–96.
11. Liu GT, Volpe NJ, Galetta SL. Neuro-opthalmology: diagnosis and management. 2nd edition. Philadelphia: W.B. Saunders Company; 2010.

12. Chan CC, Paine M, O'Day J. Steroid management in giant cell arteritis. Br J Ophthalmol 2001;85:1061–4.
13. Bruce BB, Lamirel C, Wright DW, et al. Nonmydriatic ocular fundus photography in the emergency department. N Engl J Med 2011;364:387–9.
14. Radhakrishnan K, Ahlskog JE, Cross SA, et al. Idiopathic intracranial hypertension (pseudotumor cerebri). Descriptive epidemiology in Rochester, Minn, 1976 to 1990. Arch Neurol 1993;50:78–80.
15. Daniels AB, Liu GT, Volpe NJ, et al. Profiles of obesity, weight gain, and quality of life in idiopathic intracranial hypertension (pseudotumor cerebri). Am J Ophthalmol 2007;143:635–41.
16. Galvin JA, Van Stavern GP. Clinical characterization of idiopathic intracranial hypertension at the Detroit Medical Center. J Neurol Sci 2004;223:157–60.
17. Biousse V, Rucker JC, Vignal C, et al. Anemia and papilledema. Am J Ophthalmol 2003;135:437–46.
18. Friedman DI. Medication-induced intracranial hypertension in dermatology. Am J Clin Dermatol 2005;6:29–37.
19. Liu GT, Kay MD, Bienfang DC, et al. Pseudotumor cerebri associated with corticosteroid withdrawal in inflammatory bowel disease. Am J Ophthalmol 1994;117:352–7.
20. Quinn AG, Singer SB, Buncic JR. Pediatric tetracycline-induced pseudotumor cerbri. J AAPOS 1999;3:53–7.
21. Fraunfelder FW, Fraunfelder FT, Corbett JJ. Isotretinoin-associated intracranial hypertension. Ophthalmology 2004;111:1248–50.
22. Malozowski S, Tanner LA, Wysowski DK, et al. Benign intracranial hypertension in children with growth hormone deficiency treated with growth hormone. J Pediatr 1995;126:996–9.
23. Malozowski S, Tanner LA, Wysowski D, et al. Growth hormone, insulin-like growth factor I, and benign intracranial hypertension. N Engl J Med 1993;329:665–6.
24. Fraser JA, Bruce BB, Rucker J, et al. Risk factors for idiopathic intracranial hypertension in men: a case-control study. J Neurol Sci 2010;290:86–9.
25. Wandstrat TL, Phillips J. Pseudotumor cerebri responsive to acetazolamide. Ann Pharmacother 1995;29:318.
26. Finsterer J, Foldy D, Fertl E. Topiramate resolves headache from pseudotumor cerebri. J Pain Symptom Manage 2006;32:401–2.
27. Kupersmith MJ, Gamell L, Turbin R, et al. Effects of weight loss on the course of idiopathic intracranial hypertension in women. Neurology 1998;50:1094–8.
28. Johnson LN, Krohel GB, Madsen RW, et al. The role of weight loss and acetazolamide in the treatment of idiopathic intracranial hypertension (pseudotumor cerebri). Ophthalmology 1998;105:2313–7.
29. Liu GT, Glaser JS, Schatz NJ. High-dose methylprednisolone and acetazolamide for visual loss in pseudotumor cerebri. Am J Ophthalmol 1994;118:88–96.
30. Banta JT, Farris BK. Pseudotumor cerebri and optic nerve sheath decompression. Ophthalmology 2000;107:1907–12.
31. Kurz-Levin MM, Landau K. A comparison of imaging techniques for diagnosing drusen of the optic nerve head. Arch Ophthalmol 1999;117:1045–9.
32. Optic nerve decompression surgery for nonarteritic anterior ischemic optic neuropathy (NAION) is not effective and may be harmful. The Ischemic Optic Neuropathy Decompression Trial Research Group. JAMA 1995;273:625–32.
33. Hayreh SS. Anterior ischemic optic neuropathy. Clin Neurosci 1997;4:251–63.
34. Beck RW, Servais GE, Hayreh SS. Anterior ischemic optic neuropathy. IX. Cup-to-disc ratio and its role in pathogenesis. Ophthalmology 1987;94:1503–8.

35. Newman NJ, Scherer R, Langenberg P, et al. The fellow eye in NAION: report from the ischemic optic neuropathy decompression trial follow-up study. Am J Ophthalmol 2002;134:317–28.
36. Hayreh SS. Management of ischemic optic neuropathies. Indian J Ophthalmol 2011;59:123–36.
37. Jacobson DM. Pupil involvement in patients with diabetes-associated oculomotor nerve palsy. Arch Ophthalmol 1998;116:723–7.
38. Numminen J, Tarkiainen A, Niemela M, et al. Detection of unruptured cerebral artery aneurysms by MRA at 3.0 tesla: comparison with multislice helical computed tomographic angiography. Acta Radiol 2011;52(6):670–4.
39. Chaudhary N, Davagnanam I, Ansari SA, et al. Imaging of intracranial aneurysms causing isolated third cranial nerve palsy. J Neuroophthalmol 2009;29:238–44.
40. Elmalem VI, Hudgins PA, Bruce BB, et al. Underdiagnosis of posterior communicating artery aneurysm in noninvasive brain vascular studies. J Neuroophthalmol 2011;31:103–9.
41. Hacein-Bey L, Provenzale JM. Current imaging assessment and treatment of intracranial aneurysms. AJR Am J Roentgenol 2011;196:32–44.
42. Capo H, Warren F, Kupersmith MJ. Evolution of oculomotor nerve palsies. J Clin Neuroophthalmol 1992;12:21–5.
43. Matlis A, Kleinman Y, Korn-Lubetzki I. Millard-Gubler syndrome. AJNR Am J Neuroradiol 1994;15:179–81.
44. Casero. The Millard-Gubler syndrome. Am J Ophthalmol 1948;31:344.
45. Dieterich M, Brandt T. Wallenberg's syndrome: lateropulsion, cyclorotation, and subjective visual vertical in thirty-six patients. Ann Neurol 1992;31:399–408.
46. Brandt T, Dieterich M. Skew deviation with ocular torsion: a vestibular brainstem sign of topographic diagnostic value. Ann Neurol 1993;33:528–34.
47. Chou SY, Digre KB. Neuro-ophthalmic complications of raised intracranial pressure, hydrocephalus, and shunt malfunction. Neurosurg Clin N Am 1999;10:587–608.
48. Corbett JJ. Neuro-ophthalmologic complications of hydrocephalus and shunting procedures. Semin Neurol 1986;6:111–23.
49. Cobbs WH, Schatz NJ, Savino PJ. Midbrain eye signs in hydrocephalus. Trans Am Neurol Assoc 1978;103:130.
50. Guy JR, Friedman WF, Mickle JP. Bilateral trochlear nerve paresis in hydrocephalus. J Clin Neuroophthalmol 1989;9:105–11.
51. Hart RG, Easton JD. Dissections of cervical and cerebral arteries. Neurol Clin 1983;1:155–82.
52. Rivkin MJ, Hedges TR 3rd, Logigian EL. Carotid dissection presenting as posterior ischemic optic neuropathy. Neurology 1990;40:1469.
53. Galetta SL, Leahey A, Nichols CW, et al. Orbital ischemia, ophthalmoparesis, and carotid dissection. J Clin Neuroophthalmol 1991;11:284–7.
54. Thomas JE, Yoss RE. The parasellar syndrome: problems in determining etiology. Mayo Clin Proc 1970;45:617–23.
55. Sekhar LN, Sen CN, Jho HD, et al. Surgical treatment of intracavernous neoplasms: a four-year experience. Neurosurgery 1989;24:18–30.
56. Cannon ML, Antonio BL, McCloskey JJ, et al. Cavernous sinus thrombosis complicating sinusitis. Pediatr Crit Care Med 2004;5:86–8.
57. DiNubile MJ. Septic thrombosis of the cavernous sinuses. Arch Neurol 1988;45:567–72.
58. Bhatia K, Jones NS. Septic cavernous sinus thrombosis secondary to sinusitis: are anticoagulants indicated? A review of the literature. J Laryngol Otol 2002;116:667–76.

59. Kupersmith MJ, Berenstein A, Choi IS, et al. Management of nontraumatic vascular shunts involving the cavernous sinus. Ophthalmology 1988;95:121–30.
60. Leonard TJ, Moseley IF, Sanders MD. Ophthalmoplegia in carotid cavernous sinus fistula. Br J Ophthalmol 1984;68:128–34.
61. Murad-Kejbou S, Eggenberger E. Pituitary apoplexy: evaluation, management, and prognosis. Curr Opin Ophthalmol 2009;20:456–61.
62. Fisher CM, Adams RD. Diphtheritic polyneuritis; a pathological study. J Neuropathol Exp Neurol 1956;15:243–68.
63. Lee SH, Lim GH, Kim JS, et al. Acute ophthalmoplegia (without ataxia) associated with anti-GQ1b antibody. Neurology 2008;71:426–9.
64. Yu-Wai-Man P, Griffiths PG. Steroids for traumatic optic neuropathy. Cochrane Database Syst Rev 2011;1:CD006032.
65. Yu Wai Man P, Griffiths PG. Surgery for traumatic optic neuropathy. Cochrane Database Syst Rev 2005;4:CD005024.
66. Sydnor CF, Seaber JH, Buckley EG. Traumatic superior oblique palsies. Ophthalmology 1982;89:134–8.
67. Lepore FE. Disorders of ocular motility following head trauma. Arch Neurol 1995; 52:924–6.