Neuro-Ophthalmological Emergencies

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Abstract

Neuro-ophthalmological emergencies constitute vision or life-threatening conditions if diagnosis and treatment are not promptly undertaken. Even with immediate therapy, these clinical entities carry a high rate of morbidity. They may present with diplopia, visual loss, and/or anisocoria. Arteritic anterior ischemic optic neuropathy is an ominous condition, which can cause permanent and severe vision loss, stroke, or aortic dissection, requiring immediate steroid therapy. Pituitary apoplexy may go unnoticed if only computed axial tomography is performed. Diseases affecting the cavernous sinus and orbital apex region, such as cavernous sinus thrombosis or mucormycosis, can give rise to simultaneous vision loss and diplopia and, if not treated, may extend to the brain parenchyma causing permanent neurological sequela. An isolated third nerve palsy may be the harbinger of a cerebral aneurysm, carrying a significant risk of mortality. Horner syndrome can be the initial presentation of a carotid dissection, an important cause of stroke in the young adult. The neurohospitalist should be familiar with the workup and management of neuro-ophthalmological emergencies.

Keywords

temporal arteritis, pituitary apoplexy, mucormycosis, cavernous sinus thrombosis, third nerve palsy, carotid artery dissection, emergency treatment

This article provides the neurohospitalist with a practical update on neuro-ophthalmological emergencies. We will focus our discussion on 3 different clinical scenarios that may constitute a vision or life-threatening condition if diagnosis and/or treatment are not promptly undertaken—visual loss, disturbed ocular motility, and anisocoria—highlighting those clinical causes requiring urgent management. We will start by briefly reviewing selected aspects of the clinical history and examination of a neuro-ophthalmological patient in an emergency setting.

History and Examination

A carefully obtained history provides crucial information for managing a neuro-ophthalmologic emergency. Symptoms such as vision loss, diplopia, eye pain, and headache should be explored in detail, specifically addressing its onset, duration, frequency, progression, and specific/additional features (ie, vertical vs horizontal diplopia or presence of jaw claudication). Past medical conditions and current medications can further help direct the differential diagnosis (ie, diabetes or immunosuppressant use).

A detailed and systematic examination is of outmost importance when approaching a patient heralding an emergent neuro-ophthalmological condition, including

1. Visual acuity at distance (Snellen chart at 20 ft) and near (near card at 14 in) performed in each eye

separately, with glasses or contact lens if these are normally used (if the patient's glasses are unavailable, using a pinhole device will correct most refractive errors); if visual acuity is below 20/400, the patient approaches the Snellen chart and the minimum viewing distance at which he is able to discern a specific letter is recorded; if this is not possible, acuity is quantified according to his ability to count fingers, detect hand movements, or perceive light.

2. Color vision (Ishihara, Hardy-Rand-Rittler pseudoisochromatic plates, or by simply using a red bottle top or pen to detect a difference in color perception between the 2 eyes).
3. Pupil size and reaction to light, dark, and near measured with a handheld pupil gauge, and the swinging flashlight test in dark to detect an relative afferent pupillary defect (RAPD); if 1 pupil is unreactive, a swinging flashlight test interpretation is still possible,

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if one compares the direct with consensual pupillary response in the fellow eye.

4. Visual field testing in each eye using finger confrontation in the 4 peripheral quadrants (or blink to threat in the 2 hemifields if the patient is unable to participate in more detailed examination), and Amsler grid (or asking if the patient is able to identify all parts of the examiner's face, while fixating his nose) for ruling out a central defect.
5. Eyelid marginal reflex distance (MRD) 1 measures the distance between the upper eyelid margin and the corneal light reflex, while MRD2 is the distance between the corneal light reflex and the lower lid, and levator function (measuring the excursion of the eyelid traversing from downgaze to upgaze).
6. Ocular alignment in all 9 cardinal positions of gaze (ocular excursions may be recorded as millimeters of scleral shown in different positions of gaze); formal measurements using techniques such as alternate cover or red Maddox rod with prisms further quantify the amount of deviation.
7. Direct ophthalmoscopy (through an undilated pupil, the optic disc should be assessed for margin's sharpness, color, and ratio between physiological cup and disc margin; the presence of disc edema with obscuration of retinal vessels as they pass over the disc margin, absence of the spontaneous venous pulse, retinal hemorrhages, arterial attenuation, venous dilation, and retinal emboli; if no contraindication, pharmacological pupillary dilation assists in detailed retinal examination). For a more comprehensive analysis about neuro-ophthalmological clinical history and examination, the reader is referred to classical textbooks.^{1,2}

Visual Loss

Visual loss is a common symptom presenting to the emergency setting, and similar to general neurology, the first goal in neuro-ophthalmic assessment is localization. The clinical history and examination help decide whether the underlying condition is neurological or ophthalmological. For example, if the visual acuity improves 2 or more lines on the Snellen acuity chart when using a pinhole device, then refractive abnormality is likely (Figure 1A).² Likewise, the presence of metamorphopsia (distorted images) when assessing the central 10° of visual field using an Amsler grid and a delay in visual acuity recovery (>50 seconds) after shining a bright light on each eye for about 10 seconds, both favor the presence of a maculopathy, being unusual in optic nerve disease (Figure 1B and C).^{3,4} On the other hand, the presence of an RAPD using the swinging flashlight test strongly raises the suspicion for unilateral or asymmetric optic nerve disease, especially if associated with color vision loss.¹ When neurological visual loss is suspected, determining whether the

deficit is monocular or binocular is particularly important, since it can further help localizing the lesion as anterior or posterior to the chiasm. Care must be taken though when interpreting historical information, since patients with bilateral homonymous defects are frequently unaware of their visual deficit in the eye with the nasal visual field defect and attribute their problem exclusively to the eye with the temporal visual field defect.² Especially, when transient visual loss occurs, questioning patients if they closed either eye during the symptomatic episode can provide a more accurate interpretation regarding the spatial character of visual loss.

Arteritic Anterior Ischemic Optic Neuropathy

Arteritic anterior ischemic optic neuropathy (AAION) is almost invariably caused by giant cell arteritis (GCA), a medium- and large-vessel systemic vasculitis affecting elderly patients. The estimated annual incidence of AAION is 0.36 per 100 000 population in patients older than 50 years of age.⁵ The median age at onset of ocular symptoms was 76 years in 1 study, ranging from 57 to 93 years, with a 3-fold predilection for women and caucasians.⁶ The pathogenesis of GCA likely involves T cell-mediated granulomatous inflammation in the wall of posterior ciliary artery, ultimately resulting in ischemia of the optic nerve head.⁷ Because it is a vision- and life-threatening condition, it is important to recognize symptoms early on. Sudden visual loss is the most frequent ocular symptom in GCA (up to 50% of the cases), while diplopia and eye pain occur less frequently; transient visual loss occurs in about 30% of cases and is often followed by permanent visual loss.^{6,8} The AAION is responsible for the majority of cases with vision loss (80%) in GCA, but central retinal artery occlusion, posterior ischemic optic neuropathy (optic disk edema is absent), or combinations can also be seen.⁶ Patients with GCA typically report systemic symptoms, such as jaw claudication (48%), neck pain (17%), headache (57%), scalp tenderness (20%), weight loss (40%), anorexia (31%), myalgias (28%), and malaise (37%), but importantly these may be absent in about 20% of the cases.^{6,9} Some historical features increase the likelihood of GCA, such as jaw claudication, occipital and/or neck pain, and diplopia.^{10,11}

Examination of patients with AAION frequently show marked deterioration of visual acuity and visual fields in 1 or both eyes (31%), the presence of an RAPD (in unilateral or asymmetric cases), and a characteristic pallid optic disc edema (Figure 2); retinal cotton wool spots, indicative of nerve fiber layer infarcts, may also be present. Although an absent or small cup to disc ratio is an expected feature of the nonarteritic form of anterior ischemic optic neuropathy (NAION), giant cell (arteritic) ischemic optic neuropathy has no such associations. Temporal artery tortuosity, prominence, and/or tenderness may also be found, which further increase the likelihood of GCA.^{6,10,12} Note that absence of these findings does not exclude the diagnosis. Elevation in erythrocyte sedimentation rate (ESR) and C-reactive protein

Figure 1. Techniques that can help distinguishing between ophthalmological versus neurological causes of vision loss. A, Pinhole testing. In the depicted example, visual acuity improved; more than 2 lines pinhole was used (bottom part). B, Amsler grid testing. Metamorphopsias are subjectively noted. C, Photostress testing. After shining a light for 10 seconds (middle part), the right eye has not recovered baseline visual acuity after extra 50 seconds (bottom part; see text for further explanation).

(CRP) pretreatment levels is a diagnostic hallmark of GCA, both evidencing high sensitivity (85.7% and 97.5% in 1 study, respectively) in temporal artery biopsy (TAB)-proven cases.¹³ However, it should be stressed that normal ESR and/or CRP levels can occur in GCA (normal ESR in 9.2%–14.3% of the cases depending on the formula used, normal CRP in 1.7%, and normal ESR and CRP in 0.8% in 1 study); accordingly, we routinely obtain both ESR and CRP in suspected cases.^{11,13–15} Other markers, including thrombocytosis, normocytic anemia, and leukocytosis, may also be helpful in diagnosing GCA; however, these findings are associated with a sensitivity below 60%.^{14,16} Temporal artery biopsy is the gold standard for diagnosing CGA and should be performed in all patients with GCA suspicion. Indurated or tender arterial branches 2 to 3 cm long, on the side of any visual symptoms or signs, should preferentially be obtained within 1 or 2 weeks after starting steroids in order to avoid the expected alteration in inflammation signs by steroids.^{17,18} A negative unilateral TAB is probably sufficient to rule out most cases of CGA^{11,19}; however, in the face of high clinical suspicion (eg, jaw claudication, “chalky white” disc edema,

and fever), a sequential TAB in the contralateral side should be undertaken, considering the discordance rate between sides (around 4%) and the implications of untreated GCA.^{11,20} Techniques such as color Doppler imaging, positron emission tomography, and magnetic resonance imaging (MRI) are being evaluated as potential new tools in the diagnosis of GCA; these do not replace TAB to date and further studies are needed to define their role.^{21,22} Fluorescein angiography can further help distinguish GCA from NAION by showing choroidal hypoperfusion and delayed choroidal filling soon after the visual loss.¹² Steroids are the treatment mainstay of AAION and these should be started *immediately* once the diagnosis of AAION is suspected in order to minimize the risk of further vision loss.²³ Steroid options include both oral and intravenous routes; we commonly employ intravenous methylprednisolone 1 g/d for 3 days, followed by oral prednisone 80 to 100 mg/d.^{24,25} The oral steroid taper should be done very slowly and guided by symptoms, CRP, and ESR; most patients will require steroid therapy for months to years (some indefinitely), emphasizing the importance of close vigilance in the prevention and treatment of steroid-related

Figure 2. Arteritic anterior ischemic optic neuropathy. From top to bottom, right pale disc edema with peripapillary hemorrhages, right relative afferent pupillary defect, impaired right visual acuity and color perception, and right central visual field defect.

adverse effects. Alternate day oral steroids regimens should not be used while tapering.²⁶ Unfortunately, only a minor percentage (4%) of patients will improve any visual deficit with steroids, and 4% of patients deteriorate visually even while on steroids, usually in the first 5 days.^{25,27} Adjunct immunosuppressive therapy such as methotrexate, infliximab, or adalimumab have not shown superiority to prednisone alone in terms of rate of relapses or infections in prospective trials, although these therapies should be considered when steroid-related complications occur or GCA recurs.^{26,28,29} Aspirin may reduce the risk of ischemic events and the incidence of vision loss both at presentation and at follow-up in patients with GCA, and we routinely prescribe aspirin 81 mg orally every day.³⁰

Pituitary Apoplexy

Pituitary apoplexy consists of a sudden enlargement of the gland due to hemorrhage or infarction of a pituitary tumor, usually in the setting of a previously undetected macroadenoma. Apoplexy is the presentation of 0.6% to 9.0% of all surgically managed pituitary adenomas and has a slight male

Figure 3. Pituitary apoplexy. From top to bottom, normal ocular fundi, right eye “down and out” with absent pupillary light response (right third nerve palsy), normal visual acuity, and color perception and bitemporal visual field defects. Note that occasionally, the optic nerve may be involved with subsequent abnormalities in the ocular fundi, pupil response, visual acuity, color perception, and visual fields.

predominance (about 60%), with a peak incidence in the fifth decade.³¹ Although the majority of cases are spontaneous, approximately one-third of the cases have a precipitating factor, including hypotension, malignant hypertension, or treatment with anticoagulants or dopaminergic agonists.³² The sudden enlargement of the gland causes mass effect on surrounding structures such as the optic chiasm and/or cavernous sinus. Accordingly, visual field loss (characteristically a bitemporal visual field loss or a junctional scotoma) and/or unilateral or bilateral ophthalmoplegia (most commonly third nerve palsy, followed by sixth and fourth nerve palsies) can be seen in about 50% of the cases (Figure 3). Sudden severe headache and neck stiffness are common and represent meningeal irritation. Further mass expansion compressing the brain stem and/or hypothalamus promotes reduced level of consciousness, thermoregulatory and/or cardiorespiratory dysfunction, making pituitary apoplexy a life-threatening condition. Additionally, hypofunction of the pituitary itself can promote hypothyroidism, hyponatremia, or hypercortisolism.³³ Although computed tomography

(CT) scan is usually the first neuroimaging in the emergency department, its sensitivity for pituitary apoplexy is remarkably low (46%).³⁴ Magnetic resonance imaging is the diagnostic modality of choice, not only because of superior tumor, hemorrhage, and edema demonstration but also because it provides excellent resolution of adjacent neural structures.³³ Acute management of pituitary apoplexy demands high-dose corticosteroid replacement therapy (eg, hydrocortisone 100 mg intravenously every 6 hours) followed in the majority of cases by transsphenoidal surgical decompression of the sella.^{31,33} Early decompression (ideally within the first week) improves visual acuity in 76% of the cases and visual fields in 79%.³¹ Conservative treatment using corticosteroids, bromocriptine, or radiotherapy in patients with isolated ophthalmoplegia, without severe visual loss or consciousness impairment, is a matter of debate and not our general practice pattern.³⁵

Rhino-Orbital-Cerebral Mucormycosis

Mucormycosis is an aggressive, highly destructive opportunistic fungal infection occurring almost exclusively in immunocompromised hosts, such as patients with diabetes (ketoacidosis is present in approximately 50% of cases), chronic immunosuppression, or hematological malignancies (particularly if neutropenic).^{36,37} Because iron is an essential growth factor for the Mucorales fungi, its causative agent, iron overload states and the use of desferrioxamine are also risk factors for mucormycosis.³⁸ It is a rare condition (1.7 cases/million) evidencing a male to female ratio of approximately 2:1.^{39,40} Within the various clinical forms of mucormycosis, the rhino-orbital-cerebral is the most common, constituting about 60% of the cases.⁴¹ Inhalation of sporangiospores is the usual mode of transmission.³⁸ The germinating hyphae invade the orbit, palate, mouth, and face through the paranasal sinuses. Once in the orbit, further extension to cavernous sinus may be fatal, due to invasion of the cavernous segment of the carotid artery, promoting intracranial thrombosis or mycotic aneurysm formation and subsequent infarction or subarachnoid hemorrhage.⁴² Mucormycosis can present as a painful orbital apex syndrome in which patients manifest early vision loss due to optic neuropathy and complete ophthalmoplegia, ptosis, facial anhidrosis, and decreased corneal sensation due to cavernous sinus involvement.⁴² An extensive review showed that early findings including fever (44%), nasal mucosal ulceration/necrosis (38%), periorbital and facial swelling (34%), decreased vision (30%), ophthalmoplegia (29%), sinusitis (26%), headache (25%), and facial pain (22%) are diagnostic clues, while the “classic” black eschar of skin, nasal mucosa, or palate is present only in about 20% of the patients.^{37,43} The presence of sinusitis on CT scan, especially if bone erosion is associated, and MRI evidence of extrasinus extension to orbital and cerebral tissues are important findings, but negative imaging does not exclude this entity.⁴² If high clinical suspicion

exists, paranasal sinus biopsy should be considered promptly for definite diagnosis, even if no visible mucosal lesions are present. If sinus histopathology is negative, orbital apex biopsy may be considered.^{37,42} Standard rhino-orbital mucor treatment consists of immediate antifungal therapy with amphotericin B (5-10 mg/kg/d, the latter if central nervous system involvement), reversal of underlying host risk factors (eg, ketoacidosis), and surgical debridement of the infected area when possible. The role of hydroxypyridinone iron chelators, posaconazole, echinocandins, and hyperbaric oxygen as an adjunctive and/or salvage therapy needs to be further defined.⁴⁴ Rhino-orbital-cerebral mucor is typically fatal without urgent therapy.³⁹ Late diagnosis, bilateral sinusitis, immunosuppression, presence of hemiplegia or hemiparesis, and the extent of invasion are correlated with a worse prognosis, despite surgical excision and antifungal therapy.^{45,46}

Diplopia and Disturbed Ocular Motility

The evaluation of a patient with double vision begins by establishing whether the diplopia is binocular or monocular. The former resolves when either eye is covered, while the latter persists with monocular viewing, often as an overlapping ghost image. Monocular diplopia often resolves when viewing through a pinhole, since it is usually caused by a refractive error. It should also be stressed that occasionally, ocular misalignment may be perceived by the patient as binocular blur rather than frank double vision. The orientation of diplopic images (horizontal, vertical, oblique, or torsional) and the direction of gaze with greatest image separation provide important clues regarding topographical diagnosis (eg, horizontal diplopia worse in left gaze may be left sixth nerve palsy or right internuclear ophthalmoplegia, etc). Small amounts of ocular misalignment often elude detection if the examination consists solely of “follow my finger”; accordingly, it is imperative to perform further testing with Maddox rod or alternate cover. Associated signs and symptoms can further help narrowing the diagnosis (eg, the presence of pain and proptosis favors orbital disease; dissociation between voluntary and reflex vertical gaze extend points to a supranuclear gaze palsy, that is, a limitation in the range of vertical voluntary saccades can be overcome by passively moving patient’s head vertically while he is fixating on a target, a more reflexive eye movement).^{1,47}

Cavernous Sinus Thrombosis

Cavernous sinus thrombosis (CST) is a rare but potentially life-threatening condition. It can affect any age-group, with a mean age of 22 years old reflecting the underlying etiologies.⁴⁸ Cavernous sinus thrombosis may be septic or aseptic.

Contemporary mortality and morbidity rates for the septic form of CST remain unacceptably high, despite drastic decreases since the antibiotic era (from approximately 75% to 30%).^{49,50} Septic CST is usually caused by infections spreading

through the venous system, from the middle third of the face, sphenoid and ethmoid sinus, teeth, ear, or orbit. *Staphylococcus aureus* is the causative agent in about two-thirds of the cases, while *Streptococcus pneumoniae*, gram-negative bacilli and anaerobes are less frequently identified.⁵¹ The aseptic form of CST usually occurs in the context of prothrombotic disorders (eg, polycythemia, vasculitis, pregnancy, postpartum period, or oral contraceptive use), trauma, surgery, and compression or obstruction by tumors of the skull base or nasopharynx.^{50,52}

Clinical signs of CST are related to direct damage of structures inside the cavernous sinus, impaired local venous drainage, and signs related to primary infection. Accordingly, 80% to 100% of cases with septic CST reportedly present with acute onset of fever, proptosis, chemosis, ptosis, and III, IV, and/or VI nerve palsies (initially there can be isolated involvement of the VI nerve, especially in chronic, indolent cases); 50% to 80% evidence periorbital edema, headache, lethargy, altered sensorium, optic disc edema, and venous engorgement. Less than 50% show decrease visual acuity (due to ischemic optic neuropathy, central retinal artery/vein occlusion, or corneal ulceration), sluggish or dilated pupils, periorbital and corneal sensory loss, and meningismus; rarely, seizures and hemiparesis may occur often related to venous infarction. Due to the intercavernous sinus, spread to the opposite site is common in the first days.^{50,51} Patients with aseptic CST have an analogous but less dramatic clinical presentation and signs and symptoms of sepsis or primary infection are absent.

In septic CST, laboratory findings include leukocytosis, positive blood (70%), and cerebrospinal fluid cultures (20%).^{51,53} High-resolution contrast-enhanced head CT typically shows cavernous sinus expansion and irregular filling defects (direct signs), in addition to dilated superior ophthalmic veins, soft-tissue edema, proptosis, and concurrent thrombosis of the tributary veins including the superior ophthalmic vein (indirect signs).^{54,55} High-resolution head MRI, especially spoiled gradient-recalled acquisition, is helpful to access the extension of infection.⁵⁵ Imaging can be negative initially, requiring serial imaging in cases with clinical worsening.⁵⁶ Use of gallium scintigraphy has been reported as a useful imaging modality in septic CST.⁵⁷

Two clinical conditions may resemble CST and deserve further discussion. Orbital cellulitis can also present as a painful ophthalmoplegia with proptosis, chemosis, fever, and decreased vision, but the presence of bilateral eye signs, decreased periocular sensation, and marked toxemia favor CST. Likewise, a direct high-flow carotid-cavernous fistula can present with marked periorbital edema, ophthalmoplegia, increased intraocular pressure, and decreased vision, but the presence of a supraorbital bruit and/or arterialized conjunctival vessels points to the existence of a fistula.⁵⁰ Treatment of septic CST consists of prompt therapy directed at the primary infection source, including a third-generation cephalosporin, nafcillin, and metronidazole in accord with infectious

disease consultation and consideration of early anticoagulation with low-molecular-weight heparin, which may decrease mortality and morbidity.^{51,58-60} Steroids have a controversial role in the treatment of septic CST and probably should be reserved for cases with parenchymal involvement.⁶¹ Aseptic CST is managed with primary attention to coagulation status and any underlying disease. Importantly, because clinical distinction between aseptic and septic CST can be difficult, initial management with antibiotics is recommended, until a septic etiology is ruled out.

Aneurysmal Third Nerve Palsy

Depending on the series, 9% to 36% of oculomotor nerve palsies are caused by an intracranial aneurysm. This variability probably reflects the different set of patients included in neurological versus neurosurgical series and the different sensitivity of the imaging method used (eg, CT, MRI, CT angiography [CTA], and magnetic resonance angiography [MRA]).⁶²⁻⁶⁴ Posterior communicating artery (PCA) aneurysms present with III nerve palsy 30% to 60% of the times, and approximately 40% of aneurysms are located at the level of PCA, the ophthalmic artery, and the cavernous sinus.⁶⁵⁻⁶⁷ The risk of aneurysmal rupture increases with several factors such as increasing age (peaking in the sixth decade), female gender, smoking, hypertension, alcohol consumption, positive family history for IA or subarachnoid hemorrhage, aneurysm size ≥ 10 mm, genetic conditions such as adult polycystic kidney disease, and probably aneurysm location (PCA and basilar tip have higher cumulative rupture risk at 5 years).⁶⁸⁻⁷⁰ Several mechanisms account for aneurysmal III nerve palsy, including direct compression by an enlarged aneurysmal sac, subarachnoid blood irritation, or aneurysm pulsation.⁷¹⁻⁷³

Aneurysmal III nerve palsy typically presents with pain, *mid-dilated pupil* with poor or absent light reaction, and *complete or partial external paresis* including ptosis with supra, infra, and adduction deficits (Figure 4A).⁷⁴ The early and marked pupillary involvement helps distinguishing compressive from ischemic oculomotor nerve palsy; this is thought to occur because compressive lesions usually affect both the central somatomotor fibers and the peripheral superomedial pupil fibers, while ischemic lesions spare the latter. This anatomy is the basis for the “rule of the pupil,” which states that a complete motor III nerve palsy (*complete external paresis*) with a *normal pupil* is most probably ischemic in origin and not compressive (Figure 4B). In another subset of patients with III nerve palsy, there is *no pupillary involvement* and *external paresis is incomplete*; these patients are particularly challenging and should be followed carefully, since up to 14% of these will have an aneurysm and may not evidence pupillary involvement in the early phase.⁷⁴ Hence, in patients with *partial* III nerve palsy, a normal pupil is much less telling—this may be either microvascular ischemic or compressive (Figure 4C).⁷⁵⁻⁷⁸ Finally, pupil involvement is

Figure 4. A, Complete external ophthalmoplegia (complete ptosis, supra, infra, and adduction deficit) and complete parasympathetic pupillary dysfunction—high risk of compression/aneurysm. B, The pupil rule: complete external ophthalmoplegia (complete ptosis, supra, infra, and adduction deficit) and normal pupillary function—minimal risk of aneurysm, most probably ischemic. C, Incomplete external ophthalmoplegia (in the example, complete ptosis, infra, and adduction deficit but spared supraduction) and normal pupillary function—aneurysm not ruled out. An arrow represents a normal excursion while a cross represents absence of movement.

considered to be clinically relevant if the degree of anisocoria is greater than 1 mm, since approximately 38% of patients with ischemic III nerve palsy have anisocoria less than 1 mm.⁷⁹

Digital subtraction angiography (DSA) remains the gold standard diagnostic test for cerebral aneurysms, although it carries a 1% to 2% risk of systemic or neurologic morbidity. Magnetic resonance angiography and CTA are noninvasive imaging alternatives that detect up to 95% of aneurysms in some studies, although they still don't replace DSA completely, especially with less experienced radiology readers or aneurysm size below 5 mm, which is the usual critical size limit for MRA/CTA aneurysm detection.⁷⁸ A reasonable emergency department approach to a patient with an isolated III nerve palsy in whom an aneurysm is suspected would be to perform a CTA, perhaps followed by DSA; MRA may be useful to rule other etiologies for oculomotor nerve palsy.⁸⁰ Regardless of aneurysmal treatment (surgical vs endovascular repair), 70% to 100% of surviving patients with aneurysmal III nerve palsy make a complete or partial recovery of the oculomotor deficit, usually starting with resolution of ptosis while pupillary and extraocular abnormalities may

Figure 5. Horner syndrome. Right ptosis and miosis, evidencing anisocoria greater in dark (B) than in light (A).

persist, sometimes with aberrant regeneration. Partial III nerve palsy carries a better prognosis for recovery than complete palsy.⁸¹

Anisocoria

When evaluating pupillary asymmetry (anisocoria), it is often difficult to date the onset as isolated anisocoria is often asymptomatic. Seemingly “acute” anisocoria may actually be new, or just newly discovered, perhaps by inspection prompted by another symptom such as eye pain or headache. Old photographs showing anisocoria may be extremely useful in documenting a previous abnormality. Anisocoria may be classified into disorders causing greater anisocoria in light with poor light reaction or anisocoria greater in dark with impaired dark dilation. Dilation lag refers to slowed dilation of the pupil after switching off the light, especially during the first 5 seconds; this is a useful sign of Horner syndrome and helps distinguish this entity from physiological anisocoria (Figure 5).^{1,82} Pharmacological confirmation of a sympathetic paresis (Horner syndrome) can be achieved either with cocaine (postcocaine anisocoria >8 mm) or with apraclonidine test (reversal of anisocoria), the latter test possibly showing more false negatives. Further localization of a Horner syndrome can be done with hydroxyamphetamine (at least 2 days after cocaine or apraclonidine); an increase in posthydroxyamphetamine anisocoria of >0.5 mm is indicative of a postganglionic or third-order Horner syndrome.⁸²

Carotid Artery Dissection

Carotid artery dissection occurs with intimal wall disruption, leading to intrusion of blood and subsequent intramural hematoma formation.⁸³ Carotid dissection has an incidence of about 3 per 100 000 population, with a peak incidence in the fifth decade and slight male predominance; it is responsible for up to 20% of strokes in young adults.⁸⁴⁻⁸⁶ Dissection may

be traumatic or spontaneous, sometimes related to underlying vasculopathy such as fibromuscular dysplasia or connective tissue disorder.⁸⁷ Ipsilateral headache is the most frequent symptom in carotid dissection, occurring in 70% of patients and constitutes the initial manifestation in half of these. Ipsilateral neck, eye, and ear pain are less common (10%-30%).⁸⁸ In 10% of cases, pain constitutes the only presenting symptom.⁸⁹ A painful third-order Horner syndrome occurs in nearly 60% of patients characterized by ptosis and miosis usually without notation of anhydrosis. Sudden painful Horner syndrome, especially in younger patients, should be considered cervical dissection until proven otherwise. Less frequent ophthalmological features of dissection include transient monocular vision loss, NAION, posterior ischemic optic neuropathy, central retinal artery occlusion, ocular ischemic syndrome, and ocular motor nerve palsies. It should be stressed that ophthalmologic symptoms or signs in carotid dissection may precede irreversible ocular or hemispheric ischemia with a mean interval of 6 days.⁹⁰⁻⁹³ Lower cranial nerves can be affected, and pulsatile tinnitus may be present.⁸⁸ Digital subtraction angiography has been replaced by noninvasive imaging such as CTA and MRA due to the risk of stroke and lower specificity.⁹⁴ The MRI and MRA provide a clear view of the vessel lumen, arterial wall, and intramural hematoma, demonstrating a sensitivity of 85% and specificity of 95% for dissection.⁹⁵ The CTA is probably suitable in the emergency department setting.⁹⁶ Ultrasound sensitivity is suboptimal, especially in dissections producing low-grade stenosis.⁹⁷ Treatment of carotid dissection is controversial due to the lack of randomized trials.⁹⁸ Antiplatelet or anticoagulant therapies (our usual practice) have been recommended, usually during 3 to 6 months after the event, preferentially using serial imaging to monitor dissection status.⁹⁹ Although the main mechanism of ischemic stroke in carotid dissection is thought to be embolism, 1 recent nonrandomized trial found no superiority of anticoagulation versus antiplatelet therapy in prevention of stroke.^{100,101} The role of thrombolysis and endovascular treatment needs further evaluation.⁹⁸ Clinical outcome is good for about 90% of the patients, although some series show remarkably low rates of complete recovery (29%).^{102,103} Recanalization or resolution is reported in up to 80% of dissections.¹⁰⁴ Ischemic events have a low recurrence rate after dissection (0.3%-3.4%, regardless of the preventive treatment or the degree of carotid stenosis); recurrences usually occur within the first month and may be more frequent in dissection presenting with an ischemic event (Figure 5).^{105,106}

Conclusion

The clinician should be aware of common neuro-ophthalmic emergencies including GCA, mucormycosis, CST, compressive oculomotor nerve palsies, and Horner syndrome related to carotid dissection. Prompt diagnosis and treatment of these conditions improve the possibility of favorable outcomes.

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