Neuro-ophthalmology: Disorders of the Efferent Visual Pathway

Editor:
Alireza Atri, MD, PhD
Instructor in Neurology, Harvard Medical School; Assistant in Neurology, Memory Disorders Unit, Massachusetts General Hospital, Boston, MA

Associate Editor:
Tracey A. Milligan, MD
Instructor in Neurology, Harvard Medical School; Associate Neurologist, Brigham and Women’s and Faulkner Hospitals, Boston, MA

Contributors:
Adam B. Cohen, MD
Chief Resident in Neurology, Harvard Medical School, Departments of Neurology, Massachusetts General and Brigham and Women’s Hospitals, Boston, MA

Misha L. Pless, MD
Associate Professor of Neurology, Harvard Medical School; Director, Division of General Neurology, Department of Neurology, Massachusetts General Hospital, Boston, MA

Table of Contents

Introduction ................................................. 2
Disease of the Pupil .................................... 2
Disease of an Ocular Motor Nerve ................. 7
Disease of Conjugate Eye Movement .......... 10
Summary .................................................. 14
References .............................................. 14

Cover Illustration by Kathryn K. Johnson

Copyright 2007, Turner White Communications, Inc., Strafford Avenue, Suite 220, Wayne, PA 19087-3391, www.turner-white.com. All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted in any form or by any means, mechanical, electronic, photocopying, recording, or otherwise, without the prior written permission of Turner White Communications. The preparation and distribution of this publication are supported by sponsorship subject to written agreements that stipulate and ensure the editorial independence of Turner White Communications. Turner White Communications retains full control over the design and production of all published materials, including selection of topics and preparation of editorial content. The authors are solely responsible for substantive content. Statements expressed reflect the views of the authors and not necessarily the opinions or policies of Turner White Communications. Turner White Communications accepts no responsibility for statements made by authors and will not be liable for any errors of omission or inaccuracies. Information contained within this publication should not be used as a substitute for clinical judgment.
INTRODUCTION

This manual is the second half of a 2-part review of neuro-ophthalmology. In the previous manual, diseases of the afferent visual pathway were considered. The afferent visual system includes the retina, optic nerve, optic tract, optic chiasm, and retrochiasmal pathways, including the optic radiations and the cortical/higher cognitive areas of visual representation. In this manual, the discussion focuses on diseases of the efferent visual system. The efferent component of the visual system includes the pupil and the associated autonomic pathways, neural mechanisms of ocular motility, and the cranial nerves involved in eyelid function. As in the previous manual, clinical cases are used to illustrate essential concepts guiding the physician to the location of pathology as well as the underlying process of disease.

DISEASE OF THE PUPIL

The diagnosis of a visual disturbance hinges on correctly identifying the site of pathology. Before considering specific disorders of the pupil, it is useful to begin with a brief review of the neuroanatomic pathways governing pupillary function.

CONTROL OF PUPILLARY FUNCTION

Pupillary size is under autonomic control. The parasympathetic pathway begins with light-induced activity in the retina, where signals are sent to the optic nerve and optic tract and finally to the pretectal nucleus of the midbrain and the Edinger-Westphal nucleus (via interneurons and the posterior commissure). Of note, stimulation of the Edinger-Westphal nucleus results in stimulation of the contralateral nucleus, thus producing a consensual response. Each Edinger-Westphal nucleus in turn transmits parasympathetic signals via the parasympathetic division of the ipsilateral oculomotor nerve (CN III). These parasympathetic fibers are found on the inferior portion of the oculomotor nerve. The axons synapse (activating nicotinic acetylcholine receptors) at the ciliary ganglion, which then sends short ciliary nerves (between the sclera and choroid) to the iris sphincter and ciliary muscles (activating muscarinic acetylcholine receptors). This results in pupillary constriction and lens accommodation, respectively.

The sympathetic pathway primarily begins in the insular cortex, which sends fibers to neurons in the hypothalamus. These hypothalamic cells are often considered the central, or first-order, neurons of the sympathetic pathway. From here, fibers are sent through the midbrain, pons, and lateral medulla to the intermediolateral neurons of the spinal cord (from the level of C8 to T2). The intermediolateral cells represent the second-order neurons, which in turn send projections exiting the cord at T1 to enter the sympathetic chain (via a white communicating ramus). The axons travel over the apex of the lung and continue through the inferior cervical ganglion to synapse on the superior cervical ganglion (activating nicotinic acetylcholine receptors). Cells in this latter ganglion represent the third-order neurons, which then send fibers up the internal carotid artery to the cavernous sinus. Here, the sympathetic fibers leave the carotid artery and travel first with the abducens nerve (CN VI) and then with the nasociliary nerve (which is a branch of the first division [V1] of the trigeminal nerve [CN V]) through the superior orbital fissure into the orbit. These axons reach (but do not synapse on) the ciliary ganglion in the orbit. At this point, sympathetic fibers from the ciliary ganglion (called the long ciliary nerve) finally reach the iris dilator muscles and activate noradrenergic receptors to cause pupillary dilation. These fibers also travel to the Müller’s muscles of the upper and lower eyelid, assisting in widening the palpebral fissure (ie, keeping the eye open).

THE LARGE PUPIL

Case 1 Presentation

A previously healthy 34-year-old woman presents to the emergency department (ED) with a 3-hour history of gradual-onset blurry vision of the right eye, which began while she was reading. The patient says she noticed that her right pupil is larger...
than her left pupil. She also reports mild pain in the right eye when she looks into bright lights. There is no history of trauma or ocular disease. The patient denies prior visual problems and had been feeling well until her vision became blurry. She also reports no abnormalities of alertness, cognition, language, strength, sensation, or gait.

The general examination is normal and reveals a well-appearing young woman. She has normal cognition, motor-sensory function, coordination, and plantar responses. The deep tendon reflexes are absent in the arms and legs. Slit-lamp evaluation of the anterior portions of the eyes is normal. There are no signs of inflammation (eg, redness, swelling), and the pupils are round, without signs of trauma. The intraocular pressures are normal. Best-corrected visual acuity (BVA) is 20/20 in both eyes. The Ishihara color plate, Amserl grid, and confrontation visual field tests are normal. In ambient room light, the right pupil is 6 mm and the left pupil is 4 mm. In darkness, the right pupil remains at 6 mm and the left dilates to 6 mm. Upon shining light in each pupil, the right pupil does not react but the left pupil constricts from 4 to 2 mm. There is no afferent papillary defect (APD). The extraocular movements are normal without ptosis, lid retraction, or diplopia. Fundoscopic examination (after pharmacologic dilation) is normal.

- Is this patient’s pupillary asymmetry cause for concern?

**Physiologic Versus Pathologic Anisocoria**

This patient’s right pupil is abnormally enlarged in ambient light, while the left pupil is normal in size. The right pupil also fails to react to bright light, while the left pupil constricts appropriately. Unequally sized pupils, or anisocoria, may reflect normal variation or a pathologic process. Because roughly 20% of cases are physiologic, it is important to distinguish this benign situation from pathologic anisocoria, the possible causes of which include potentially life-threatening conditions.

In physiologic anisocoria (also referred to as simple anisocoria), pupillary size difference is usually small (≤ 1 mm) and does not change appreciably in bright versus dark conditions. This latter point is crucial in determining a possible pathologic pupil. With a pathologically small pupil, anisocoria increases in darkness; the pathologically small pupil usually remains small while the normal pupil dilates, augmenting the anisocoria seen in ambient light. Conversely, with a pathologically large pupil, anisocoria typically is more pronounced with the lights turned on. In the dark, the normal pupil dilates, reaching the size of the pathologically large pupil. When the lights are on again, the normal pupil constricts, while the pathologically large pupil fails to constrict.

- What are diagnostic considerations in a patient with an enlarged pupil?

**Differential Diagnosis of an Enlarged Pupil**

An abnormally enlarged pupil, or mydriasis, suggests a disruption of the parasympathetic nerve supply, with resultant unopposed sympathetic stimulation. Any different structure responsible for parasympathetic pupillary control could be the source of the problem in this patient. Diagnostic efforts are therefore focused on pathology of the midbrain nuclei and interconnections, oculomotor nerve, ciliary ganglion, short ciliary nerves, and iris sphincter muscle.

**Midbrain lesions.** Beginning in the midbrain, most pathologic processes will produce additional neurologic findings because of the small size of the nuclei/tracts and close proximity among these structures. When midbrain pathology is the culprit, large pupils are termed tetral pupil. Midbrain lesions are often accompanied by deficits of the oculomotor nuclei and may also exhibit features of Parinaud’s syndrome, including upgaze paresis, convergence retraction nystagmus, and eyelid retraction. Although the pupils may not constrict when light is present, there may be constriction due to a near stimulus (ie, light-near dissociation), depending on the precise site of pathology. Lesions might include hydrocephalus, pineal tumors, or focal demyelination. A midbrain lesion is less likely in this patient given the paucity of additional neuro-ophthalmologic or general neurologic findings (eg, level of arousal; motor, sensory, or coordination).

**Disorders of the oculomotor nerve.** An oculomotor nerve disorder often results in pupillary enlargement. However, at least 1 of the muscles innervated by the oculomotor nerve (an extraocular muscle or the levator palpebrae superioris) will usually be dysfunctional. Nevertheless, there are rare cases when a third nerve palsy produces an isolated pupillary enlargement. Oculomotor neuropathy may result from intrinsic disease of the nerve, nerve ischemia (as seen in patients with hypertension and/or diabetes), or inflammation. Alternatively, oculomotor neuropathy may result from extrinsic disease of the nerve with uncal herniation or arterial aneurismal formation, which is commonly seen at the posterior communicating artery. Third nerve pathology is possible but not likely in the case patient because she has isolated mydriasis.

**Disorders of the ciliary ganglion/short ciliary nerves.** Various disorders may preferentially affect the ciliary ganglion and short ciliary nerves, causing pupillary
enlargement and/or abnormal response to near stimuli as the only sign of disease. Hence, either of these locations could be the pathologic site in this patient. The iris sphincter itself may be the primary site of pathology in the setting of local trauma, medications, infection, or inflammation. Similarly, acute angle-closure glaucoma produces an enlarged pupil with photophobia, redness, and pain. However, the patient’s normal intraocular pressures and slit-lamp examination rule out most of these entities.

**Pharmacologic causes.** Finally, local (often anticholinergic) agents may cause pupillary dilation; for example, this may occur via intentional administration as part of the dilated fundoscopic examination or unintentionally in the case of nebulized ipratropium or transdermal scopolamine. In these cases, the medicines bypass the blood-ocular or blood-nerve barrier to gain access to the relevant structures, causing pupillary dilation—often to a size (> 7 mm) that would be unexpected in other settings. Because of these blood barriers, it is exceedingly rare for systemic medicines (eg, paralytic agents) to cause fixed and dilated pupils. Agents that cross these barriers (eg, tricyclic antidepressants, atropine) may cause fixed and dilated pupils.

- **How might further evaluation assist in localizing the pathologic site to the ciliary ganglion or short ciliary nerves?**

**Evaluation**

Parasympathetic fibers from the ciliary ganglion cause iris sphincter muscle contraction not only to a light stimulus (direct light reflex) but also to a near stimulus (accommodation [near reflex]). The postganglionic accommodative (near reflex) fibers outnumber the light reflex fibers by 30 to 1. Thus, an injury to the ganglion is more likely to cause defective pupillary constriction to light than to a near stimulus. In this scenario, the pupil is large because of devastated postganglionic light reflex fibers, but the near reflex is intact as a result of relative preservation of the accommodative fibers. Instilling dilute pilocarpine (0.125%) into a normal pupil causes no change in pupil size; however, because of denervation hypersensitivity, the abnormal pupil will constrict. Pupillary enlargement, light-near dissociation (light reflex is absent or abnormal but near reflex is intact), slow redilation after constriction due to a near stimulus, and denervation hypersensitivity constitute the *tonic pupil*.

**Case 1 Continued**

When the patient is asked to hold her thumb 6 in from her nose and then look at her thumb, both pupils constrict to 2 mm. The redilation phase is abnormally slow.

- **What are the causes of a tonic pupil?**

**Tonic Pupil**

The most common cause of a tonic pupil is Holmes-Adie syndrome, a neurologic disorder characterized by an enlarged pupil exhibiting light-near dissociation. Patients often are young adult women who may also exhibit absence of deep tendon reflexes. Holmes-Adie syndrome is believed to be a disorder of the ciliary and dorsal root ganglions. For this disorder, the pupil often slowly becomes miotic over time and most patients become asymptomatic; specific treatment is not available.

A variety of other disorders may affect the ciliary ganglion or short ciliary nerves. These include local trauma, inflammatory diseases such as giant cell arteritis and Sjögren’s syndrome, infectious illnesses including Lyme disease and syphilis, and paraneoplastic syndromes. Disorders of widespread autonomic dysfunction (eg, an acute inflammatory demyelinating neuropathy) may also affect the ciliary ganglion. Although patients with syphilis may develop tonic pupils, they more often develop the Argyll Robertson pupil. Here, the pupils are typically small and demonstrate light-near dissociation. The Holmes-Adie pupil, although initially large, may become small after several months and, thus, appear similar to the Argyll Robertson pupil. As a result, these disorders may be difficult to distinguish.

**Case 1 Conclusion**

To evaluate for intracranial pathology and arterial aneurysm, gadolinium-enhanced magnetic resonance imaging (MRI) of the brain and magnetic resonance angiography (MRA) are ordered. Both are normal. A serum rapid plasma reagin test is also normal. In the setting of a tonic pupil, areflexia, and normal brain/blood vessel imaging, the patient is diagnosed with Holmes-Adie syndrome. Over the next few months, the patient’s enlarged pupil decreases in size and her photophobia and blurry vision resolve.

**THE SMALL PUPIL**

**Case 2 Presentation**

An 86-year-old man with a history of hypertension, hyperlipidemia, coronary artery disease, and a 30 pack-year smoking history presents to the ED with sudden-onset gait unsteadiness and drooping of the left eyelid. The patient had been well until 1 hour ago. He had been standing on a chair, painting his ceiling.
when he suddenly felt unsteady and had difficulty using his left arm. He quickly stepped down from the chair and called his wife for help. The wife noticed that the patient’s left eyelid was drooping, and she called 911. During the ambulance ride, the patient was overcome by nausea and vomited twice. The wife estimates that they arrived at the ED 20 minutes after the patient’s symptoms began.

Examination reveals a somewhat ill-appearing elderly man. The patient looks fatigued and nauseated but is not in distress. The general examination is remarkable for an irregularly irregular heart rhythm. Cognition, motor strength, and plantar responses are normal. There is hypesthesia to pinprick and temperature sensation on the left side of the face and in the right hemibody. Facial movements and hearing are normal and symmetric, but there is hypophonia and dysarthria.

The deep tendon reflexes are mildly diminished in the right upper and lower extremities. Dystonia is apparent on left upper extremity finger-to-nose and left lower extremity heel-to-shin movements. There is past-pointing of the left arm with mirror testing. The patient feels uncomfortable standing but is able to walk. His gait is moderately wide-based, and he stumbles to his left. Romberg testing is positive, as the patient again falls to the left.

BVA is 20/25 in both eyes. The Ishihara color plate, Amsler grid, and confrontation visual field tests are normal. In ambient room light, the right pupil is 3 mm and the left pupil is 2 mm. In darkness, the right pupil dilates to 5 mm and the left dilates to 3 mm. Upon shining light in each pupil, both constrict to 1 mm. When the patient is asked to hold his thumb 6 in from his nose and then look at his thumb, both pupils constrict to 1 mm. There is no APD. A left-sided ptosis is apparent, with the upper lid covering 25% of the pupil. The left lower eyelid is slightly elevated compared with the right lower eyelid. A slight right hypertropia is apparent. This is seen at rest and made worse with left gaze but is visible in all directions of gaze. The patient denies any diplopia. Nystagmus is absent.

• Which pupil is abnormal?
• Could all the neurologic findings in this patient originate from the same location within the neuraxis?

Like the patient in case 1, this patient presents with anisocoria plus a host of other neuro-ophtalmologic as well as non–neuro-ophtalmologic abnormalities. Although the non-ophtalmologic signs may be a starting point for localizing the site of the pathology, it is often helpful to begin with the eye findings.

In this case, the anisocoria is greatest in darkness: the left pupil fails to dilate while the right pupil dilates normally. In ambient light, the right pupil constricts and nearly matches the size of the left pupil, making the anisocoria less pronounced. Thus, the left pupil is pathologically small. An abnormally small pupil, or miosis, suggests a disruption of the sympathetic pathway to the eye. The case patient also has left-sided ptosis and lower eyelid elevation. Thus far, the examiner may be confident that a left-sided sympathetic lesion exists, likely stemming from the left lateral medulla.

The patient’s skew deviation (right hypertropia) could conceivably originate from various locations within the brainstem such as the cranial nerve nuclei that control vertical gaze or the tracts connecting these nuclei (eg, medial longitudinal fasciculi). The crossed sensory findings in the left side of the face and the right hemibody implicates the left medulla as the site responsible for the skew deviation. The left-sided ataxia offers additional evidence for a lesion of the left lateral medulla, with probable inferior cerebellar peduncle involvement.

• What are the diagnostic considerations in a patient with a small pupil? What is the most likely diagnosis in this patient?

Differential Diagnosis of a Small Pupil

Aside from physiologic anisocoria, Horner’s syndrome is probably the most important and common cause of a small pupil. Horner’s syndrome consists of miosis, ptosis, lower eyelid elevation, and facial anhidrosis (loss of sweating).18–20 Other diagnostic considerations include Argyll Robertson pupil, chronic tonic pupil, and inflammatory and traumatic processes involving the iris. Finally, pupillary constriction may be caused by systemic and local administration of various medications (often via noradrenergic blockade or cholinergic activation) and by certain toxins (eg, various pesticides).

The case patient presents with classic features of Horner’s syndrome (miosis, ptosis, lower lid elevation), making this a strong diagnostic consideration. Although anhidrosis was not reported, the pattern of anhidrosis in Horner’s syndrome assists in localizing the site of the lesion. Lesions of the hypothalamus produce ipsilateral hemibody loss of sweating. More distal lesions produce 2 main patterns of facial anhidrosis.21 Because sudomotor fibers travel with the common carotid artery, lesions at this location cause hemifacial anhidrosis. At the carotid bifurcation, sudomotor fibers destined for the upper face travel with the internal carotid artery while those responsible for lower face sweating travel with the external carotid artery. Thus, in the setting of a left lateral medullary lesion, the case patient would be
expected to have anhidrosis from at least the entire left side of the face.

• What are the causes of Horner’s syndrome, and what clinical features aid in localizing a lesion to first-order, second-order, or third-order neurons?

Causes and Clinical Features of Horner’s Syndrome

The causes of Horner’s syndrome vary in their clinical presentation based on the location of the lesion in the first-order, second-order, or third-order neurons.

First-order syndromes. Lesions of the first-order type begin with hypothalamic disturbances (ie, tumors, infections, or primary inflammatory disorders); these rarely, however, present as an isolated Horner’s syndrome. Concomitant hypothalamic-diencephalic signs (eg, altered level of arousal, endocrine dysfunction, disrupted sleep patterns) would be expected. Low dorsal midbrain or pontine lesions may also produce Horner’s syndrome. With midbrain lesions, a contralateral fourth nerve palsy would also be expected because of the close geographic association between the descending sympathetic tract and the trochlear nucleus/fascicle.

Large pontine lesions (eg, hemorrhages) often produce small pupils because of descending sympathetic tract disruption. Lateral medullary strokes are perhaps the most common cause of first-order type Horner’s syndrome. The constellation of Horner’s syndrome, ipsilateral facial numbness, contralateral body numbness, hypophonia, and ipsilateral body ataxia is referred to as Wallenberg (or lateral medullary) syndrome. Horner’s syndrome is present in most patients with Wallenberg syndrome. With this in mind, a lateral medullary stroke is quite likely in the case patient. Here, an atherosclerotic lesion of the vertebral artery or posterior inferior cerebellar artery (PICA) would be expected, but primary embolic disease may also account for the stroke. In addition to stroke, tumors and inflammatory lesions may cause Wallenberg syndrome.

Second-order syndromes. Second-order lesions responsible for Horner’s syndrome include Pancoast (apical lung) tumor, trauma, syringomyelia, neoplasia, transverse myelitis, and cord infarction. Ipsilateral arm pain with Horner’s syndrome is suggestive of a brachial plexus lesion and common with Pancoast tumors. Additional clinical clues to second-order lesions, such as the Brown-Séquard syndrome or bowel/bladder disturbances, may localize pathology to the upper spinal cord.

Third-order syndromes. Finally, 2 important considerations of the third-order type of Horner’s syndrome are diseases of the internal carotid artery (eg, dissection, thrombosis) and disease of the cavernous sinus (eg, inflammation, thrombosis). Horner’s syndrome is the most common neuro-ophthalmologic manifestation of a carotid dissection. Patients with a carotid dissection commonly have lower cranial nerve (ie, IX, X, and XII) involvement. Other commonly reported symptoms include retro-orbital headache, facial pain, neck pain, and pulsatile tinnitus. The cranial nerves are affected through ischemia, compression, or stretching. If carotid narrowing becomes hemodynamically significant or thrombotic emboli form, ipsilateral ischemic symptoms will be present. Although some patients with carotid dissection report overt neck trauma, most have no obvious inciting factor or report seemingly trivial injury. Additional causes of the third-order type include orbital disease, cluster headaches, neck or intraoral trauma, and iatrogenic injury via chest tubes, central venous catheters, and other thoracic surgical procedures.

• How might further testing assist in localizing the site of sympathetic pathway disruption in patients presenting with Horner’s syndrome?

Pharmacologic Testing for Horner’s Syndrome

In the case patient, the history and additional sensory and coordination findings help elucidate the pathologic site, offering localization to the first-order pathways (in the medulla). Further ocular testing is probably unnecessary in this case, as a first-order neuron lesion is nearly certain. Similarly, in a patient with miosis and an ipsilateral apical lung tumor, a second-order neuron lesion is most likely. Although the history of illness, symptoms, and examination findings are most helpful in localizing the site of pathway disruption in patients presenting with Horner’s syndrome, pharmacologic testing may assist in some situations.

Confirming Horner’s syndrome. When uncertainty exists, pharmacologic testing often begins with instillation of a noradrenergic reuptake inhibitor (eg, cocaine) into the pathologic eye. Normally, a low baseline level of norepinephrine is emitted from the third-order neuron to the iris dilator muscle. Thus, cocaine would decrease norepinephrine reuptake and produce a relative increase in norepinephrine concentration, resulting in pupillary dilation and widening of the palpebral fissure. If there is a disruption of the oculosympathetic pathway (at any point in the pathway) norepinephrine will not be emitted from the third-order neuron and reuptake inhibition will not change norepinephrine concentrations. Thus, with a disruption at any level, cocaine will have no effect on pupillary size or width of the palpebral fissure. Therefore, when cocaine fails to produce these changes, Horner’s syndrome is diagnosed.
Localizing the lesion. One to 2 days after confirming the presence of Horner’s syndrome, hydroxyamphetamine eye drops are used to determine more precisely the site of pathology. Hydroxyamphetamine enhances the release of norepinephrine from the third-order neuron. Because the release of norepinephrine depends only on the state of the third-order neuron, hydroxyamphetamine will result in norepinephrine release even when the first-order or second-order pathway is damaged. Thus, hydroxyamphetamine helps distinguish a first- or second-order lesion from a third-order lesion. If the third-order pathway is intact, hydroxyamphetamine will result in pupillary dilation and widening of the palpebral fissure. Although not performed in the case patient, cocaine would be expected to have no effect on the pupil or palpebral fissure, while hydroxyamphetamine should produce pupillary dilation and widening of the palpebral fissure.

- Are additional tests indicated for management of the case patient?

As noted, additional pharmacologic or radiologic tests to evaluate for a second- or third-order cause of Horner’s syndrome would not be needed in the case patient, as he most certainly has a first-order syndrome. Given the constellation of Horner’s syndrome, acute neurologic signs and symptoms, and an irregularly irregular cardiac rhythm in a patient with multiple cardiovascular risk factors, lateral medullary stroke is the most likely diagnosis. Thus, imaging of the brain and cerebral and neck vessels would be a top priority. A standard evaluation for stroke risk reduction (eg, lipid evaluation) and etiology (eg, cardiac biomarkers) may begin in the ED. An electrocardiogram may confirm suspected atrial fibrillation.

When a second- or third-order cause of Horner’s syndrome is a possibility, further testing is indicated. Suspicion of carotid dissection mandates special imaging of the neck vessels (eg, computed tomography angiography [CTA] or fat-suppression MRI). Imaging of the spinal cord, chest, cavernous sinus, and/or orbit is dictated by the clinical setting. For example, Horner’s syndrome with abnormal or painful eye movements and facial anesthesia (first and second division of the trigeminal nerve) may suggest the need for special imaging dedicated to the cavernous sinus. Subacute or chronic presentations suggest a neoplastic or inflammatory process, in which case contrast-enhanced imaging would be indicated.

Case 2 Conclusion

The patient undergoes MRI and MRA of the brain and neck, which reveal a left lateral medullary stroke without PICA territory inferior cerebellar involvement (Figure 1). MRA shows scattered areas of mild arterial narrowing but not severe stenosis. Two hours after symptom onset, the patient receives tissue plasminogen activator (tPA) and is transferred to the neurologic intensive care unit. Twenty-four hours after tPA administration, the patient is started on anticoagulation for treatment of new-onset atrial fibrillation. He is later discharged to rehabilitation and makes steady improvements in gait and balance. Over the next year, the patient’s Horner’s syndrome slowly resolves, but a slight skew deviation persists.

DISEASE OF AN OCULAR MOTOR NERVE

CASE 3 PRESENTATION

A 65-year-old woman with a history of diabetes mellitus, hypertension, and previously treated stage II colon cancer presents to the clinic with a 3-day history of double vision and aching around her right eye. The patient’s symptoms developed relatively suddenly, when she noticed that objects appeared to be on top of one another. Upon covering either eye, the diplopia would disappear. The patient says she bumped her head on a cabinet the day before the symptoms began, but she reports no other trauma. Other aspects of her vision have seemed normal. Aside from the recent vision problems, the patient has felt well, without weight loss, fevers, sweats, joint or muscle pain, malaise, melena, hematochezia, weakness, numbness, dyscoordination, or gait disturbance.

- What are possible sites of pathology in this patient?

Diplopia may stem from a problem in nearly every aspect of the visual pathway. The extraocular muscles may harbor disease or may be dysfunctional as a result of a disorder of an ocular motor nerve or the brainstem.
Alternatively, pathology of intraocular structures of the eye itself (e.g., cataract, retinal detachment) may also produce diplopia.

The case patient reported disappearance of diplopia with monocular occlusion, which makes primary ocular disease less likely. She also reported pain around the eye, which makes primary hemispheric or brainstem disease less likely and draws attention to pain-sensitive structures. The evaluation then centers on processes affecting the ocular motor nerves (in the subarachnoid space, cavernous sinus, or posterior orbit) and the extraocular muscles (also in the orbit). In the setting of vertical diplopia, sixth nerve or lateral rectus dysfunction is less likely. Therefore, the evaluation focuses on the third and fourth cranial nerves and their associated extraocular muscles.

**CASE 3 CONTINUED**

Examination reveals a well-appearing woman. The general examination is unremarkable. Cognition, motor strength, sensation, coordination, and plantar responses are normal. The deep tendon reflexes are absent at the ankles; elsewhere, they are diminished but symmetric. BVA is 20/20 in both eyes. Color vision, Amsler grid, and confrontation visual field tests are normal. Pupillary responses to light are normal, with both pupils constricting from 3 to 2 mm. Eyelids are normal, without ptosis. Slit-lamp examination and exophthalmometry (to evaluate for proptosis) also are normal. The patient’s head is tilted toward her left shoulder. A right hypertropia is present and made worse on leftward gaze. There is limitation of right eye depression, which is worse upon right eye adduction. Nystagmus is absent. Fundoscopic examination (after pharmacologic dilation) and intraocular pressures ae normal.

- **Is this a third or a fourth nerve palsy?**
- **Once the dysfunctional nerve is identified, how does the examination further assist in localizing the site of pathology?**

**Clinical Clues to a Third or Fourth Nerve Palsy**

Because the trochlear nerve (CN IV) innervates the superior oblique muscle, trochlear nerve dysfunction produces deficits primarily in depression and intorsion of the eye, with resultant unopposed action of the functional inferior oblique muscle causing elevation and extorsion of the eye. Thus, in primary gaze, the eye is elevated and extorted, which causes the lower image to be tilted. The patient brings the eye back to the neutral position by tilting the head toward the contralateral shoulder. To produce binocular alignment, the functional contralateral eye intorts. The patient may also tilt the head forward (chin to chest) to correct the unwanted elevation. Because the inferior oblique muscle most effectively elevates the eye in adduction, the unopposed action of this muscle is most evident when the eye is adducted in contraversive gaze (Figure 2). As the case patient demonstrates right hypertropia that is made worse in left gaze and worse in right head tilt, right superior oblique muscle or trochlear nerve dysfunction is most likely.

Although oculomotor nerve (CN III) dysfunction may also produce vertical diplopia and head tilt, expected findings would include pupillary enlargement and ptosis (Figure 3) along with exotropia (resulting from unopposed action of the lateral rectus muscle) and depression (from unopposed action of the superior oblique muscle). The complete syndrome is not always seen. For example, because the third nerve divides into superior and inferior branches in the cavernous sinus, lesions anterior to the division produce incomplete palsies.

**Localizing the Lesion**

Assuming dysfunction of fourth nerve structures, the evaluation focuses on identifying a site of pathology along the pathway of the trochlear nerve. After the...
trochlear nerve exits the dorsal midbrain and passes into the subarachnoid space, it wraps around the midbrain and proceeds into the cavernous sinus to the superior orbital fissure and, finally, into the orbit. Although lesions of the trochlear nucleus or fascicle (dorsal midbrain structures) are possible, additional midbrain signs would be expected. Superior dorsal midbrain involvement may manifest as convergence, vertical gaze, or oculomotor nerve dysfunction. Disease of the inferior dorsal midbrain in the vicinity of the trochlear nucleus might affect the medial longitudinal fasciculus (manifesting as internuclear ophthalmoplegia or skew deviation), the superior cerebellar peduncle (contralateral ataxia), or descending oculosympathetic pathways (Horner’s syndrome).

In the setting of primary brainstem disease, right trochlear nucleus disease results in left trochlear nerve or left superior oblique dysfunction because fibers from the trochlear nuclei cross the midline to subserve the contralateral trochlear nerve. Although the patient’s pain suggests possible disease of the cavernous sinus, superior orbital fissure, or orbit, additional symptoms and signs consistent with such pathology are not evident. In the case of cavernous sinus or superior orbital fissure disease, additional findings might include other ocular motor signs, facial sensory loss (distribution of the first division of the trigeminal nerve), Horner’s syndrome, proptosis, eyelid swelling, and conjunctival redness. Given the lack of findings that would be expected with midbrain, cavernous sinus, or orbital pathology, isolated painful superior oblique dysfunction supports primary disease of the trochlear nerve along its pathway between the midbrain and the cavernous sinus.

- What is the differential diagnosis of trochlear nerve dysfunction? What is the most likely cause in this patient?

Differential Diagnosis of Trochlear Nerve Dysfunction

Due to the close anatomic relationships of the oculomotor, trochlear, and abducens nerves, when a disease in any of these nerves is discovered, dysfunction of the others should be suspected. Because more than 1 ocular motor nerve can be involved, a combination of symptoms and signs may be seen. Diagnostic considerations include traumatic, vascular, inflammatory, infiltrative, and neoplastic processes.

Head trauma (major or minor) is the most commonly identified cause of acquired fourth nerve dysfunction.34–37 The purported mechanism is debated, but damage may occur as the nerve exits the brainstem, where it abuts the tentorial free edge. The patient’s recent mild head trauma makes this etiology possible.

Vascular causes include ischemia, arterial malformations (eg, aneurysms), and cavernous sinus disease (eg, carotid-cavernous fistulae). In patients older than 50 years of age with cardiovascular risk factors, acute painful oculomotor nerve dysfunction may present as an isolated clinical syndrome. The presumed mechanism is through nerve ischemia, which is another etiologic possibility in the case patient. Isolated third nerve palsy is more common than a fourth nerve palsy. Additional vascular considerations include giant cell arteritis38 and arterial aneurysmal compression.39 Giant cell arteritis should be considered in any patient older than 50 years, particularly in the presence of other characteristic signs (eg, headache, jaw claudication, fevers, sweats, weight loss). Aneurysmal compression is possible but is an uncommon cause of fourth nerve palsy. In cases of third nerve palsy (especially those with pupillary involvement), a posterior communicating aneurysm should be strongly considered.

Neoplastic processes affecting the trochlear nerve include schwannomas/neurinomas,40–42 meningiomas (at the skull base or in the cavernous sinus), chordomas,43 chondrosarcomas,44 and metastases (eg, carcinomatous meningitis). Given the case patient’s history of breast cancer, a metastasis is a consideration. Infectious processes such as bacterial, fungal, or tuberculous meningitis and septic thrombosis of the cavernous sinus are additional diagnostic considerations. Possible inflammatory or infiltrative causes include systemic lupus erythematosus,45 sarcoidosis, and Tolosa-Hunt syndrome (a rare, idiopathic inflammatory disorder of the cavernous sinus causing painful ophthalmoplegia). Finally, myasthenia gravis and Graves’ disease, both common entities, produce a myriad of eye findings and may mimic primary trochlear nerve palsy.

- What should the diagnostic work-up for this patient include?

Although traumatic or ischemic fourth nerve palsies seem most likely in this patient, neoplastic and/or cavernous sinus disease also must be considered. Thus, gadolinium-enhanced MRI with special attention to the upper brainstem, base of the brain, cavernous sinus, and orbit would be indicated. Although aneurysmal compression produces oculomotor palsies much more commonly than trochlear palsies, CTA (which is more sensitive than MRA) would be considered for aneurysmal evaluation. The common form of ischemic trochlear palsy is evaluated by assessing classic vascular risk factors, whereas inflammatory ischemic etiologies require a separate evaluation. This may include an erythrocyte...
sensation rate (ESR), C-reactive protein, and even a temporal artery biopsy. In the setting of possible infection or carotid artery/thrombotic meningitis, a lumbar puncture (LP) with cytologic evaluation would be considered. Finally, evaluation for thyroid disease and myasthenia gravis may be indicated.

**CASE 3 CONCLUSION**

The patient undergoes MRI and MRA of the brain; results on both studies are unremarkable. Thyroid-stimulating hormone level is normal, and ESR is 27 mm/min (normal in a diabetic patient and therefore not supporting systemic inflammation, as in giant cell arteritis). LP is not pursued. In light of the patient’s age, diabetes, and hypertension, the troclear nerve dysfunction is presumed to be secondary to ischemia, although a traumatic contribution is not ruled out. Over the next 6 weeks, the patient makes a full recovery.

- **How are ischemic ocular motor neuropathies treated?**

The main treatment is supportive and may include ocular occlusion (ie, eye patching) or eyeglass prisms. Injection of botulinum toxin into the unopposed muscle may be helpful when there is persistent double vision (eg, injecting the medial rectus when there is lateral rectus weakness). Although most cases resolve over weeks to months, some patients do not experience complete recovery. In these cases, corrective surgery would be considered. Finally, aggressive risk factor reduction should be pursued.

**DISEASE OF CONJUGATE EYE MOVEMENT**

Conjugate eye movements (synchronous movements of both eyes in the same direction) include saccades (saccadic eye movements), pursuits (smooth pursuit movements), and the vestibulo-ocular reflex. Conjugate eye movements pertain to both horizontal and vertical gaze; saccades and pursuits are gaze shifting mechanisms, and the vestibulo-ocular reflex is a gaze stabilizing mechanism. Abnormalities of conjugate eye movement imply intracerebral pathology (eg, frontal eye field). When gaze abnormalities are dysconjugate (the eyes move in opposite directions), pathology may be intracerebral (eg, brainstem ocular motor nuclei) or extracerebral (eg, ocular motor nerves).

**MECHANISMS OF CONJUGATE EYE MOVEMENT**

**Gaze Shifting Mechanisms**

Saccades (rapid, simultaneous eye movements to direct the eyes on a new visual target) may be spontaneous, reflexive (in response to an auditory or peripheral visual stimulus), or voluntary. Each type of saccade is generated by a particular cortical area or network. These areas include the frontal eye fields (at the posterior middle frontal gyri), supplementary eye fields (in the supplementary motor regions), and parietal eye fields (in the posterior parietal cortex). Activation of the frontal eye fields, for example, produces a conjugate eye movement to the contralateral visual field; thus, a lesion in this area tends to produce an ipsilateral conjugate deviation because of unopposed activity of the contralateral (normal) corresponding area.

Smooth pursuit movements enable the eyes to track a slow moving visual target. Smooth pursuit primarily begin with activation in areas near the junction of the occipital, temporal, and parietal lobes. The cortical saccadic areas are likely involved in generation of smooth pursuit movements as well.

The cortical generators of saccadic and smooth pursuit eye movements send fibers to the brainstem to act on the ocular motor nuclei to direct gaze. The cortical saccadic areas send projections down toward the brainstem, crossing at the level of the third and fourth cranial nerve nuclei, and finally synapsing on the contralateral paramedian pontine reticular formation (PPRF).

To test saccades, the patient is asked to redirect gaze from the primary position to a new horizontal or vertical direction. For example, while a patient is looking straight ahead, he is then asked to “look left,” and thus, a leftward volitional saccade is produced. Pursuits are tested by asking the patient to visually track a slow-moving object such as the examiner’s finger.

**Horizontal gaze control.** To produce a horizontal saccade, the PPRF projects to the ipsilateral pontine abducens nucleus. The PPRF also immediately sends projections returning across the pons in the medial longitudinal fasciculus (MLF). These fibers travel back up to the contralateral midbrain oculomotor nucleus (medial rectus subnucleus). Thus, the left-sided cortical saccadic areas produce a saccade to the right by activating the right-sided PPRF, right-sided abducens nucleus, and left-sided medial rectus subnucleus of the oculomotor nucleus complex. Of note, additional brainstem areas help to facilitate, produce, or maintain saccades and include the contralateral superior colliculus, burst cells of the rostral interstitial nucleus of the MLF (riMLF), the cerebellar flocculus, perihypoglossal complex, and medial vestibular nuclei. Other areas inhibit unwanted saccades and include the omnipause neurons of the raphe interpositus nucleus.

To produce a horizontal pursuit, a double decussation pathway is achieved: the cortical pursuit areas...
converge upon the posterior limb of the ipsilateral internal capsule and eventually reach the dorsal pons. At this point, fibers cross the midline to the contralateral cerebellar flocculus and posterior vermis. Cer- ebellar outflow from the inferior cerebellar peduncle projects to the medial vestibular nucleus, which sends projections back across the midline to the abducens nucleus.

**Vertical gaze control.** As with horizontal gaze, vertical gaze includes both saccadic and smooth pursuit movements, and generation begins in the cortex. The anatomic focus of vertical gaze control lies in the dorsal midbrain, specifically the pretectum and tectum. Above the red nuclei in the midbrain, neurons of the riMLF initiate upward and downward saccades. Projections from the riMLF then descend to the relevant portions of the oculomotor nuclear complex and trochlear nuclei to produce upgaze or downgaze. Interestingly, bilateral projections exist for upgaze, but there are only unilateral projections for downgaze. This may explain why lesions of the riMLF are more likely to affect downgaze than upgaze. The interstitial nucleus of Cajal (inC), which lies slightly inferior and dorsal to the riMLF, functions as a neural integrator of signals from the riMLF, cortex, and vestibular nuclei. The inC then sends projections dorsally in the midbrain, across the posterior commissure, to also act upon the (more inferiorly placed) relevant portions of the oculomotor nuclear complex and trochlear nuclei to mediate upgaze or downgaze. Lesions of the riMLF, inC, or posterior inC commissure may all cause a disturbance of conjugate (saccadic or pursuit) vertical eye movements.

**Gaze Stabilizing Mechanism**

The vestibulo-ocular reflex is a smooth movement of both eyes that helps to maintain a visual target centered and stabilized on the retina while the head moves. These movements are generated by neural activity of the semicircular canals of the inner ear. Projections from the semicircular canals reach the vestibular nuclei, which in turn project to the MLF and relevant oculomotor nuclei. Thus, a leftward head turn elicits smooth rightward conjugate eye movements when the left horizontal semicircular canal becomes relatively more active than the right horizontal canal. Neural signals, through the vestibular nuclei, travel via the MLF to the right abducens and left medial rectus subnuclei. Thus, this vestibulo-ocular reflex pathway bypasses both the cortical areas and the PPRF. It may be tested by passive head turns (oculocephalic maneuver) or through caloric stimulation of the horizontal canal (e.g., cold water irrigation).

**DISEASE OF HORIZONTAL GAZE CONTROL**

**Case 4 Presentation**

A 72-year-old man presents to the ED with a history of visual problems that began earlier in the day while he was driving his car. Upon attempting to look to the left, he suddenly experienced extreme difficulty moving his eyes and instead had to move his head to focus on the approaching vehicles. He had slight nausea and dizziness but no headache, diplopia, or other symptoms. He pulled to the side of the road and called his wife, who picked him up and drove him home. Later in the day, his wife brought him to the ED. The patient has a history of hypertension, hyperlipidemia, and gastroesophageal reflux disease but no prior visual disturbances.

- **What are the symptoms of conjugate gaze deficits?**

Patients with isolated deficits of gaze control are rarely aware of the specific deficit and may report vague symptoms such as blurred or double vision or dizziness. Further, most patients who harbor deficits of gaze control also have other signs and symptoms referable to lesions that disrupt neighboring structures. Nevertheless, some patients, such as the case patient, specifically report loss of gaze control or production. Given the lack of reported “neighborhood signs” such as weakness, sensory changes, or gait disturbance, this patient appears to have an isolated problem with horizontal gaze control. The examination then is focused on isolating the particular area of gaze control causing such a deficit.

**Case 4 Continued**

Examination reveals a well-appearing man. The general examination is unremarkable with the exception of a systolic blood pressure of 220 mm Hg. Cognition, motor strength, sensation, deep tendon reflexes, coordination, and plantar responses are normal. BVA is 20/20 in both eyes. Pupillary response to light and eyelids are normal. Color vision, Amsler grid, and confrontation visual field tests are normal. Conjugate eye movements are normal on rightward and vertical gazes. On attempted production of a leftward saccade, however, the eyes either do not move or drift slightly upward. A test of the vestibulo-ocular reflex (oculocephalic maneuver) could not elicit a normal conjugate leftward gaze with rightward head turns. Rightward and vertical saccades are normal, as are smooth pursuits to the right. Fundoscopic examination (after pharmacologic dilation) is normal.

- **What type of lesion is suggested by these examination findings?**
As noted, an impairment of leftward saccades could stem from pathology of various cortical areas in the right hemisphere, the descending connections, or the final nuclear targets in the midbrain or pons. Because the right frontal eye fields lie adjacent to the somatic motor areas, one would expect a concomitant left-sided hemiparesis. A left PPRF lesion is suspected because a leftward volitional saccade could not be produced and leftward conjugate eye movements were not seen with the oculocephalic maneuver. Although a lesion of the cortical saccadic network or descending pathways is possible, the case patient’s isolated findings suggest a small lesion in the left PPRF, since additional signs or symptoms referable to nearby pontine structures are not seen. Expected findings with a larger lesion might include ipsilateral lateral rectus or nuclear/fascicular-type facial weakness from involvement of the abducens and facial motor nuclei or fascicles, respectively. Additionally, one might find a contralateral arm and leg weakness because of ipsilateral descending corticospinal tract involvement.

In this elderly patient with cerebrovascular risk factors and an acute neurologic decline, a small-vessel ischemic stroke or intraparenchymal hemorrhage of the left pons would be most likely. Although atherosclerosis would be the typical cause of stroke in this case, giant cell arteritis would also be a consideration. Alternative etiologies include pontine myelinolysis, various infections (eg, arboviral encephalitis), and an episode of acute demyelination (eg, multiple sclerosis, acute disseminated encephalomyelitis).

**Case 4 Conclusion**

Brain MRI shows an intraparenchymal hemorrhage of the left-sided pontine tegmentum ([Figure 4](#)). The patient’s hypertension is treated with only moderate success, and his clinical status deteriorates. On repeat examination, systolic blood pressure remains above 190 mm Hg and the patient demonstrates decreased arousal, paralysis of leftward eye movements, a left complete facial droop, and right-sided weakness of the arm and leg. Controlled escalation of blood pressure treatment ensues. Repeat brain imaging via computed tomography shows expansion of the pontine hemorrhage. The patient is taken to the intensive care unit, where he is stabilized. He slowly improves over the next few weeks and is discharged to a rehabilitation hospital. He ultimately is left with moderate right-sided weakness, mild left facial weakness, and a left lateral rectus palsy without a primary leftward gaze disturbance.

**DISEASE OF VERTICAL GAZE CONTROL**

**Case 5 Presentation**

An 85-year-old woman with a remote history of breast cancer presents to the clinic for evaluation of progressive difficulty walking down the stairs. For the past few years, the patient’s family has noted that she appears stiff when she walks. They also have noticed slight memory trouble and possible personality changes, including being somewhat withdrawn. The patient reports that the gait imbalance has become more noticeable lately and that, over the past few weeks, she has become unsteady while walking downstairs. On a few occasions, she has nearly fallen down the stairs.

Examination reveals a well-appearing woman. The general examination is unremarkable. On cognitive testing, the patient has a mild paucity of speech and shows mild deficits in memory and executive function. Slight dysarthria is noted. The stance is upright, but the gait is moderately slow and shuffling. On motor examination, there is increased tone in the neck and trunk as well as mild bradykinesia without tremor. Motor strength, sensation, deep tendon reflexes, coordination, and plantar responses are normal. BVA is 20/20 in both eyes. Color vision, Amsler grid, and confrontation visual field tests are normal. Pupillary responses to light and near stimuli are normal. Eyelids are slightly retracted bilaterally. There are normal conjugate pursuit eye movements.

---

**Figure 4.** Left pontine tegmentum intraparenchymal hemorrhage. This axial gradient echo magnetic resonance imaging sequence shows an intraparenchymal hemorrhage (arrow) in the region of the paramedian pontine reticular formation.
in all directions of gaze (while tracking the examiner’s finger). There is marked limitation and slowness of volitional production of upward saccades; downward saccades are absent. Horizontal saccades are normal, as is the vestibulo-ocular reflex with both vertical and horizontal oculocephalic maneuvers. Fundoscopic examination (after pharmacologic dilation) is normal.

- What findings might be encountered with vertical gaze disorders?
- What types of diseases may cause disorders of vertical gaze?

Unlike horizontal gaze, it is not typical to have isolated vertical gaze defects from cortical lesions alone. A major consideration with vertical gaze defects is the so-called pretectal syndrome. In addition to vertical gaze defects or deviations, patients with the pretectal syndrome may have pupillary light-near dissociation, eyelid retraction, and convergence-retraction nystagmus. Unlike in Holmes-Adie syndrome, light-near dissociation in pretectal syndrome does not stem from disease of the ciliary ganglion but rather from disruption of the incoming fibers from the retina. The pretectal syndrome has various causes, including obstructive hydrocephalus (which may result in the syndrome through third ventricular and Sylvian aqueduct dilation via subsequent pretectal compression), pineal region or thalamic tumors, pineal cysts, midbrain infection (tuberculosis or toxoplasmosis), or midline thalamic strokes and hemorrhages.

Vertical gaze disturbances may also be seen in oculogyric crises from antidopaminergic agents (as well as a host of other medicines and illnesses) and thiamine deficiency, which affects a variety of structures including the midbrain. Limitation of upgaze is believed to be a normal part of aging in some elderly individuals.

A variety of degenerative pathologic states may limit vertical gaze, including progressive supranuclear palsy (PSP), dementia with Lewy bodies, Hallervorden-Spatz disease, and Huntington’s disease. Of these latter degenerative entities, PSP is perhaps most commonly associated with vertical gaze defects.

Other diseases that may cause prominent vertical gaze defects include cerebral infection with Tropheryma whippelii (Whipple’s disease), Niemann-Pick disease, Wilson’s disease, and various paraneoplastic illnesses. Many of these illnesses have additional characteristic or ancillary findings that clue the examiner to the correct diagnosis. Thus, many would not be considered for the case patient.

- Which disease entity is most likely to blame for the vertical gaze deficits in this patient?

The combination of slowly progressive deficits of gait and cognition in the setting of parkinsonian features, axial rigidity, lid retraction, and decreased vertical eye movements all point to PSP. Pathologic findings are prominent in the midbrain, basal ganglia, and cerebellum. Because chronic hydrocephalus and even a chronic infectious state (eg, Whipple’s disease) would be a consideration in this patient, brain imaging would be pursued. In PSP, brain MRI may show signal changes in the putamen and midbrain along with atrophy of the superior cerebellar peduncles and midbrain. There are no treatments that show consistent benefit for PSP, but dopaminergic agents may be tried.

CASE 5 CONCLUSION

Results on gadolinium-enhanced brain MRI are consistent with PSP and do not show hydrocephalus or any enhancing mass or space-occupying lesions. The patient is started on levodopa/carbidopa and shows modest benefit in gait and motor performance.
SUMMARY

Neuro-ophthalmologic cases require an intimate knowledge of anatomy as a starting point in the evaluation. The patient’s history guides the examiner to the site of pathology, which in turn sheds light on the correct diagnosis as well as proper treatment. Thanks to the wide-reaching fingers of the visual network within the nervous system, visual dysfunction is a common representative of neurologic disease. Similarly, systemic diseases may also manifest neuro-ophthalmologically. Thus, instead of pertaining only to a narrow subset of a subspecialty, neuro-ophthalmologic cases are instructive to all neurologists and physicians alike.

REFERENCES

32. Kline LB. The neuro-ophthalmologic manifestations of spontaneous dissection of the internal carotid artery.


