Presentation of Case

Dr. Aaron Savar (Neuro-Ophthalmology): A 26-year-old man was seen in the Neuro-Ophthalmology Clinic of the Massachusetts Eye and Ear Infirmary (MEEI) because of blurred vision in the right eye.

Approximately 8 days earlier, vision in the right eye became hazy, and periorbital pain developed. Six days earlier, he was evaluated in the emergency department of this hospital. He had recently had an upper respiratory infection and nasal congestion, for which he was taking pseudoephedrine. The vital signs and general physical examination were normal. He was referred to the emergency department of the MEEI. He rated the discomfort of the right eye as 2 to 3 on a scale of 0 to 5, where 5 is the most severe. Visual acuity, with eyeglasses, was 20/50 in the right eye and 20/20 in the left eye. The pupils were 4 mm in diameter. Motility was normal, as were the results of a confrontational visual-field examination (whereby the examiner sits directly in front of the patient, who, with one eye covered, is asked to look at the examiner’s eye and announce when the examiner’s hand is visible as it moves from the periphery toward fixation) and a slit-lamp examination. A diagnosis of blepharitis was made, and treatment with warm compresses was recommended.

During the next 5 days, visual acuity in the right eye gradually decreased, and the patient felt mild discomfort with movement of the eye. Nasal congestion and headache persisted, and he continued to take pseudoephedrine. One day before admission, he returned to the emergency department of the MEEI. He again rated the discomfort of the right eye as 2 to 3. On reexamination, the blood pressure was 150/83 mm Hg and the pulse 104 beats per minute. Visual acuity, with eyeglasses, was 20/60 +1 in the right eye and 20/20 in the left eye. Both pupils constricted more after illumination of the left eye than after illumination of the right eye (indicating a relative afferent pupillary defect in the right eye). Motility and a confrontational visual-field examination were normal in both eyes, and applanation tonometry revealed intraocular pressures of 16 mm Hg on the right and 17 mm Hg on the left. On funduscopic examination, the optic nerve of the right eye appeared swollen.

Magnetic resonance imaging (MRI) scans, obtained before and after the administration of gadolinium, revealed bilateral nasal polypoid lesions, a finding consis-
tent with inflammatory polyps, mucosal thickening in all paranasal sinuses, and expansion of a left anterior ethmoid air cell, thought to represent a mucocele. The left aspect of the bony sella was elevated, with superior displacement of the normal-appearing pituitary gland, which abutted the optic chiasm. No signal abnormality was noted in the optic nerves on $T_2$-weighted images. There was no enhancement along the course of the optic nerves. Intranasal corticosteroids and a tapering course of methylprednisolone were begun. The next day, the patient was seen by the Neuro-Ophthalmology Service.

The patient did not have rashes, fevers, myalgias, numbness, weakness, or ataxia. He had had chronic sinusitis for approximately 5 years. He was born in India and had immigrated to the United States 2 years earlier. Medications included pseudoephedrine, intranasal steroids, and methylprednisolone. He had no allergies to medications, and he did not smoke, drink alcohol, or use illicit drugs.

On examination, the patient was alert, oriented, and cooperative. There was nasal congestion and copious discharge. The best corrected visual acuities were 20/40 in the right eye and 20/15 in the left eye, with no improvement with pinhole testing (viewing the chart through a pinhole). Results of the Ishihara color-vision test revealed that he was colorblind in the right eye and had normal color vision in the left eye. Testing with the use of an Amsler grid showed diffuse metamorphopsia (distortion of the straight lines of the grid) on the right. The pupils were equal in size, and constricted in response to light and while focusing on an approaching object (near stimulus). The right relative afferent pupillary defect was again demonstrated. External examination of the eyes and orbits was normal. The eyelids were in normal position and ocular motility was normal. The slit-lamp examination revealed normal anterior segments bilaterally. Applanation tonometry revealed pressures of 17 mm Hg in both eyes. Automated perimetry testing (also known as Humphrey visual-field testing) was performed reliably in both eyes and was normal in the left eye. The right eye showed a diffusely decreased visual field with an area of relative sparing superonasally. Stereoscopic funduscopy performed while the pupils were dilated revealed swelling of the right optic nerve, more prominent nasally than temporally. There were no optociliary collateral vessels. The left optic nerve was normal. The maculae and mid-peripheral retinas were normal in both eyes.

The next day, computed tomography (CT) of the orbits and sinuses, performed after the administration of contrast material, revealed extensive radiodense material in the paranasal sinuses, the ethmoid air cells, and the sphenoid sinuses, with expansion of ethmoid air cells and the sphenoid sinuses. There was erosion of both optic canals, the floor of the sphenoid sinus, and the sella turcica. There was mass effect on the pituitary gland, which was displaced superiorly and to the right by the expanded left sphenoid sinus.

The next day, the patient was admitted to the MEEI and a diagnostic procedure was performed.

Differential Diagnosis

Dr. Dean M. Cestari: I participated in this patient’s care and am aware of the diagnosis.

Approach to a Patient with Loss of Vision

When a patient such as this one presents with blurred vision, the first and most important task is to determine whether the vision loss is optical (i.e., refractive) or related to an ophthalmic, medical, or neurologic disorder. If the visual acuity improves when the patient looks through a pinhole, it means that the vision loss is caused by optical or refractive error. If the vision loss is not corrected by using the pinhole, the patient needs a more thorough evaluation, since a lack of improvement may indicate a more serious ophthalmic or neurologic process. We do not have a record of whether pinhole testing was done during the patient’s initial visits to the emergency department; however, his visual acuity did not improve when he looked through a pinhole during my examination, raising the possibility that the vision loss was of retinal or neurologic origin.

Localization of the Lesion

The next step is to localize the defect within the visual pathway, which includes prechiasmal components (e.g., the retina and optic nerve), the optic chiasm, and the postchiasmal structures (e.g., the optic tract, lateral geniculate nucleus, optic radiation, and striate cortex), by assessing visual acuity, color vision, pupillary function, the appearance of the fundus, and visual fields.
A unilateral prechiasmal lesion can reduce visual acuity, but only when both the crossing and noncrossing fibers are affected. Therefore, it is important to remember that visual acuity is not always a sensitive test of optic-nerve function and that it may remain normal in the setting of a profound optic neuropathy. In this patient, a unilateral decrease in acuity with dyschromatopsia (acquired loss of color vision) was present, strongly implicating the optic nerve. Newly acquired ipsilateral dyschromatopsia is a very sensitive indicator of optic-nerve dysfunction and, as in this patient, usually indicates the presence of an acquired optic neuropathy.

Perhaps more important, this patient’s right eye had a relative afferent pupillary defect — one of the most highly localizing signs in all of neurology. During the swinging-flashlight test, light shone into the healthy eye causes symmetrical pupillary constriction. Light directed into the abnormal eye causes bilateral pupillary dilatation, because of the reduced neural input that reaches the pretectal region of the midbrain. A relative afferent pupillary defect is typically found in the presence of a unilateral optic neuropathy and occasionally, but only rarely, with large macular abnormalities. It is usually present ipsilateral to the side of an injured optic nerve, whereas a postchiasmal optic-tract lesion will cause a contralateral relative afferent pupillary defect. The neuroophthalmic findings in this patient are consistent with a right optic neuropathy.

The natural history and specific patterns of visual-field loss are perhaps the most useful means of localizing lesions in the visual pathways. Acute visual-field loss is typical of vascular and demyelinating events. A gradual, progressive loss of visual acuity, visual field, or both is typical of slowly growing compressive lesions. In this setting, monocular visual-field defects generally indicate involvement of the optic nerve. Chiasmal involvement produces a temporal defect in both eyes, whereas homonymous hemianopic visual-field defects with normal visual acuity are the hallmark of a unilateral retrochiasmal lesion. This patient had a unilateral visual-field defect, which had apparently progressed over a period of 8 days, consistent with an optic neuropathy. This finding alone is not sufficient to confidently make a clinical diagnosis of an optic neuropathy.

Finally, the appearance of the optic nerve on ophthalmoscopic examination differs according to the site of injury. Compressive lesions can cause chronic optic-disk swelling or atrophy. Optic-nerve pallor may develop with any lesion of the afferent pathway that is presynaptic to the lateral geniculate nucleus, since the axons of the retinal ganglion cells extend from the retina to the lateral geniculate nucleus via the optic nerve. This patient had swelling of the right optic disk, consistent with an optic neuropathy.

Overall, this 26-year-old man presented with progressive loss of vision in the right eye over a period of 1 week, periorbital pain, decreased visual acuity, dyschromatopsia, a relative afferent pupillary defect, a swollen optic nerve, and a generalized reduction of sensitivity on automated right visual-field testing. The combination of these findings localizes this problem to the right optic nerve.

**OPTIC NEUROPATHY**

**Glaucoma**
The most common cause of an optic neuropathy in the general population is open-angle glaucoma; it is often asymptomatic and results in slowly progressive peripheral visual-field constriction over a period of years. Central acuity is not affected until late in the course of the disease. The acute loss of vision, dyschromatopsia, swelling of the optic nerve, and the normal intraocular pressure rule out this diagnosis.

**Optic Neuritis**
Optic neuritis — inflammation of the optic nerve, usually associated with demyelination — is an important consideration in this patient, since it is by far the most frequent cause of optic-nerve dysfunction in young adults. Although it is most common in patients with multiple sclerosis, it may occur as an isolated phenomenon; when it does, it is often followed by the development of multiple sclerosis. Although it presents with many features that this patient had — loss of central vision, pain with eye movement, dyschromatopsia, a relative afferent pupillary defect (when unilateral), visual-field loss, and swelling of the optic disk (in one third of cases) — it usually develops more quickly, over several hours to days. Nonetheless, this patient’s clinical history and examination findings are consistent with optic neuritis. MRI will be useful in ruling out this diagnosis,
since it should show intrinsic abnormalities of the optic nerve.  

**Ischemic Optic Neuropathy**
The next most common optic neuropathy is anterior ischemic optic neuropathy; this is characterized by swelling of the optic disk and peripapillary hemorrhages that are visible on funduscopic examination. It can be divided into arteritic (associated with giant-cell arteritis) and nonarteritic. Typically, there is painless loss of vision with dyschromatopsia and a relative afferent pupillary defect. Visual-field defects are universal and tend to involve the lower portion of the field. This patient’s age, ethnic background, and periorbital pain are atypical for this diagnosis.

**Compressive and Infiltrative Optic Neuropathies**
In addition to intracranial lesions such as meningiomas and pituitary adenomas, lesions of the orbit, optic canal, or sinuses (by direct extension) may compress the optic nerve, resulting in an optic neuropathy, with or without disk swelling (Table 1). In most cases of anterior compressive optic neuropathy, progressive visual loss is associated with proptosis. Visual loss tends to be gradual over a period of months or even years when it is due to a slow-growing lesion such as a meningioma. When visual loss is acute, as it was in this case, it is most often because of an infectious cause such as severe sinusitis. In view of this patient’s history of severe sinusitis and the presence of decreased visual acuity, dyschromatopsia, visual-field abnormalities, and disk swelling accompanied by periorbital pain, my leading diagnosis at this point was compressive optic neuropathy due to a sinus infection, but other entities in the differential diagnosis could not be ruled out. MRI of the orbits should help to differentiate among nonarteritic anterior ischemic optic neuropathy, optic neuritis, and a compressive optic neuropathy. May we see the MRI?

**Dr. Mary E. Cunnane:** MRI of the orbits reveals no evidence of signal abnormality or enhancement in the optic nerves (Fig. 1A and 1B), a finding that would be expected in optic neuritis but not in anterior ischemic optic neuropathy. There is opacification of the left sphenoid sinus and mucosal thickening in the ethmoid and sphenoid sinuses (Fig. 1C), with expansion of the left anterior ethmoid, indicating a mucocele. The right anterior clinoid does not show normal marrow signal but, rather, shows low signal consistent with air and is thus probably pneumatized (Fig. 1C, arrows; and 1D). The sphenoid sinus immediately abutting the right optic-nerve canal also shows an absence of signal on the MRI. Signal void in a paranasal sinus may be a normal finding, reflecting normal aeration, but can also be caused by the presence of very dense material in the sinuses.

**Dr. Cestari:** The MRI helped to rule out optic neuritis but did not explain the findings on the clinical examination, which clearly indicated a right optic neuropathy. Instead, the MRI showed abnormal sinuses on the left but not the right. Although findings of hypointensities in the sinuses on T1-weighted sequences are consistent with aerated sinuses, they are also typical of fungal sinusitis. CT is a better means of showing this abnormality.

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<th>Table 1. Differential Diagnosis of an Optic Neuropathy.</th>
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<td><strong>Inflammatory</strong></td>
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<td>Sarcoidosis</td>
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<td><strong>Vascular</strong></td>
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<td>Arteritic anterior ischemic optic neuropathy</td>
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<td>Nonarteritic anterior ischemic optic neuropathy</td>
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<td><strong>Compressive</strong></td>
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<td>Meningioma</td>
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<td>Thyroid ophthalmopathy</td>
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<td><strong>Toxic effects and metabolic and nutritional deficiencies</strong></td>
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<td>Vitamin B12 deficiency</td>
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<td>Toxic effects from methanol</td>
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<td><strong>Hereditary</strong></td>
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<td>Leber’s hereditary optic neuropathy</td>
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<td>Dominant optic atrophy (Kjer’s disease)</td>
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<td><strong>Traumatic</strong></td>
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Dr. Cunnane: CT of the sinuses showed complete opacification of all the paranasal sinuses due to material consistent with densely inspissated secretions (Fig. 2A and 2B). There is expansion of the walls of the sphenoid sinus and erosion along the floors of both optic-nerve canals (Fig. 2C and 2D, arrows). Dense secretions are a finding typical of allergic fungal rhinosinusitis. The marked inspissation seen in this disease causes the increased density of the secretions on CT, but it can substantially reduce the signal intensity of these secretions on MRI. In addition, aspergillus, one of the common causes of fungal sinusitis, tends to concentrate metallic ions from its surroundings, causing a paramagnetic effect that accentuates the hypointensity on MRI. The com-

Figure 1. MRI of the Orbit and Sinuses.
Coronal short-tau inversion-recovery images (Panel A) and coronal T1-weighted images obtained after the administration of contrast material (Panel B) show no evidence of a mass lesion along the course of the right optic nerve and no enhancement in the nerve itself. Axial T2-weighted images (Panel C) and T1-weighted images obtained after the administration of contrast material (Panel D) show mucosal thickening throughout the visualized paranasal sinuses. There is signal dropout in the right sphenoid sinus and in a pneumatized right anterior clinoid (Panel C, arrows).
Comparison of the MRI and the CT indicates how much more sensitive CT is for this particular entity.

Dr. Cestari: Because this patient was immunocompetent, this condition was unlikely to be an invasive fungal sinusitis, and the most likely diagnosis was allergic fungal sinusitis. However, an invasive process could not be ruled out on the basis of the clinical examination alone. Therefore, I asked Dr. Metson to evaluate this patient for a debulking procedure, which I hoped would be both diagnostic and curative.

Summary

Dr. Ralph B. Metson: This patient presented with many symptoms seen in sinusitis, including an upper respiratory infection, nasal congestion, and periorbital discomfort. The findings of high densities within the sphenoid sinuses on CT and low signal in the same region on T₂-weighted MRI were strongly suggestive of allergic fungal sinusitis. The sphenoid sinus is surrounded by the maxillary branch of the trigeminal nerves, the carotid arteries, and the optic canals. A layer of bone...
typically protects the optic nerve from any disease process in the sphenoid sinus, but if the bone is eroded in severe sinusitis, compression of the optic nerve can occur. All the clinical and radiologic features of this case strongly suggested such a condition as the cause of the patient's visual loss. To confirm the diagnosis and to provide relief to the patient, we performed a transnasal endoscopic exploration of the sphenoid sinus.

**INTRAOPERATIVE FINDINGS**

At time of surgery, the right nasal cavity was filled with inflammatory polyps, which were removed with a motorized shaver (see the video, available with the full text of this article at www.nejm.org). In the sphenoid sinus, thick brown material with a peanut-butter–like consistency was encountered, a classic finding for allergic fungal sinusitis. The debris was filling the opticocarotid recess — the space between the optic nerve and carotid artery — and exerting pressure against the optic nerve. This material was cleared from the sphenoid cavity, and a 5-mm area of bony erosion of the optic canal, with exposure of the optic nerve, was identified. The nerve itself appeared to be intact. Once this material was removed, the sinuses could begin to drain and re-establish mucociliary clearance.

Surgical drainage of the obstructed sinus cavity is sufficient treatment for most patients with allergic fungal sinusitis. Corticosteroids, either oral or as topical nasal sprays, are prescribed after surgery in an attempt to control the regrowth of inflammatory nasal polyps that are associated with this disease. Daily saline rinses of the nasal cavity appear to be of benefit as well.

The use of systemic antifungal therapy or topical agents has not been shown to improve the clinical outcome in immunocompetent patients.

**CLINICAL DIAGNOSIS**

Allergic fungal sinusitis with compression of the right optic nerve.

**PATHOLOGICAL DISCUSSION**

Dr. William C. Faquin: Microscopical evaluation of the sinus contents revealed edematous polypoid fragments of tissue with an attenuated respiratory epithelial lining. A marked chronic inflamma-
tory stromal infiltrate was present that consisted of plasma cells, lymphocytes, and many eosinophils. The eosinophils had nuclei with two lobes and cytoplasm with coarse granules (Fig. 3A and inset). Abundant allergic, eosinophilic mucin, characterized by thick extracellular mucin with numerous eosinophils, was present in the sinus contents (Fig. 3B). Charcot–Leyden crystals, a by-product of eosinophil degranulation, were identified in the allergic mucin (Fig. 3B inset, arrow). A silver stain revealed occasional septate fungal hyphae with acute-angle branching that were compatible with aspergillus species (Fig. 3C). These features confirm the diagnosis of allergic fungal sinusitis.

In contrast to invasive fungal sinusitis, which is a rare, acute, life-threatening condition seen primarily in immunocompromised patients, allergic fungal sinusitis is a chronic condition that typically occurs in immunocompetent patients such as this one.5 A variety of fungal organisms that show geographic variations in frequency have been identified within the allergic mucin of patients with allergic fungal sinusitis, including aspergillus species and various other fungi such as bipolaris, curvularia, fusarium, and alternaria.6,7

Allergic fungal sinusitis may be an immune reaction to ubiquitous fungal allergens, similar to allergic bronchopulmonary aspergillosis; however, several studies have shown that even healthy persons without sinonasal disease have evidence of fungal organisms within their nasal mucin, so the role of fungus as an initiating factor in this disorder is somewhat controversial.6,7,12,13

Dr. Cestari: The day after surgery, the patient noted rapid improvement in his vision. His visual acuity improved from 20/40 to 20/13, which was almost as good as that in the left eye, which was 20/10. Color vision completely normalized, and I could no longer detect a relative afferent pupillary defect. His visual fields improved, showing substantially less reduction in sensitivity.

A Physician: Does fungal sinusitis occur as a complication of chronic bacterial sinusitis?

Dr. Metson: It can occur in patients with chronic bacterial sinusitis. The common initiating factor for both conditions is most likely blockage of the sinuses.

Dr. Mandakolathur R. Murali (Allergy and Immunology): Should Wegener’s granulomatosis be considered in the differential diagnosis?

Dr. Metson: The initial presenting findings could have been due to Wegener’s granulomatosis or other granulomatous processes that can affect the sinonasal tract and the eye and orbit. However, such processes do not have hyperplastic mucosa with polyps; rather, they have atrophic mucosa, dry membranes, crusting, and septal perforations.

Dr. Cestari: For the practicing clinician, I think the take-home points for this case are as follows: when you see a patient with loss of vision, do a pinhole test; when you suspect an optic neuropathy, test for dyschromatopsia and a relative afferent pupillary defect; and always remember that your findings on physical examination are real, even if they are not supported by neuroradiologic findings (MRI may miss some findings that are evident on CT).

ANATOMICAL DIAGNOSIS

Allergic fungal sinusitis.

No potential conflict of interest relevant to this article was reported.

REFERENCES


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