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Three Cases of Fungal Disease with Neuro-Ophthalmic Manifestations Associated with Post-Hurricane Environment

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Abstract

Allergic fungal sinusitis (AFS) is thought to represent an immunologic response to exposure to dematiaceous fungi. These fungi are known to cause disease more frequently in hot, humid climates and seasons. Three patients presented with unusual manifestations of fungal disease after exposure to environments recently affected by hurricanes. Two patients had AFS, one with gradual painless visual loss from an AFS mass extending into the suprasellar region and one with orbital apex syndrome. Another patient had invasive fungal disease and developed orbital apex syndrome. The cases underscore the importance of clinical recognition of fungal disease in patients with sinus, orbital, or skull base involvement as well as its potential for causing permanent visual loss. This report suggests a potential association between fungal disease and tropical storm exposure.

Keywords

Allergic Fungal Sinusitis; Orbital Apex Syndrome; Cranial Nerve Palsy; Compressive Optic Neuropathy

Fungal disease of the sinuses is classified into four subtypes: chronic noninvasive infection, chronic indolent infection, fulminant invasive disease, and allergic fungal sinusitis (AFS) (1). AFS is the most recently described form, thought originally to be an allergic response to aspergillus species (2). It is now known that dematiaceous fungi such as *Bipolaris* and *Drechslera* are the principle organisms involved (3). AFS is relatively common, accounting for up to 7% of sinus disease in patients undergoing sinus surgery (4). The exact pathogenesis of AFS is unknown but is thought to involve both type 1 (immediate, IgE mediated) and type 3 (immune complex, IgG mediated) immunologic reactions to fungal antigens after fungal colonization of the sinuses (5).

AFS is usually seen in immunocompetent individuals with long-standing sinus disease symptoms (6). Most commonly AFS occurs in hot and humid environments (7). The dematiaceous fungal species that cause AFS have been demonstrated to cause disease more frequently in warmer and more humid months as well (8). Despite being “noninvasive” by definition, AFS is not benign and may cause destructive inflammation extending through the sinuses into the orbit and cavernous sinus leading to ophthalmoplegia (9,10).

We report three patients with fungal disease associated with exposure to post-hurricane environments. Two patients had AFS and one patient had invasive fungal infection. The cases underscore the importance of clinical recognition of fungal disease in patients with sinus, orbital, or skull base involvement as well as its potential for causing permanent visual loss.

Case Reports

Case 1

A 25-year-old Miami school teacher presented with a ten-month history of painless vision loss in the left eye that worsened in the week prior to presentation. She had a history of seasonal allergies and migraine headaches. She was present in Miami when both Hurricane Katrina and Wilma passed through south Florida and worked in a hurricane damaged classroom.

Best-corrected visual acuity was 20/20, right eye and 5/200, left eye with a left relative afferent pupillary defect. Extraocular movements were full. The right fundus was normal and the left optic disc had pallor and temporal cupping. Manual kinetic perimetry disclosed a left central scotoma and optical coherence tomography was consistent with retinal nerve fiber layer thinning in the left eye.

Magnetic resonance imaging (MRI) revealed a sphenoid sinus mass, hypointense on T2 weighted images, extending superiorly displacing the pituitary gland and optic chiasm (Fig 1). The lesion also extended posteriorly to displace and distend the prepontine cistern and compress the basilar artery.

The patient underwent transsphenoidal surgical intervention with removal of a large necrotic mass with bony fragments from the left sphenoid sinus. Histopathologic examination revealed septated fungal hyphae and several eosinophils mixed with mucus and necrotic material (Figure 2). Fungal culture grew *Drechslera* species.

The patient was diagnosed with AFS and placed on intravenous methylprednisolone and oral voriconazole. The patient's Goldmann visual fields improved over the next few months with near resolution of the left central scotoma. Repeat MRI nine months after surgery revealed persistent AFS, but the patient did not follow-up thereafter.

Case 2

A 58-year-old Caribbean woman was referred with a six-month history of left-sided headaches with recent development of diplopia. Medical history was remarkable for hypertension and hypothyroidism managed with oral medication. About two years prior to presentation she worked in a hotel with hurricane damage in the Cayman Islands and was involved in cleaning the damaged rooms.

Best corrected visual acuity was 20/25, right eye, and 20/20-3, left eye, with no relative afferent pupillary defect. The patient had a left sixth nerve palsy and decreased sensation in the ophthalmic branch (VI) of the left trigeminal nerve. Ophthalmoscopic exam was unremarkable.

MRI showed left sphenoid and posterior ethmoid sinus expansion extending around the left internal carotid artery into the cavernous sinus. The sinuses appeared to be filled with a central, non-enhancing material demonstrating peripheral mucosal enhancement (Figure 3).

The patient underwent emergent left trans-sphenoidal decompression with removal of a large necrotic mass. Histopathology revealed numerous eosinophils and septate hyphal fragments consistent with allergic fungal sinusitis.

The patient was placed on a short course of IV methylprednisolone and a one-year course of voriconazole. One month later the patient's sixth nerve palsy decreased V1 sensation had resolved. At two year follow-up the patient was asymptomatic with no headaches or sinus congestion. MRI showed residual left sphenoid sinus disease.

Case 3

A 64-year-old Federal Emergency Management Agency (FEMA) inspector was referred with a three-month history of vision loss in the right eye as well as right ptosis and ophthalmoplegia. He had been previously evaluated elsewhere for severe right-sided temporal headaches associated with weight loss and was treated with oral corticosteroids for presumed giant cell arteritis. Over the next three months he experienced rapid deterioration of vision in the right eye followed by diplopia and ptosis. The patient was a diabetic and in the year prior to presentation had been working without any respiratory protection as an inspector of mold-infested trailers in the areas of Louisiana affected by Hurricane Katrina.

Visual acuity was no light perception, right eye and 20/25, left eye. The right pupil demonstrated both an afferent and efferent pupillary defect. There was complete right upper lid ptosis with near complete ophthalmoplegia with only minimal abduction of the right eye. The fundi were normal as was function of the trigeminal and facial nerves.

MRI revealed an enhanced area involving the right optic nerve and cavernous sinus (Fig 4). The patient underwent transsphenoidal biopsy the following day which revealed fungal hyphae. He was treated with oral cortisone, oral voriconazole and IV micafungin.

Two months later, the area of infection appeared more extensive on MRI and a right orbital exenteration was considered. The patient declined surgery and medical therapy was changed to micafungin and voriconazole both given intravenously for an additional ten months. The patient's headaches and ophthalmoplegia gradually improved with full extraocular movements at one year following initial presentation. Visual acuity remained NLP, right eye. The patient had stable neuroimaging studies during three years of follow-up.

Discussion

As our first two cases demonstrate, AFS must be considered in the differential diagnosis of patients who have sinus disease and ophthalmic symptoms and signs (11). As many as 17% of patients can present with orbital symptoms (12). Although proptosis is the most common orbital sign, diplopia and visual loss in the absence of proptosis and pain have been reported as presenting complaints (6,13). The pathophysiology of AFS involves destructive inflammation extending through the sinuses and orbit into the cavernous sinus and resulting in ophthalmoplegia (9,10). The mechanism of visual loss is thought to be secondary to either orbital inflammation causing a contiguous inflammatory optic neuritis or optic nerve ischemia secondary to increased intraorbital pressure (14).

If the diagnosis of AFS is suspected clinically, neuroimaging with attention to the paranasal sinuses and orbital structures is necessary. MRI classically reveals decreased T2 weighted intensity in the involved sinus with high signal of the surrounding mucosa (15). This imaging finding is thought to be due to both the accumulation of desiccated mucosal secretions and high concentrations of manganese, iron, and calcium in the fungal

concretions (16,17). Definitive diagnosis depends on positive fungal culture and histopathology of tissue revealing extensive mucin, eosinophils, and septate hyphae (18).

Treatment of AFS consists of surgical removal of the fungal mass and post-operative use of systemic corticosteroids to reduce risk of recurrence (19). There is no evidence to either support or discredit the use of intravenous and oral antifungal agents (19).

In Case 1, the patient lived in Miami and began developing symptoms two months after two major hurricanes affected the region. Ten months later, she presented with unilateral visual loss from an optic neuropathy secondary to suprasellar exterior inflammatory process, an infrequently reported finding in AFS (6). Imaging is exceptionally helpful in guiding appropriate therapy, because glucocorticoids treatment without surgery could have resulted in permanent vision loss (12).

In case 2, our patient cleaned hurricane-damaged hotel rooms in the Cayman Islands. Eighteen months later she began having severe headaches, and in another five months she presented with a right cavernous sinus syndrome. This was confirmed on MRI and treatment was made early enough to prevent any further clinical deterioration. Orbital apex syndrome is a very uncommon manifestation of AFS, occurring in only 2% of AFS patients with orbital symptoms (9).

In Case 3, the patient had a prolonged stay in Louisiana in the aftermath of Hurricane Katrina. Nine months after starting his job with FEMA he began experiencing right temporal headaches followed by right-sided blindness, ptosis, and ophthalmoplegia. MRI revealed enhancement of the right orbital apex, which led to a transphenoidal biopsy revealing fungal hyphae. The patient's ophthalmoplegia resolved with treatment but there was no improvement in vision.

What factors might facilitate fungal disease occurring in the post-hurricane environment? Soil-dwelling fungi that induce fungal disease and AFS have been shown to cause more disease in wetter and warmer months. It is known that a water-rich environment is conducive to the growth of mold species (8). Hurricanes can create such an environment due to flooding and water damage. In the aftermath of Hurricane Katrina, aspergillus species were found to be more concentrated than normal in both general urban air quality studies and tests of the air in homes undergoing renovation (20,21). Six months after Hurricane Katrina, a direct correlation was demonstrated between exposure to water-damaged homes and respiratory symptoms (22).

Although it is impossible to assign causality, our three patients may all have developed fungal disease secondary to living and working in areas recently affected by inclement weather and flooding. They developed signs and symptoms over a three to eighteen month period, consistent with the slow, indolent course of AFS and fungal infection.

In conclusion, fungal disease including AFS is an important diagnostic consideration in the otherwise healthy patient presenting with symptoms including visual loss, diplopia, facial numbness and unilateral temporal headache. A potential association between tropical storm exposure and fungal disease including AFS requires further investigation.

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Figure 1.

Case 1. Coronal MRI shows a sphenoid sinus mass extending superiorly displacing the pituitary gland and displacing the chiasm (arrows) upward. The mass shows contrast enhancement on T1 scan (A) and low signal on T2 image (B).

Figure 2.

Case 1. Histopathology of sphenoid sinus mass. A. eosinophils mixed with mucus and necrotic material. (hematoxylin and eosin $\times 40$). B. septated fungal hyphae (Gomori methenamine silver $\times 40$).

Figure 3.
Case 2. Initial contrast-enhanced T1 axial (A) and coronal (B) MRI with fat suppression reveals left sphenoid and posterior ethmoid sinus disease with left orbital apex involvement.

Figure 4.
Case 3. Contrast-enhanced T1 axial (A) and coronal (B) MRI with fat suppression demonstrates an area of enhancement involving the area of the right orbital apex and cavernous sinus (arrows).