

Catastrophic Allergic Fungal Sinusitis: A Report of Two Cases

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Background: Allergic fungal rhinosinusitis (AFRS) is a common condition in which sinusitis develops as an IgE-mediated response to common sinonasal fungal organisms. If that response leads to blockage of sinus ostia, bone expansion and erosion by expansive cysts containing dense inspissated debris may occur with the potential for critical neurovascular compression including damage to the anterior visual pathway.

Methods: Review of clinical and imaging features of 2 patients who sustained catastrophic clinical outcomes.

Results: The first patient had pansinusitis with massive mucocoele-like cysts expanding the sphenoid sinus and cranial base and causing compression of the anterior visual pathway that led to persistent severe vision loss despite extensive sinus surgery. The second patient developed sphenoethmoidal expansion with a marked inflammatory response and presumed conversion to invasive fungal sinusitis that caused anterior visual pathway vision loss, bilateral ocular motor palsies from extension into the cavernous sinuses, and death from a large middle cerebral artery stroke.

Conclusions: Although AFRS is most often benign and treatable, it may rarely produce catastrophic outcomes, especially if the sphenoid sinus is involved. Irreversible vision loss may occur from compression, and ocular motor palsies and death from conversion to invasive fungal disease. Close ophthalmologic and imaging monitoring is necessary in patients with expanded sinuses, and prophylactic sinus surgery may be indicated in certain cases.

Journal of Neuro-Ophthalmology 2019;00:1–7

doi: 10.1097/WNO.0000000000000833

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Allergic fungal rhinosinusitis (AFRS) is a form of IgE-mediated, eosinophil-predominant Type 1 hypersensitivity initiated by exposure of sinonasal mucosa to fungal glycoproteins and carbohydrate antigens (1). Occurring primarily in young immunocompetent patients with atopy, AFRS is not considered an infection of the sinonasal tract, but an exuberant humoral and cellular immune response to chronic infestation by the fungus. The paranasal sinuses display polyposis and are filled with a thick mucin, clusters of eosinophils, Charcot–Leyden crystals, sloughed epithelial cells, cellular debris, and rare fungal hyphae (1).

Classic manifestations of AFRS are protracted nasal congestion, thick and discolored nasal discharge, and facial pain. In some cases, sinus drainage can become obstructed, and mucocoele-like expansion may occur in the paranasal sinuses, resulting in dysfunction of the anterior visual pathway (2–8). The process is extradural, causing damage by compression, not by invasion. Treatment of AFRS consists of surgical debridement of the affected sinuses and corticosteroids without the use of antifungal agents, and results are almost universally favorable when intervention is performed promptly (2,5,6,9).

Invasive fungal rhinosinusitis (IFRS) is unlike AFRS in that fungal organisms transgress the paranasal sinus mucosa, bone, and dura to invade blood vessels, causing thrombosis and infarction (1,10,11). This invasive process, which typically occurs in immunocompromised patients, must be treated with aggressive and often deforming surgery to remove the infected tissue, supplemented with parenteral antifungal agents. Even such aggressive treatment may be unable to forestall blindness, stroke, and death.

We present 2 cases of AFRS in immunocompetent patients who sustained disastrous outcomes. One patient had persistent severe optic neuropathy from expansile cystic compression. The other patient died of stroke from occlusion of the cavernous carotid artery, perhaps owing to conversion to IFRS. These cases illustrate the consequences of delayed recognition and treatment of AFRS.



FIG. 1. Case 1. Axial CT of paranasal sinuses, performed 6 years before presentation with vision loss, shows complete opacification and mild expansion of the left ethmoid air cells. All paranasal sinuses display high density. CT, computed tomography.

CASE REPORTS

Case 1

A 23-year-old woman had a 10-year history of chronic nasal congestion and previous nasal polypectomy. There was no history of diabetes or other immune-compromising conditions. Serial computed tomography (CT) scans (Fig. 1) demonstrated pansinusitis with polyposis and cystic expansion of the frontal sinuses, cribriform and sphenoid walls. Despite a recommendation for follow-up, there was a gap in care. Toward the end of a pregnancy, she began to note progressive vision loss in the left eye. Three days after an uneventful delivery, she noted vision loss in the right eye as well.

Best-corrected visual acuities were 20/25 in the right eye and finger counting in the left eye. There were no signs of orbital congestion. The pupils were normal in size, but there was a left afferent pupil defect. Formal (Humphrey) visual field examination of the right eye disclosed a dense temporal hemianopia with a mean deviation of -19.33 dB

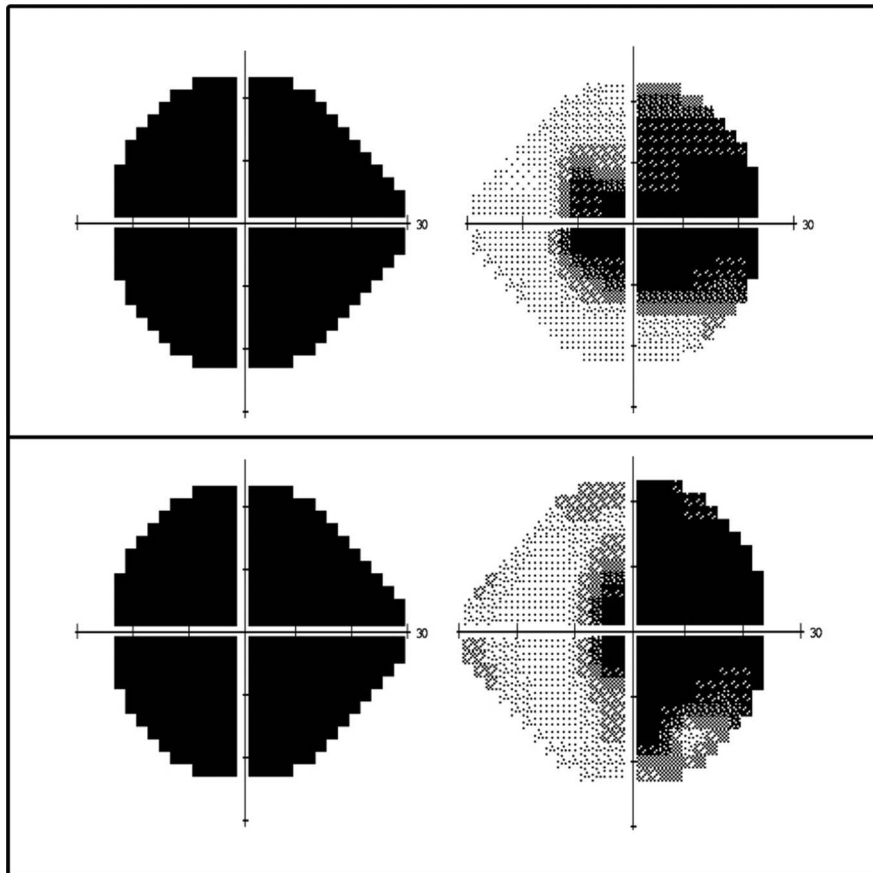


FIG. 2. Case 1. Top: Humphrey visual field 24-2 performed 2 days before sinus surgery shows complete extinction of the visual field in the left eye and a central scotoma with temporal field loss in the right eye. Bottom: Identical visual field protocol performed 2 months after sinus surgery shows minimal if any improvement relative to preoperative examination.



FIG. 3. Case 1. Coronal (A) and axial postcontrast computed tomography (CT) (B) performed 2 days before sinus surgery shows sphenoid sinus filled with high-density material. Axial bone window CT (C) discloses erosion of sphenoid sinus walls.

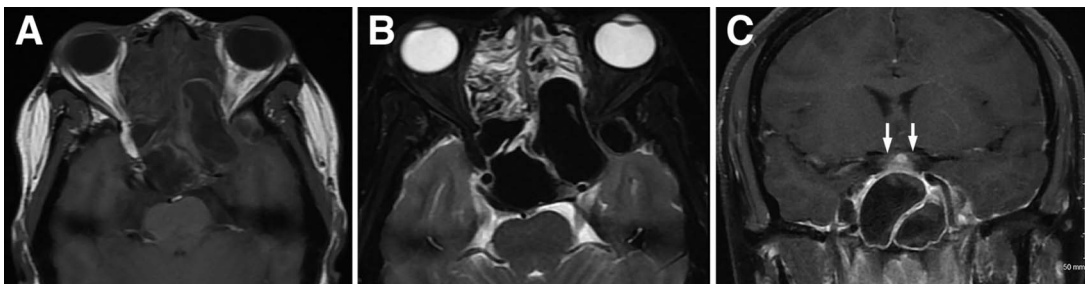


FIG. 4. Case 1. Axial precontrast T1-weighted (A), T2-weighted (B), and coronal postcontrast (C) MRI performed 2 days before sinus surgery confirms expansion of multiple paranasal sinuses exhibiting hypointense signal due to highly proteinaceous contents. Coronal image (C) shows expanded sphenoid sinus with displacement of the pituitary gland, optic chiasm (arrows), and cavernous sinuses.

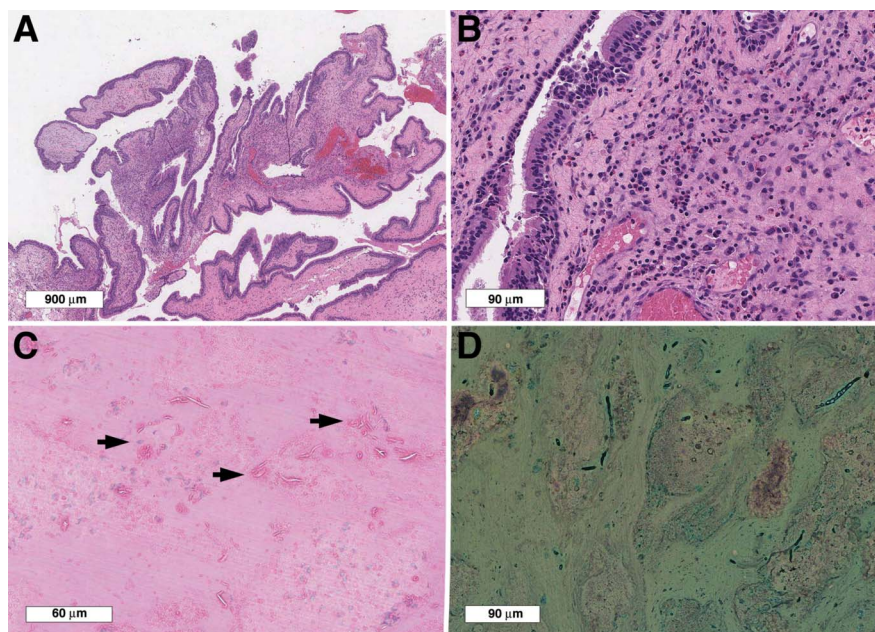


FIG. 5. Case 1. Surgical pathology. A. Hematoxylin and eosin staining shows multiple nasal polyps with edema and infiltration of chronic inflammation. B. Higher magnification demonstrates numerous eosinophils and plasma cells. C. Medium power of mucocoele with refringent hyphal organisms (arrows). D. Gomori methenamine silver staining highlights the fragmented branched hyphal fungal organisms. These abnormalities are consistent with a diagnosis of allergic fungal sinusitis.



FIG. 6. Case 1. Postoperative coronal reformatted CT shows mild improvement in the mass effect on the optic chiasm as compared to the preoperative MRI (Fig. 4C). CT, computed tomography.

and, in the left eye, a diffuse depression with a mean deviation of -34.66 dB (Fig. 2). The eyes displayed normal movements and alignment. Ophthalmoscopy disclosed mild optic disc pallor in both eyes.

CT showed expansion of all paranasal sinuses with marked thinning and remodeling of the sinus walls, including the medial (Fig. 3). Brain MRI showed peripherally enhancing polyps and expansile cysts containing debris that was hypointense on T1 and T2, together with superior displacement of the optic chiasm (Fig. 4).

She underwent prompt bilateral endoscopic ethmoidectomy, sphenoidotomy, maxillary antrostomies, and frontal sinusotomies, with removal of polyps and thick inspissated allergic fungal debris and decompression of the optic nerves. The surgical specimen showed several nasal polyps with edema,

chronic inflammation, including eosinophils and plasma cells and large mucocoeles with rare septate hyphae (Fig. 5). Postoperative CT confirmed slight decompression of the optic chiasm (Fig. 6). The patient was treated with oral corticosteroid.

Follow-up neuro-ophthalmologic examination 2 months later showed no improvement in visual function in either eye (Fig. 2). Both optic discs were profoundly pale.

Case 2

A 35-year-old man with a long history of allergic rhinitis gradually developed headaches and right-sided proptosis. He had no history of diabetes or other immune-compromising conditions. Brain CT and MRI reportedly showed expansion of multiple sinuses filled with hyperdense material. For a presumed diagnosis of AFRS, he underwent endoscopic bilateral ethmoidectomy, maxillary antrostomies, and sphenoidotomies with polypectomy and removal of debris at an outside hospital. The surgical specimen reportedly showed rare *Aspergillus* species.

Three weeks later, he acutely developed a dramatic headache with dysarthria and left upper and lower extremity weakness. CT (Fig. 7A) and MRI (Fig. 7B) showed expansion of both ethmoid sinuses, including bilateral Onodi cells (ethmoid cells extending over the sphenoid sinus), thickening and enhancement of the right cavernous sinus, and no flow void in the cavernous segment of right internal carotid artery. CT angiography (Fig. 8) showed no flow in the right cavernous carotid artery and minimal flow through the right middle cerebral artery, which was fed by the right posterior cerebral artery. MRI (Fig. 9) showed restricted diffusion in the domain of the right middle cerebral artery, confirming a recent right hemisphere ischemic stroke. The imaging could not clearly distinguish between compressive and arteritic occlusion of the carotid artery. Therefore, he was treated with a combination of voriconazole, dexamethasone, and antibiotics and transferred to our hospital for further management.

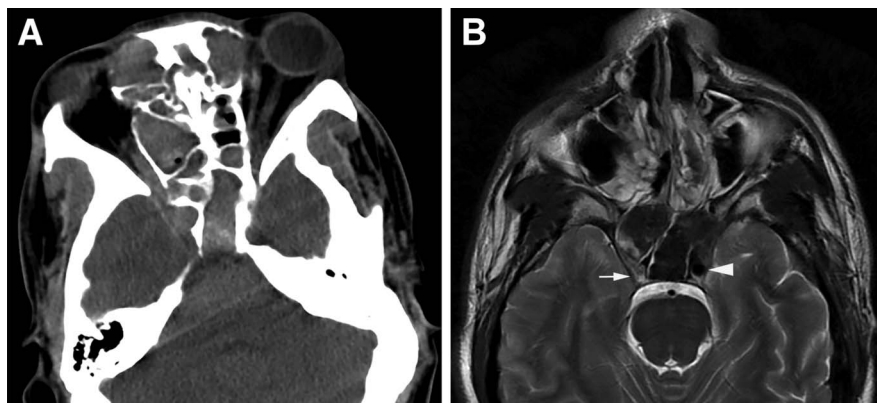


FIG. 7. Case 2. **A.** Axial CT performed after first sinus surgery and before second sinus surgery shows residual expansion of paranasal sinuses filled with high-density material. **B.** Axial T2-weighted MRI shows markedly hypointense signal within the sinuses. Loss of flow void of right internal carotid artery is also noted (arrow), compared with normal carotid artery on opposite side (arrowhead). CT, computed tomography.



FIG. 8. Case 2. **A.** Axial arterial phase computed tomography (CT) angiogram shows absent contrast opacification within the cavernous segment of the right carotid artery (arrow). **B.** Coronal reformatted image of arterial phase CT angiogram again shows absent opacification of the right intracavernous carotid artery, together with reduced opacification of the middle cerebral artery (arrow), which was supplied by the posterior communicating artery.

Neuro-ophthalmologic examination disclosed visual acuities of hand movements in the right eye, 20/70 in the left eye. He was too drowsy for a reliable confrontation visual field test. There was partial right upper lid ptosis. Both eyes were proptotic. There was markedly limited adduction, supraduction, and infraduction of the right eye and slightly reduced ductions in all directions of the left eye. Pupils measured 2 mm in dim illumination in the right eye, 3 mm in the left eye, neither constricting fully to direct light, and there was an afferent pupil defect in the right eye. Ophthalmoscopy through clear media disclosed elevation of both optic discs with obscuration of the peripapillary nerve fiber layer and scattered peripapillary hemorrhages, features considered to indicate papilledema. These abnormalities were interpreted as consistent with dysfunction of

the anterior visual pathway on both sides, ocular motor nerves in the right (and possibly left) cavernous sinus, and increased intracranial pressure. The proptosis was attributed to orbitocavernous venous congestion and expansion of the ethmoid bulla cells bilaterally.

Two days later, the patient underwent endoscopic debridement and an open subcranial procedure to debride the anterior cranial base. The surgical specimen (Fig. 10) disclosed abundant necrosis and sparse fungal hyphae, consistent with aspergillosis. Gomori methenamine silver stain disclosed numerous fungal hyphae. Tissue Gram stain revealed the presence of rare clusters of Gram-positive cocci. No angioinvasion was identified.

Several days later, the patient suffered a generalized seizure and a decline in consciousness. Brain CT disclosed enlargement of the ischemic brain edema with subfalcine and uncal brain herniation, and so he underwent a decompressive right hemisectomy (Fig. 11). Despite intensive medical management, intracranial pressure remained high. When neurologic function continued to decline, the family withdrew care and the patient died. An autopsy was not performed at the family's request.

DISCUSSION

We have described 2 patients with AFRS who sustained catastrophic outcomes—irreversible optic neuropathy in Case 1 and optic neuropathy, ocular motor palsies, and death in Case 2. In Case 1, the mechanism was believed to be cystic expansion of the sphenoid sinus with compression of the optic nerves and optic chiasm. In Case 2, cystic compression of the optic nerves and optic chiasm caused

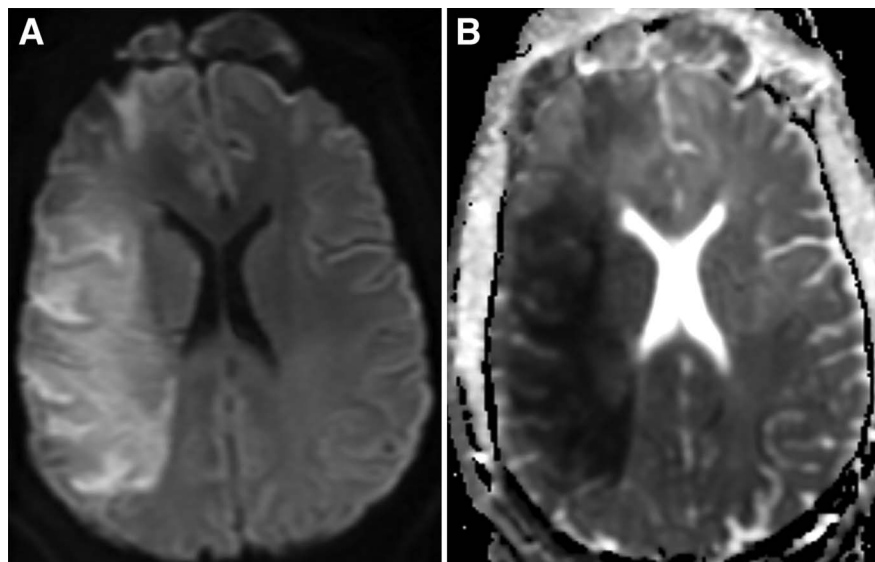


FIG. 9. Case 2. **A.** Axial diffusion-weighted MRI shows large area of restricted diffusion in the right middle cerebral artery distribution. **B.** Apparent diffusion coefficient MRI shows hypointense signal in the corresponding area, suggestive of acute right middle cerebral artery territory infarction.

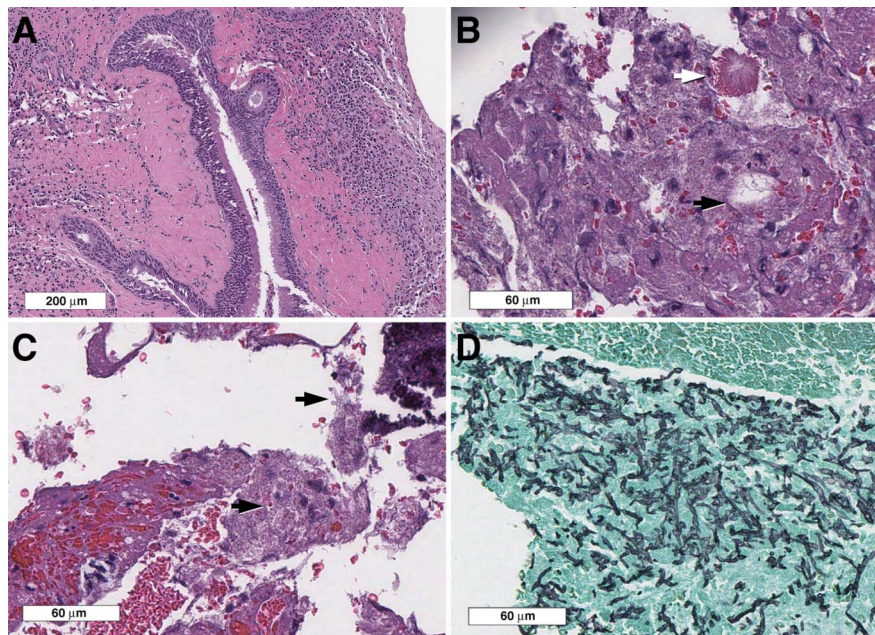


FIG. 10. Case 2. Surgical pathology. **A.** Hematoxylin and eosin (H&E) stain shows chronic sinusitis and fibrosis. **B.** Abundant necrosis with hyphal organisms (black arrow) and bacterial colonies (white arrow). **C.** Higher magnification shows translucent branching and septated hyphal fungal organisms (arrows). **D.** Gomori methenamine silver staining highlights plentiful *Aspergillus* hyphal forms not so evident in the necrotic specimen stained with H&E (**B**).

profound vision loss; compression or fungal invasion of the cavernous sinuses presumably accounted for occlusion of the right cavernous carotid artery and subsequent right middle cerebral artery territory infarction.

Compression of the anterior visual pathway in AFRS by ethmoid, frontal, and sphenoid sinuses has been well documented (2–5,7,8,12). An ethmoid mucocoele often appears to be the site of damage to the ipsilateral optic nerve in the orbit, (6,13) but an additional, and possibly more important, site of damage may be the optic canal when the lateral recess of an expanded sphenoid sinus bends the medial wall of the canal inward, as probably occurred in our Case 1. Compression of the optic nerve can also occur intracranially, where the optic nerve meets the optic chiasm. Such a site of compression can be inferred when the visual field loss displays a junctional pattern, as it did in our Case 1. Compression can also reach into the cavernous sinus to cause ocular motor palsies and even carotid artery occlusion, (2) as occurred in our Case 2.

Anterior visual pathway compression by AFRS involving the sphenoid sinus has been reported in 28 cases (2–4,7,8). In these cases, preoperative and postoperative imaging and visual fields have not generally been well documented, and the diagnosis of AFRS has not always been explicitly supported by surgical pathology (2–4,7,8). When surgery has followed within 30 days of discovery of vision loss, visual improvement has generally occurred. But only a single patient has sustained improved vision when surgery has occurred a month or more after discovery of vision loss (2–4,7).



FIG. 11. Case 2. Axial noncontrast CT, performed after patient developed marked left hemiplegia and reduced consciousness, shows marked hypodensity affecting the right cerebral hemisphere with loss of gray-white matter demarcation. There is marked hemispheric displacement despite right decompressive hemicraniectomy. CT, computed tomography.

There have been no reports of death from AFRS alone. Moreover, occlusion of the cavernous carotid artery and subsequent middle cerebral artery stroke, as occurred in our Case 2, has not been described in purely compressive AFRS. Thus, we presume that our Case 2 suffered conversion from AFRS to IFRS, a phenomenon that has been reported in immunocompetent patients (10). In that report, the authors described 3 of their own cases and reviewed 26 previously reported cases in which the invasive nature of fungal infection was established by histopathological examination of surgical specimens. Nine patients died of fungal disease, all of whom had involvement of the sphenoid sinus. When the sphenoid sinus was not involved, death did not occur. The authors did not provide information about imaging or vision status in those cases, nor was there mention of the cause of death. Duration of symptoms was a key prognostic factor, with doubling in the mortality rate when symptoms were present for more than 6 months. In our Case 2, the surgical specimen was necrotic, but fungal elements were profuse enough to sustain a presumption of conversion to invasive fungal sinusitis.

The lesson of these cases is that sphenoid sinus expansion in AFRS may be an ominous sign mandating close monitoring and even periodic imaging of patients with such imaging abnormalities. Prophylactic sinus surgery might be indicated even before vision begins to fail.

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REFERENCES

1. **Montone KT**. Pathology of fungal rhinosinusitis: a review. *Head Neck Pathol*. 2016;10:40–46.
2. **Thakar A**, Lal P, Dhiwakar M, Bahadur S. Optic nerve compression in allergic fungal sinusitis. *J Laryngol Otol*. 2011;125:381–385.
3. **Chen L**, Jiang L, Yang B, Subramanian PS. Clinical features of visual disturbances secondary to isolated sphenoid sinus inflammatory diseases. *BMC Ophthalmol*. 2017;17:237.
4. **Gupta AK**, Bansal S, Gupta A, Mathur N. Visual loss in the setting of allergic fungal sinusitis: pathophysiology and outcome. *J Laryngol Otol*. 2007;121:1055–1059.
5. **Alaraj AM**, Al-Faky YH, Alsuhailani AH. Ophthalmic manifestations of allergic fungal sinusitis. *Ophthalm Plast Reconstr Surg*. 2018;34:463–466.
6. **Tong J**, Jefferson N, Chaganti J, Fraser CL. Compressive optic neuropathy from allergic fungal sinusitis. *Neuroophthalmology*. 2015;39:236–239.
7. **Herrmann BW**, White FV, Forsen JW. Visual loss in a child due to allergic fungal sinusitis of the sphenoid. *Otolaryngol Head Neck Surg*. 2006;135:328–329.
8. **Brown P**, Demaerel P, McNaught A, Revesz T, Graham E, Kendall BE, Plant G. Neuro-ophthalmological presentation of non-invasive *Aspergillus* sinus disease in the non-immunocompromised host. *J Neurol Neurosurg Psychiatry*. 1994;57:234–237.
9. **Sacks PL IV**, Harvey RJ, Rimmer J, Gallagher RM, Sacks R. Antifungal therapy in the treatment of chronic rhinosinusitis: a meta-analysis. *Am J Rhinol Allergy*. 2012;26:141–147.
10. **Clancy CJ**, Nguyen MH. Invasive sinus aspergillosis in apparently immunocompetent hosts. *J Infect*. 1998;37:229–240.
11. **Kalin-Hajdu E**, Hirabayashi KE, Vagefi MR, Kersten RC. Invasive fungal sinusitis: treatment of the orbit. *Curr Opin Ophthalmol*. 2017;28:522–533.
12. **Marple BF**, Gibbs SR, Newcomer MT, Mabry RL. Allergic fungal sinusitis-induced visual loss. *Am J Rhinol*. 1999;13:191–195.
13. **Miller NR**, Newman NJ, Biouesse V, Kerrison JB. Walsh and Hoyt's Clinical Neuro-Ophthalmology. 6th edition. Philadelphia, PA: Lippincott Williams and Wilkins; 2005:2778–2883.