

Allergic fungal sinusitis secondary to *Acremonium* species causing unilateral visual loss

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A wide range of fungi have been associated with Allergic Fungal Sinusitis (AFS) or Eosinophilic fungal rhinosinusitis (EFRS) as it is known in some institutions. To our knowledge, this is the first reported case of aggressive, invasive AFS due to *Acremonium* species occurring in an immunocompetent patient and leading to unilateral visual loss. Literature on AFS is reviewed.

Key words: Eosinophilic fungal rhinosinusitis, Allergic fungal sinusitis, *Acremonium* species, visual loss.

Introduction

Allergic fungal sinusitis (AFS) or Eosinophilic fungal rhinosinusitis (EFRS) as it is known in some institutions, was first appreciated by Millar et al in 1981 due to its histological similarity to Allergic bronchopulmonary aspergillosis (ABPA)¹. Criteria for the diagnosis of AFS were proposed by Bent and Kuhn² in 1994. They found five characteristics in all 15 patients they reported: These were;

1. Evidence of type 1 hypersensitivity.
2. Nasal polyps.
3. Characteristic CT scan findings.
4. Eosinophilic mucus.
5. Demonstration of fungi.

There are six associated features. They include:

1. Asthma.
2. Unilateral predominance.
3. Radiographic bone erosion.
4. Fungal culture.
5. Charcot-Leyden crystals and serum eosinophilia.

Controversy exists as to whether this is an IgE mediated disease or not. Because the presence of eosinophils in the allergic mucin, not a type 1 hypersensitivity, is probably the common denominator in the pathophysiology of AFS, the Mayo Clinic group proposed a change in the name from Allergic fungal sinusitis to Eosinophilic fungal rhinosinusitis^{3,4}.

A wide range of fungi have been shown to be associated with AFS. These include *Alternaria*, *Aspergillus* sp. and various dematiaceous fungi such as *Bipolaris* and *Culvulari*⁵. Visual loss in

AFS is uncommon⁶. To our knowledge, we report the first case of AFS caused by *Acremonium* species leading to a unilateral visual loss and we review the literature on AFS.

Case report

A 48 year old immunocompetent lady presented to her general practitioner (GP) with a three week history of unilateral right-sided nasal obstruction and headaches localized to the right frontal and occipital areas. The GP requested plain film x-rays which showed opacification of all sinuses on the right. She was commenced on Co-Amoxiclav and nasal decongestant drops, but a week later suffered sudden blindness in the right eye and an aggravation of symptoms of nasal obstruction and headaches. After urgent referral to an otolaryngologist, a CT scan (*figure 1*) of the sinuses was performed. This showed opacification of the right frontal, ethmoid and both sphenoid sinuses. Thinning of the right lamina papyracea and widening of right infundibulum was present. MRI showed (*figure 2a & b*) a hypo-intense mass extending into the right anterior clinoid process and compressing the optic nerve. There was no intracranial extension and the cavernous sinuses appeared normal. Both CT and MRI had features consistent with fungal sinusitis.

The patient went for an endoscopic examination under anaesthesia and biopsy. PAS stains showed thin fungal pseudohyphae and the final culture grew *Acremonium* species. She was started on intravenous Amphotericin B and a week later on corticosteroids. The reason for the delay was the invasive nature of the disease with fulminant fungal sinusitis not completely

excluded. A complete sphenoidectomy was performed after the initial culture results and complete macroscopic clearance was obtained. She continued with intravenous Amphotericin-B for another week and was discharged on oral Fluconazole and systemic corticosteroids. She has since regained full peripheral vision.

Discussion:

Fungal sinusitis in immunocompetent patients is not a rare condition^{7,8}. Five basic diagnostic categories of fungal rhinosinusitis disorders are recognised. Three types of fungal rhinosinusitis are true tissue-invasive infectious diseases: acute necrotising fungal rhinosinusitis, chronic invasive fungal rhinosinusitis, and granulomatous invasive (indolent) fungal rhinosinusitis. The two non-invasive fungal rhinosinusitis disorders are fungal ball (sinus mycetoma) and allergic fungal sinusitis (AFS). AFS, indolent and fungal ball are usually found in immunocompetent individuals^{7,9}. His classification does not take into account the acute fulminant type which has been reported by other authors^{10,11}

The patient was classified as allergic fungal sinusitis based on clinical features, immunocompetence, radiological features, mycologic findings and presence of macroscopic allergic mucin. Although AFS has been described since the early 1980s, there are still no established criteria for diagnosis and management. Most authors take into account presence of atopy, characteristic radiographic findings, positive fungal culture and stain, in addition to presence of allergic mucin^{12, 13}. Currently it appears that presence of more than one of these features may satisfy the diagnosis of AFS and not just the presence of one factor.

Controversy surrounds the aetiology and pathogenesis of fungal sinusitis. Non-invasive fungal sinusitis usually occurs in individuals with a poorly draining maxillary sinus. Hamilos et al¹⁴ postulates six steps in the pathogenesis of EFRS which also emphasise the role of the Eosinophil. 1) The host becomes sensitised to fungal antigens. 2) fungal spores become trapped in nasal or sinus mucus and germinate into viable hyphae. 3) The large local fungal load elicits a localised immune response; this may explain disease localisation. 4) Eosinophils attack fungal hyphae and degranulate. 5) the

eosinophilic inflammatory process releases multiple cytokines and growth factors, which may contribute to airway remodelling and nasal polyp formation. 6) Damage occurs to mucosa, facilitating bacterial penetration of the mucosa that leads to bacterial infection and further perpetuates the inflammatory process.

A wide range of fungi have been shown to be associated with AFS. *Aspergillus* is the most prevalent pathogen in both invasive and non-invasive fungal sinusitis^{8,12}. Other causative organisms include *Alternaria* species, *Curvularia lunata*, *Candida albicans*, *Bipolaris* species¹³. This is the first case to our knowledge of AFS being caused by *Acremonium* species and leading to visual loss. *Acremonium* species are environmentally widespread as saprobes in soil and as pathogens of plants and insects and rarely are opportunistic pathogens of humans and other mammals. Although definitive identification of these species requires culture, they often can be identified provisionally in tissue sections by a combination of histologic features, including hyaline septate hyphae and characteristic reproductive structures known as phialides and phialoconidia. *Acremonium* species have been associated with diseases like keratomycosis and mycetoma

Involvement of the orbit in fungal sinusitis forms a major component of the symptomatology of the patients. Therefore most patients do present to the Ophthalmologist first and then referred to the Otolaryngologist. Carter and associates looked at the ophthalmic manifestations of allergic fungal sinusitis and all of their six patients had proptosis. One patient had symptomatic diplopia and the other had visual loss¹⁵. The index patient had complete visual loss in the right eye and this is the most devastating ophthalmic symptom although it does not appear to be the common presenting ophthalmic symptom.

Three modes of treatment are generally employed in managing AFS and these are surgery, antifungals and corticosteroids. Kuhn et al³ highlights the role of each mode of treatment and he also discusses the role of immunotherapy which though it has been described as effective means of controlling AFS, can actually worsen the patients' symptoms if therapy is started before a 'significant antigenic' load is removed. Surgery is the mainstay mode of treatment coupled with corticosteroids especially where

there is visual loss. Antifungals are naturally used where there is demonstration of fungi in the specimens but their role is unclear.

Conclusion

This is to our knowledge, the first case of invasive AFS due to *Acremonium* species leading to unilateral visual loss. Knowledge of AFS continues to evolve and an understanding on the pathogenesis of this mysterious disease will in future help us diagnose it more efficiently and of course manage it properly. At the moment a combination of vigilance, radiological and histological methods are quite helpful by way of diagnosis and the treatment methods described above together with close follow up are essential in managing the condition.

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