



## Allergic Fungal Sinusitis

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### Introduction

Allergic fungal sinusitis is a benign noninvasive sinus disease, believed to be an allergic reaction to aerosolized environmental fungi. It has been almost three decades when in 1976 Safirstein noted that the combination of polyposis, crust formation and sinus cultures yielding aspergillus was similar to the constellation of findings observed in allergic bronchopulmonary aspergillosis(1). Subsequently allergic fungal sinusitis was initially described by Millar in 1981(2). Over the past two decades allergic fungal sinusitis has been increasingly identified. It is probably the most frequently occurring fungal rhinosinusitis disorder(3). Continuing research has high lightened some aspects of the disease and has led to an improved understanding of allergic fungal sinusitis and its treatment. In this article, we review current data regarding the etiology, pathophysiology, clinical presentation, diagnosis and roles of various surgical and nonsurgical therapies in the treatment of allergic fungal sinusitis.

### Incidence

The incidence of allergic fungal sinusitis in cases of chronic rhinosinusitis treated surgically has been approximately 6 to 7%.(4) The incidence of aspirin sensitivity has been demonstrated to be 27% in patients with allergic fungal sinusitis(4). Asthma has been associated in 65% of the patients.(5) Incidence of allergic fungal sinusitis is high in temperate regions with relatively high humidity. Mean age according to large series is 23 - 42 years(4,6).

### Etiology and Pathophysiology

Allergic fungal sinusitis is thought to be an allergic reaction to fungi. The causative fungi usually are dematiaceous. Among these *Bipolaris spicifera* has been

reported to be the commonest(7). Other genera include *Curvularia*, *Exserohilum*, *Alternaria*, *Drechslera*, *Helminthosporium*, *Fusarium* and *Aspergillus*. Both type I and type III hypersensitivity reactions (Gell and Coombs classification) have been postulated to play role in the development of allergic fungal sinusitis. Once atopic host is exposed to fungi via normal nasal respiration, it initiates antigenic stimulus. The initial inflammatory response ensues as a result of both Gell and Coombs type I (IgE-mediated) and type III (immune complex-mediated) hypersensitivity reactions. The resulting tissue edema and obstruction of the sinus ostia lead to stasis of secretions within the sinuses. This creates an ideal environment for further proliferation of the fungus, thus increasing the antigenic exposure(8). It may expand to involve other sinuses causing bony expansion and erosion(9).

### Clinical Features

The clinical features of the patients with allergic fungal sinusitis may be similar to those of chronic sinusitis. There may be nasal blockage, purulent rhinorrhoea, postnasal discharge or headache. Incidence of nasal polyposis has been reported to be almost 100%(7). Facial dysmorphism may be present in the form of proptosis, telecanthus and malar flattening. Based on the clinical findings in 16 patients, Bent and Kuhn proposed 5 criteria for the diagnosis of allergic fungal sinusitis (10). (1) type I hypersensitivity (atopy) diagnosed by history, positive skin test, or serology (2) nasal polyposis (3) characteristic CT scan findings (4) positive fungal smear and (5) allergic mucin. These are now referred to as major criteria. The other six minor criteria are (1) asthma, (2) unilateral predominance, (3) radiographic bone erosion,

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(4) fungal culture, (5) charcot leyden crystals and (6) serum eosinophilia. These are probably the most widely accepted criteria for diagnosis of allergic fungal sinusitis. An atopic patient who lacks nasal polyps, but has characteristic CT scan findings or a positive fungal culture is still diagnosed to have allergic fungal sinusitis(11).

#### **Laboratory Diagnosis**

The suggested work up for a patient with allergic fungal sinusitis includes total eosinophil count, total serum IgE, antigen specific IgE for both fungal and other inhalants, fungal antigen specific IgG, precipitating antibodies, microscopic evaluation and fungal culture of mucin evacuated intra operatively(11).

Previously the diagnosis of allergic fungal sinusitis could not be confirmed in a number of patients who had clinical and radiological evidence of allergic fungal sinusitis. It was probably because the methods used to collect mucus were inadequate to identify the fungi. Ponikau *et al* (12) described the principle of maximum mucus preservation which enabled the pathologist to find allergic mucin and fungal elements within the mucus. As fungi colonize within the nasal mucus, the increased amount of mucus collected for culture and histologic examination leads to higher chances of isolation of the pathogen. Multiple sections from different areas of the nose and paranasal cavities should be prepared as the fungi may be found scattered. The sections must be routinely stained with Gomori methenamine silver to identify the fungi and with hematoxylin and eosin to identify the eosinophils in the mucus. Fontana Masson stain can help in distinguishing dematiaceous fungi from other septate fungi(13).

#### **Imaging studies**

Allergic fungal sinusitis has a highly specific radiographic appearance based on CT scan and MRI(9). CT scan shows central area of hyperattenuation in the sinus cavity which represents the allergic mucin. In MRI, this area is seen as the area of hypointensity on T1 weighted images and signal void on T2 weighted images. The triad of nasal polyps, characteristic CT scan findings and specific immunoglobulin E titers has been shown to have a sensitivity of 70% and a specificity of 100% for

the preoperative diagnosis of allergic fungal sinusitis(14). The expanding allergic mucin may cause thinning and erosion of the bone. Orbital and intra cranial spread may also be seen. Almost one half of the patients with allergic fungal sinusitis have unilateral involvement(7).

#### **Treatment**

Previously an aggressive surgical approach was adopted because of a perceived risk of fungal invasion. This led to open antrostomies with radical removal of mucosa, intranasal sphenoethmoidectomies and Lynch frontoethmoidectomies. Despite such aggressive therapy, recidivism remained high and most patients required multiple surgical procedures. As it is widely accepted that immunological hypersensitivity plays a major role in allergic fungal sinusitis, there have been changes in its management.

There are various options in the treatment of allergic fungal sinusitis. It includes surgical as well as medical modalities. If we look back in surgical treatment for allergic fungal sinusitis, radical surgery has given way to more conservative tissue-sparing approaches. Endoscopic sinus surgery has been shown to be preferable to open sinus techniques.(15) Medical therapy includes corticosteroids, antifungal agents and immunotherapy. For best results, all these modalities should be given in combination. The various treatment options are as follows.

**Surgical Treatment:** The findings in allergic fungal sinusitis can vary from a minimal edema to severe polyposis and bony erosions. These can lead to intra operative disorientation and increased chances of complications. Therefore certain authors recommend preoperative steroids with antibiotics to reduce the edema and chances of postoperative bacterial sinusitis respectively.(16,17)

Nasal polyposis occasionally can facilitate the surgery. The expansile behavior of slowly growing nasal polyps and accumulating allergic fungal mucin expand the involved paranasal sinuses and the surgical route to the involved sinuses. Enlargement of the nasal cavity, middle meatus and frontal recess increases the accessibility.

One should try to remove all the allergic mucin and fungal debris and try to give permanent drainage and



ventilation to affected sinuses. The allergic mucin should be sent for histopathological examination to confirm the diagnosis of allergic fungal sinusitis. The fungal elements and mucin can be sent for culture to identify the fungus responsible for the disease. Examination of allergic mucin shows eosinophils, charcot leyden crystals along with fungal hyphae(18).

Endoscopic surgery for allergic fungal sinusitis may be associated with more complications when compared to endoscopic sinus surgery for other pathologies. Extensive disease may cause spatial disorientation. There may be areas of bony dehiscence, which may confuse or distort anatomic boundaries, causing increased risk of orbital and intracranial complications. It includes penetration of dura or periorbita resulting in diplopia, blindness, intracranial hemorrhage or cerebrospinal fluid rhinorrhoea(16). Occasional cases of fungal invasion into adjacent tissues have also been described(19).

Follow up is very important postoperatively as allergic fungal sinusitis is known for recurrence. Recurrence can be in the form of mucosal edema, polyps, scarring, allergic mucin, or fungal debris. Kupferberg *etal* (20) has refined endoscopic follow up which are as follows.

**Stage 0:** No mucosal edema or allergic mucin.

**Stage I:** Mucosal edema with or without allergic mucin.

**Stage II:** Polypoid edema with or without allergic mucin.

**Stage III:** Sinus polyps with fungal debris or allergic mucin.

Therefore use of steroids, antifungals and immunotherapy has been described in post operative period. Total serum IgE levels can be followed postoperatively as they can be prognostic for recurrent disease.

**Systemic steroids:** The potent anti-inflammatory and immunomodulatory effects of corticosteroids appear to control recurrence of disease in postoperative period. But there is no uniformity in optimal dosing regimen and length of therapy. Kuhn and Javer(21) recommend oral prednisolone starting with 0.4mg/kg body weight postoperatively and slowly tapering it to 0.2 mg/kg body weight. After maintaining normal mucosa for four months period, the dose is reduced to 0.1 mg/kg body weight for another two months and stopped. Major side effects of

systemic steroids include growth retardation, diabetes mellitus, hypertension, psychotropic effects, gastrointestinal side effects, cataracts, glaucoma, osteoporosis, and aseptic necrosis of the femoral head. Topical steroid preparations can also be used as they have fewer adverse effects than systemic corticosteroids.

**Antifungal agents:** Antifungal agents have shown mixed results in the treatment of allergic fungal sinusitis. A study by Kuhn and colleagues showed amphotericin B and ketoconazole to be most effective agents in vitro(22). Supportive data regarding the usage of these agents are pending. Fluconazole nasal spray has also been used with encouraging results(23).

**Immunotherapy:** Immunotherapy is gaining an important role in treating allergic fungal sinusitis. Previously it was contraindicated because it was thought that antigens administered could provoke a Gel and Coomb type III reaction worsening the patient's condition. Recently it was shown that surgery is able to remove the inciting fungal load from the paranasal sinuses. Therefore immunotherapy might achieve sufficient immunomodulation to benefit the patient(24). A study conducted by Mabry et al showed immunotherapy can reduce the reliance on the systemic and topical steroids(25). Another study conducted by them showed no recurrence in follow-up period of 7 to 17 months(26). Although initial work suggests that a role may exist for immunotherapy in the overall treatment strategy for allergic fungal sinusitis additional studies are necessary to support it.

### Conclusion

Controversy still exists regarding the exact criteria for diagnosis and the exact regimen for treatment. Recent evidence supports the theory that allergic fungal sinusitis represents an immunologic rather than infectious disease process. An improved understanding of this underlying disease process has led certain changes in treatment concepts. Medical therapy has begun to shift from an emphasis on systemic antifungal therapy to various forms of topical treatment and immunomodulation. Likewise, surgical treatment of allergic fungal sinusitis has shifted from radical to a more conservative but complete, usually endoscopic approach. Although important, surgery alone



does not lead to a long-term disease free state. At the present time, it is not possible to predict recurrence of this disease(27). A comprehensive management plan incorporating medical, surgical and immunologic care remains the most likely means of providing long-term disease control for allergic fungal sinusitis.

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