

# Allergic Fungal Rhinosinusitis

**Paul Samuel**

a. Cosmopolitan Hospital, Thiruvananthapuram\*

## ABSTRACT

Published on 27<sup>th</sup> September 2011

Allergic fungal sinusitis is a benign non-invasive sinus disease, believed to be an allergic reaction to aerosolized environmental fungi mainly of dematiaceous species. It occurs mainly in immunocompetent persons in contrast to other invasive fungal diseases which occur chiefly in immunocompromised patients. It is a cause of recurrent or refractory sinusitis in immunocompetent patients. This entity is probably under diagnosed and should be considered in patients with chronic, intractable sinusitis if there is a history of atopy or asthma. When fungal elements are detected by histopathology or culture from sinus material, AFRS must be differentiated from invasive disease, as treatment and prognosis are radically different.

It is widely accepted that immunological hypersensitivity plays a major role in allergic fungal sinusitis. This has necessitated changes in management methods. 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. Medical therapy includes corticosteroids, antifungal agents and immunotherapy. For best results, all these modalities should be given in combination.

Follow up is very important postoperatively as allergic fungal sinusitis is known for recurrence. Rate of recurrence is high despite of complete surgery (10-100%). Recurrence can be in the form of mucosal edema, polyps, scarring, allergic mucin, or fungal debris.

**Keywords:** Allergic sinusitis, Fungal, Endoscopic sinus surgery, Corticosteroids, Immunotherapy.

\*See End Note for complete author details

Fungus has been connected to the history of human civilization from time immemorial. In the BC era, Egyptians sought the help of fungus for making bread and wine. Ever since that time, fungus has been useful to man in different ways. From bread to alcohol, we need their help. But along with it, the harmful effect it causes in our daily life cannot be ignored. It rots fruits and vegetables and ruins our food if kept outside for a long time. The diseases caused by fungi were a big menace to the medical world. Fungal diseases were a real nightmare in the field of medicine. Measures to combat it by way of drugs have been accomplished, but only partly. Many of the fungal diseases are deadly. In the field of Otorhinolaryngology also, fungal diseases were dreaded for a long time. Fungal diseases were always related to immunocompromised patients. But now with discovery of a new entity called as ALLERGIC FUNGAL RHINOSINUSITIS, the above mentioned dictum has changed. Fungus affects nasal cavity and paranasal sinuses in different ways.

Fungal diseases of the nose can be classified into 5 types:<sup>1</sup>

- Acute fulminant invasive - < 4 weeks duration

- Chronic invasive: > 4 weeks duration
  - Granulomatous
  - Non-granulomatous
- Fungal ball.
- Saprophytic colonization
- Allergic fungal sinusitis.

## HISTORY

The combination of nasal polyposis, crust formation, and sinus cultures yielding *Aspergillus* was first noted in 1976 by Safirstein who observed the clinical similarity which this constellation of findings shared with Allergic Broncho pulmonary Aspergillosis (ABPA).<sup>2</sup> In 1981, Millar et al described five cases of chronic *Aspergillus fumigatus* sinusitis in which the sinus exudates appeared histologically similar to the inspissated bronchial mucus plugs in patients with ABPA.<sup>3</sup> The authors named the condition "allergic Aspergillosis of the paranasal sinuses". Histologically the extra mucosal material was characterized as "allergic mucin"- degenerating eosinophils, desquamated respiratory epithelial cells, and Charcot-Leyden crystals.

### Corresponding Author:

Dr. Paul Samuel, MBBS, DLO, DNB (ENT), Consultant ENT Surgeon, Cosmopolitan Hospital, Thiruvananthapuram.  
Mobile: 9447290255, E-mail: paulsamuel1978@gmail.com

Fungal stains showed fungal hyphae in the allergic mucin, but not in the mucosa. There was no histologic evidence for tissue invasion by the fungi. Many others also reported identical findings thereafter and more cases have been described since then, not only with *Aspergillus* spp. but with other fungi such as *Bipolaris*, *Alternaria*, *Curvularia*, and *Exserohilum*. Allergic fungal sinusitis (or allergic fungal Rhinosinusitis (AFRS) was a term introduced by Robson et al in 1989. It is probably the most frequently occurring fungal Rhinosinusitis disorder.

Allergic fungal sinusitis is a benign non-invasive sinus disease, believed to be an allergic reaction to aerosolized environmental fungi mainly of dematiaceous species. It occurs mainly in immunocompetent persons in contrast to other invasive fungal diseases which occur chiefly in immunocompromised patients. It is a cause of recurrent or refractory sinusitis in immunocompetent patients. This entity is probably underdiagnosed and should be considered in patients with chronic, intractable sinusitis if there is a history of atopy or asthma. When fungal elements are detected by histopathology or culture from sinus material, AFRS must be differentiated from invasive disease, as treatment and prognosis are radically different.

### Aetiology

Exactly aetiology is not known. The most accepted one is allergic or hypersensitivity response to the presence of extra mucosal fungi in the sinus cavity. It is more common in atopic individuals. 70% of them may have allergic rhinitis, serum IgE will be raised in 90% and 50% will have asthma. AFRS will be the diagnosis in 5 – 10% of patients with chronic rhinosinusitis.<sup>4</sup> It occurs most common in areas with high temperature and high humidity. The most common fungi implicated are<sup>5</sup>

- Dematiaceous fungi:
- *Bipolaris* spp.
- *Curvularia lunata*.
- *Alternaria*
- *Exserohilum rostratum*

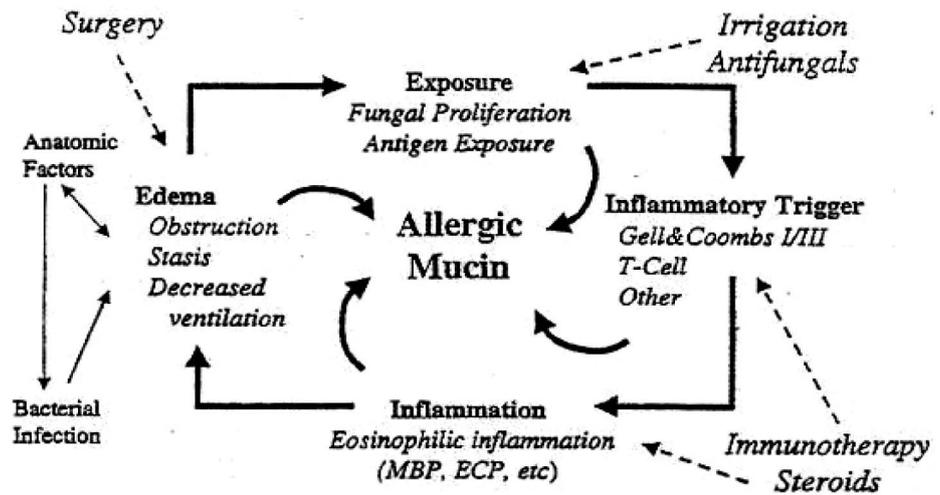


Figure 1. The cycle of AFRS and the rationale for its various treatments. (From Marple BF. Allergic fungal Rhinosinusitis: Current Theories and Management Strategies. Laryngoscope 2001;111:1006-19.)

- *Helminthosporium*
- *Drechslera*
- *Fusarium*
- *Aspergillus*
- *Aspergillus Flavus*

The pathophysiology involved in AFRS is depicted in Figure 1.

### CLINICAL FEATURES

Patients typically present with

- Gradual nasal airway obstruction and production of semisolid nasal crusts that, on inquiry, match the gross description of allergic fungal mucin.
- The development of nasal obstruction may have been so gradual that the patient is unaware of its presence.
- Pain is uncommon among patients with AFRS and suggests the concomitant presence of a bacterial rhinosinusitis.
- Patients with AFRS are atopic but generally have been unresponsive to antihistamines, intranasal corticosteroids, and prior therapy. The use of systemic corticosteroids may produce some relief of symptoms, but relapse typically follows completion of therapy.

Physical findings on examination range from nasal obstruction to gross facial disfigurement and orbital or ocular abnormalities. Skull base involvement can occur rarely.

Diagnostic nasal endoscopy will reveal 'allergic mucin'. Grossly, it is thick, tenacious, and highly viscous in

consistency; its color may vary from light tan to brown or dark green similar to 'peanut butter'. Histologic examination reveals branching noninvasive fungal hyphae within sheets of eosinophils and Charcot-Leyden crystals.

### Radiology

Soft tissue attenuation areas with internal hyperdensity are seen on non-contrast CT scans. This finding in CT is termed 'starry sky appearance'(Figure 2).These findings are although not specific for AFRS, but they are relatively characteristic and provide preoperative information supportive of the diagnosis of AFRS. The presence of accumulations of heavy metals (iron, manganese) and calcium salt precipitation within the inspissated allergic mucin is the most likely cause of these radiologic findings. On MRI, presence of hypointense central T1 signal, central T2 signal void, and increased peripheral T1/T2 enhancement is highly specific for AFRS as compared with other forms of fungal sinusitis. The high protein and low water concentration of allergic fungal mucin, coupled with the high water content within surrounding edematous paranasal sinus mucosa, gives rise to specific MR characteristics.

### Laboratory findings

**Immunologic tests:** Total IgE levels is a useful indicator of AFRS clinical activity. It is generally elevated to more than 1000 U/ml. Patients usually demonstrate positive skin test and in vitro ( RAST) responses for both fungal and nonfungal antigens.

**Culture of fungi** Fungal cultures provide some supportive evidence helpful in diagnosis and subsequent treatment of AFRS, but it is important to realize that the diagnosis of AFRS is not established or eliminated on the results of these cultures. Special stains like Fontana mason melanin stain and Grocott silver stain has to be used for identifying the fungi.

**Diagnosis** Although certain signs and symptoms, as well as radiographic, intraoperative, and pathologic findings, may cause the physician to suspect allergic fungal sinusitis, no standards had been defined for establishing the diagnosis. Parameters which enhanced the index of suspicion were as stated by Waxman et al (Laryngoscope 1987):

- (1) Young adults,
- (2) Recurrent polyposis,
- (3) History of asthma,
- (4) Multiple affected sinuses,
- (5) History of poor response to medical management,
- (6) Multiple surgical procedures,
- (7) Thick inspissated intracavity mucus,
- (8) Atopic patients with nasal polyps.

Many others used the combination of radiologic, laboratory and histologic parameters to distinguish AFRS from other forms of rhinosinusitis. In 1994, Bent and Kuhn laid down the diagnostic criteria, which are the most widely accepted.<sup>6</sup>

### These are as follows

#### 1. Major criteria:

- Type 1 hypersensitivity.
- Nasal polyps.
- Characteristic CT finding.
- Positive fungal smear\*
- Eosinophilic mucus

#### 2. Minor criteria:

- Asthma.
- U/L prominence.
- Radiographic bone erosion.
- Positive fungal culture.
- Charcot-Leyden crystals.
- Serum eosinophilia

\*(now this has been modified to include positive fungal culture, so it now reads positive fungal smear and/or culture).<sup>7</sup>



Figure 2. Non contrast CT of paranasal sinus in the axial view showing starry sky appearance in the sphenoid sinus

### MANAGEMENT

Previously an aggressive surgical approach was adopted because of a perceived risk of fungal invasion. Despite such aggressive therapy, recidivism remained high and most patients required multiple surgical procedures. As it is widely accepted that immunological hypersensitiv-

ity 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. 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:-

Treatment essentially consists of

1. Surgery
2. Steroids
3. Immunotherapy
4. Antifungals
5. Follow-up

Treatment goals can be summarised into

1. Eliminate the inciting allergen
2. Lessen allergic response AFRS has to be approached with these goals in mind.

### Surgery

Goals of surgical treatment are

- a) Eradicate all allergic mucin and fungal debris.
- b) Provide permanent drainage to the paranasal sinuses.
- c) Provide adequate ventilation route for paranasal sinuses.

Surgery is usually by the endoscopic approach. Endoscopic clearance of the sinus cavity has to be done as much as possible. 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.<sup>8,9</sup> 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. 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 dis-

orientation. 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 rhinorrhea.<sup>8</sup> Rarely, inaccessible intracranial or intraorbital extension may have to be approached by craniotomy or frontoethmoidectomy.

**Systemic steroids** Preoperative use of steroids aid in decreasing inflammation and reducing the size of polyps. The potent anti-inflammatory and immunomodulatory effects of corticosteroids appear to control recurrence of disease in postoperative period. It will also help in controlling the co-existent allergic rhinitis. But there is no uniformity in optimal dosing regimen and length of therapy. Kuhn and Javer<sup>10</sup> 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. Topical steroid preparations can also be used as they have fewer adverse effects than systemic corticosteroids. Nasal steroid sprays can be used at thrice daily for upto one year. Steroids are helpful in reducing the recurrence rate also.

**Antifungal agents** Role of antifungal therapy is controversial. Antifungal agents have shown mixed results in the treatment of allergic fungal sinusitis. Some studies have shown that it decreases the progression to invasive form. Also it is suggested that it can decrease steroid dependence and recurrence, Supportive data regarding the usage of these agents are pending. Itraconazole has been the drug that is most commonly used now.<sup>11</sup> The dosage is 200mg twice daily for 6 weeks. Voriconazole is a newer drug which is being used. But cost factor and drug related morbidity limits the use in our scenario. Fluconazole nasal spray has also been used with encouraging results in some studies.<sup>12</sup>

**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.<sup>13</sup> A study conducted by Mabry et al showed immunotherapy can reduce the reliance on the systemic

and topical steroids. Another study conducted by them showed no recurrence in follow-up period of 7 to 17 months.<sup>14</sup> 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.

### Follow up

Follow up is very important postoperatively as allergic fungal sinusitis is known for recurrence. Rate of recurrence is high despite of complete surgery (10-100%). Recurrence can be in the form of mucosal edema, polyps, scarring, allergic mucin, or fungal debris. Kupferberget al has refined endoscopic follow up which are as follows.<sup>15</sup>

- Stage 0** No mucosal edema or allergic mucin.
- Stage I** Mucosal edema with or without allergic mucin.
- Stage II** Polypoid edema with or with out 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. Salina nasal douche have to be tried postoperatively for clearance of residual mucin. Periodic nasal endoscopy in the follow-up period is vital for detection of recurrence early.

### AFRS in children

AFRS in children, although rare, needs special care. It is more aggressive in pediatric population. Also bone erosion is severe in children. Extension to intraorbital region is high and intracranial extension is more aggressive. Treatment protocol doesn't alter much for pediatric cases.

### CONCLUSION

Allergic fungal sinusitis represents an immunologic rather than infectious disease process. It should be considered in all patients with intractable sinusitis and a history of atopy or asthma.. Early diagnosis of noninvasive sinusitis may prevent multiple surgical procedures and lead to effective treatment. Endoscopic sinus surgery is the main stay of therapy even for intracranial or intra orbital involvement. Although important, surgery alone does not lead to a long-term disease free

state. Postoperative follow-up is critical as the relapse rate is very high. 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.

### END NOTE

#### Author Information

Dr. Paul Samuel, MBBS, DLO, DNB (ENT)  
Consultant ENT Surgeon, Cosmopolitan Hospital,  
Thiruvananthapuram. Mobile: 9447290255.  
E-mail: paulsamuel1978@gmail.com

**Conflict of Interest:** None declared

**Cite this article as:** Paul Samuel. Allergic Fungal Rhinosinusitis. Kerala Medical Journal. 2011 Sep 27;4(3):103-107

### REFERENCES

1. Schubert MS. Allergic fungal sinusitis. *Otolaryngol Clin North Am.* 2004 Apr;37(2):301–26.
2. Safirstein BH. Allergic bronchopulmonary aspergillosis with obstruction of the upper respiratory tract. *Chest.* 1976 Dec;70(6):788–90.
3. Millar JW, Johnston A, Lamb D. Allergic aspergillosis of the maxillary sinuses. *Thorax* 1981; 36: 710.
4. Cody DT, Neel HB, Ferreiro JA, Roberts GD. Allergic fungal sinusitis: the Mayo Clinic experience. *Laryngoscope.* 1994 Sep;104(9):1074–9.
5. Manning et al *Arch Otolaryngology and Head & Neck Surgery*;1991,117:174-178
6. Bent JP, Kuhn FA. Diagnosis of allergic fungal sinusitis. *Otolaryngol Head Neck Surg.* 1994 Nov;111(5):580–8.
7. Kuhn FA, Javer AR. Allergic Fungal Sinusitis: A Four-Year Follow-Up American Journal of Rhinology May-June 2000, Vol. 14, NO.3 p149-156
8. Marple BF: Allergic fungal rhinosinusitis. *Surgical Management.* *Otolaryngol Clin North Am* 2000; 33: 409-18.
9. Marple BF, Mabry RL. Comprehensive management of allergic fungal sinusitis. *Am J Rhinol.* 1998 Aug;12(4):263–8.
10. Marple BF. Allergic fungal rhinosinusitis: current theories and management strategies. *Laryngoscope.* 2001 Jun;111(6):1006–19.
11. Kuhn FA, Javer AR. Allergic fungal rhinosinusitis: perioperative management, prevention of recurrence, and role of steroids and antifungal agents. *Otolaryngol Clin North Am.* 2000 Apr;33(2):419–33.
12. Jen A, Kacker A, Huang C, Anand V. Fluconazole nasal spray in the treatment of allergic fungal sinusitis: a pilot study. *Ear Nose Throat J.* 2004 Oct;83(10):692, 694–5.
13. Mabry RL, Mabry CS. Allergic fungal rhinosinusitis. The role of Immunotherapy. *Otolaryngol Clin North Am* 2000; 33: 433-40.
14. Mabry RL, Marple BF, Mabry CS. Outcomes after discontinuing immunotherapy for allergic fungal sinusitis. *Otolaryngol Head Neck Surg.* 2000 Jan;122(1):104–6.
15. Kupferberg SB, Bent JP, Kuhn FA. Prognosis for allergic fungal sinusitis. *Otolaryngol Head Neck Surg.* 1997 Jul;117(1):35–41.