

## ROLE OF POSTOPERATIVE MEDICAL TREATMENT IN THE MANAGEMENT OF ALLERGIC FUNGAL SINUSITIS

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### ABSTRACT

**Objectives:** To evaluate the effectiveness of postoperative medical treatment in the management of allergic fungal sinusitis with orbital and/ or skull base erosion.

**Study design:** -Descriptive study.

**Place and Duration of Study:** This study was conducted in the Department of ENT and Head & Neck Surgery, Khyber Medical College & Khyber Teaching Hospital Peshawar between January 2002 and April 2007.

**Patients and Method:** Eighteen cases of allergic fungal sinusitis with orbital and/ or skull base erosion were selected for the study. Demographic Data like, name, age, sex, address, clinical features, labs and imaging studies were recorded, clinical data including the pre and post-operative medical treatment, operative findings and postoperative results, recurrence of disease were recorded. All patients were divided into three groups on the basis of postoperative medical treatment.

**Results:** Study revealed that Allergic Fungal Sinusitis (AFS) is a disease of younger age, mainly occurring in 2nd & 3rd decade of life, with male to female ratio 1:1.25. The recurrence was 100% in group-1 who were on oral antifungal therapy postoperatively. The recurrence of disease was 40% in patients of group-2 who were on topical nasal steroid, antihistamine and saline irrigation postoperatively. The recurrence rate was much lower 11% in group-3 patients who received oral and topical nasal corticosteroids postoperatively.

**Conclusion:** - AFS is a disease of young immunocompetent adults. Surgical debridement and drainage combined with topical and oral corticosteroids can lead to resolution of disease in majority of the cases and prevent recurrences. Antifungal medication has no role in the treatment of allergic fungal sinusitis.

**Keywords:** Allergic fungal sinusitis, Skull base erosion, Orbital erosion, Role of corticosteroids, Antifungal medication

### INTRODUCTION

Allergic fungal sinusitis (AFS) is a relatively recently defined pathological entity. Allergic fungal sinusitis (AFS) was first described in early 1980, when Millar & others noticed a clinical entity of sinus disease that was similar in many ways to allergic

bronchopulmonary aspergillosis (ABPA).<sup>1,2</sup> The pathological features of AFS have been known for two decades. Earlier, the condition was misdiagnosed for sinus mucocele, invasive fungal infections, undifferentiated neoplasm and fungal mycetoma.<sup>3</sup> The incidence of allergic fungal sinusitis (AFS) in cases of chronic rhinosinusitis (CRS) treated surgically has been approximately 5-10%.<sup>4</sup> Patients with non-invasive form have intractable sinusitis

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that fails to respond to repeated courses of antibiotics and surgical procedures.

Bent and Kuhn published the diagnostic criteria of AFS in 1994, 1)- nasal polyposis, 2)-allergic mucin, 3)-CT Scan findings consistent with CRS, 4)-fungus found in histopathologic analysis or culture and 5)-type-1 hypersensitivity as determined by history, serology or positive skin test. DeShazo and Swain also proposed diagnostic criteria.<sup>6</sup> Some patients may present with clinical and histopathological features similar to AFS but without fungal hyphae in allergic mucin by both special stain and culture.<sup>7</sup> This has recently been described a distinct clinicopathologic entity by Ferguson as eosinophilic mucin rhinosinusitis (EMRS).<sup>8</sup>

Patients with AFS have a high incidence of bone erosion of the skull base and orbit, which is best demonstrated on CT scanning.<sup>9</sup> The incidence of bone erosion has considerable variation in different regions, races and gender. Wise et al demonstrated the erosion rate of 44.7% in AFS patients.<sup>10</sup> The ophthalmologic findings are said to occur in as many as 18.3% of cases, varying from proptosis and diplopia to impaired vision and rarely sudden visual loss.<sup>11</sup> The presence of bony erosion of the skull base and orbital in AFS has been well documented in the literature.

Surgery has emerged as a universally accepted component and first step of the treatment. However, surgery alone without other adjuvant therapy frequently leads to recurrence of the disease. Being relatively recently discovered, there are many controversies regarding medical management of the disease. The postoperative medical therapies may include systemic corticosteroids, antifungal agents, or immunotherapy.<sup>12, 13</sup>

This study was done to see the postoperative clinical response of different modalities of medical treatment in AFS with orbital and /or skull base erosion.

## **MATERIALS AND METHODS**

This is a descriptive study conducted in the

department of Otorhinolaryngology, Head and Neck Surgery, Khyber Teaching Hospital Peshawar a tertiary care, referral center between January 2002 and April 2007. The sampling was by convenience. Eighteen (18) diagnosed patients of allergic fungal sinusitis with orbital or base of skull erosion were included in this study.

**Inclusion Criteria;** Allergic fungal sinusitis with bone erosion.

**Exclusion Criteria;** Allergic fungal sinusitis without erosion of bone. Allergic fungal sinusitis without fungal hyphae on staining .All Other form of sinusitis both invasive and non-invasive.

Based on CT Scan findings patients were diagnosed as having orbital and/ or skull base erosion.

The medical records of 18 patients were analyzed in terms of clinical profile, investigative profile (ophthalmologic findings, CT Scan, MRI), operative findings and postoperative results in terms of nasal symptoms, headache and visual improvement. All patients were evaluated for common conditions that could contraindicate the use of oral corticosteroids or any other medication.

All these patients underwent surgery, which included complete removal of allergic fungal mucin from involved sinuses and creating wide access to these sinuses for ventilation and postoperative care. The surgical approach was based on the extent of the disease according to the findings of CT Scan. All the allergic mucin and polyp/sinus mucosa removed was sent for histopathological examination. Pathologist was requested for special fungal staining such as PAS (Periodic acid-Schiff) and GMS (Gomori methanamine silver stain) or KOH preparation. Postoperatively, all patients received antibiotics for one week.

On the basis of postoperative medical treatment received, patients were divided into three groups.

Group-1; patients who received oral antifungal postoperatively for 3 months.

Group-2; patients who received postoperatively

topical nasal steroids and antihistamine for 3 months

Group-3; patients who received topical and oral corticosteroids treatment for three months postoperatively Follow up; the minimum follow up was up to 8 months.

The follow up period ranged from 8 to 84.4 months.

Details of postoperative treatment, relief in symptoms, examination finding and recurrences if any and side effect of drugs if any, appropriate treatment given that is, uses of antifungal, topical or systemic corticosteroids were recorded.

## RESULTS

On the bases of the Schubert diagnostic criteria 18 patients of allergic fungal sinusitis with orbital and/or skull base erosion were selected.<sup>14</sup> Only 7 cases presented with recurrence. The clinical features, age, sex, extent of disease, number of previous surgeries and incidence of recurrence are shown in the Table-1 and 2.

**Table 1:**

S.No.	Clinical Features	No.	%
1	Nasal obstruction	17	94%
2	Nasal discharge	16	89%
3	Rhinorrhoea	16	89%
4	Facial pain	08	44%
5	Headache	09	50%
6	Polyposis	17	94%
7	Proptosis	16	89%
8	Telecanthus	02	11%
9	Impaired Vision	02	11%
10	Previous surgeries	07	39%

**Table 2:**

Number of Patients	Sex	Sex		Recurrence	Extend of disease in recurrence		Sex ratio in recurrence	
		M	F		Unilateral	Bilateral	M	F
Group-1	Four	1	3	Four (100%)	2	2	1	3
Group-2	Five	2	3	Two (40%)		2		2
Group-3	Nine	5	4	One (11%)		1	1	

The male to female ratio was 1:2, while among the recurrent cases two were male and 5 were female. The youngest was 11 years and the oldest was 45 years (average 19 years). This study revealed that AFS is a disease of young adults, mainly occurring in the 2nd & 3rd decade of life. The disease was unilateral in thirteen (72%) of 18 patients and bilateral in 5 patients. Among the recurrent 7 cases 4 patients had bilateral & 2 had unilateral disease. Fungal hyphae were seen in allergic fungal mucin on histopathological examination in all cases. Cultures were performed in only 5 cases, in which *Aspergillus* was isolated. 13 cases presented with nasal allergy and one was a known case of bronchial asthma. History of previous sinonasal surgeries for rhinosinusitis with polyposis was elicited in eight (39%) cases.

## DISCUSSION

With heightened awareness and sophisticated laboratory diagnostic techniques and imaging, an increasing number of reports are being published. A full consensus among rhinologists and immunologists worldwide concerning diagnostic criteria for AFS is still awaited. We employed Schubert criteria<sup>14</sup> for diagnosis of AFS in our patients. This study describes the effectiveness of postoperative medical treatment in minimizing the recurrence of disease and improving the symptomatology with which patients presented. All patients in our series were immunocompetent and young. The mean age at presentation was 20 years and 83% were in 2nd & 3rd decade of life, which is similar to studies reported in the literature.<sup>6,16</sup>

The male to female ratio of 1:1.25, has also been reported by Scott C Manning.<sup>15</sup> Conversely Thahim K et al and Richard D deshazo found male predominance in their study.<sup>6,16</sup>

In our study the disease was unilateral in 13 (73%) patients and bilateral 5 (18%) patients. Bent & Kuhn<sup>5</sup>, Sohail et al<sup>19</sup> and Thahim et al<sup>16</sup> also reported unilateral predominance in allergic fungal sinusitis. On the other hand Bradley Marple<sup>17</sup> found 51% bilateral disease in 45 patients. The recurrence is more common in female in the study and in that group of patients

having bilateral disease; five of 7 patients had bilateral disease in recurrent cases.

Regarding management of AFS, adequate sinus surgery is a universally accepted component and the first step in the treatment of any patient with AFS<sup>14</sup>. Although no studies are available to compare different techniques, it has been suggested that limited functional endoscopic sinus surgery has been associated with higher rates of AFS recurrence than more aggressive surgical procedures that remove all dysfunctional obstructive hypertrophic/ polypoidal sinus mucosa as well as all inspissated allergic mucin.<sup>4,18</sup> Aims of surgical treatment regardless of surgical techniques are complete removal of all allergic mucin and fungal debris, permanent drainage and ventilation of the affected sinuses while preserving the integrity of the sino-nasal mucosa and access for postoperative care. Keeping in mind the aims of surgical treatment, we adopted more radical approaches in surgery. Endoscopic sinus surgery with preservation of structures is popular procedure in most centers.<sup>20</sup>

In Group-1 patient's recurrence was observed in all cases (100%). Similar poor responses were observed in different studies.<sup>4,17,21,22,28,30</sup> The use of topical and systemic antifungal agents is controversial. No indication exists for the use of toxic antifungal agents to treat noninvasive fungal sinusitis. Since AFS is thought to be an allergic (hypersensitivity) disease caused by extrinsic fungal antigen rather than a true infection, systemic antifungal should be ineffective.<sup>14, 24</sup> Itraconazole, a relative benign oral antifungal agent was used in four patients postoperatively in our study with no beneficial effects. However in some cases antifungal agents were added to oral corticosteroids in the treatment of allergic fungal sinusitis with additional clinical benefits.<sup>25,26</sup>

In Group-2 patient's recurrence was observed in two cases (40%) that received nasal corticosteroids and antihistamine postoperatively. Topical intranasal steroids spray, antihistamine and saline irrigation have minimal side effects and are commonly used in postoperative management of ASF. However the duration and effectiveness of steroids sprays in AFS

has not been proven scientifically.<sup>4,13,18,27</sup>

In this study Group-3 patients who underwent surgery followed by oral and topical corticosteroids showed very good response, regarding relief from symptoms and recurrence. In this group of patients only one case (11%) presented with recurrence. Use of oral corticosteroids postoperative in AFS is well established and supported by many studies.<sup>4,17,18,28,29</sup> Although no fully controlled studies have been published for any treatment for AFS, the origin of corticosteroids therapy for long-term management of AFS arose directly from the analogy of AFS to ABPA. The potent anti-inflammatory and immunomodulatory effect of corticosteroids appears to be well suited to control recurrence of disease. Bent and Kuhn<sup>30</sup> noted eventual universal recurrence of AFS in their patients who were not receiving systemic corticosteroids. Schubert and Goetz<sup>17</sup> studied the role of systemic corticosteroids in the postoperative management of AFS, demonstrating a significant decrease in recurrence of AFS, much improvement in relief of symptoms and quality of life in patients who received prolonged courses of postoperative systemic steroids. Systemic steroids have been used successfully in cases of recurrence of AFS, but the potential side effects limits their use and the dosing regime and length of therapy remain unclear. A modified protocol of systemic corticosteroids regime for AFS from that used for ABPA has been suggested and used by Schubert and Goetz<sup>18</sup> in their cases.

This study did encounter some limitations. The time taken to transport the specimen to the histopathology and mycology laboratory could not strictly be observed. Because of budget constraints, fungal culture and fungal-specific IgE and IgG, which are good screening tools, were not performed.

## CONCLUSION

AFS is a disease of young immunocompetent adults. Skull base & orbital erosion is seen in majority of the cases. Surgical debridement and drainage combined with topical steroids and oral steroids can lead to resolution of disease in majority of the cases and prevent recurrences. Antifungal medication has



no role in the treatment of allergic fungal sinusitis. Allergic fungal sinusitis should be considered in all patients with refractory chronic sinusitis.

## REFERENCES

1. Millar JW, Johnston A, Lamb D. Allergic aspergillosis of the maxillary sinuses *Prod Scot Thor Soc* 1981; 36:710.
2. Katzenstein AA, Sale SR, Greenburger PA, Allergic Aspergillus sinusitis: a newly recognized form of sinusitis. *J Allergy Clin Immunol* 1983; 72:89-93.
3. Torres C, Ro JY, El-Naggar AK, Sim SJ, Weber RS, Ayala AG. Allergic fungal sinusitis: A clinicopathologic study of 16 cases. *Hum Pathol* 1996; 27:793-99.
4. Schubert MS, Medical treatment of allergic fungal sinusitis. *Ann Allergy Asthma Immunol* 2000; 85: 90-101.
5. Bent JP 3rd, Kuhn FA. Diagnosis of allergic fungal sinusitis. *Otolaryngol Head Neck Surg* 1994, 111: 580-8.
6. deShazo RD, Swain RE, Diagnostic criteria for allergic fungal sinusitis. *J Allergy Clin Immunol* 1995; 96:24-35.
7. Ramadan HH, Quraishi HA. Allergic mucin sinusitis without fungus, *Am J Rhinol* 1997; 11:145-7.
8. Ferguson BJ. Eosinophilic mucin rhinosinusitis: a distinct clinicopathological entity. *Laryngoscope* 2000; 110:799-813.
9. Ghegan MD, Lee F, Schlosser RJ. Incidence of skull base and orbital erosion in allergic rhinosinusitis. *Otolaryngol Head Neck Surg* 2006; 134:592-5.
10. Wise SK, Ventatraman G, Wise JC, Del Gaudio JM. Ethnic and gender differences in bone erosion in AFS. *Am J Rhinol* 2004; 18:397-404.
11. Carter KD, Graham SN. Ophthalmic manifestation of allergic fungal sinusitis. *Am J Ophthalmol* 1999; 13:189-95.
12. Marple BF, Mabry RL. Allergic fungal sinusitis: Learning from our failures. *Am J Rhinol* 2000, 14: 223-6.
13. Ferguson BJ. What role do systemic steroid, immunotherapy and antifungal drugs play in the therapy of allergic fungal rhinosinusitis? *Arch Otolaryngol Head Neck Surg* 1998; 124:1174-8.
14. Schubert MS. Allergic fungal sinusitis. *Otolaryngol Clin North Am* 2004; 37:301-26.
15. Manning SC, Mabry RL, Schaefer SD, Close LG. Evidence of IgE-mediated hypersensitivity in allergic fungal sinusitis. *Laryngoscope* 1993; 103:717-21
16. Thahim K, Jawaid MA, Marfani MS. Presentation and management of allergic fungal sinusitis. *J Coll Physican Surg Pak* 2007; 17: 23-7.
17. Marple BF. Allergic fungal rhinosinusitis: current theories and management strategies. *Laryngoscope* 2001; 111:1006-19.
18. Schubert MS, Goetz DW. Evaluation and treatment of allergic fungal sinusitis. II. Treatment and follow-up. *J Allergy Clin Immunol* 1998; 102:395-402.
19. Sohail MA, Al Khabori MJ, Hyder J, Verma A. Allergic fungal sinusitis: Can we predict the recurrence. *Otolaryngol Head Neck Surg* 2004; 131:704-10.
20. Iqbal J, Raza SN Endoscopic sinus surgery versus intranasal polypectomy for ethmoidal nasal polyposis. *Pak J otolaryngol* 2007; 23:3-5.
21. Schubert MS, Goetz DW. Evaluation and treatment of allergic fungal sinusitis I. Demographics and diagnosis. *J Allergy Clin Immunol* 1998; 102:387-94.
22. Leonard CT, Berry GJ, Ruoss SJ. Nasal-pulmonary relations in allergic fungal sinusitis and allergic bronchopulmonary aspergillosis. *Clin Rev Allergy Immunol* 2001; 21:5-15.
23. Bent JP 3rd, Kuhn FA. Antifungal activity against allergic fungal sinusitis organisms. *Laryngoscope* 1996; 106:1331-4.
24. Mian MY, Kamal SA, Allergic fungal rhinosinusitis:

- Current status. Pak J Otolaryngol 2002; 18:36-40
25. Ande D, Proctor R, Bush RK, Pasic TR. Report of successful prolonged antifungal therapy for refractory allergic sinusitis. Clin Infect Dis 2000; 31:202-4.
26. Rains BM 3rd, Mineck CW. Treatment of allergic fungal sinusitis with high-dose Itraconazole. Am J Rhinol 2003; 17:1-8.
27. Manning SC, Vuitch F, Weinberg AG, Brown OE. Allergic aspergillosis: a newly recognized form of sinusitis in the paediatric population. Laryngoscope 1989;99:681-5.
28. Kupferberg SB, Bent JB. Allergic fungal sinusitis in the pediatric population. Arch Otolaryngol Head Neck Surg 1996;122:1381-4.
29. Safirstein B. Allergic bronchopulmonary aspergillosis with obstruction of the upper respiratory tract. Chest 1976; 70:788-90.
30. Bent JP 3rd, Kuhn FA. Allergic fungal sinusitis/polyposis. Allergy Asthma Proc 1996; 17:259-68.











