PRESENTATION AND DIAGNOSIS OF ALLERGIC FUNGAL SINUSITIS

Zakirullah, Ghareeb Nawaz, Syed Fazle Sattar
Department of Otorhinolaryngology, Head & Neck Surgery, Khyber Medical College, Peshawar, Pakistan

Background: Allergic fungal sinusitis (AFS) is a form of fungal disease that has recently been considered a distinct clinicopathologic entity. Other forms of fungal sinusitis include acute-fulminant (invasive), chronic indolent (invasive) and mycetoma (non-invasive). Objectives were to assess the presentation and to describe the diagnostic techniques for allergic fungal sinusitis in our setup. **Method:** Descriptive study was conducted in the Department of ENT and Head & Neck Surgery, Khyber Medical College and Khyber Teaching Hospital, Peshawar from January 2002 to April 2008. Twenty-three cases of allergic fungal sinusitis (ASF) were selected for the study. Data like, name, age, sex, address, clinical features, labs (Eosinophil count) and imaging studies (CT and/or MRI) were recorded, including the pre- and postoperative treatment, operative findings and postoperative results, recurrence of disease were also recorded. Surgical procedures were performed on all cases followed by medical treatment. **Results:** Study revealed that AFS is a disease of younger age, mainly occurring in 2nd & 3rd decade of life, with male to female ratio 1:1.3. Allergic rhinitis (91%) and nasal polyposis (91%) were important associated factors. Nasal obstruction (96%), nasal discharge (91%), post-nasal discharge (87%) and unilateral multi sinus extension were important clinical features. Increased eosinophil count and increased IgE level was found in 78% cases. Histopathological analysis showed fungal hyphae in all cases and aspergillus was predominant organism on culture. Orbital erosion was seen in 78% and skull base erosion was observed in 9%. Recurrence of disease was seen in nine cases. **Conclusion:** Allergic fungal sinusitis (AFS) is a disease of young immunocompetent adults. Nasal obstruction, nasal discharge, nasal allergy and proptosis were the most common presentations. Initial diagnosis of allergic fungal sinusitis requires high index of suspicion in patients presenting with chronic rhinosinusitis, such cases should be properly evaluated. Differentiation from invasive forms of fungal sinus disease is crucial.

Keyword: Sinusitis, Allergic Fungal Sinusitis, Skull base erosion, Orbital erosion, Fungal

INTRODUCTION

Allergic fungal sinusitis (AFS) is a form of fungal disease that has recently been considered a distinct clinicopathologic entity. Other forms of fungal sinusitis include acute-fulminant (invasive), chronic indolent (invasive) and mycetoma (non-invasive). Allergic fungal sinusitis a non-invasive pansinusitis that occurs in young immunocompetent individuals, with a strong history of atopy and elevated levels of total immunoglobulin (Ig)E and peripheral eosinophilia. It is histologically characterised by the presence of allergic mucin and scattered fungal hyphae.[1] Allergic fungal sinusitis (AFS) was first described in the literature in the early 1980s, when Millar *et al* noticed a clinical entity of sinus disease that was similar in many ways to allergic bronchopulmonary aspergillosis (ABPA).[2,3] Patients with allergic fungal sinusitis (AFS) have intractable sinusitis that fails to respond to repeated courses of antibiotics and surgical procedures. Criteria for the diagnosis are still evolving. Bent *et al*[4] published the diagnostic criteria of AFS in 1994[4] and deShazo *et al* in 1995[5]. Recently Schubert prospectively evaluated his patients with allergic fungal sinusitis and discovered 4 characteristic findings for the diagnosis as diagnostic criteria.[6] 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.[7] This has recently been described a distinct clinicopathologic entity by Ferguson as oesinophilic mucin rhinosinusitis (EMRS).[8]

The diagnosis is based, by analogy with the findings in bronch-pulmonary aspergillosis, on the presence of allergic mucin within the sinus.[9] Macroscopically, the secretions are thick, viscous, and green and microscopically, the allergic mucin contains eosinophilic polynuclear cells, Charcot-leyden crystals, and scattered mycelial filaments without tissue invasion. Clinically, allergic fungal rhinosinusitis should be suspected in the presence of chronic rhinosinusitis refractory to several medical or surgical treatments.[9–11] CT scan shows heterogeneous opacities or calcifications. The presence of bony erosion of the skull base and orbital in AFS has been well documented in the literature.[12–14]

The aim of this study was to assess the presentation of allergic fungal sinusitis and describe the techniques of diagnosis in our setup.

MATERIAL AND METHODS

This was a descriptive study conducted in the department of Otorhinolaryngology, Head and Neck Surgery, Khyber Medical College/Khyber Teaching Hospital, Peshawar. The cases presenting with clinical features of allergic fungal sinusitis were enrolled in the study between January 2002 and April 2008.

Allergic fungal sinusitis with bone erosion was included. Allergic fungal sinusitis without erosion of bone, fungal hyphae on staining and other forms of fungal sinusitis invasive and non- invasive were excluded from the study.

All patients were subjected to a detailed history, thorough physical and nasal examination. Medical management in the form of topical steroids, antihistamines for a period of one month were given to all cases and some patients were also given antibiotics for ten days. Those patients who failed to respond to the medical treatment were subjected to CT scans of the paranasal sinuses. The cases with evidence of polypoidal changes/polypi and radiological typical evidence of presence of allergic fungal sinusitis with bone erosion were included in this study. A record regarding the characteristic clinical presentation, radiological extent of the disease, labs (IgE and eosinophil count) operative details including the area involved were noted as well as postoperative results (nasal symptoms, headache and visual improvement), recurrence and the treatment given was maintained. Medical specialist pre-operatively evaluated all patients for common conditions that could contraindicate the use of oral corticosteroids. 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 and KOH preparation. Pathologist was alerted for special fungal staining such as PAS (Periodic acid-Schiff) and GMS (Gomori methanamine silver stain). Postoperatively all patients received antibiotics for one week. Patients whose allergic mucin was negative for fungal hyphae on KOH preparation as well as on special staining were excluded from this study.

The follow-up period ranged 6–80 months. Details of postoperative course, recurrences if any, appropriate treatment given that is, use of antifungal, topical or systemic corticosteroids were recorded.

Table-1: Diagnostic criteria for allergic fungal sinusitis

1	Surgically obtained characteristic inspissated allergic mucin must be seen histopathologically or grossly at surgery
2	The allergic mucin must be positive for fungal hyphae on fungal staining, or properly obtained surgical sinus fungal culture must be positive in an otherwise characteristic patient
3	There should be no histopathological evidence for mucosal necrosis, granulomata or giant cells
4	Other fungal rhinosinusitis disorder must be excluded

RESULTS

Twenty-three diagnosed patients of allergic fungal sinusitis with bone erosion were evaluated. The clinical features, age, gender, extent of disease, number of previous surgeries and incidence of recurrence are shown in Tables- 2, 3.

Patients comprised 10 (43.0%) male and 13 (57.0%) were female (male to female ratio 1:1.3), among the recurrent cases three were male and 6 female. The youngest patient was 11 years and the oldest was 45 years (average 21.52 years) Mean age was 20 years. The disease was unilateral in 16 patients and bilateral in 7 patients. Nine cases presented with recurrent disease. Fungal hyphae were found on histopathological analysis with special stain for fungus in all cases. Cultures performed on 5 specimens, Aspergillus was the predominant organism in all specimens. Twenty-one cases presented with nasal allergy and 5 were known cases of bronchial asthma. History of previous sinonasal surgeries for rhinosinusitis with polyposis was elicited in 8 (39%) cases.

Table-2: CT scan findings (n=23)

CT Scan Findings	No.	%
Unilateral involvement of nose & PNS	16	70.0
Bilateral involvement of nose & PNS	7	30.0
Double density sign	14	61.0
Orbital involvement	18	78.0
Intracranial involvement	2	9.0

Table-3 Clinical presentations (n=23)

Clinical Features	No.	%
Nasal obstruction	22	96.0
Nasal discharge	21	91.0
Postnasal discharge	20	87.0
History of allergic rhinitis	21	91.0
Allergic nasal cast production	15	65.0
Loss of smell	12	52.0
Facial asymmetry	15	65.0
Facial pain	9	39.0
Headache	13	57.0
History of asthma or reactive airway	5	22%
Intolerance to aspirin	2	9.0
Polyposis	21	91.0
Proptosis	18	78.0
Telecanthus	3	13.0
Impaired Vision	2	09.0
Previous surgeries	9	39.0

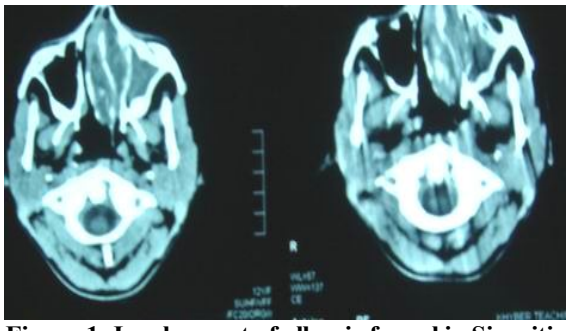

Figure-1: Involvement of allergic fungal in Sinusitis

DISCUSSION

Allergic fungal sinusitis is being increasingly seen in various parts of the world with higher incidence in Southwestern states of the USA[15], Sudan[16], northern India[17], and Saudi Arabia[18]. The authors have experience a rising trend in ASF in Northern part of Pakistan. Nasal obstruction and discharge have been seen to be common complaints in allergic fungal sinusitis compare with invasive disease. Similarly nasal polyps on anterior rhinoscopy were predominantly present in ASF.

This study describes the frequency of symptoms and techniques used for diagnosis of AFS in our patients. All patients in our series were immunocompetent and young with a mean age at presentation 20 years and 83% were in 2nd and 3rd decade of life, which is similar to studies reported in the Literature.[5,15] The male female ratio is 1:1.3, similar male female ratio reported by Scott C Manning.[18] Conversely Thahim *et al*[19] and Richard D deshazo[5] found male predominance in their study. However the M/F ratio may be age dependent and different in children and adults. In the review of patients at UT Southwestern, in children, male dominated (M/F ratio 2.1:1; average age=13 year) and in adults females dominated (M/F ratio 1:1.4; average age 36 year).[20] The paediatric group in our study were six, they presented with an aggressive disease mainly proptosis, extensive polyposis, facial deformity and telecanthus, Gupta *et al* also reported a more aggressive nature of ASF in children than in adults mandating an early diagnosis, proper management and regular follow up in children.[21]

Nasal obstruction, nasal discharge, symptoms of allergic rhinitis or sinusitis and headache were the main presentation in our patients. Patients typically complain of gradual nasal airway obstruction and production of semi-solid nasal crusts that upon inquiry match the gross description of allergic fungal mucin. The clinical features depend upon the extension of the disease, involvement of orbital or intracranial structures and presence of the concomitant bacterial rhinosinusitis. Patients with AFS are atopic, but generally their symptoms have been unresponsive to medical and surgical treatment for common allergic rhinosinusitis and chronic sinusitis. The overall incidence of AFS is estimated at 5–10% of all hypertrophic sinus disease cases going to surgery.[22] The ASF must be distinguished from other forms of fungal rhinosinusitis before a treatment plan can be instituted on the basis of clinical features.[6]

Nasal polypi, proptosis, nasal discharge, mucin cast, Telecanthus and facial asymmetry were seen in our patients. The clinical findings in both local and international literature are more or less the same with insignificant difference in frequencies of the symptoms.[6,18,23,24] Proptosis was predominantly present (18 cases) and dimness of vision in two patients in our study; this high prevalence may be due to our selection criteria. Ophthalmic findings are said to occur probably due to close proximity of the orbit to paranasal sinuses and extension of the disease leads to proptosis, impaired vision and facial asymmetry. Such extrasinus extension of AFS is caused by bone resorption from pressure from the expanding allergic mucin mass and is not caused by invasion of fungi into sinus mucosa, bone or other tissue.[13] A higher incidence of proptosis, facial deformity, intraorbital/ intracranial extension and a higher rate of recurrence in children were reported by Gupta *et al*.[21]

In our study the disease was unilateral in 16 (70%) patients and bilateral 7 (30%) patients Bent & Kuhn[4], Sohail *et al*[24] and Thahim *et al*[18] also reported unilateral predominance in allergic fungal sinusitis. On the other hand Bradley Marple[26] found 51% bilateral disease in 45 patients. The recurrence is more common in female and in that group of patients having bilateral disease; 6 of 9 patients had bilateral disease in recurrent cases.

Operative details showed extensive polyposis and characteristic thick peanut-buttery tan to dark-green allergic mucin in all cases, concomitant bacterial sinusitis with pus under tension in 7 cases. Similar findings are reported in world literature.[4–6,15,17] Histopathological analysis showed fungal hyphae in all allergic mucin in our cases. We utilised various histological staining techniques to help to identify the variety of components within allergic fungal mucin. Hematoxylin and eosin (H&E) staining accentuates the mucin and cellular components of allergic fungal mucin. Using this stain, background mucin often takes on a chondroid appearance, while eosinophils and Charcot-Leyden crystals are heavily stained and become easily detectable. Fungi fail to stain using this technique and therefore may be difficult to identify. The Gomori methenamine silver (GMS) stain, which turns fungi black or dark brown were used along with PAS stain. The use of a fungal stain complements the findings of initial H&E stain and is extremely important in the identification of fungus.

No financial support was utilized so due to budget constraints and lack mycology lab in our region, all allergic mucin were not cultured. Aspergillus was found in 5 specimens cultured in our study, showing prevalence of the organism in this region.[17,18,21] A positive fungal culture does not confirm the diagnosis of AFS, nor does a negative culture exclude it. For example, fungi may proliferate as saprophytic growth in diseased sinuses. Furthermore, mycology laboratories vary in capability, and specimen handling significantly influences the rate of positive fungal cultures in a clinical setting. Allergic

mucin remains the most reliable indicator of AFS. Because nasal polyposis and fungal disease in the sinuses are not unique to AFS, other mycotic diseases in the differential diagnosis must be defined.[15]

The CT scan findings suggested 70% unilateral and 30% bilateral involvement of nose and paranasal sinuses and 61% double density sign. Although these findings are not specific for AFS, they remain relatively characteristic of the disease and may provide preoperative information supportive of a diagnosis of AFS. Expansion, remodelling, or thinning of involved sinus walls is common in AFS and is caused by the expansile nature of the accumulating mucin and polypi. Areas of high attenuation are found within the expanded paranasal sinuses in all patients. Other diseases can cause similar radiographic findings. Bony erosion of the sinus walls and extension into adjacent cavities have been mentioned in many reports.[15,27,28]

Lab investigations showed increased level of total IgE in all our cases. Our results are matching reports of other studies. Total IgE values generally are elevated in AFS, often to more than 1,000 U/mL. Total IgE level traditionally has been used to monitor the clinical activity of allergic bronchopulmonary fungal disease. On the basis of similar IgE behaviour associated with recurrence of AFS, total IgE levels have been proposed as a useful indicator of AFS clinical activity.[29]

Regarding management of AFS, adequate sinus surgery is a universally accepted component and the first step in the treatment of any patient with AFS[26]. 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. In our study patients who underwent surgery followed by oral and topical corticosteroids showed very good response, regarding relief from symptoms and recurrence.[30]

Initial diagnosis of allergic fungal sinusitis requires high index of suspicion on the part of the attending physician. Keeping in mind the results of this study and the reports of different studies showing a high prevalence of the disease, it is recommended that the diagnostic criteria for allergic fungal sinusitis should be followed strictly. Every patient of chronic rhinosinusitis should be properly evaluated with a detailed history, though clinical examination, radiological investigations (CT scan), laboratory investigation (IgE level), allergic mucin along with polypoidal tissue removed from sinus should be subjected histopathology staining. Fungal genus or species can be accurately identified on sinus allergic mucin culture, and nasal specimen for culture should be avoided.[15] Differentiation from invasive forms of fungal sinus disease is crucial, because systemic antifungal medication and extensive surgical tissue debridement are not required in allergic fungal sinusitis.

Because of budget constraints, fungal culture, MRI, and fungal-specific IgE and IgG, which are good screening tools, were not performed on all cases.

CONCLUSION

The AFS is a disease of young immunocompetent adults. Nasal obstruction, nasal discharge, nasal allergy and proptosis were the most common presentations. Skull base and orbital erosion is seen in majority of the cases. Orbital erosion is more common than skull base erosion. Initial diagnosis of allergic fungal sinusitis requires high index of suspicion in patients presenting with chronic rhinosinusitis, such cases should be evaluated properly. Allergic fungal sinusitis should be considered in all patients presenting with chronic rhinosinusitis. Differentiation from invasive forms of fungal sinus disease is crucial.

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Address for Correspondence:

Dr. Zakirullah, House No. 301, Street 15, Sector F-7, Phase-6, Hayatabad, Peshawar, Pakistan. **Cell:** +92-314-9028861
Email: zakirent@yahoo.com