

Allergic fungal sinusitis in children in Saudi Arabia

Jamil N. Al-Swiahb, MD, Ahmed Al-Ammar, MD, FRCS, Surayie H. Al-Dousary, MD, FRCS.

ABSTRACT

Objectives: To report the allergic fungal sinusitis (AFS) in children in Saudi Arabia and to review the experience of King Abdul-Aziz University Hospita in diagnosis and management of AFS in children.

Methods: Hospital charts of 45 children reviewed retrospectively. Clinical presentation, radiological and operative findings, management and outcomes studied. Only 25 patients had ≥ 4 diagnostic criteria, treated endoscopically between January 2000 and December 2005 and followed at least 2 years in KAUH, Riyadh, Kingdom of Saudi Arabia.

Results: Twenty-five patients had at least 4 criteria for AFS. All patients underwent functional endoscopic sinus surgery (FESS) with high recurrence rate, 44%. Twenty-eight percent needed revision surgery even with medical treatment post operatively. Moreover, no other complications were reported in this study. *Aspergillus spp* is the most common fungal type in our review.

Conclusion: Allergic fungal sinusitis in children is underestimated and understudied associated with poor outcome and high recurrence rate because of difficulty in management. Therefore, the most effective approach of AFS management in children is to have a high index of suspicion, adequate preoperative evaluation, medical preparation preoperatively, meticulous surgery, medical management, postoperative including topical and systemic corticosteroids and close clinical follow-up with endoscopically guided debridement.

Saudi Med J 2007; Vol. 28 (11): 1711-1714

From the Department of Otorhinolaryngology, Head & Neck Surgery, King Abdul-Aziz University Hospital, Riyadh, Kingdom of Saudi Arabia.

Received 21st March 2007. Accepted 9th June 2007.

Address correspondence and reprint request to: Dr. Jamil N. Al-Swiahb, Department of Otorhinolaryngology, Head & Neck Surgery, King Abdul-Aziz University Hospital, PO Box 245, Riyadh 11411, Kingdom of Saudi Arabia. Tel. +966 (1) 2355769. Fax. +966 (1) 2350220. E-mail: ziad8026@hotmail.com/fawaz8026@yahoo.com

In less than 2 decades, allergic fungal sinusitis (AFS) has evolved from a curiosity to an increasingly recognized condition. Previous study observed the clinical similarity to allergic bronchopulmonary aspergillosis, first noted the combination of nasal polyposis, crust formation, and sinus cultures yielding *Aspergillus* in 1976. This description was followed by reports of “allergic aspergillosis of the paranasal sinuses” and “allergic *Aspergillus* sinusitis”.¹ The term “allergic fungal sinusitis” was introduced in 1989 following reports indicating that this condition could be caused by a number of different fungi.² Only few studies were carried out in pediatric age group.¹⁻⁸ This study focuses on the characteristic features of pediatric allergic fungal sinusitis in all aspects of the disease including early diagnosis, management and the recurrence pattern.

Methods. A retrospective study conducted at the Department of Otorhinolaryngology, Head and Neck Surgery, King Abdul-Aziz University Hospital (KAUH), Riyadh, Kingdom of Saudi Arabia (KSA). The Ethical Committee Group of KAUH reviewed and approved the study. A total of 25 pediatric patients, clinically diagnosed with immunocompetent chronic rhino sinusitis (CRS), who underwent endoscopic sinus surgery between January 2000 and December 2005 were included in the study. All children were diagnosed with AFS if ≥ 4 of Kuhn and Swain AFS diagnostic criteria were present.⁹ Criteria for exclusion were age above 18 years, radiological and histological evidence of diagnosis other than chronic rhinosinusitis (CRS) or demonstration of hyphae invading tissue. All patients underwent endoscopic sinus surgery. Outcome of surgical, medical management and complication observed for at least 18 months. We retrospectively reviewed the demographic information, history, physical examination, laboratory and radiological findings, preoperative, intra-operative and postoperative management and follow up reports. All data were entered into a computerized database, and data analysis was conducted using the NCSS 2000/PASS 2000 statistical package.

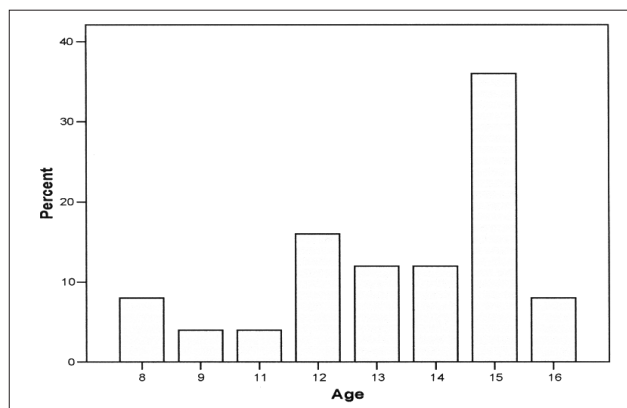


Figure 1 - Distribution of the children according to the age.

Results. The average age of the study population was 13.3 years. Ranging between 8-16 years with 14 males (56%) and 11 females (44%) (**Figure 1**). All were Saudi children living in the central area of KSA. Previous sinus surgery was found in 28% (n=7). The common clinical presentations are summarized in **Table 1**. Other findings include halitosis in 4% (n=1), visual impairment in 12% (n=3), ear symptoms in 20% (n=5), left cheek swelling in 8% (n=2), right cheek swelling in 4% (n=1). The average duration of symptoms at time of presentation was 3 months to one year. Nasal polyps were seen in 25 children, graded according to Lund and Mackay classification.¹⁰ Grades 3-4 in 88% (n=22), and Grades 1-2 in 12% (n=3). Eosinophilia was significantly high in 36% (n=9) of cases. Total IgE, fungal specific IgE, and fungal specific IgG were seen in 5 patients. The total IgE increased in 2 patients, while fungal specific IgE increased in one patient, none of our patient had abnormal fungal specific IgG titer. Radiological studies revealed that 60% with bilateral disease, 40% with unilateral disease and from both 80% of the cases had left side sinuses disease (n=20), and 64% had right sinuses disease (n=16). Seventy-six of the CT scans showed heterogeneous opacity. The Lamina papyracea was pushed in 12% of the cases (n=3), and eroded in 32% (n=8). Sinus wall was expanded in 60% of cases (n=15), and eroded in 16% (n=4), with orbital extension in 24% (n=6). However, none of the patients had intracranial extension. Large amount of allergic mucin was found in 60% of the cases (n=15), with fungal hyphae in 52% of the cases (n=13). The most common fungus grown from the culture was *Aspergillus fumigatus* seen in 32% of the cases (n=8), 2 other cases had *Dematiaceous fungi* grown. Different forms of treatments were used. Oral prednisolone was used preoperatively for 10-15 days in 12% of the cases (n=3), and in 64% (n=16) postoperatively. Local nasal

Table 1 - Most common clinical findings.

Symptoms and signs	n	(%)
Nasal obstruction	24	(96)
Nasal polyposis (grade 3-4)	22	(88)
Deviated nasal septum	17	(68)
Allergic rhinitis	16	(64)
Snoring	15	(60)
Purulent nasal discharge	13	(52)
Mouth breathing	13	(52)
Hyposmia	13	(52)
Postnasal discharge	9	(36)
Bronchial Asthma	9	(34)
Headache	7	(28)
Orbital proptosis	7	(28)
Nasal polyposis (grade 1-2)	3	(12)

treatment included normal saline, nasal irrigation, and steroid nasal spray was used preoperatively in 96% of the cases (n=24), and in 100% (n=25) postoperatively. All cases underwent endoscopic sinus surgery. Recurrence of the disease occur when polypoid mucosa obstruct the middle meatus or sinus ostium, which occurred after the first visit (2-4 weeks) in one patient, after the second visit (6-12 weeks) in 12% (n=3), and after the third visit (>12 weeks) in 44% (n=11). Revision surgery was carried out in 28% of the cases (n=7) when disease progress symptomatic and refractory to the medical treatment.

Discussion. Allergic fungal sinusitis is a non-invasive form of fungal sinusitis that seen in highly atopic individuals with sinusitis and nasal polyposis.⁷ Chronic fungal sinusitis results when large accumulations of eosinophil-rich allergic mucin containing sparse fungal elements cause mucous impaction and obstruction of the ostiomeatal complex.⁶ Mucous plugs may become an expanding mass. Multiple sinuses are usually involved and bony erosion of the sinus walls is present in as many as 50% of patients.⁹ Ninety-three percent of chronic rhino-sinusitis (CRS) cases were found to meet the diagnostic criteria for AFS, which makes it likely that AFS and CRS represent varying degrees of allergic response to the same fungal antigens.⁷ In our study, only 25 patients out of 45 children with CRS had ≥ 4 AFS diagnostic criteria. Allergic fungal sinusitis has been described in children with a mean age of 13.6,⁸ and 12.5.⁷ In our series, the mean age was 13.3 years. The male to female ratio of our cases was almost similar

to some published reports (male to female ratio 1.5-1). Many authors have noted nearly equivalent rates of unilateral and bilateral presentation of AFS overall,^{3,9} although children tends to present more often with unilateral disease (70%).³ We found that the bilateral involvement of the sinuses was more common (60%). Patients with AFS presents with nasal obstruction, nasal discharge, and headache. Previous studies reported that these symptoms were the most common presenting symptoms.^{3,7} Other symptoms such as history of snoring, mouth breathing, and hyposmia commonly noted in this study but not commonly reported in other series. Allergic rhinitis found in 64% of our cases, which is nearly similar to that mentioned in other studies.^{11,12} Many studies have shown that AFS patients suffer from atopy and more than half of AFS patients have concomitant bronchial asthma.^{7,9,13,14} In our study, only 34% of the cases had bronchial asthma. Aspirin sensitivity was not documented in any of our patients. Visual loss has been described to complicate AFS.^{15,16} However, in this study only 3 patients (12%) had documented visual impairment. Proptosis was the most common facial deformity in our findings (20% of the cases). It was also reported to be seen in 16-50% of patients with AFS.^{3,7,17-19} Many authors described telecanthus and diplopia in approximately 17% of the cases.^{1,20,21} In our study, we found telecanthus in 8% of the cases with widening nasal bridge; facial swelling in 12%, and no diplopia. Other clinical findings also noted such as deviated nasal septum (68%), inflamed nasal mucosa with turbinate hypertrophy (88%) and nasal polyposis (100%). Skin tests show molds positive. One study reported in their cases to have 52% molds allergies.²² Immunologic characteristics of patients with AFS include 1) elevated total IgE; 2) peripheral eosinophilia; 3) immediate and late cutaneous reactivity to specific fungal antigens; 4) positive serum precipitins; 5) fungal antigen-specific IgE and IgG antibodies and; 6) elevated fungal IgE. In addition, eosinophilic inflammatory mediators have been demonstrated within allergic mucin. The immunologic evidence points to a fungal-antigen triggered, IgE- and IgG-mediated, predominantly eosinophilic inflammation cascade leading to the clinical manifestations of AFS.^{2,23} In our finding, the total IgE was elevated in 2 of 5 tested patients, and one patient had a positive fungal specific IgE. The first report of both CT and MRI finding in cases of AFS was from Jay et al in 1988.¹⁶ Many authors described the radiological finding of AFS,^{2,9,24} which include an expansile nasal and sinus mass of single or multiple sinuses. It had been noted that the mass has discrete wispy areas of hyper-attenuation which is a characteristic finding of AFS often with associated thinning of the bone which may give the appearance

of bone erosion.⁸ Magnetic resonance imaging is not typically used for evaluation of AFS, but it may indicate to assess suspicious sinonasal mass or when there is bone erosions with extension to the surrounding structure such as the brain. Magnetic resonance imaging usually shows a central area of low signal on both T1 and T2 imaging along with T2 evidence of peripheral mucosal inflammation.²⁵ Magnetic resonance imaging can also be extremely useful in documenting precisely any areas of persistent or recurrent allergic mucin in previously treated patients.²⁵ In this study, CT finding showed involvement was usually bilateral asymmetrical with expansion in 60%, lamina papyracea erosion with orbital extension in 24% and no patient with CNS extension. Bone erosion as reported in many study may occur in 20-93% of AFS cases in both adult and pediatric age group.^{3,7} In one report, 50% of pediatric patients had bone erosion.⁷ The important regimen in treatment of AFS is a combination of surgery and long-term medical management. Early reports used classic non-endoscopic techniques with good results. The advent of endoscopic sinus surgery has led to replacement of conventional surgery in most areas with enough removal of sinus disease and rare significant complication, but even with surgical removal of disease and drainage alone the recurrence is common.²⁶ So adjuvant therapy with systemic steroids have been suggested for the treatment of AFS.² Oral steroid should be tapered in pediatric patients as soon as possible to avoid adverse effects.² Some authors suggest that debridement, nasal hygiene and topical steroids are effective without systemic steroids.^{1,14} The antifungal agents have been used in a few reported cases and have not been shown to be effective.^{2,7} This was supported by the histopathological findings which was characterized by an eosinophilic allergic response to a non-invasive fungi. Some authors suggested the use of irrigation with antifungal solution to speed the clearance of the causative organisms.^{2,7} One recent uncontrolled series of AFS patients on specific antifungal immunotherapy reported a very low recurrence rate after initial surgery.²² Many patients need periodic reevaluation and removal of recurrence disease and cleansing of the fungal growth in such cases, short infrequent bursts of steroid may facilitate control of disease. In this study, all patients were treated with functional endoscopic sinus surgery with careful removal of all polypoid disease and inspissated fungal mass and mucin with careful attention to preserve any normal anatomical landmarks. Allergic mucin, mostly in our patients, reveal fungal hyphae in 52% and positive fungal culture in 32% with *Aspergillus sp* (*Aspergillus fumigatus* and *Flavus*) in 6 patients and dematiaceous (*Curvularia* and *Alternaria*) in 2 patients. In addition to surgical management, all patients received postoperatively antibiotics (cefuroxime, amoxil, or

augmentin), 64% treated with prednisolone in addition to local nasal irrigation and steroids. Outcome of disease management were difficult to evaluate in this study because of poor compliance with follow up visits and treatment regimen. Forty-four percent of children experienced disease recurrence and 28% needed revision surgery in this study and other patients disease controlled with medical treatment and follow up.

In conclusion, AFS diagnosis is difficult and required a high index of suspicion. A confirmatory diagnosis made from testing the inspissated mucus, clinical and CT findings, along with careful communication with the investigating microbiologist about the possibilities of fungal growth. A comprehensive management plan including endoscopic sinus surgery, steroids and local treatment needed, and might provide long-term control of AFS. Long-term follow up is mandatory. Further studies needed to evaluate more in the pathophysiological aspects of the disease and the optimum medical treatment in pediatric age group.

References

- Manning SC, Vuitch F, Weinberg AG, Brown OE. Allergic aspergillosis: a newly recognized form of sinusitis in the pediatric population. *Laryngoscope* 1989; 99 (7 Pt 1): 681-685.
- Muntz HR. Allergic fungal sinusitis in children. *Otolaryngol Clin North Am* 1996; 29: 185-122.
- McClay JE, Marple B, Kapadia L, Biavati MJ, Nussenbaum B, Newcomer M, Manning S, Booth T, Schwade N. Clinical presentation of allergic fungal sinusitis in children. *Laryngoscope* 2002; 112: 565-569.
- Gupta AK, Ghosh S, Gupta AK. Sinonasal aspergillosis in immuno-competent Indian children: an eight-year experience. *Mycoses* 2003; 46: 455-461.
- Kupferberg SB, Bent JP. Allergic fungal sinusitis in the pediatric population. *Arch Otolaryngol Head Neck Surg* 1966; 122: 1381-1384.
- Gupta AK, Bansal S, Gupta A, Mathur N. Is fungal infestation of paranasal sinuses more aggressive in pediatric population. *Int J Pediatr Otorhino-Laryngol* 2005; 70: 603-608.
- Jenny M, Campbell MD, Melissa Graham MD, Heather C. Gray MD. Allergic fungal sinusitis in children. *Ann Allergy Asthma Immunol* 2006; 96: 286-290.
- Kupferberg SB, Bent JP. Allergic fungal sinusitis in the pediatric population. *Arch Otolaryngol Head Neck Surg* 1996; 122: 1381-1389.
- Mukherji SK, Figueroa RE, Ginsberg LE. Allergic fungal sinusitis: CT findings. *Radiology* 1998; 207: 417-422.
- Lund VJ, Kennedy DW. Staging for rhinosinusitis. *Otolaryngol Head Neck Surg* 1997; 117 (3 Pt 2): S35-S40. Review.
- Sobol SM, Love RG, Stutman HR, Pysher TJ. Phaeoophomycosis of the maxilloethmoid sinus caused by *Drechslera spicifera*: a new fungal pathogen. *Laryngoscope* 1984; 94: 620-627.
- Rinaldi MG, Phillips P, Schwartz JG, et al. Human Curvularia infections: report of five cases and review of the literature. *Diagn Microbiol Infect Dis* 1987; 6: 27-39.
- Cody DT, Neel HB, Ferreiro JA, Roberts GD. Allergic fungal sinusitis: the Mayo clinic experience. *Laryngoscope* 1994; 4: 1074-1079.
- Waxman JE, Spector JG, Sale SR, Katzenstein AL. Aspergillus sinusitis: concepts in diagnosis and treatment of a new clinical entity. *Laryngoscope* 1987; 97: 261-266.
- Pratt MF, Burnett JR. Fulminant *Drechslera* sinusitis in an immuno-competent host. *Laryngoscope* 1988; 97: 1343-1347.
- Jay WM, Bradsher RW, Snyderman N, Augtuaco EJ. Ocular involvement in mycotic sinusitis caused by *Bipolaris*. *Am J Ophthalmol* 1988; 5: 366-670.
- Torres C, Ro JY, El-Naggar AK, Sim SJ, Weber RS, Ayala G. Fungal sinusitis: a clinicopathologic study of 16 cases. *Hum Pathol* 1996; 27: 793-739.
- Chhabra A, Handa KK, Chakrabarti A, Mann SB, Panda N. Allergic fungal sinusitis: Clinicopathological characteristics. *Mycoses* 1996; 39: 437-441.
- Friedman GC, Warren R, Hartwick J, et al. Allergic fungal sinusitis: report of three cases associated with Dematiaceous fungi. *Am J Clin Pathol* 1991; 96: 368-372.
- Rolston KV, Hopfer RL, Larson DL. Infections caused by *Drechslera* species: case report and review of the literature. *Rev Infect Dis* 1985; 7: 525-529.
- Khan DA, Cody DT 2nd, George TJ, Gleich GJ, Leiferman KM. Allergic fungal sinusitis: an immunohistologic analysis. *J Allergy Clin Immunol* 2000; 106: 1096-1101.
- Mabry RL, Manning SC, Mabry CS. Immunotherapy in the treatment of allergic fungal sinusitis. *Otolaryngol Head Neck Surg* 1997; 116: 31-35.
- Bent JP, Kuhn FA. Diagnosis of allergic fungal sinusitis. *Otolaryngol Head Neck Surg* 1994; 111: 580-8.
- Bent JP, Kuhn FA. Allergic fungal sinusitis/polypoidosis. *Allergy Asthma Proc* 1996; 17: 259-268.
- Corey JP, Delsupehe KG, Ferguson BJ. Allergic fungal sinusitis: allergic, infectious, or both? *Otolaryngol Head Neck Surg* 1995; 113: 110-119. Review.
- Manning SC, Merkel M, Kriesel K, Vuitch F, Marple B. Computed tomography and magnetic resonance diagnosis of allergic fungal sinusitis. *Laryngoscope* 1997; 107: 170-176.