Allergic fungal rhinosinusitis

Report of 4 cases from Saudi Arabia

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ABSTRACT

Allergic fungal rhinosinusitis is a newly recognized clinical entity of chronic rhinosinusitis. Over the past 3 years, 4 such patients were treated in our hospital. The clinical and pathological features of these 4 cases which merited the criteria for such diagnosis, are described. All the 4 cases had history of nasal polyps, asthma, or both with radiographical evidence of pansinusitis. Histologically, the thick greenish-brown inspissated material specimens which were collected and submitted to the laboratory showed, eosinophils, Charcot-Leyden crystals but no fungal elements were detected on routine hematoxylin and eosin sections and no tissue invasion was noted. However, scanty *aspergillus hyphae* were detected on sections stained with silver. All 4 cases grew *Aspergillus flavus* only from the swabs and no other fungi were seen and all were treated by surgical debridement, aeration, oral itraconazole with no steroids.

Keywords: Allergic fungal rhinosinusitis, paranasal sinuses aspergillosis.

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Aspergillus is the most common fungal infection of the nose and sinuses.[1] Many forms of nasal and paranasal aspergillus infection have been described: invasive, fulminant and the non-invasive which includes Aspergilloma (fungal ball) and Allergic Aspergillus Sinusitis (AAS). This last variant affects more than one sinus and occurs in healthy adults with asthma, polyps or both. It is characterized by the presence of thick inspissated mucus in the sinus with marked eosinophilic reaction and Charcot-Leyden crystals. Fungal hyphae are very scanty and only shown by Grocott silver stain but not by routine hematoxylin and eosin (H&E) stain.[2,3] However, a variety of other fungi, such as *Curvularia lunata* among other species, were grown from the eosinophilic mucin concretions.[4] Thus, more recently, the term allergic fungal rhinosinusitis (AFRS),[5] a broader term, replaced the former AAS. We present here 4 such cases encountered over the last 3 years in our hospital. Their clinical picture, pathological features and management are discussed below.

Case Report.

Patient 1. A 27 year old male Saudi school-teacher, presented with a history of excessive lacrimation of the right eye for 4 months as well as nasal obstruction for 7 months. History of dental surgery at the right upper molar gingiva and bronchial asthma was found to be positive. Clinical examination showed large right nasal polyps. Sinus x-rays revealed totally opaque right maxillary antrum, ethmoidal and sphenoidal sinuses. When right Caldwell-Luc procedure was performed, it

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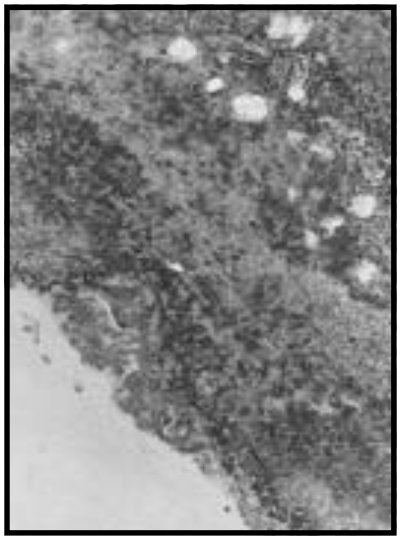

Figure 1 - Photomicrograph of clusers of chronic inflammatory cells (dark areas) and the Charcot-Leyden crystals (pale areas) on a homogenous background of inspissated mucin (H&E stains; x 100).

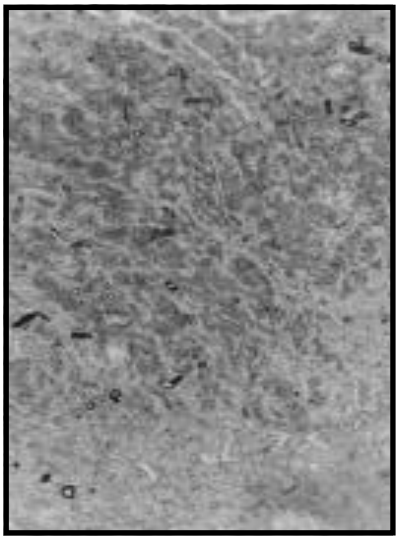

Figure 2 - Histological section of mucin showing scanty septate branching of Aspergillus hyphae (Grocott silver stain x 400).

revealed inspissated greenish-brown mucus filling the right maxillary antrum, ethmoidal and sphenoidal sinuses. The histology showed oedematous inflammatory polyps and the inspissated mucus was found to contain numerous prominent eosinophils and the typical Charcot-Leyden crystals (Figure 1). Fungal hyphae were not detected in H&E stain but they were seen in sections stained with Grocott-silver stain, as scanty pale hyphae with dichotomous branching, typical of the *Aspergillus species* (Figure 2). The fungus isolated was identified to be *Aspergillus flavus*. Post-operatively, the patient was put on oral itraconazole (Sporonox) capsules, 100mg daily for one month after checking the liver and kidney functions. Follow up for 6 months revealed no symptoms.

Patient 2. A 14 year old Saudi female student, presented with a 4 year history of left rhinorrhoea, nasal blockage, secondary to nasal polyps, and a recent left proptosis for which she sought clinical advice in both endocrinology and ophthalmology clinics. Examination revealed left nasal polyp. Sinus x-rays showed left maxillary and ethmoidal opacity. The CT scan of the paranasal sinuses showed chronic granulomatous tissue with marked calcifications characteristic of fungal infection, in the left paranasal sinuses including the sphenoidal sinus. The chest x-ray was clear. At left Caldwell-Luc and nasal polypectomy, the left ethmoidal and left maxillary sinuses were impacted with yellowish-green inspissated thick mucus and the septae were all destroyed forming one large cavity. The floor of the orbit was thinned out by the impacted mucus with secondary proptosis. The histopathology of the material removed from the sinuses was similar to the findings in patient one. The swab culture also grew *Aspergillus flavus.* Post-operatively she was put on itraconazole oral capsules after checking the liver and kidney functions. She remained symptom-free for the 3 month follow up period after surgery.

Patient 3. A 17 year old Saudi female, presented with a 2 year history of gradual right nasal obstruction and marked right proptosis with no diplopia and recurrent frontal headaches and rhinorrhoea. Sinus x-rays showed opaque right pansinusitis, and CT scan showed radio-opaque masses with calcifications in all the right paranasal sinuses. Right nasal polypectomy coupled with Caldwell-Luc procedure and transmaxilary ethmoido-sphenoidectomy were performed. Necrotic greenish-brown, thick, inspissated mucus, with polypoidal masses were removed from all these sinuses. The impaction resulted in pressure necrosis and thinning out of the right antral roof and medial walls, as evidenced by the right proptosis. At histology the diagnosis of allergic aspergillus sinusitis was made. The culture of the inspissated mucus grew *Aspergillus flavus*. She received oral itraconazole capsules after surgical debridment and aeration. She has remained symptom-free at regular follow up visits for the last 3 years.

Patient 4. A 16 year old Saudi school-girl presented with left nasal obstruction for 2 months and gradual left proptosis. She is not asthmatic but her mother and uncle are known asthmatics. Examination revealed a large polyp filling the left

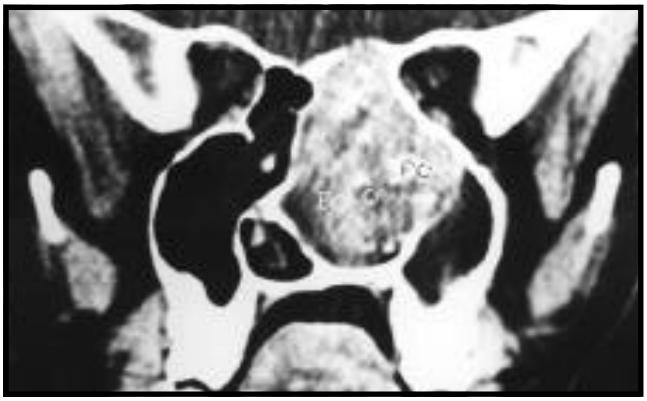

Figure 3 - An axial CT scan showing soft tissue mass in the left maxillary, ethmoidal and sphenoidal sinuses with marked typical calcifications in the sinuses; marked A, B, and C.

nasal fossa pushing the septum markedly to the right. CT scan (Figure 3) showed, a large soft tissue mass in the left nasal cavity with extensive calcifications and extensions into the left ethmoidal and sphenoidal sinuses. The medial wall of the left maxillary sinus was thinned out and pushed laterally. The MRI confirmed the same findings as the CT scan. At nasal polypectomy, large amounts of soft, cheesy brownish-green material, with characteristic moldy odor, was removed from the anterior and posterior ethmoidals. The material was extending intracranially through the ethmoidal clefts and cells, open superiorly with the dura exposed in some areas. All the areas involved, including the sphenoid sinuses, were debrided by the functional endoscopic sinus surgery. Histopathology showed the same picture as the previously mentioned 3 patients and the culture grew *Aspergillus flavus*. Postoperatively, she received intravenous cephradine and metronidazole for one week with no early complications. Further management plan included oral itraconazole 200mg daily for one month after complete investigations. So far, no recurrences have been seen.

Discussion. Millar et al[6] were the first to describe AAS in 1981, due to its histological similarity to that of allergic bronchopulmonary aspergillosis (ABPA), described by Hinson et al.[7] In 1983, Katzenstein[2] and her co-authors termed the histopathological presence of eosinophilic mucin secretions with Charcot-Lyden crystals and hyphal fragments of *Aspergillus* species as AAS. Subsequently, it was recognized that other fungi can be grown from the mucin secretions of the sinuses in addition to various *Aspergillus* species, and the term was changed to AFRS[5] to reflect this finding. It has been extensively documented in rhinological literature in the past 15 years by many authors including Kinsella[8] and Marple et al.[9] Although aspergillosis of the paranasal sinuses is almost endemic in neighboring Sudan[10,11,12] few cases were reported from different regions of Saudi Arabia. Geographical location may play a role in determining the particular *Aspergillus* species causing infection. All the cases in our series from Qassim Region, grew *Aspergillus flavus*, similar to the ones reported from Asir[13] Region and Sudan[10,11] while *Aspergillus fumigatus* was mostly isolated in Western[14] and Eastern[15,16] Regions. Qassim Region is the center of the agricultural activities of Saudi Arabia, thus when we reviewed the available literature, no previous reports were found of this special entity of fungal disease. It seems to us that the diagnosis of AFRS is overlooked and poorly recognized in this region by both clinicians and pathologists. The diagnosis, however, could be easily made if only the possibility is always considered. The points that raised the index of suspicion for diagnosing AFRS among our patients, were as follows. Clinically, they were all atopic young adults presenting with nasal obstruction, chronic pansinusitis, or with history of asthma, or both. Examination of the nose, showed nasal polyps and thick greenish mucus secretions. Radiologically, unilateral opaque, multiple sinuses involvement was evident in plain sinus x-rays and CT scan. The characteristic calcifications in CT are due to deposition of heavy metals in the fungal concretions or mud. At surgery, apart from the nasal polyps, the characteristic features were the presence of thick greenish-brown inspissated mucus, which was difficult to remove and the presence of a moldy smell. Histopathology of the material submitted to the laboratory showed oedematous nasal polyps and pale basophilic or eosinophilic mucin containing sloughed respiratory epithelial cells, chronic inflammatory cells with prominent eosinophils and Charcot-Leyden crystals which appeared as hexagonal in cross-section and bipyramidal in longitudinal section (Figure 1). Fungal hyphae were not seen by routine H&E stain, nevertheless few septate aspergillus hyphae with the characteristic dichotomous branching at 45° were observed by Grocott silver stain (Figure 2). No evidence for tissue invasion was recognized. All the paranasal sinuses, including the sphenoidal sinuses were involved at least unilaterally, indicating extensive disease but not necessarily invasive. In view of the extensive nature of the disease with orbital and sphenoid sinuses involvement, surgical debridement, aeration and oral itraconazole post-operatively were our treatment of choice as recommended in the literature.[17,18] The predisposing factors and the exact pathogenesis of AFRS are uncertain and still speculative[19] and the pros and cons of the use of postoperative systemic steroids as an adjunct to surgery and antifungals, are not yet settled.[20]

Therefore, no steroids were advocated in our series and as the follow up periods were short, it is difficult at this stage to comment on recurrence.

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