Allergic Fungal Rhinosinusitis Caused by Aspergillus flavus

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Summary

Allergic fungal rhinosinusitis is a chronic inflammatory disorder of the sinonasal mucosa, with or without nasal polyps, which is frequently associated with microbial colonization including fungi. A case of fungal rhinosinusitis in Aseer area, Saudi Arabia, is described. The patient was admitted with common symptoms including nasal obstruction accompanied by itching, sneezing, rhinorrhea, epistaxis and recurrent headache. The patient was examined clinically and by CT scan. Nasal sinus swabs and a biopsy specimen were submitted for microbiological analysis. Polyps were surgically removed during functional endoscopic sinus surgery. Histopathology showed the presence of acute and chronic inflammatory cell infiltrates (rich in eosinophils) in the covering epithelium layers. *Aspergillus flavus* was isolated

and identified from the lesions. The patient was discharged after showing good recovery, and home follow-up revealed no recurrences.

Key words: Paranasal sinuses, Polypoidal disease, Rhinorrhea,

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Introduction

Chronic rhinosinusitis (CRS) comprises a spectrum of diseases including fungal rhinosinusitis. Allergic fungal rhinosinusitis (AFRS) is one form which is defined as chronic inflammation of the nose and nasal sinuses, with or without nasal polyps (1). Patients suffering from AFRS report nasal obstruction and secretion, olfactory impairment, head and facial pain. These symptoms also impact quality of life considerably (2). The mechanisms by which fungi can generate an effect on sinus mucosa in susceptible individuals is not fully understood (3, 4). Chronic rhinosinusitis is a challenging problem, bearing in mind the rising morbidity and the lack of consensus on accepted measures for diagnostics and treatment of this condition.

Many factors predispose to the development of AFRS (3). The pathogenic mechanisms of AFRS remain to be elucidated despite a wealth of publications devoted to this problem. The results of many evidence-based investigations are different and even conflicting. Both diagnostic techniques and characteristics of AFRS vary broadly depending on the standards adopted in different countries (5).

Treatment is prescribed according to the Classification Schemes for Chronic Rhinosinusitis with Nasal Polyposis Endotypes (6), but 38–51% of CRS patients do not respond to the recommended medical therapies (6, 7). In general, antifungal medication is not usually prescribed in case of non-invasive fungal infections (1, 6, 8).

Fungal sinusitis caused by Aspergillus species has become a major cause of morbidity and mortality among immunocompromised patients. Aspergillus fumigatus is the most frequently isolated pathogen while *Aspergillus terreus* is less common (9). *Aspergillus* spp. are associated with unilateral nasal polyps and a significant recurrence rate, necessitating frequent endoscopic sinus surgery and aggressive antifungal medication. *Aspergillus* spp. are ubiquitous in the environment and rarely cause infections though many authors consider them mere saprophytes (9). Nevertheless, fungal colonization without invasion of tissue is to blame for initiation of AFRS (3). A rare case of fungal sinusitis caused by *Aspergillus flavus* in an immunocompetent patient is described.

Case report

Maxillary sinusitis was diagnosed in an adult female patient admitted with symptoms of sinusitis: nasal obstruction accompanied by itching, sneezing, rhinorrhoea, epistaxis and recurrent headache. The patient was examined clinically and using CT scan. Nasal sinus swabs and a biopsy specimen were submitted for histopathology and microbiology analyses. CT scan of head showed sinonasal polypoidal disease involving ethmoid, frontal and sphenoid sinus, right nasal fossa and extended to maxillary sinuses bilaterally. Increased density of the sphenoethmoidal recess was noted. Adjacent brain parenchyma and orbital structure were not affected (Fig. 1). Polyps were surgically removed during functional endoscopic sinus surgery (Fig. 2). Histopathology showed presence of acute and chronic inflammatory cell infiltrates (rich in eosinophils) in the covering epithelium layers. Aspergillus species was isolated from the lesions. As this was a non-invasive fungal infection, no antifungal was used in this case. The patient was discharged

after showing good recovery, and home follow-up revealed no recurrences. Histopathology [H&E] examination of tissue section showed multiple white yellowish pieces. The sections of the specimen labelled nasal polyp showed oedematous polyp lined by respiratory epithelium and infiltrated by chronic inflammatory cells covered by respiratory epithelial overlying oedematous stroma, which contained mucus glands infiltrated by lymphocytes, neutrophils, macrophages and plasma cells, were evident. Inflammatory nasal polyp associated with abscess formation was seen. The sections showed partially necrotic tissue with a dense, acute on chronic inflammatory cell infiltrate. Abscess formation and eosinophilic material are also seen.

The fungus was identified when colony morphology appeared on Sabouraud dextrose agar (SDA) and using microscopic features following recommended standard methods (10). Heavy fungus growth on SDA from the purulent material was obtained after 3 days of incubation at 30 °C (Fig. 3A). Under the microscope, the fungus showed septate hyaline hyphae, conidial heads with vesicles, septate hyaline hyphae, and many spores (Fig. 3B). Such structures are characteristic of *Aspergillus flavus*.

Discussion

This case study was diagnosed as allergic fungal rhinosinusitis from the clinical, pathological and mycological evidence. Fungal rhinosinusitis is classified into two major groups: extra mucosal (non-invasive) and invasive. The non-invasive form includes superficial sinonasal mycosis, fungal ball and AFRS. The present case falls in the AFRS category given the clinical, pathological and mycological evidence. The invasive form includes chronic invasive (indolent) and acute (fulminant) fungal rhinosinusitis (1). Invasive forms of fungal rhinosinusitis are usually caused by hyaline mold fungus (Aspergillus, Zygomycetes and Fusarium), while the most common cause of the non-invasive form is the dematiaceous mold fungi (Bipolaris, Curvularia, Pseudallescheria) (11, 12). The patient usually presents with headache, nasal congestion, epistaxis, proptosis and other symptoms of chronic rhinosinusitis. This form of infection is most commonly present in individuals who are immunocompromised with uncontrolled diabetes (13), and a high index of suspicion is necessary to make proper diagnosis. The fungus Aspergillus flavus was detected in the present case and no evidence of invasion was documented. Hence it was classified as non-invasive CRS form with superficial sinonasal mycosis CRS with nasal polyposis (6). Fungi are found in 96% of patients with chronic sinusitis; the most commonly isolated fungi species are Alternaria, Penicillium, Cladosporium, Aspergillus, Candida and Fusarium, especially in those with defective immunities resulting from HIV and hepatitis C (14). A. flavus is a common saprophyte considered an opportunistic pathogen. It is likely to cause invasive, disseminated disease



Figure 1. CT scan axial cut of a patient with sinonasal polypoidal disease involving sphenoid, right ethmoidal, frontal and the right nasal fossa. Increased density of the sphenoethmoidal is noted. Adjacent brain parenchyma and orbital structure are not affected.

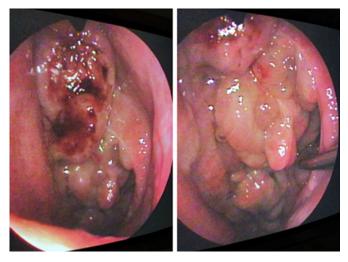


Figure 2. Endoscopy using 30 $^{\rm o}$ showing left nasal polyps grade 3 originate from ethmoid.

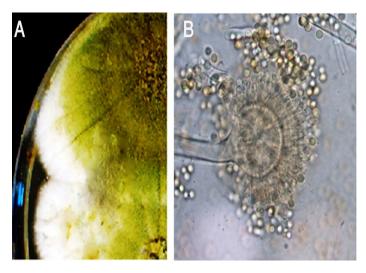


Figure 3. Colonies of *Aspergillus flavus* grown on Sabouraud dextrose agar at 30 °C for 7 days (A), and a microscopic slide showing the presence of conidial heads with vesicles, septate hyaline hyphae, and many spores (B), characteristic of *Aspergillus flavus*.

in a manner similar to other *Aspergillus* species such as *A. fumigates* and *A. niger*. These opportunists are especially important risks in immunocompromised patients.

Treatment for this case, as for other non-invasive fungal rhinosinusitis, consisted mainly of surgical removal. No antifungal is needed against non-invasive fungal infections (1, 6, 8). Also, intranasal corticosteroids to reduce disease activity, and frequent sinus irrigation with warm isotonic saline to prevent impaction of mucus are recommended. Surgical treatment consists of endoscopic polyp resection, debridement and sinus aeration. Postoperative oral and intranasal corticosteroids should be administered. These measures improve patient symptoms, although recurrence rate remains high. Treatment of chronic invasive fungal rhinosinusitis should also include control of any underlying metabolic or immunologic disorders (8).

Outcome measurements are chosen according to experience in the field. Patient symptoms are thought to be an important parameter because patients seek medical advice in case of symptoms, regardless of the extent of disease visible on nasal imaging or with nasendoscopy (15). The indication for FESS in the management of chronic rhinosinusitis is based primarily on practical facts. National and international clinical guidelines recommend drug treatment for no less than one month prior to surgical intervention. Drug treatment consists of nasal corticosteroids supplemented with systemic corticosteroids or a longer course of antibiotics (16). Patients failing drug treatment are offered a choice between more intensive drug treatment and surgery. Shared decision-making between the otorhinolaryngologist and the patient decides the moment that surgery is needed to relieve symptoms. Because of the chronic nature of the (mucosal) disease, the optimal treatment would be local treatment with medication combined with surgery (17).

Conclusion

This report concludes that early mycological diagnosis and appropriate medical and surgical interventions are prerequisites for improved patient care outcome. The treatment of the case was successful with functional endoscopic sinus surgery. This is in accordance with literature that ESS can significantly improve the condition (15).

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