Asparagillosis of the Sinonasal Tract

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ABSTRACT

This paper presents seven patients demonstrating the four patterns of sinonasal tract aspergillosis and reviews the clinicopathological spectrum of the disease.

The allergic aspergillosis patient presents with long standing nasal obtruction and polyps. X-rays usually show opaque multiple sinuses sometimes with areas of increased density. The affected sinuses are filled with thick mucin containing the fungus hyphae. Treatment is by surgical debridement followed by steroid therapy. The non-invasive aspergillosis usually presents as persistent unilateral chronic sinusitis in otherwise healthy patient. Radiology disclose single opaque sinus; sometimes associated with metal-dense shadows. The fungus is present extra mucosaly in the lumen. Treatment is surgical clearance and aeration. The invasive type appears clinically and radiologicaly as slowly progressive sinus mass extending beyond the bony walls. Histologicaly the fungus is invading the tissue inducing a granulomatous reaction. It is treated by debridement and often with systemic antifungal agents. The fulminant aspergillosis occurs as rapidly progressive destructive necrotizing mucoperiostitis in immunocompromised patients. Treatment is by systemic antifungal agents combined with surgical removal of the disease.

INTRODUCTION

Aspergillosis of the nose and paranasal sinuses is not a common disease, despite an increase of the reported cases over the last two decades (McGuirt and Harrill 1979, McGill et al. 1980 , Van Haacke 1984, Quiney et al.1988 and Manning et al. 1989). This increase may be due to hightened awareness and improved diagnostic methods. This paper reports a series of seven patients with paranasal sinuses aspergillosis seen at King Abdul Aziz Hospital, Riyadh, Over four years. All the four basic patterns of this disease are presented in the series.

CASE REPORTS

Case 1

A 9 years old asthmatic girl, presented with bilateral nasal polypi and bilateral exophthalmos. She gave history of nasal polypectomies twice over the previous 18 months. She was investigated for cystic fibrosis but results were negative. X-rays showed opacities of all paranasal sinuses with displacement of both eyes (Fig.1). Bilateral intranasal ethmoidectomies and sphenoidostomy showed thick mucosa, polypi and tenacious mucus. The examination of the later showed scanty fungal hyphae.

Case 2

A 27 years old, asthmatic female patient presented with recurrent bilateral nasal polypi. X-rays examination showed expansion of both maxillary antra, opacification of all the paranasal sinuses, with areas of increased densities on the left maxillary, posterior ethmoid and part of the left sphenoid sinusis (Fig.2). Bilateral Caldwell Luc and intranasal ethmoidectomies were performed to remove thick mucosa and polypi from the nose and the sinuses. Thick mucoid material were isolated from the left antrum and its microscopical examination showed respiratory epithelium cells and eosinophils with scanty aspergillus hyphae. Diagnosis of allergic aspergillosis was made and the patient was put on topical beclamethazone. Eighteen months post-operatively she has no recurrence.

Case 3

A 29 years old lady was presented with three months history of right facial pain and post-nasal

discharge refractory to medical treatment and antral lavage. Plain X-ray (Fig.3) showed two very high attenuated densities laying an opaque left maxillary antrum. Left Caldwell Luc operation was performed to remove thick antral mucosa and greasy greyish material which was filling the lumen. Histological examination of this material illustrated aspergilus fungus with no invasion of the mucosa. Diagnosis of non-invasive aspergillosis was made and no further treatment was needed. Patient remained symptoms free for 4 years post- operatively.

Case 4

A 23 years old lady was admitted for routine septoplasty to treat persistent right nasal obstruction. She had no history of nasal discharge or facial pain. Pre-operative plain X-ray showed a high density shadow in the left maxillary antrium. A CT scan confirmed this finding (Fig 4). Left Caldwell Luc operation was carried out to show greasy greenish material which turned to be fungal debris when examined microscopically.

Case 5

A 24 years old lady who was 32 weeks pregnant was admitted because of severe epistaxis from the left nostril. Examination showed polypoidal lesion in the left nasal cavity and mild left proptosis. The bleeding was controlled by anterior nasal packing. A CT scan showed a lesion in the left nasal cavity, maxillary antrum, ethmoid and orbit with bone erosions (Fig. 5a). Repeated biopsies of the nasal cavity lesion were inconclusive. After the patient gave birth, the nose and sinuses were explored via lateral rhinotomy approach to remove blackish greasy material. Histological examination showed granulomatous lesion with aspergillus fungus confirming diagnosis of invasive aspergillosis (Fig. 5 b & c). No systemic anti fungal treatment was given. The patient had to leave the country immediately after the operation.

Case 6

A 17 years old lady presented by recurrent left single nasal polyp which was diagnosed as antro choanal polyp. However, X-rays showed shadow of increase densities in the left maxillary and nasal cavity (Fig.5). Diagnosis of aspergillosis was confirmed by histological examination of the removed polypi.

Case 7

A 25 year old lady, who was under treatment of acute lymphocytic leukaemia developed headache and fever with foul smelling blood stained nasal discharge, proptosis and loss of vision in the left side. The symptoms were of sudden onset and were rapidly progressive for two weeks. Examination showed extensive ulceration in nasal mucosa with friable haemorrhagic lesion in the middle meatus, left eye proptosis, restriction of the eye movements and loss of pupilary reflex. Laboratory investigation showed WBC of only 700 with no granulocytes. A CT scan showed large lesion of all the left paranasal sinuses with extension in the orbit and the anterior cranial fossa (Fig.7). A biopsy taken from nose showed extensive tissue necrosis with a spergillus hyphae. The patient refused to have cranio facial resection of the disease. Instead limited surgery was performed to debride part of the disease through lateral rhinotomy approach. Amphotericin B was started post-operatively but it failed to halt the progress of the disease and the patient expired from intracranial infection two weeks later.

DISCUSSION

Aspergillus is the most commonly encoutered fungus in man's environment (Waxman et al.1987). It is a spore forming fungus commonly found as saprophyte in soil, dust and decaying organic material. The fungus grows best as an anaerobe, especially in warm and damp climate.

Infection of the sino-nasal tract is more commonly caused by Aspergillus fumigatus or A. flavus. Other species like A. niger, A. oryzae and A. nidulans are less frequently implicated as sinus pathogens (Jahresdoerfer et al. 1979). The geographical location may influence the particular Aspergillus species causing infection.

Aspergillosis is not transmissible between humans and is always contracted from an exogenous

source. Although the fungus may be introduced into the sinuses during a surgical procedure or following trauma (Kley and Draf, 1971), most infections probably occur after inhalation of airborne spores. What makes a common saprophytic fungus to become pathogenic is not fully understood.

It is postulated that mechanical obstruction of the nose and paranasal sinuses secondary to septal deviation, nasal polypi and chronic rhinitis; induce hypoxic environment which foster the growth of this anaerobic organism (Sarti et al. 1988). However, the fact that aspergillosis is more common in the lungs argues strongly against this theory. The progression of the disease is believed to be dependent upon its location (Nielson et al. 1983), immunocompetence (McGill et al. 1980), duration (Stammberger et al. 1984) and the presence of allergy (Katzenstein et al. 1983).

The maxillary antrum is the common single sinus to be affected with other single sites occuring only rarely (Jahresdoerfer et al.1979). However, in the majority of cases a combination of sinuses and the nasal cavity are involved and this probably represents late presentation and/or multiple primary infections (Quiney et al. 1988). In this series, the infection was confined to a maxillary sinus in two patients (Cases No. 3 and 4), to the maxillary and nasal cavity in one patient (No. 6) while in all other cases multiple sinuses were involved.

The pathology and clinical features of aspergillosis very according to the type as it will be discussed below. However, the diagnosis of aspergillosis, in general, is established by identification of the fungus by microscopical examination and by its culture. Histological examination should not only be limited to the mucous membrane, but must include any secretions or crusts found in the nose or the sinuses. The specimen submitted for microscopy should be stained with hematoxylin and eosin, silver, or periodic acid schift. The later two are more selective stains that identify the septate hyphae, the dichotmous branching and the 45 angle branching of the organism (Fig.5c). Material for culture should be placed on Sabouraud's agar with an antibiotic to inhibit bacterial growth. Culture of the fungus may be very difficult due to the low viability of the organism present in the specimen. In fact, the results of culture were found to be negative or inconclusive in up to 60% of cases (Jahresdoerfer et al.1978). In this seven patients series, culture was not necessary to establish the diagnosis.

Classification

Aspergillosis of the paranasal sinuses is classified into four distinct pathoclinical forms: allergic, non-invasive, invasive and fulminant. In the first two forms (allergic and non-invasive) the fungus is present in the lumen of the sinus with no invasion of the tissue. In the other two types (invasive and fulminant) the organism invades tissue inducing a granulomatous reaction in the former and necrotizing reaction in the later.

1- Allergic aspergillus sinusitis

The incidence of allergic aspergillus sinusitis is not established yet. Since its description first by Katzenstein et al., in 1983, 32 cases have been reported (Hartwick and Batsakis 1991). The pathophysiology of allergic aspergillus sinusitis is speculative. It is postulated that the disease is a combination of both type I (IgE) and type III (immune complex) immunologic reaction. The disease begins by the inhalation and trapping of Aspergillus spores in viscid mucous. Aspergillus antigens then react with IgE sensitized mast cells. This is followed by the cascade of immunologic events resulting in a state of chronic inflammation, leukocytosis, and tissue destruction (Waxman et al. 1987).

In allergic aspergillosis the sinuses are filled with firm, white-tan mucoid material. Microscopically this material consists of mucin containing numerous eosinophils, sloughed respiratory epithelial cells, Charcot-Leyden crystals and scattered aspergillus hyphae (Katzenstein et al.1983). There may be acute and chronic inflammatory cells in the mucosa but invasion of tissue by the fungus is not seen (Hartwick and Batsakis 1991). The patient usually presents with

long standing history of progressive nasal obstruction and sinus disease refractory to medical and surgical treatment. Facial deformity resulting from long-standing progressive expansile sinusitis may occur particulary in children (Manning et al. 1989). Thick inspissated allergic mucin is seen in the sinuses. Radiologically multiple sinuses show opacification; sometimes with discrete areas of high density (Fig.1). Expansion (Fig.2) or bone erosion may occur in the involved sinuses especially in the paediatric patients (Manning et al. 1989 and Zinreich et al. 1988). Serology can aid in the diagnosis, although most tests are still relatively non specific and may be positive when other chronic respiratory tract disease are present (Manning et al. 1989).

The optimal therapy for allergic aspergillosis has not been established. Surgical debridement and aeration of the involved sinuses with or without corticosteroids appear to be the range of therapeutic options (Waxman et al. 1987). Although some cases may be "cured" by surgery alone; steroid is given to prevent recurrence which may otherwise occur. Most cases respond well to topical corticosteroid but some cases will only respond to systemic administration.

2-Non invasive aspergillosis (Aspergilloma)

This type of sinus Aspergillosis usualy appears in otherwise healthy persons as noncontagious sporadic disease without predilection for age or race , but with a predilection for female patients. The significance of the last finding is uncertain (McGuirt and Harrill, 1979). In distinction to mucormycosis there is no increased incidence in diabetic patients (Quiney et al.1988). The non- invasive aspergillosis is characterized pathological by the presence of a "fungus ball" in the sinus (extramucosal); and the histology shows tangled mycelium of aspergilli with little inflammatory response. The hyphae are arranged in concentric layers like onion rings with each layer corresponding to a growth episode of the fungus. Although it may be asymptomatic (like Case No.4) the clinical feature of the non-invasive Aspergillosis usually resembles chronic bacterial sinusitis with symptoms of unilateral nasal obstruction, pressure feeling and drainage of a foul, gelatinous, grey or green substance. Often flecks of grey membrane will be blown from the nose (McGuirt and Harrill 1979). Basically the symptoms progress over months or even years. Examination of the nose may show polyps or/and pale oedematous turbinates. Repeated irrigation of the maxillary sinuses are frequently made, while no exact diagnosis is given and the patients do not recover completely. Sinus washout may reveal greasy and darkish material; but more often it is unrewarding due to the inspissated nature of the material. However, Nishioka et al. (1989) reported a high diagnostic rate by examination of sediment obtained by antral lavage stained by papanicolaou and by using cell blocks. On the other hand, sinuscopy may be more useful, showing red swollen mucosa with petechial haemorrhage and showing green yellow greasy intra cavitary material (Quiney et al. 1988).

Radiography usually shows a single cloudy sinus, most often the maxillary sinus. Fluid levels are not usually seen. Frequently there are extremely radiation-dense shadows in the lumen (Fig.3,4). Stammberger et al.(1984) demonstrated that these metal-dense X-ray shadows are due to local accumulation calcium phosphate within the fungal mass, and they regarded them as pathognominic of the disease .

The treatment of this form of aspergillosis is primarily surgical. Most cases are cured by surgical excision of the disease with aeration and drainage of the involved sinus (McGuirt and Harrill 1979).

3- The invasive sinus aspergillosis

This type of aspergillosis also occurs in immunocompotent patients. It is characterized pathologically by tissue necrosis and granulomatous reaction with fibrosis surrounding the organism. Aspergillus hyphae are scanty and not easily seen with routine stains appearing as halos in giant cells; but can be easily identified with fungal stains (Fig.5c).

Clinically it usually pressents as paranasal

sinus neoplasm with extension to the adjacent sinuses, Orbit or to the intra cranial structures. The term "sino-orbital" aspergillosis is often applied to the disease when it involves the orbit (Case5). The symptoms are usually nasal obstruction, rhinorhea, facial pain, eye displacement and blurring of vision. The symptoms are usually slowly progressive over few months . Roentgenography of the invasive aspergillosis shows signs of a paranasal mass (with sometimes areas of increased density) causing bony erosion and invasion of contiguos structures (Fig.5a,6) The differenital diagnosis consists of neoplasm. osteomyelitis. mucopyocele, mucormycosis and granulomatous disease (McGuirt and Harrill 1979).

The treatment is conservative excision of all visible granuloma with concomitant sinus aeration (McGuirt and Harrill 1979). Some authors reported that residual granuloma next to vital structure such as dura and sclera may regress and heal by fibrosis following excision of the gross disease with concomitant drainage and aeration of the involved sinus (Bahadur et al.1983). However this view is not shared by others who advocate complete excision of the disease (Yomoto et al. 1985) . In conjuction with surgery, many authors advise systemic anifungal agents e.g. intravenous amphotericin B (Jahresdoerfer, et al.1979, Bahadur, et al. 1983, Quiney et al. 1983 , Sarti et al. 1983). Amphotericin B is sometimes ineffective and it may cause liver and kidney dysfunction. Combination of amphotericin B with rifampin or 5-fluorocytosine is reported to give better results (Yu et al. 1980). Antibiotics and corticosteroid have no effect on fungal infection.

4-The fulminant sinus aspergillosis

This form of aspergillosis was first described by McGill et al.1980) . It occurs in patients whose defeneses have been compromised by a primary disease or immunosuppressive therapy. The greatest susceptability occurs in children with acute leukaemia undergoing chemotherapy and irradiation (Violliер et al 1986 and Kavanagh et al. 1991) Prolonged granulocytopenia is probably the single most important causative factor for aspergillosis in those patients. Other factors include prolonged hospitalization and the administration of broad-spectrum antibiotics (Violliер et al. 1986). The incidence of aspergillus sinusitis in immuno-suppressed patients is not well established. However, Violliер et al (1986) in a study of 1331 immuno-suppressed patients with cancer found an incidence of 2 per cent (21 patients) of aspergillus sinusitis.

The basic pathological feature fulminant aspergillosis is rapidly progressive necrotizing mucoperiostitis with little reaction and without granulomatous response (Hartwick and Batsakis 1991). Destruction of the sinuses walls rapidly occurs with extension into the orbit and the brain. The rapidity with which the condition progresses is entirely dependent on the immunocompetence of the host (McGill et al 1980). Extensive paranasal involvement is usually associated with disseminated aspergillosis with particular involvement of the lungs, liver and spleen (McGill et al. 1980). Patients with fulminant aspergillosis usually present with fever, pain, swelling, nasal obstruction and rhinorrhea, (McGill et al. 1980 and Kavanagh et al. 1991). Prominent non-tender facial cutaneous erythema and oedema may be an early manifestation (Weingarten et al. 1987). Examination of the nose shows crustings on the mucosa. Removal of the crusts reveals ulcerated gangrenous and insensitive mucosa. Within few days the lesion extend to the lateral nasal wall, paranasal sinuses, orbit or to the brain. Extension to the anterior cranial fossa by direct extension or along vascular channels usually herald a fatal outcome.

The differential diagnosis of fulminant aspergillosis included mucormycosis and Wegener's granulomatosis. For fulminant aspergillosis antifungal agents should be given intravenously to all pateints combined with surgical removal of all macroscopic disease with a generous margin of healthy tissue (McGill et al 1980). Following surgery, continuous irrigation of the nasal cavity and sinuses must be instituted to prevent crusting and further invasion by Aspergillus. Treatment also include possible use of granulocyte transfusion and bone marrow transplant. Violliер et al. (1986)stressed

the importance of an early treatment of aspergillus sinusitis in immunodeficient patients; and recommended initiating empiric treatment if a number of the risk factors favoring a diagnosis of aspergillosis are present , even in the absence of microbiological proof.

The prognosis of sinus aspergillosis depends on the location and the immunologic status of the patient. the intracranial extension of the disease carries poor prognosis. Jahresdoerferet al. (1979) in their review of 103 cases reported outside Sudan, found 17 deaths, sixteen of them occured in nonimmunocompromised patients due to intracranial extension of the disease. Aspergillus may give rise to arthritis which results in thrombosis occlusion or aneurysms; the internal carotid and middle cerebral arteries are commonly affected (Yomoto et al. 1985).

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Fig. (1) : An axial C.T. scan of patient No. 1 showing opacities of both ethmoids and left sphenoid with areas of increased densities. Exophthalmus is noted especially of the right eye (Allergic type).

Fig. (2) : Plain X-ray of patient No. 2 showing marked expansion of opaque maxillary antre (Allergic type).

Fig. (3) : Plain X-ray of patient No. 3 showing two very high attenuated densities in the left maxillary sinus (non-invasive).

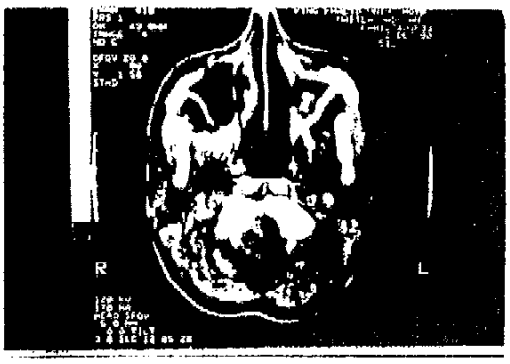

Fig. (4) : A metal-density small shadow seen in the left maxillary antrum (non-invasive).

Fig. (5a) : A coronal CT of patient No. 5 showing a lesion in the left ethmoid, nasal cavity, maxillary sinus and the orbit with bone destruction.

Fig. (6) : A CT scan showing a high density lesion in the left maxillary sinus and nasal cavity (Invasive).

Fig. (5b) : A section showing fungal elements appearing as hyphae or single cells.

Fig. (7) : A coronal CT scan showing a lesion involving the antrum, nasal cavity, ethmoid, orbit and left anterior cranial fossa (Fulminant).

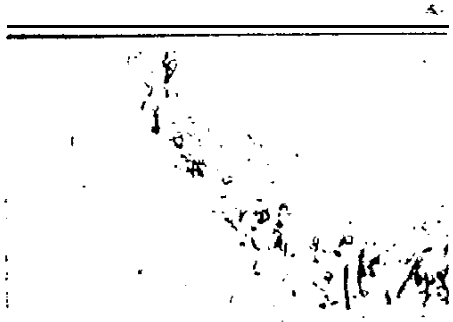

Fig. (5c) : The same section stained by silver metheramine stain.

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