CASE REPORT

Invasive *aspergillosis* in an immunocompetent host

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ABSTRACT
Aspergillosis is a common opportunistic fungal infection affecting the nose and paranasal sinuses. The disease presents in various forms ranging from non-invasive to invasive, destructive and allergic types. We report here a rare case of invasive *aspergillosis* in an immunocompetent host with the literature review.

Key words: A flavus, *aspergillosis*, invasive *aspergillosis*, opportunistic

INTRODUCTION

The genus *Aspergillus* is a group of filamentous fungi found in the atmosphere and is often the blue green mould found on the bread. There are several species of this genus. *A. Fumigatus* and *A. flavus* are the most commonly isolated spores of the disease process "*aspergillosis*".[1] Inhalation of *Aspergillus* spores can lead to colonization in the upper and lower respiratory tract with allergic response or invasive destruction.[2] The paranasal sinuses are most commonly involved.[3]

A. fumigatus is the species mainly held responsible for the infection of the paranasal sinuses.[4,5] But *A. flavus* is considered most destructive in paranasal sinuses because of its potent toxins.[6]

This fungus contaminates the paranasal sinuses by two routes. In the first or the aerogenic route the spores are inhaled directly into the antrum where they multiply best in the anaerobic medium.[6] The second route involves an iatrogenic model where spores are introduced into antrum via an oroantral communication formed due to root canal perforation or dental extraction.[6-8] Once the spores are introduced they act as opportunistic pathogens and colonize the maxillary sinus, particularly when condition that decrease sinus ventilation such as bacterial sinusitis already exist[9] *Aspergillosis* of paranasal sinuses is commonly seen in normal healthy individual. This condition may present as mycetoma, or occasionally as an invasive form of the disease.[10-12] In patients with history of asthma and recurrent nasal polyps, an allergic *aspergillosis* may occur.[13-15] However it presents as invasive and fulminant variant in cancer patients with impaired host defense,[16,17] disease and treatment-induced leucopenia, long-term use of antibiotics or corticosteroids.[18] This article is reported because of the rarity of the invasive variant occurring in immunocompetent host.

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CASE REPORT

A 47-year-old female reported to the outpatient department at Government Dental College, Rohtak, with complaint of pain and foul discharge from upper left region of the jaw, distortion of left eye and nasal stuffiness for last three months. There was history of extraction of left maxillary canine 7 months back. There was no relevant medical history. Left infraorbital prominence was lacking with eyeball pushed upward, prominent lower sclera and difficulty in eye movement. Intraorally there was a sinus at the site of healed socket in the left maxillary canine region. The overlying mucosa was normal and the adjacent teeth were free of caries or any other periodontal pathology [Figure 1].

Paranasal sinus view showed destruction of left infraorbital margin along with increased radiodensity of left maxillary sinus [Figure 2]. CT scan showed prominent and radiodense left maxillary sinus and thinned out infraorbital plate [Figure 3]. Routine blood investigations showed leucocytosis with selective eosinophilia Total leucocyte count was 9900/ mm^3, polymorphs: 62, lymphocytes: 28%, eosinophils: 8%, and monocytes: 2%. The lesion was surgically managed. Postoperative course was uneventful.

Histopathology of H and E stained specimen revealed chronic granulation tissue with faint hyphae [Figure 4]. Methanamine silver staining revealed septate hyphae with branching at 45 degree angle, suggestive of *aspergillosis* [Figure 5].

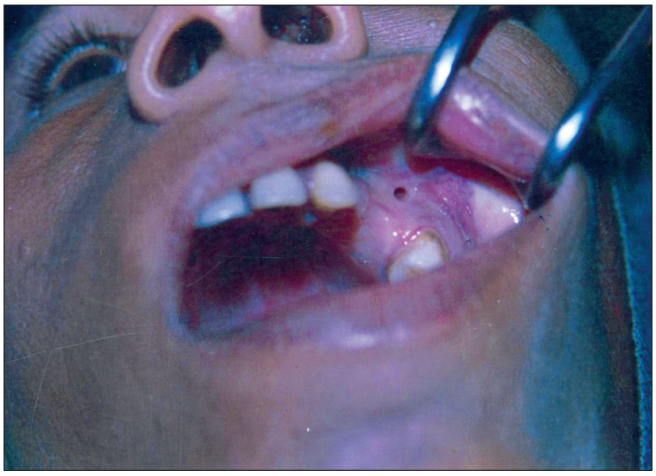

Figure 1: Photograph showing intraoral sinus at the site of extracted left maxillary canine

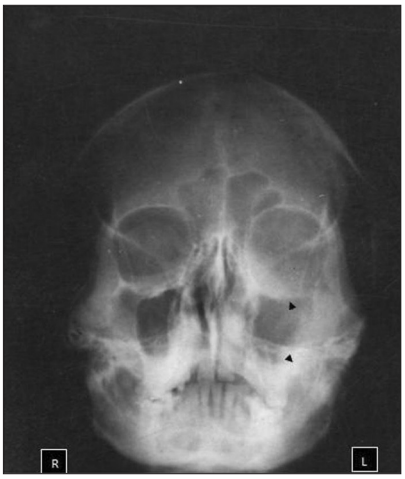

Figure 2: PNS view showing increased radiodensity of left maxillary sinus and destruction of left infraorbital margin

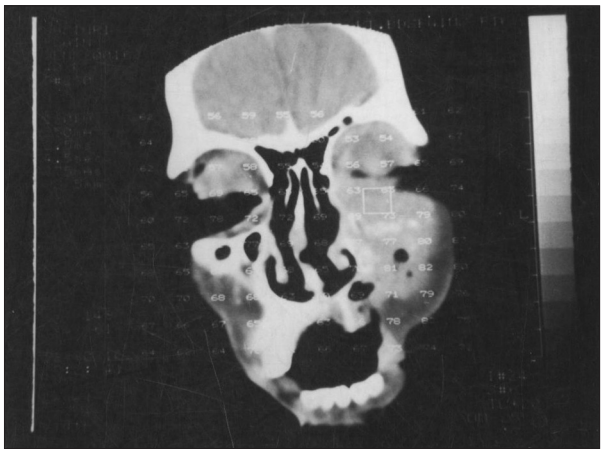

Figure 3: CT scan showing hyperdense mass in left maxillary sinus and thinning of infra orbital margin

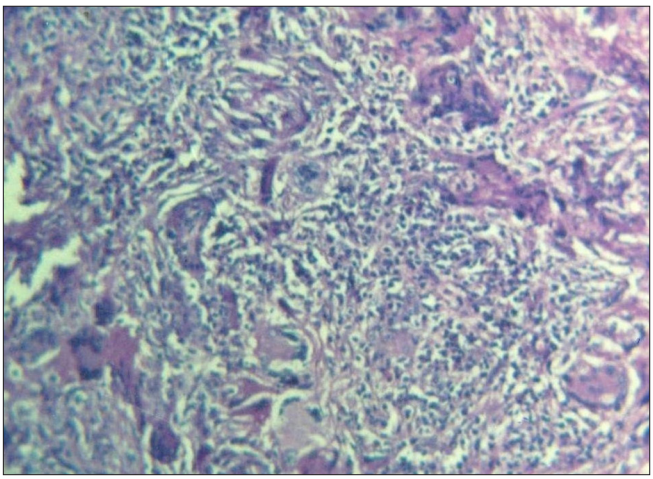

Figure 4: Photomicrograph showing scattered multinucleated giant cells, some Langhans type in granuloma formations with lymphocytic infiltration (H and E, ×25)

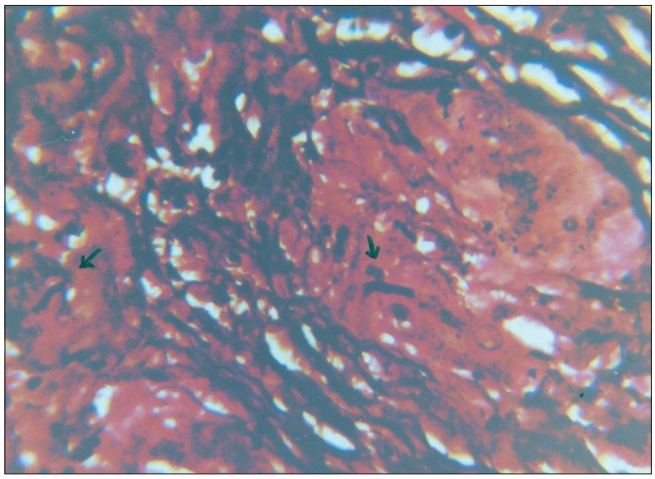

Figure 5: Photomicrograph of aspergillum organism in granulomas showing typical branching septate hyphae (Methenamine silver ×25)

The patient was treated with oral itraconazole 100 mg twice daily for 3 months and was followed biannually. At follow up the patient remains free of clinical disease.

DISCUSSION

Aspergillus infection was first identified by Sluyter in 1847.[19] Zarnico first reported *Aspergillus* infection of the maxillary sinus in 1885.[20] Initially Hora in 1965 classified the infection of nasal and paranasal sinuses as non-invasive and invasive![11] This classification was based mainly on the fact whether bone has been involved or not. Sarti and Lucenten gave four clinical variants of *Aspergillus* in 1988[21] as allergic *Aspergillus* sinusitis, non-invasive type, invasive type and fulminant type.

Rowe Jones in 1994 classified *aspergillosis* into three chief variants: Invasive, Non-invasive and non-invasive destructive type.[22] Non-invasive type is further classified into Aspergilloma, Fungal ball, Mycetoma (usually affecting one sinus) or allergic *Aspergillus* sinusitis (involving more than one sinus). Invasive type represents true fungal tissue invasion that can be either slow progressive and destructive (non-fulminant) or highly aggressive and lethal (fulminant). Destructive non-

invasive variant is locally destructive but shows no tissue invasion. Solitary *aspergillosis* of the maxillary sinus occurs almost exclusively in otherwise healthy patients and has no tendency to recur after complete removal of the mycotic masses (Aspergilloma, Mycetoma, Fungal ball). Invasive and fulminant types are common in immunocompromised patients, whose inherited response to pathogen predispose to the progressive infiltrating disease. The invasive lesion of the *aspergillosis* comprises of a chronic inflammatory granulomatous reaction that includes giant cells and a large amounts of septate mycelial filament. The invasiveness of fungus becomes most lethal once the hyphae enter blood vessels, where thrombi are formed, precipitating embolism and necrosis. However invasive form in healthy hosts is very rare. In addition to immunocompromised status, occupations like milling and farming are also the predisposing factors for *aspergillosis*.[23]

A. Flavus is most destructive in paranasal sinuses and oral cavity because of its potent toxin producing abilities. Paranasal *aspergillosis* can manifest as localized disease or destructive and invasive and even extend up to intracranial structures[13] or oral cavity causing palatal perforation. The initial picture of *aspergillosis* in healthy individuals is non-typical. The symptoms of chronic, sometimes acutely exacerbating sinusitis, progress over a month or even years.

The invasive form of disease follows a much less benign course like the mycetoma.[11] Symptoms such as pain and swelling are generally isolated to only one sinus. Nasal obstruction and rhinorrhea may also develop with the late development of ocular and neurological signs due to local compression or direct invasion.[24]

The clinical picture of paranasal *aspergillosis* can therefore be similar to that of malignant disease, although chronic sinusitis with osteomyelitis, mucormycosis and inverted papilloma must also be considered.

Fulminant *aspergillosis* of paranasal sinuses is rapidly progressive and occurs in immunocompromised patients. The *Aspergillus hyphae* invade local blood vessels, leading to ischemic tissue necrosis and bony destruction. Only biopsy with or without culture of fungus is confirmatory. Grossly, the infective tissue exhibits yellowish, brown, grey or black color, cheesy in consistency containing dirty or muddy material.[25]

Radiographic changes in non-invasive mycetoma include the presence of radiodense foci in association with homogeneous opacification of the sinus. In addition, it is found to affect only one sinus at a time. Radiographically invasive and fulminant *aspergillosis* may appear similar; unlike the invasive form fulminant *aspergillosis* involves multiple sinuses. In present case, there was partial destruction of inferior wall of the orbit and left maxillary sinus on PNS.

Histopathologically, invasive lesions are made up of chronic granulomatous reaction and are similar to sarcoidosis, midline lethal granuloma or foreign body granuloma. If Langhans type giant cells are seen then pre-existing TB granuloma has to be ruled out. To see hyphae clearly selective special staining with PAS or methanamine silver is required. They appear as septate hyphae with branching at 45^{o} angles and are about 2-4 micrometer in diameter. This fungus can be differentiated from mucormycosis where broader non-septate hyphae with dichomatous branching at 90^{o} angle are observed. As culture may be negative even after employing Sabouraud agar, demonstration of hyphae in tissue sections are more reliable and conclusive but species cannot be confirmed. Management of *aspergillosis* mycetoma requires the removal of the mycotic mass while the restoration of mucociliary drainage and sinus ventilation is simultaneously ensured, sinceTreatment of invasive *aspergillosis* consists of antifungal drugs with concomitant surgery. In allergic *aspergillosis*, surgical debridement and aeration of the antrum with or without use of systemic steroids is advocated.

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