

Fungal infections involving maxillary sinus – a difficult diagnostic task

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Abstract

Fungal infections of the paranasal sinus are increasingly recognized entity both in normal and immunocompromised individuals. Aspergillosis and Mucormycoses being the commonest of all the fungal infections involving maxillary sinus manifests as two distinct entities, a non-invasive and invasive infection. It is important to distinguish the invasive disease from the non-invasive as the treatment and prognosis are different in each. These infections present a diagnostic and therapeutic challenge to the physicians. Early diagnosis is essential in order to avoid high morbidity and mortality associated with the destructive disease and to instigate treatment before irreversible condition arise. The purpose of this paper is to add a few more cases of fungal infections involving maxillary sinus to the literature in both immunocompetent and immunocompromised patients with an emphasis on the fact that early diagnosis is vital in these infections, because delay in initiation of treatment can be life threatening due to propensity of fungi to invade adjacent blood vessels and embolize to distant organs.

Key words: Fungal Infection, aspergillus, mucormycoses, immunocompetent host.

Introduction

Mycology, the study of fungal infections has gained a remarkable impetus in the past few decades, owing at least in part to the fact that fungal diseases are far more common than was previously suspected. A variety of different causative organisms are responsible for paranasal mycoses, *Aspergillus* and *Mucor* being the commonest (1). Paranasal mycoses manifests as two distinct entities, a benign or non-invasive infection and the more serious invasive infection, which occurs in immunocompromised individuals. It is important to distinguish the invasive disease from the non-invasive because treatment and prognosis are different in each. Since fungal infections occur infrequently, they might pose a diagnostic and therapeutic dilemma for those who are not familiar with its clinical presentation. Early diagnosis is vital in these infections as delay in initiation of treatment can be life threatening due to propensity of the fungi to invade adjacent blood vessels and connective tissue produces thrombosis and ultimately necrosis of the hard and soft tissues. We report cases of mucormycoses and aspergillosis involving maxillary sinus.

Case Report

A male patient aged thirty years reported to the department of oral medicine and radiology, Subharti dental college. Patient reported with the complain of pus discharge in the posterior region of the upper jaw along with the exposed bone (Fig. 1). Patient gave a history of hospitalization for Dengue, suffered from multi-organ failure and was on ventilator 1 year back and was prescribed various antibiotics and antifungal drugs. He complained of multiple periodontal abscesses and treated for the same. Patient underwent extraction of his upper first molar and the socket did not heal and bone was exposed at the extraction site. Patient was provisionally diagno-



Fig. 1. Photograph of a patient with pus discharge in the posterior region of the upper jaw along with the exposed bone.

sed as a case of osteomyelitis but the cause not known. Patient was referred to the department of oral and maxillofacial surgery where fungal infection was suspected because of the following reasons- history of ventilatory support and intensive care unit for almost one month, history of recent extraction and unhealed socket, osteolysis of maxilla-fungus more common cause, mobility of dentoalveolar segment, palatal swelling and maxillary occlusal radiograph indicated gross and massive osteolysis.

Patient was planned for sequestrectomy, nasal antrostomy of inferior meatus, the debridement and irrigation of maxillary sinus through oro-antral opening and antral packing with bismuth idoform paraffin packing (BIPP) was done. During antral lavage and debridement black color granulation tissue was completely debrided and sent for histopathological and microbiological examination.

Histopathological Examination:

The histopathology examination of the received specimen showed stratified squamous epithelium which was ulcerated with intraepithelial split formation; underlying connective tissue stroma showed large amounts of necrotic tissue with cellular degeneration and debris. Fungal hyphae were seen with neutrophils infiltration and generalized chronic inflammatory cell infiltrate. Hyphae were aseptate, broad, dichotomous branching at 90 degree angle, suggestive of mucormycoses (Fig. 2). Culture grown in Sabouraud's dextrose agar medium showed cotton wool growth of mucor (Fig. 3).



Fig. 2. Hyphae were aseptate, broad, dichotomous branching at 90 degree angle, suggestive of mucormycoses.

Case Report - Aspergillosis

A 45 year male patient reported to the department of oral medicine and radiology in Subharti dental college. Patient complained of pain in upper left back tooth region since 10 days. Patient gave a history of intraoral swelling since 2 months and had undergone extraction 10 days back but there was no relief and patient developed dry socket and pain in upper left teeth. On examination



Fig. 2. Culture growth in Sabouraud's dextrose agar medium showing cotton wool growth of mucor.

patient had exposed bone in the left maxillary back tooth region (Fig. 4). Provisional diagnosis of osteomyelitis was made. Patient was planned for sequestrectomy, nasal antrostomy of inferior meatus, the debridement and irrigation of maxillary sinus through oro-antral opening and antral packing with BIPP was done. During antral lavage and debridement black color granulation tissue was completely debrided and sent for histopathological and microbiological examination.



Fig. 4. Photograph of a patient with pus discharge in the posterior region of the upper jaw along with the exposed bone.

Histopathologic Examination:

The histopathology of received specimen in both the cases showed granulation tissue with intense chronic inflammation with multiple congested blood vessels. One specimen also showed necrotic tissue. Areas of hemorrhage were evident with masses of eosinophilic, entangled hyphae like structures and spores. The hyphae like structures were flat, broad, refractile, branching at acute angle and septate, suggestive of Aspergilliosis (Fig. 5) and culture showed smoky grey-green colonies of As-

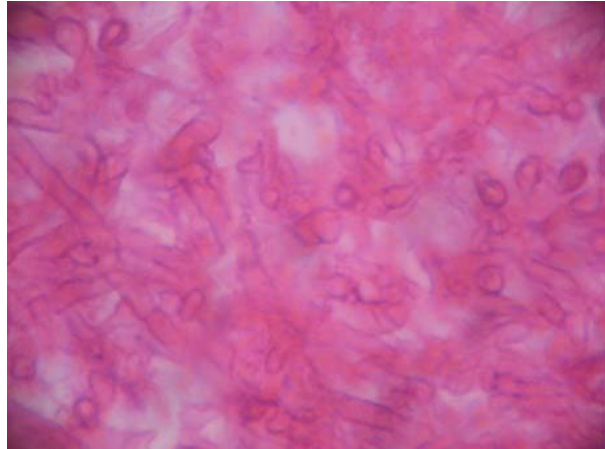


Fig. 5. Hematoxylin & eosin stained section (10x) showing fungal hyphae dichotomously branched at 45° angles with conidiospores

pergillus fumigates (Fig. 6). During follow-up patient's clinical outcome was found to be satisfactory and culture was negative for any fungal growth.



Fig. 6. Culture growth in Sabouraud's dextrose agar medium showing smoky grey-green colonies of *Aspergillus fumigates*.

Discussion

Fungal infection of the paranasal sinuses is an increasingly recognized entity both in normal and immunocompromised individuals. Paranasal mycoses manifest as two distinct entities, a benign or non-invasive infection and the more serious invasive infection, which occurs in immunocompromised individuals, is characterized by its rapid onset, ability to invade tissues and destruction. Mucormycoses is a rare fulminating opportunistic fungal infection caused by a fungus of the order mucorales (2). Although the fungi and spores of mucorales shows minimal intrinsic pathogenicity towards normal persons, they can initiate aggressive and fulminating infection in the patients whose resistance is lowered by immunocompression (3), diabetes, malignant disease, burns, trauma and rarely by steroids or in solid organ transplanted patients. Auluck et al (4) in 2007 observed that immunocompromised or immunosuppressed patient having

bone necrosis following tooth extraction should alert a clinician of possible mucormycoses infection. In contrast, *Aspergillus* hyphae have the propensity to penetrate mucous membranes, to invade and grow in the walls of small to medium sized arteries or veins producing thrombosis, infarction and necrosis (5). In the diabetic ketoacidotic patient, there is incidence of mucormycoses as seen in our case reports which is said to be caused by *Rhizopus oryzae*, also known as *Rhizopus arrhizus*, because they produce the enzyme ketoreductase, which allows them to utilize the patients ketone bodies. Aspergillosis of the paranasal sinuses is most commonly seen in patients who are otherwise fit as seen in our reported cases. Shoham and Levitz (6) in 2005 reviewed the current understanding of the role and relative importance of innate and adaptive immunity to common or emerging fungal pathogens in decisions regarding use of currently available antifungal therapies and in the design of new therapeutic modalities. The immune response varies with respect to the fungal species and morphotype encountered. The risk for particular infections differs depending upon which aspect of immunity is impaired. Each form of paranasal aspergillosis has a specific radiologic profile. The presence of radiodense foci in association with homogenous opacity of the sinus is highly suggestive of a non-invasive mycetoma. Opacity of the sinus with or without destruction may be demonstrated in the invasive form. Mucormycoses show opacification of the sinus (7) which was seen in our cases also. CT is a more sensitive diagnostic tool than plain radiography and is the best way to identify bony destruction. Magnetic resonance image (MRI) (8,9) was found to be even more sensitive than CT diagnosing fungal sinusitis. Microscopically, *Aspergillus* can be identified as a filamentous structure with a diameter of 3 to 6 µm and with septate hyphae. *Aspergillus* must be distinguished from *mucor*, which form broader, non-septate hyphae and can be identified by dichotomous branching at 90 degree angle (12) while *aspergillus* shows branching at acute (45 degree) angle (Table 1). In a study done by Ferry et al (3) in 1983 and Yohai et al (10) in 1994. They reported sinus involvement in 69%-79% of mucormycoses respectively. Special histological stains such as Grocott or PAS should be used to find fungal hyphae. Fungal cultures on Saboraud's dextrose agar are needed to confirm the

diagnosis. The effective management of paranasal sinus fungal infection requires early diagnosis, histological classification and surgery and when appropriate chemotherapy. Treatment in invasive fungal sinusitis involves radical surgery in addition to intravenous amphotericin B/lipid complex of liposomal amphotericin B with or without flucytosine. The optimum dose and duration of treatment is still unclear. Endoscopic surgery has been found to be feasible and efficient, enabling excellent local control and less morbidity than traditional approaches (11-13). Sinus surgery must be performed as soon as feasible. The prognosis is directly related to the severity of the underlying disease, the extent of the disease when treatment begins, and the aggressiveness of the treatment. Both of our cases showed good prognosis and the clinical outcome was satisfactory on follow-up. Repeat fungal culture performed 15 days after treatment was negative for growth of any fungal pathogens. Fungal infections of the paranasal sinuses are usually seen in both immunocompromised and immunocompetent individuals, so clinicians should be aware that chronic sinusitis that is unresponsive to usual management is highly suggestive of mycoses of the paranasal sinuses. Because the numbers of reported cases are increasing, its inclusion as part of the differential diagnosis in antral disease is important, particularly because not all forms follow a benign course and the prognosis is dependent on early diagnosis. Tissue invasion by the hyphae of *Aspergillus fumigatus* and *mucor* must be seen microscopically to establish the diagnosis, but culture is required to identify the fungal species involved. We thus emphasize that early diagnosis and prompt treatment are essential to avoid the high morbidity and mortality associated with this destructive disease.

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MUCORMYCOSES	ASPERGILLOSIS
<ul style="list-style-type: none"> • Hyphae: • Larger in size (6 - 50 µm) • Irregular • Branching at 90 degree angle • Ribbon like • Devoid of septa 	<ul style="list-style-type: none"> • Hyphae: • Relatively smaller in size (3 – 6 µm) • Regular • Dichotomously branching at 45 degree angle • Distinct cross - septa

Table 1. Microscopic observations of Fungal Infections

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