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Fungal Infection Emerging Into Oral Cavity: A Rare Case Report with Review of Literature.

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ABSTRACT

Mucormycosis is an opportunistic, frequently fulminant invasive fungal infection caused by a saprophytic fungus. Mucormycosis originating in paranasal sinuses and nose involves oral cavity secondarily presenting as palatal necrosis or ulceration. This case report and review describes emergence of mucormycosis in the oral cavity of an immunocompromised patient and importance of early diagnosis and management by antifungal drugs, surgery and control of underlying diseases in controlling mortality.

Keywords: Mucormycosis, palatal ulceration, immunocompromised

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INTRODUCTION

Mucormycosis is a life-threatening opportunistic fungal infection caused by saprophytic fungi of the order Mucorales mainly Rhizopus and mucor and, rarely other species. Infection arises by inhalation of the spores that are deposited in the pulmonary alveoli. It also arises due to contamination of the traumatized tissues and direct inoculation. The fungus preferentially erodes arteries, resulting in thrombosis with subsequent necrosis of the surrounding tissues [1].

Case Report

A 60 years old male patient came with chief complaint of painful and unhealed wound in relation to the extracted socket of the left upper back teeth region for past 1month.History revealed that he had his left upper back tooth extracted 1 month back as the tooth was painful and shaking. Following this, the wound did not heal and as it was painful, he visited the dentist again for which he was given a dressing on the extracted site with a white paste and medications (antibiotics and pain killers). Pain persisted even after this and the patient came to the department as he developed a swelling in the left cheek region. He also noticed a small painless wound in the palate. He gave a history of fever for past 10 days before visiting the dental hospital. His past medical history revealed that he is a diabetic and not under regular medication. Was hospitalized for hematuria in 2000 due to uncontrolled diabetes

Extra oral examination revealed Left side mild facial asymmetry (Fig 1). Mild diffused swelling on left side of face with mild pain present. Left periorbital was oedema present. Skin over the swelling is normal in colour. No scar or sinus. On palpation the swelling is soft in consistency and tender. The skin over the swelling is not warm.

On intra oral inspection a well defined ulcer in the mid palatal region, irregular in shape of size 1x2cms was noticed (Fig 2). The margins are raised with the floor covered with necrotic slough. There is no discharge from the ulcer.

Provisional Diagnosis

Based on the history and clinical presentation, a provisional diagnosis of deep fungal infection was made.

Investigations

Haematology

Haematological test showed WBC increased to 12300 cells/mm^3 and Biochemical test showed HbA1c - 8.7, Blood sugar random - 290 mg/dl, Creatinine – 2.1, BUN – 21.7.

Conventional radiography

Occlusal radiograph of maxilla showed an irregular and ill defined radiolucent area in the mid-hard palatal region present (Fig 3). Paranasal sinuses showed radiopacity involving left maxillary sinus (Fig 4). Computed tomography scan of paranasal sinuses showed soft tissue mass lesion of the left maxillary sinus eroding and destroying the medial and lateral walls of maxillary sinus extending further medially involving the left upper jaw and the hard palate with pathological fracture of the upper jaw with loss of teeth (Fig 5&6). Frontal sinus, Ethmoidal sinus, Sphenoidal sinus appeared normal.

The H&E stained slide shows normal parakeratinized stratified squamous epithelium. The underlying fibrous connective tissue shows dense inflammatory cells in the subepithelial area. Connective tissue shows non-septate hyphae branched at 90 degrees, certain areas of necrosis and focal areas of thrombus formation (Fig 7). These non septate hyphae stained positive with PAS suggestive of Mucormycosis.

Medical management with antimicrobials were not effective. Patients referred to tertiary care center for surgical management.

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Figure 1: Extra Oral View

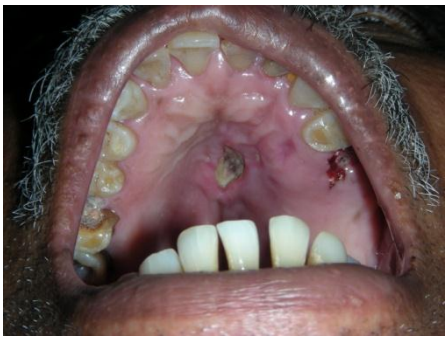

Figure 2: Intraoral view presenting as palatal ulcer

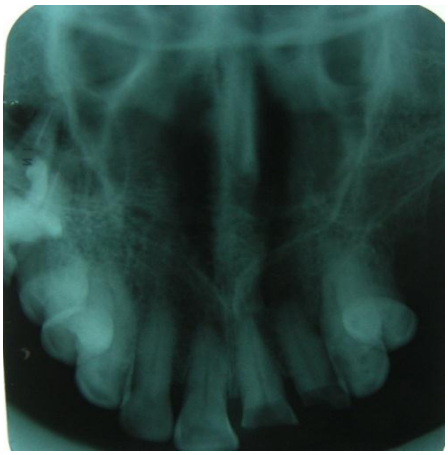

Figure 3: Occlusal radiograph of maxilla showed an irregular and ill defined radiolucent area in the mid-hard palatal region present

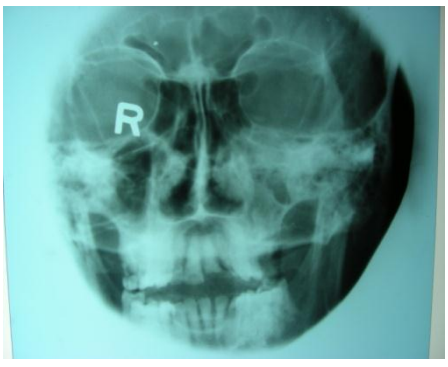

Figure 4: PNS view Opacity seen in left side sinus.

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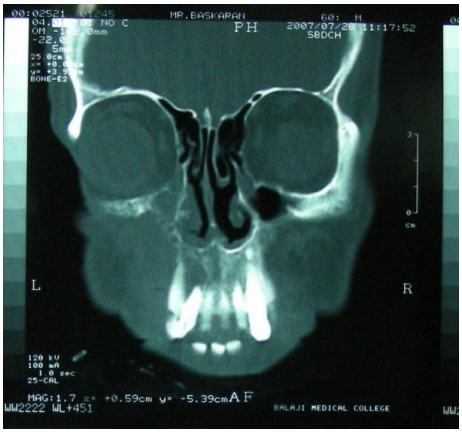

Figure 5: Coronal view shows soft tissue lesion of the left sinus.

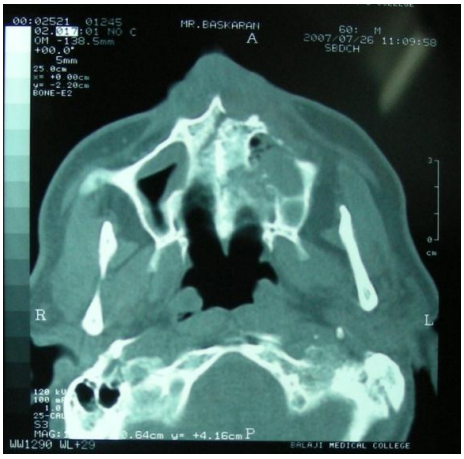

Figure 6: Axial view shows erosion of the left maxillary sinus.

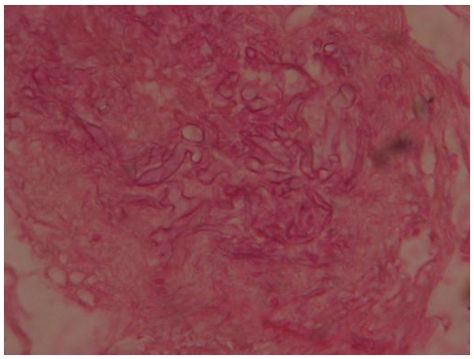

Figure 7: Fungal hyphae staining showing non-septate hyphae.

DISCUSSION

Mucormycosis are ubiquitous, found throughout the world on fruit and bread, in air and in soil, where they exist as saprophytes. Although the fungi and spores of Mucorales show minimal intrinsic pathogenicity towards normal persons, they can initiate aggressive and fulminating infection in the immune compromised host as people with uncontrolled diabetes with ketoacidosis, in immuno-suppressed - granulocytopenia and in declined CD4 +T cells, in dialysis patients-deferoxamine therapy - makes iron availability to fungus easily at even low concentration, in extreme malnutrition and use of contaminated medical equipment and patients receiving steroids and cancer therapy [3,4]. Depending on the immunological status of the host, the disease may manifest in six different ways depending on the affected site: rhinocerebral, pulmonary, cutaneous, gastrointestinal, central nervous system and Disseminated. For example,

patients with diabetes mellitus usually have the rhinocerebral and pulmonary forms of disease. Patients who are malnourished usually have the gastrointestinal forms of disease. High fatality with diabetes is due to the angioinvasive character of the Mucor, thereby causing thrombosis of blood vessels and tissue necrosis. Mucorales are ferrophilic fungi. Acidosis reduces the binding of iron to transferrin; in turn, available free iron helps in proliferation of the Mucorales [4].

In the diabetic ketoacidotic patient, there is a high incidence of mucormycosis caused by Rhizopus oryzae, also known as Rhizopus arrhizus, because they produce the enzyme ketoreductase, which allows them to utilize the patient's ketone bodies. It is also likely that the hyperglycemia stimulates fungal growth, and the diabetic reduction in chemotaxis and phagocytic efficiency permit these otherwise innocuous organisms to proliferate.

Fungal sinusitis generally affects only debilitated patients. The mucormycosis and Aspergillus organisms are common opportunistic pathogens in the milieu of immunologically compromised patient; so mucormycosis should also be differentiated from aspergillosis. Histopathological features show in mucormycosis the hyphae tend to branch at 90 degree angles whereas for aspergillosis the hyphae shows tendency to branch at acute angle [2]. Radiographically in aspergillosis, radiopaque concretions may be identified whereas mucormycosis shows opacification of sinus, as also seen in the present case. Suspicion of mucormycosis requires a CT scan of the maxilla orbits and brain. In particular, evidence of intracranial brain abscesses and orbital extensions is critical. Sinus and orbital extensions are recognized by membrane or periosteal thickenings as well as bony disruption [5].

Routine blood studies will show a leukocytosis in the 12,000-20,000/L range and usually a left shift (Schilling shift to the left, indicative of immature neutrophil). Neutrophils are known to play a crucial role in the protective host response to fungal colonization. Neutropenia, in association with haematological malignancy, restoration of adequate numbers of functional neutrophils must be achieved for mucormycosis to be resolved [6]. If the patient is diabetic, a full workup of serum glucose, electrolytes, blood chemistries and blood gases is required. Diabetic ketoacidosis require insulin, correction of acidosis with sodium bicarbonate and rehydration.

Mucormycosis is appropriately diagnosed histologically when broad, irregularly shaped, nonseptate hyphae with right angle branching are seen invading the tissue with H & E; but are better visualized with PAS or silver stains. Detection of fungal DNA and antigens are promising technology for detection of invasive fungal disease [7].

Medical management alone is not effective because of poor drug delivery to the infection site due to extensive vascular thrombosis. Aggressive control of the underlying disease and aggressive debridement are needed. Patients should undergo a resection-type debridement as soon as they are physiologically stable. The subsequent wound is best left open for care and irrigation but may be obturated with a removable prosthesis-obturator to support speech and feeding [8].

Amphotericin B usually given in intravenously at a dose of 0.6-1.0mg/kg/day therapy should also be initiated as soon as possible. A lipid formulation of amphotericin B can maintain high blood levels with lower toxicity and may be more efficacious (IV Liposomal Amphotericin (AMBISOME, FUNGISOME), IV Lipid complex (AMBECET)-1mg -5mg/kg, Oral suspension Posaconazole (NOXAFIL)- 600-800mg/day) [9,10]. Adjunctive hyperbaric oxygen should also be used when available. Evidence now shows a better prognosis with the use of hyperbaric oxygen, probably because it reverses the hypoxia in local tissues and enhances neutrophil- and macrophage-killing ability [11].

Prognosis depends on several factors such as infection site, rapidity of diagnosis, type and severity of immunosuppression. A surviving mucormycosis requires rapid diagnosis and aggressive coordinated medical and surgical therapy.

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