REFRACTORY MUCORMYCOSIS: A POSSIBLE CAUSE FOR MAXILLARY NECROSIS

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ABSTRACT

Mucormycosis (Zygomycosis or Phycomycosis) is an opportunistic fungal infection caused by a saprophytic fungus that belongs to the class of phycomycetes. It is commonly associated with immunocompromised patients. Such patients may present with extensive jaw bone necrosis and pose a diagnostic challenge for an oral physician. Here, we describe our clinical experience of a 55 year old diabetic, hypothyroidism female with extensive necrosis of the maxilla due to refractory mucormycosis, a lethal fungal infection which necessitates multidisciplinary approach for treatment.

KEY WORDS

necrosis, diabetes, mucormycosis, fungus, maxilla

INTRODUCTION

Mucormycosis is an opportunistic infection usually occurring in immuno-compromised patients such as uncontrolled diabetes, hematological malignancies, renal failure, patients on chemotherapy, patients on long term steroids and AIDS.(1,2) It is considered as the third most common opportunistic fungal infection after candidiasis and aspergillosis(3) The common genera causing this disease are Rhizopus, Rhizomucor and Absidia(4) Rhinocerebral form of mucormycosis frequently presents with oral manifestations and may lead to considerable dilemma in clinicians unfamiliar with this entity, which in turn may worsen the prognosis for the patient. The present case report is of refractory pulmonary and maxillary sinus mucormycosis presenting with necrosis of maxilla causing exposure of the underlying bone. The aim of this report is to discuss the role of oral physicians in the management of mucormycosis.

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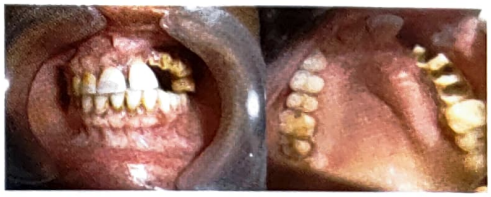
Case Report

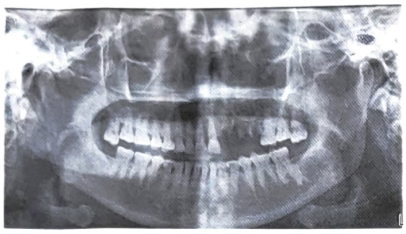
A 55- year female patient reported to the department of oral medicine and radiology with a chief complaint of halitosis and chronic non-healing wound of the left maxillary region since 1 month. It was associated with sudden exfoliation of maxillary left teeth over a period of past 2 weeks. She also experienced difficulty in eating, drinking and complained of nasal regurgitation. The patient was a known hypothyroidism taking thryroxine since 3 years. She was diagnosed 5 months back for pulmonary and maxillary sinus mucormycosis. The previous Computed Tomography (CT) images, revealed areas of dense consolidation in right middle lobe and left lower lobe of lungs. She was treated with intravenous amphotericin-B injections and regular surgical debridement of maxillary sinuses. At the time of primary mucormycosis infection her fasting glucose level were high and was also diagnosed to be suffering from uncontrolled diabetes. Since then she was taking insulin injections and oral hypoglycemics.

On Extra-oral examination, there was a mild diffuse swelling over the left cheek region. An intra-oral examination revealed exposed, necrotic yellow-coloured alveolar bone in the left maxillary canine-premolar region. 22, 23, 24 and 25 were missing with exposed sockets and covered with slough. There was oro-antral fistula present through the buccal cortical plate breach in second premolar region (figure 1)

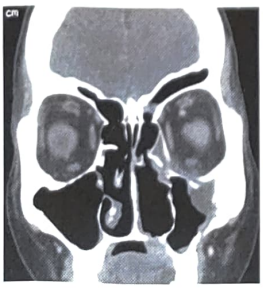


Considering the patient's medical history and extensive denuded, necrotic maxilla, a provisional diagnosis of refractory mucormycosis of maxilla was made. The differential diagnosis of osteomyelitis was considered.

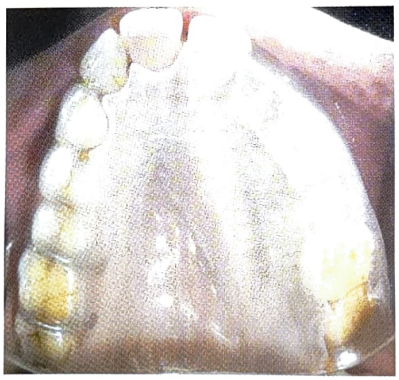
Later the patient was subjected to blood investigations which revealed raised ESR and fasting blood sugar around 200 mg%. A panoramic radiograph showed haziness of the left maxillary sinus with erosion of maxillary sinus walls (figure 2).



A fresh CT scan was performed which showed mucosal thickening of the left maxillary, sphenoid and posterior ethmoid sinuses. At the floor of left maxillary sinus, erosion was seen with its extension to the alveolar margins of left maxilla and hard palate (figure 3). There was superior extension into the left orbit through the eroded orbital wall, superomedially extension to left ethomoidal air cells with erosion of the inferior ethmoid air septa. Posteriorly there was extension of mucosal thickening through the eroded maxillary wall into the sphenopalatine recess and the pterygopalatine fossa. Further extension into the left sphenoid sinus through the eroded anterior and anterio-inferior wall of sphenoid sinus was noted (figure 3).



The incisional biopsy and culture of the tissue from left maxillary sinus was suggestive of mucormycosis of the maxilla. The patient was admitted, her blood sugar level were managed by the physician, and frequent regular local debridement of maxillary sinus was done under general anesthesia by otolaryngologists. Following surgery the patient was administered a single daily dose of lip os om al amphotericin- B 1 mg/kg body weight as an infusion in 100 ml of 5% dextrose over 1–2 h for a period of 15 days. The blood urea and creatinine levels were regularly monitored for nephrotoxicity. She was rehabilitated with heat cure, clear acrylic, removable interim obturator with its extension into buccal sulcus to close the oro-antral fistula (Figure 4).



Patient was satisfied post-treatment and was followed up for 6 months uneventfully.

DISCUSSION

Mucormycosis is one of the most rapidly progressing fungal infection in humans. It becomes pathogenic when the patient's general resistance has been altered by metabolic disorders, immunosuppressive therapy, malignancy or other chronic debilitating disorders. An underlying disease, frequently diabetes mellitus, is almost always present5. Infection arises through inhalation of spores and contamination of the traumatized tissue, ingestion and direct inoculation. These fungi have a tendency to erode and invade small blood vessels that leads to thrombosis, ischemia and tissue necrosis6. From sinuses, infection may extend to involve oral cavity inferiorly and orbit superiorly. Thrombosis of internal maxillary artery or descending palatine artery results in necrosis of maxilla. Cranial involvement leads to meningoenchephalitis, resulting in patient's death, and hence the time between diagnosis and initiation of treatment is critical for prognosis. A high mortality rate has been reported, 16% for Cutaneous mucormycosis, 67% for Rhinocerebral, 83% for Pulmonary and 100% for GIT and disseminated form.(7)

In diabetic patients there is a high incidence of mucormycosis caused by Rhizopus arrhizus, because they produce the enzyme ketoreductase, which allows them to utilize the patient's ketone bodies. Ketoacidosis inhibits the binding of iron to transferrin, allowing serum iron levels to rise. The growth of these fungi is enhanced by iron, and the patients who are taking deferoxamine (an iron chelating agent used in the treatment of diseases such as thalassemia) are also at increased risk of developing mucormycosis.(8) It is also likely that the hyperglycemia reduces

chemotaxis and phagocytic efficiency permitting innocuous organisms to proliferate5.

A clinical suspicion of mucormycosis requires confirmation by radiological examination, biopsy and culture of tissue. With regard to radiological examination, preferably a CT scan of the maxilla and orbit, showing membrane or periosteal thickening and bony disruption is helpful. Although magnetic resonance imaging (MRI) is presumed to be a better diagnostic tool for fungal infection of the head and neck region but for visualizing bone destruction a CT scan is considered better than MRI. Moreover the cost effectiveness of CT scans as compared to MRI is also an important factor.(9)

Differential diagnosis of such rare oral presentation can include spectrum of reasons- chemical or mechanical trauma, necrotizing sialometaplasia, post-surgery, post-radiation consequences, infections like syphilis, tuberculosis, histoplasmosis or coccidiomycosis, neoplastic like squamous cell carcinoma or T-cell lymphoma and collagen vascular disease such as wegener's granulomatosis.(10,11)

Definitive diagnosis of mucormycosis is based on histopathologic examination which shows extensive areas of tissue necrosis and the presence of numerous fungal hyphae aseptate with non-dichotomous branching at right angle and with areas of focal dilatations.

Treatment of mucormycosis consists of surgical debridement; systemic anti fungal therapy and treatment of any underlying systemic disease. Control and prevention of opportunistic fungal infection in patients suffering from debilitating diseases such as diabetic ketoacidosis, immunosuppression, blood dyscrasia, solid organ transplant, patients on long term steroids and bone marrow transplant is very important. Once mucormycosis infection diagnosed in debilitated patients, it must be treated promptly, without any delay, by multidisciplinary approach involving medical physicians medically and surgically.

Though amphotericin B formulations have remained the mainstay of treatment for mucormycosis, recent studies have demonstrated that posaconazole, an extended-spectrum triazole agent, has in vitro activity against zygomycetes and may represent a therapeutic option for patients with serious invasive fungal infections. A few microbiological studies have confirmed in vitro activity comparable to amphotericin B against Rhizopus and Mucor.(12)

Once the maxilla is involved, surgical resection and debridement of the necrosed areas can result in extensive maxillary defects. The defect may be in the form of a small opening resulting in communication from the oral cavity into the maxillary sinus, or it may include portion of the hard and soft palate, alveolar ridge and the floor of the nasal cavity.(13) Rehabilitation (closure of the oronasal and/or oroantral fistulae) can be done surgically or by construction of a prosthetic appliance, usually an obturator. (14)

Moreover, patients previously diagnosed with mucormycosis are prone to develop recurrent infection, so long-term follow will help in reducing high mortality rate associated with this condition.

In the above presented case, our aim was to improve quality of life of patient by enabling her to perform functions of chewing, swallowing, speech and to provide an acceptable esthetic appearance.

A poor prognosis is primarily related with uncontrolled underlying disease. Other associated prognostic factors are the extent of disease including orbital or intracranial extension. Surgical debridement is essential for a good prognosis, but timely intervention and complete aggressive debridement is not always needed in all patients.(15)

For managing such fatal cases of refractory rhinocerebral mucormycosis, a multidisciplinary team is required which includes an oral physician, otorhinolaryngologist for diagnosing and surgical management of maxillary necrosis, radiologist for estimating extent of disease, pathologist for giving histopathological confirmation and general physician for medical management as well as control of underling systemic diseases. Prosthodontist along

with speech therapist provide oral rehabilitation which acts as a boon to improve the overall quality of life for the patient.

CONCLUSION

A diabetic patient with exposed necrotic bone and a history of previous mucormycosis should alert the clinician about the possibility of a refractory mucormycotic infection. In such cases goal of treatment is directed towards improving the quality of life and which can be achieved successfully with a multidisciplinary approach involving a team of doctors from different specializations.

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