

Rhino Orbital Mucormycosis Presenting as Palatal Ulcers - A Report of Two Cases: Case Report

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ABSTRACT

Mucormycosis is a life threatening fungal infection caused by fungi of the order Mucorales and is one of the fulminant and fatal opportunistic infections, characterized by very acute onset, with a high mortality rate. Rhinocerebralmucormycosis is the most common type and its extension to the orbit and brain is quite usual. It is commonly reported in immunocompromised patients such as poorly controlled diabetics, immunosuppression with corticosteroids, hematological malignancy, solid malignancy, iron overload and burns. Mucormycosis is on the rise with an increase in incidence of Diabetes mellitus and HIV infection leading to immunocompromised status of the patient. Here in, reporting two cases of rhinocerebralmucormycosis in two diabetic patients with palatal perforation in both cases and this is a rare and late occurrence. One was in a known systemic lupus erythematosus (SLE) patient, which is a very rare incidence. Both the patients were successfully treated with a combination of surgical debridement and systemic amphotericin B administration. By presenting these two case reports we would like to point out that mucormycosis should be included in the differential diagnosis of hard palate ulcers and cellulitis, especially in diabetic patients.

Key words: Mucorales, rhino orbital, subtotal maxillectomy, vascular thrombosis.

INTRODUCTION

Mucormycosis (also known as zygomycosis or phycormycosis), is a rare life-threatening infection caused primarily by fungi from the order Mucorales⁹. It was first described by Paulltauf in 1885¹⁴. Typically developed by poorly controlled diabetic patients, this opportunistic infection is characterized by a very acute onset. It produces vascular thrombosis and tissue necrosis and the most frequent form is the rhino-orbito-cerebral⁶. The sites of pre-dilection for this infection are the nose and paranasal sinuses from where it involves the orbital structures and at times intracranial structures such as the cavernous sinus and the cerebral hemispheres¹¹. Poorly controlled diabetics, immunosuppression with corticosteroids,

hematological malignancy, solid malignancy, iron overload and burns are some of the conditions which predispose patients to the development of this disease¹³. Six clinical variants of mucormycosis such as "rhinocerebral, pulmonary, cutaneous, gastrointestinal, central nervous system, disseminated type" have been recognized so far¹⁶. The prognosis is poor, with severe sequelae and high mortality even in patients with a prompt diagnosis and correct treatment.

Here, we present two clinically and histopathologically proven cases of rhinomaxillarymucormycosis, clinically presented as deep palatal ulcers in diabetic patients. One case was in a known Systemic systemic lupus erythematosus (SLE) patient, which is a very rare occurrence.

Case report 1

A 30 year old female patient reported to the Department of Oral Medicine and Radiology, Tamilnadu Government Dental College and Hospital, Chennai -3, with a complaint of nasal regurgitation of food associated with a purulent discharge from the nasal cavity for the past 30 days. Patient gave a history of spontaneous exfoliation of maxillary anterior teeth since two months (**Fig 1**). Patient is a known type 2 diabetic since 4 years and hypertensive since 2 years. Patient was moderately built and debilitated. Examination of the nasal cavity revealed eschar of the right and left nasal septum. Intra oral examination revealed, denudation of gingiva in relation to maxillary teeth, extending from mesial of tooth #16 to mesial of tooth #26, with necrosis of underlying alveolar bone. There were empty tooth sockets in relation to # 13,12,11,21,22,23. A 3 x 1.5 cm sized oval perforation was noticed in the anterior region of the hard palate, exposing the bone of the hard palate (**Fig 2**). A through and through opening was formed due to perforation in the palate creating an oronasal fistula. Based on the history and clinical findings, a provisional diagnosis of mucormycosis was made. Random blood sugar was 368mg/dl.

Paranasal sinus view radiograph was taken which revealed, destruction of nasal septum, floor of right nasal cavity and roof of right maxillary sinus. There was evidence of destruction of floor of right orbit also (**Fig 3**).

Orthopantomograph revealed destruction of floors of right nasal cavity, right orbit and roof of

right maxillary sinus. CT revealed destruction of nasal septum, and right nasal bone with soft tissue density lesion occupying the roof and posterior wall of right maxillary sinus. There was destruction of floor of right orbit. The lesion was seen to displace the nasal septum to the left (**Fig 4**).

Biopsy was taken from nasal eschar, and it revealed non-septate hyphae with branches at right angles which confirmed the diagnosis of rhinocerebral mucormycosis. An antifungal regimen of amphotericin B 1mg/Kg/day was initiated. A subtotal maxillectomy was done and the same antifungal regimen continued. The patient was on review for about a month, after which she failed to turn up for review.

Case report 2

A 29 year old female, reported to the Department of Oral Medicine and Radiology, Tamilnadu Government Dental College and Hospital, Chennai -3, with a chief complaint of pain and swelling on the right side of upper face for one month duration. The patient gave history of fever, before one month. The patient gave a history of diabetes mellitus for 2 years duration and diagnosed to have Systemic lupus erythematosus, nephrotic syndrome, along with lupus nephritis. The patient is moderately built and moderately nourished.

On extraoral examination, there was diffuse swelling in relation to periorbital region of the right eye, with evidence of surgical scar in relation to right upper cheek region, 4 cm inferior to



Fig. 1: Empty exfoliated teeth sockets with necrosis and exposure of maxillary alveolar bone



Fig. 2: Denuded Palatal mucosa with exposure of underlying palatal bone

the right lower eyelid (**Fig 5**). Intra oral examination revealed, denudation of right palatal gingival, extending anteroposteriorly from, distal of #14 to distal of #18, and mediolaterally from, right upper buccal vestibular sulcus medially 3cm towards the midline of palate, not crossing the midline (**Fig 6**). The surface of the exposed bone was mildly necrotic with tenderness on palpation. The smear was taken from the necrotic bone and studied . It showed presence of non septate hyphae, branched at right angles. On the basis of history, clinical

examination, and smear study a provisional diagnosis of rhino orbital mucormycosis was made. The patient was reluctant to undergo treatment because of domestic reasons, inspite of repeated advice was discharged from Government General Hospital , Chennai-3, where she was admitted for other systemic problems. The same patient reported after exactly a year, with similar complaints of severe pain and nasal discharge . On extraoral examination, the patient was unable to close the right upper eyelid, with loss of wrinkles on the right

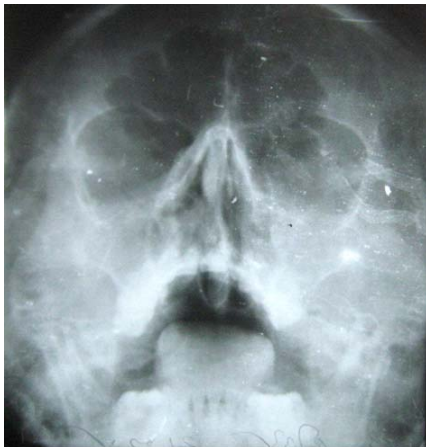


Fig. 3: Destruction of nasal septum, floor of right nasal cavity and roof of right maxillary sinus, floor of right orbit

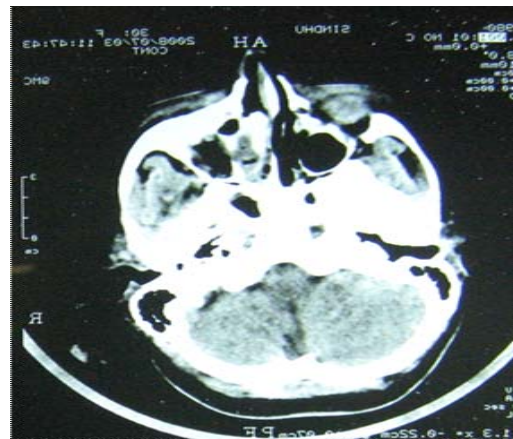


Fig. 4: CT revealed destruction of nasal septum, and right nasal bone with soft tissue density lesion occupying the roof and posterior wall of right maxillary sinus.



Fig. 5: Diffuse swelling in relation to periorbital region of the right eye, with evidence of surgical scar



Fig. 6: Denudation of right side palatal mucosa in relation to #14,15,16,17

side of forehead when the patient was asked to frown, with drooling of saliva from right corner of the mouth (**Fig 7**). Intraoral examination revealed, denudation of right maxillary gingiva, from distal of 12 to distal of 18, with underlying necrotic bone exposed, with characteristic black areas on the surface. The denudation extended from right upper buccal vestibular sulcus, medially 3.5 cm, not crossing the midline (**Fig 8**). The margins of the

gingiva were rolled out. Empty tooth sockets in #13,14,15 were observed. The alveolar segment from distal of #12 to distal of #18 was mobile.

CT was taken, which revealed complete destruction of the right posterior ethmoidal sinuses, floor of right maxillary sinus, displacing the nasal septum to the left with necrosis of right palatal bone (**Fig 9**). Histopathological examination was done,



Fig. 7: Bell's palsy on the right side of face



Fig. 8: Denudation of right side palatal mucosa, with necrosed underlying bone and exfoliated teeth sockets #13,14,15.

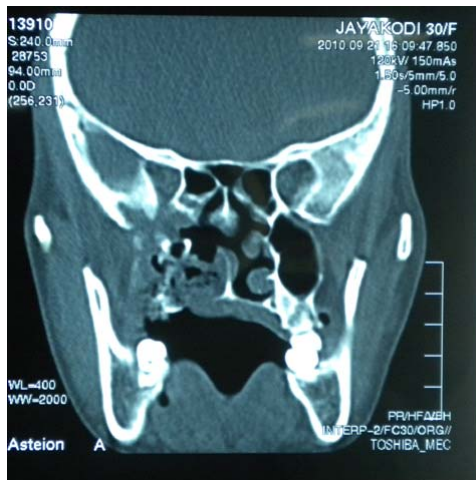


Fig. 9: CT revealing complete destruction of the right posterior ethmoidal sinuses, floor of right maxillary sinus, displacing the nasal septum to the left with necrosis of right palatal bone



Fig. 10: Post operative- right subtotal maxillectomy done

which finally confirmed the diagnosis of mucormycosis. The patient was taken up for emergency surgery, right subtotal maxillectomy was done (**Fig 10**). Intravenous amphotericin B was started. The patient was under regular follow up for about one year, without any recurrence of the lesion.

DISCUSSION

Mucormycosis is a rare, invasive, fungal infection caused by fungi of the class phycomycetes². It usually acts as an opportunistic pathogen¹⁴. There are six clinical forms of mucormycosis: rhino-orbito-cerebral, respiratory, gastrointestinal, cutaneous/widespread and mixed. The most frequent one is the rhino-orbitocerebral, with or without CNS involvement, but almost always with ocular damage¹⁴. Pterygopalatine fossa is considered to be the main reservoir for rhinocerebralmucormycosis, and extension into the orbit and facial soft tissues usually follows this route. After proliferation in the nasal cavity, the mucor reaches the pterygo-palatine fossa, inferior orbital fissure and finally the retroglobal space of the orbit, resulting in ocular signs¹¹.

The sites of pre-dilection for this fungal infection are the nose and the paranasal sinuses from where it progresses to involve the orbit and at times intracranial structures such as the cavernous sinus and the cerebral hemispheres¹¹.

Rhinocerebralmucormycosis begins with colonization of the nasal mucosa by air borne spores. Mucorales hyphae have a predilection for the growth into the artery and lymphatic systems. The fungi invade the nerves, fatty tissue and bone but muscles are usually spared. Angioinvasion by the hyphae produces a fibrin reaction and the development of "mucor thrombi" which occludes the artery and lead to ischemia and infarction and consequence formation of black necrotic eschar of the skin and mucous which is characteristic of rhinocerebralmucormycosis, is observed only in 20-40% of patients, and is a bad prognostic sign^{12, 14}. The infection spreads rapidly to adjacent sinuses and orbit and continue into the cranium via the ethmoid bone or orbital vessels¹².

Rhino-cerebral mucormycosis mainly occurs in immunocompromised patients¹³. Poorly controlled diabetics, immunosuppression with corticosteroids, hematological malignancy, solid malignancy, organ transplant, chemotherapy, chronic renal insufficiency, iron overload and burns are some of the conditions which predispose patients to the development of this disease^{13,14}.

It has been established that high glucose concentrations enhance fungus growth. In 1943 Gregory *et al.*, reported 3 patients of RCM with fatal diabetic ketoacidosis¹. About 70% of rhinocerebral cases (occasionally referred to as craniofacial) are found in diabetic patients in ketoacidosis⁴. Rhinocerebralmucormycosis continues to be the most common form of the disease, accounting for between one-third and one-half of all cases of mucormycosis³.

Ulceration of the palate, is the commonest oral sign in mucormycosis, which results from necrosis due to invasion of a palatal vessel. Extension of the infection from the paranasal sinuses into oral cavity causes painful, black necrotic ulcerations in the hard palate. The palatal lesion is characteristically large and deep, causing denudation of the underlying bone. Differential diagnosis of a lesion presenting as palatal perforation should include mechanical trauma, tertiary syphilis, leprosy, cancrum oris, intranasal cocaine abuse, malignancies such as nasal T cell lymphomas, Wegener's granulomatosis and midline non-healing granuloma. But, evidence of diabetes or immunosuppression in a patient presenting with necrotic lesions of the palate and nasal cavity strongly favours the diagnosis of a deep fungal infection¹².

One of our patients presented with facial palsy on the right side. According to Alireza Mohebi *et al.*, no obvious pathophysiology for facial nerve paralysis has been proposed yet. Some researchers believe that infection can reach from the pterygopalatine fossa to inferior orbital fissure, orbital apex, and infratemporal fossa. Whether or not the facial nerve is involved at stylomastoid foramen via mentioned pathway is not completely obvious¹⁷.

Both of our patients presented with oral and nasal symptoms with some orbital symptoms and CT scan revealed paranasal sinuses involvement without any evidence of CNS involvement. Erosion of bone is only the later manifestation of the disease. It has been suggested that any diabetic patient in a ketoacidotic state who presents with clinical and radiographic findings of rhino sinusitis should be suspected as having mucormycosis until proven otherwise ⁷.

Computed tomography or magnetic resonance imaging are useful modalities to assess the extent of the disease. Paranasal sinuses were involved in both of our patients, as seen in computed tomography images. Radiographically, rhinocerebralmucormycosis has been associated with nodular thickening of sinus mucosa, sinusopacification without fluid levels, spotty destruction of the bony walls of paranasal sinuses ¹⁵.

All these radiological findings were present in both of our patients. Radiological findings are helpful in assessing the stages of disease rather than making a definite diagnosis as because early lesions of rhino-orbitocerebralmucormycosis may mimic simple rhino sinusitis. Early diagnosis and treatment are of extreme importance for successful eradication of this invasive fungal infection and for patient survival. For a definitive diagnosis of mucormycosis, the histopathological specimen need not be of the isolated fungus, but may be a sample of the necrotic tissue from the site in question. The Grocott-Gomori methenamine silver stain is the most effective for identifying fungi. However, haematoxylin and eosin, periodic acid schiff or calcofluor white stains may also be used ¹⁵. The detection of aseptate hyphae with right angled branching is pathognomonic ⁵. Because initial cultures of diseased tissue may be negative, histopathological examination is essential for early diagnosis ¹⁵. Mok CC *et al* ¹⁰, reviewed the literature from 1970 till 2002, reported that only eight cases of mucormycosis in Systemic lupus erythematosus patients were reported, worldwide. Even in this, Mok *et al* observed that disseminated form of mucormycosis was the most common presentation compared to rhino-orbito-cerebral, which lists one among the two of our cases to be a very rare case.

Amphotericin B is usually administered for the management of mucormycosis, and is administered intravenously, usually at a dose of 1mg/kg/day to a total dose of 3-3.5 gms, confers proven survival benefits in patients with mucormycosis ⁸.

Nowadays, we use liposomal amphotericin B, that although more expensive has less renal toxicity, fewer adverse effects, and a better solubility in the CNS. Hence the dose can be safely increased. Renal function as well as potassium and magnesium must be rigorously monitored during the treatment, that usually lasts for 3 to 7 months ¹⁴.

The use of other drugs has been reported, such as the combination of rifampicin and amphotericin. In the US, posaconazole is employed in amphotericin resistance or intolerance, with good results. It can be administered orally, and is well tolerated with a high response rate. We can also find promising results with the use of granulocyte-monocyte colony stimulating factor in patients with hematologic diseases ¹⁴.

Amphotericin B is partially effective therefore surgical debridement becomes essential. Antral wash, lateral rhinotomy, pansinusectomy, orbital exenteration, and sometimes intracranial surgery are performed depending upon the extent of the disease. Extensive orbital involvement by mucorales required orbital exenteration ¹¹.

CONCLUSION

Rhino-orbito-cerebral mucormycosis is an acute opportunistic mycosis that predominantly occurs in the patients with diabetes mellitus and in immunocompromised conditions. The dental surgeon may see patients with this deadly fungal infection in its earliest stages, presenting as palatal ulceration with other nasal and orbital symptoms. Early diagnosis, prompt controlling of predisposing factors like blood sugar control in diabetic patients, aggressive surgical debridement and, high dose amphotericin B are the most important factors to decrease the morbidity and mortality from this fungal disease.

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