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Case Series

Rhino-orbital mucormycosis with palatal involvement: series of four cases

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ABSTRACT

Mucormycosis (Zygomycosis) is a rare, opportunistic fungal infection caused by mucorales. The clinical hallmark of invasive mucormycosis is angioinvasion and subsequent thrombosis. Palate is the least common site and ulceration with palatal perforation is late occurrence. Involvement of oral cavity usually appears as palatal ulceration or necrosis with denudation of bone and later perforation of palate. In our cases, the patients had both debilitating conditions resulting from poorly controlled diabetes and acute inflammatory immune response due to COVID-19 infection. Radiographically opacification of sinuses may be observed in conjunction with patchy effacement of bony walls of sinuses. Potassium hydroxide smear of lesion can reveal non septate fungal hyphae. Culture on sabouraud's dextrose agar is preferred but histopathological examination of biopsy specimen is conclusive. Successful treatment of mucormycosis consists of rapid diagnosis of the condition followed by radical surgical debridement of infected necrotic tissue with systemic administration of antifungal drugs. Mucormycosis, along with other deep fungal infections, should be considered as an important outcome of SARS-CoV-2 infection.

Keywords: Mucormycosis, Palate, Rhino-orbital

INTRODUCTION

Mucormycosis (Zygomycosis) is a rare, opportunistic fungal infection caused by mucorales, belonging to the class of zygomycetes (phycomycetes).[1] Depending on the immunological status of the patient, the disease may manifest in different ways depending on the affected site as rhino-cerebral, rhino-orbital ,pulmonary, cutaneous, gastrointestinal, central nervous system or disseminated forms. It is commonly reported in immunocompromised patients such as poorly controlled diabetes mellitus, blood dyscrasias, malnutrition, neutropenia, iron overload, organ transplant, and immunosuppressive therapy. The clinical hallmark of invasive mucormycosis is tissue necrosis resulting from angioinvasion and subsequent thrombosis. Diagnosis is confirmed by histopathological demonstration of the organism in the affected tissue.[2] In case of mucormycosis, palate is the least common site; and ulceration with palatal perforation is late occurrence. Early diagnosis and treatment of mucormycosis is extremely important due to the aggressive course of the disease. Control of underlying disease must be established, metabolic abnormalities corrected and antifungal therapy should be combined with surgical debridement of all necrotic tissues.[3] The aim of this article is to report such rare cases of mucormycosis with palatal ulceration and add it to the literature. Here in, reporting 4 cases of rhino-orbital mucormycosis with palatal perforation which were treated by a combined approach involving, medical and surgical management.

CASE SERIES

Case report 1

A 50-year male patient was presented to our ENT OPD with chief complaint of ulcer and eschar in right side of the palate with severe halitosis for last 15 days. It was associated with nasal regurgitation of food, purulent discharge from both side nostril and right orbital swelling. Past history revealed patient was a known case of type 2 diabetes mellitus since 7 years and on insulin therapy. He had history of COVID-19 infection 1 month back for which he was hospitalised and under gone oxygen and steroid therapy. On examination of nasal cavity revealed eschar of inferior turbinate of both the nostril along with eschar of right side of nasal septum with exposure of bony septum. Intraorally 4cm×3 cm circular perforation was noticed in anterior region of hard palate with blackish eschar with necrosis and ulceration. Ulcer margins was irregular and slough present. Based on the history and clinical presentation a provisional diagnosis of mucormycosis was made.

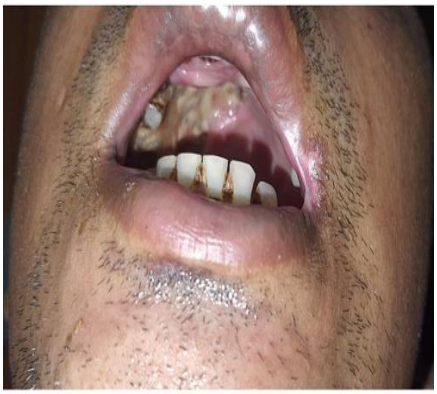

Figure 1: Clinical picture showing ulceration and slough with perforation of anterior part of hard palate.

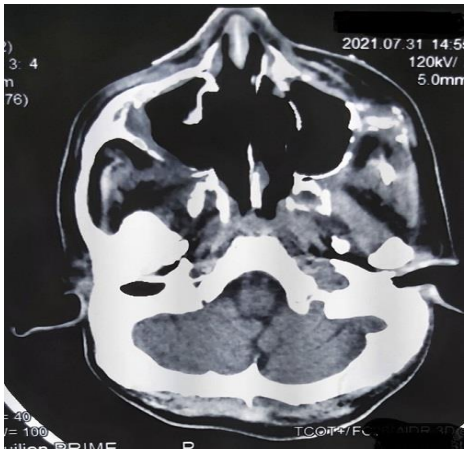

Figure 2: MRI showing bilateral ethmoid and maxillary fungal sinusitis and perforation of nasal septum and bone erosions involving hard palate and maxilla.

Patient was subjected to various biochemical investigation and radiological investigations such as MRI, culture sensitivity test, KOH mount and histopathological examination were advised.

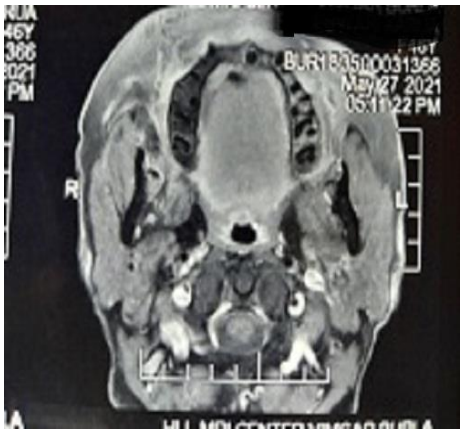

Figure 3: MRI suggesting maxillary sinus opacification with soft tissue density over right side of hard palate.

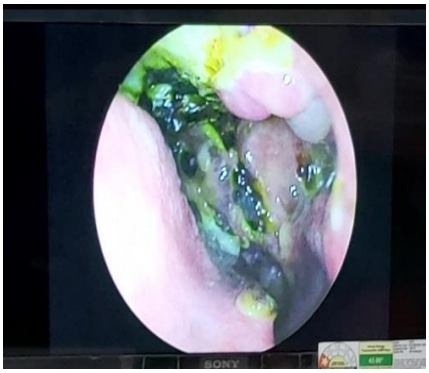

Figure 4: Diagnostic nasal endoscopy showing blackish crust with necrosis of lateral wall of right side of nasal cavity.

MRI revealed bilateral ethmoid and maxillary, right frontal and sphenoid fungal sinusitis and bone erosions involving hard palate and maxilla. KOH mount revealed the presence of few broad, aseptate, branched fungal hyphae. Biopsy was performed from hard palate and tissue sample was taken. Histopathological examination showed branched, nonseptate, broad, fungal hyphae, necrotic tissue, and haemorrhagic material. Fungal culture SDA showed cottony to woolly fungal growth. Emergency medical management of diabetes was started by administration of insulin which resulted in optimal glycaemic control. The patient was started on intravenous liposomal amphotericin B 50 mg in 3 divided doses and metronidazole 1 g intravenously every 12 hour. Surgical debridement of necrotic tissues of nasal cavity and palate was done under endoscopic guidance by modified denkers approach and partial maxillectomy was done under general anaesthesia following which an obturator was constructed for the patient. The patient was advised

daily administration of insulin and to maintain glycaemic control, scrupulous oral and general hygiene. Patient was followed up.

Case report 2

A 47-year female patient was reported to our ENT OPD with complaint of pain over right upper and lower jaw since 8 days. Swelling over right cheek and right periorbital region since 5 days. Pain was contineous, throbbing in nature radiating to head and neck region which was relieved on taking over analgesics. Past history revealed patient had history of COVID-19 infection 15 days back for which she was admitted to near hospital and undergone oxygen therapy. She was recently diagnosed with Diabetes mellitus and under insulin therapy. No history of steroid therapy or any chronic illness. On examination of oral cavity-mouth opening inadequate. Slough present over anterior aspect of right side of the hard palate. No tooth disruption. Nose; mild swelling present over right nasolabial fold. Blackish crusts present over right-side nasal cavity. Left side nasal cavity was normal. Eye: right periorbital edema present.

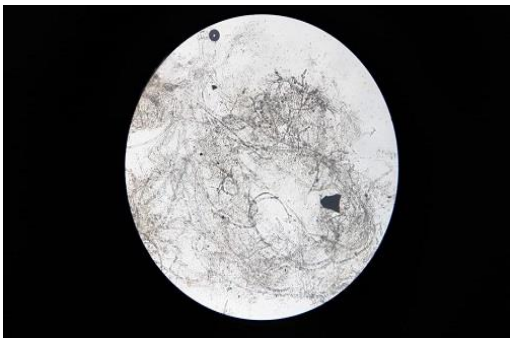

Figure 5: Histopathology report showing broad septate hyphae suggesting mucormycosis.

NCCT scan of paranasal sinus view revealed haziness on right maxillary sinus region. MRI suggested right ethmoid, frontal, and maxillary sinus opacification with soft tissue density over right hard palate.

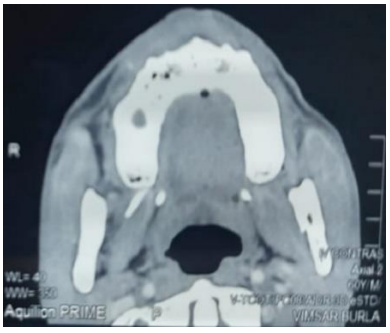

Figure 6: MRI of nose and PNS showing heterogenous mucosal thickening and soft tissue in right maxillary sinus eroding the sinus wall and extending to premaxillary right side of the face, right nasal cavity and hard palate.

Diagnostic nasal endoscopy was performed under local anaesthesia. On examination of right nasal cavity the lateral nasal wall found to be necrosed and studded with thick blackish coloured crusts. Tissue biopsy was performed and sent for histopathology study and KOH mount. KOH mount suggestive of plenty of broad, aseptate fungal hyphae likely Mucormycosis. Sino-nasal debridement was performed by Modified denker's approach under endoscopic guidance and partial maxillectomy with removal of anterior wall of maxilla along with palatal debridement was done under general anaesthesia and tissue was sent for fungal culture and histopathology study suggestive of mucormycosis. Following surgery an obturator was constructed for reconstruction. Based on the above findings a final diagnosis of the rhino-orbital mucormycosis with palatal involvement was confirmed. Human actrapid 30 IU was administered in 3 divided doses till blood glucose levels were within the normal range. Parenteral Ceftriaxone 1gm and liposomal amphotericin B 50 mg diluted in 500 ml normal saline per day was prescribed for 7 days and injection amphotericin B 50 mg once a day for 2 months was advised. Nasal wash with saline was advised for 2 months. Her condition improved dramatically and is under follow up.

Case report 3

52-year female patient was presented to our ENT OPD with chief complaint of pain over right side of the face and right-side unilateral headache which was associated with pain and swelling over right upper molar tooth since 15 days.Past history revealed patient was diagnosed with COVID RAT positive 2 months back for which she was hospitalised in a nearby private hospital and undergone steroid and oxygen therapy. Patient was a known case of diabetes mellitus and hypertension and under medication. On examination of oral cavity-mouth opening adequate. Swelling present over right side of upper molar tooth region and right side of the hard palate without tooth disruption. Nose-mild DNS to left with pale mucosa present over right side of the nostril. Eye-right periorbital edema present. Patient undergone biochemical, radiological and diagnostic nasal endoscopy.

MRI nose and PNS revealed extensive mucosal thickening, soft tissue and retained secretion in right maxillary sinus eroding bony sinus walls and extending to right retro-maxillary space and further to right masticator space with involvement of the all masticator muscles and hard palate. lesion extending to and filling the right nasal cavity, right ethmoid and bilateral sphenoid sinuses. Diagnostic nasal endoscopy under local anaesthesia was performed. yellowish discharge was found in middle meatus and choana. Papery thin bony specules with cheesy discharge coming out of right maxillary sinus. Swab was taken for KOH mount and fungal culture. Tissue was sent for culture and sensitivity. KOH mount suggestive of mucormycosis.

Surgical debridement of the lesion along with right Partial maxillectomy was performed under general anaesthesia. Underlying muscle and mucosa were healthy so kept in situ. Facial defect was reconstructed using temporalis myofascial graft. Necrotic tissue was sent for fungal culture and histopathology study. Histopathology report suggestive of mucormycosis. Based on the above findings final diagnosis of the rhino-orbital mucormycosis with palatal involvement was confirmed. Human actrapid 20 IU was administered in 3 divided doses till blood glucose levels were within the normal range. Parenteral liposomal amphotericin B was prescribed for 2 months which resulted in clinical improvement. Post operative Ryle's tube feeding was given for 15 days. Patient was under follow up and there was no clinical recurrence.

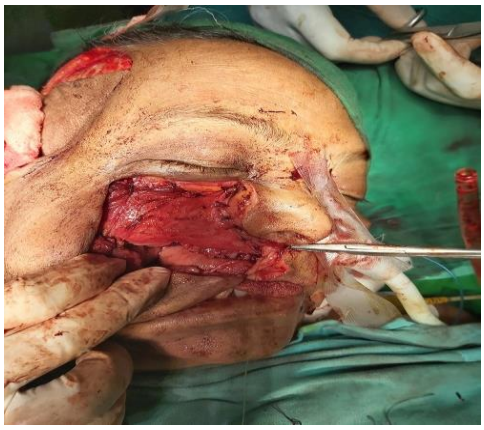

Figure 7: Clinical picture showing the surgical procedure of Partial maxillectomy with reconstruction with temporalis myofascial graft.

Case report 4

A 45 year male patient was presented to ENT OPD with complaint of diffuse swelling over right side of the face and swelling over hard palate for 2 months which was associated with intermittent episodes of bleeding from right nostril. Past history revealed patient was diagnosed with RAT positive COVID 19 infection 2 months back for which he was hospitalised in COVID CARE ICU. He had undergone steroid therapy and oxygen therapy for COVID 19 infection. He was an unknown case of Type 2 diabetes mellitus and on insulin therapy. On examination of oral cavity-mouth opening adequate, swelling present over hard palate of size about 3 cm×3 cm, no disruption of tooth present.

Nose-crusting present over right nostril with clots, pale mucosa over left nasal cavity**.** Eye-right periorbital edema present. Patient undergone biochemical, radiological and diagnostic nasal endoscopy. MRI nose and PNS suggestive of heterogenous mucosal thickening and soft tissue in right maxillary sinus eroding the sinus wall and extending to premaxillary right side of the face, right nasal cavity and hard palate. It extending to right ethmoid and right frontal sinuses. It likely represents invasive fungal sinusitis, most likely mucormycosis. Diagnostic nasal endoscopy under local anaesthesia was performed and crust with tissue from right nasal cavity was sent for KOH mount and fungal culture. After confirmation of mucormycosis surgical debridement of the right nasal cavity was performed by Endoscopic Denker's approach and maxillectomy was performed for palatal involvement by submandibular approach under general anaesthesia.

Reconstruction of the facial defect was performed with masseter myofascial graft. Specimen was sent for histopathology study and HP reports confirmed invasive fungal mucormycosis with palatal involvement. Post operative Ryle's tube feeding was prescribed for 15 days. Post operative broad spectrum intravenous antibiotics and intravenous liposomal amphotericin B was prescribed for 2 months. Patient was under follow up with strict monitoring of all blood parameters.

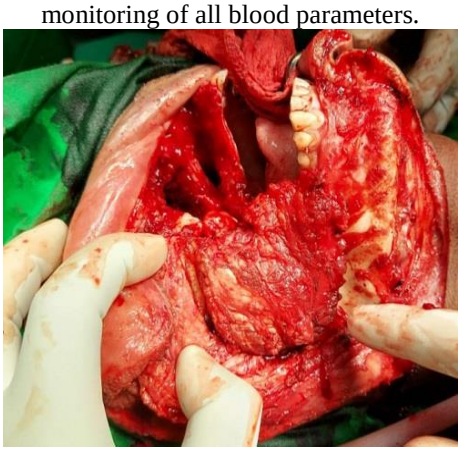

Figure 8: Clinical picture showing surgical debridement with partial maxillectomy with masseter myofascial reconstruction.

DISCUSSION

Mucormycosis is a rare and potentially lethal invasive fungal infection caused by saprophytic aerobic fungi Rhizopus, Rhizomucorpp and Cunninghamella genera of the or order Mucorales, now called Rhidopodaceae which colonize the oral and nasal mucosa and paranasal sinuses.[4] The major predisposing factors responsible for mucormycosis are uncontrolled diabetes mellitus, metabolic acidosis, debilitating diseases such as leukaemia or lymphoma, and immunosuppression.[5] This disease rarely affects patients with no underlying condition. Mucormycosis infection in human is usually acquired through airborne fungal spores, contamination of traumatized tissue, ingestion and direct inoculation.[6] The most common clinical presentation of mucormycosis is sinusitis (rhino-orbital infection), followed by pulmonary, cutaneous/subcutaneous, and disseminated diseases. Tissue necrosis is the hallmark of mucormycosis, resulting from angioinvasion and subsequent vascular thrombosis. Oral manifestations of mucormycosis usually include bone exposure and necrosis, which demands histopathological examination

to confirm the diagnosis because of its nonspecific features and possible similarities to bacterial osteomyelitis, trauma, and iatrogenic infections. The highly fatal rhino-orbito-cerebral form which is invasive and may involve ophthalmic and internal carotid arteries, the other one being the rhinomaxillary form which is seen most commonly in individuals with uncontrolled diabetes and involves sphenopalatine and greater palatine arteries resulting in thrombosis of turbinates and necrosis of the palate. Fungal hyphae produces a substance called Rhizoferrin which binds iron ardently. This Iron-Rhizoferrin complex is then taken up by fungus and becomes available for vital intercellular process.[7]

The low pH, hyperglycemic state and iron rich environment in diabetic and COVID 19 infection patients favours the fungal growth. Mucormycosis is also caused by Rhizopus arrihzus species, in diabetic patients, due to their ability to produce enzyme Ketoreductase which allows them to utilize patient's ketone bodies for their nutrition.[8] Involvement of oral cavity usually appears as palatal ulceration or necrosis with denudation of bone and later perforation of palate. Visual disturbances with concurrent proptosis and symptoms related to orbital cellulitis is often present which were also seen in our cases.[9] In long standing diabetics with poor glycemic conditions, there is atherosclerosis and microangiopathy of blood vessels which further compromise the vascularity and predispose the patient to osteomyelitis . In our cases, the patients had both debilitating condition resulting from poorly controlled diabetes and acute inflammatory immune response due to COVID-19. All of these cases of oral mucormycosis share a debilitating condition, and we considered COVID-19 as one of these, besides diabetes. In a review study on the association between COVID-19 and fungal infection, Song et al. suggested that invasive mycoses are more likely to occur in patients with COVID-19, especially those who are severely ill or immunocompromised.[10]

According to their study, the most important risk factors of invasive mucormycosis in these patients are diabetes, glucocorticoid use, prolonged oxygen therapy, hemopoietic malignancies, prolonged neutropenia, allogeneic hematopoietic stem cell transplant, and solid organ transplant. Radiographically opacification of sinuses may be observed in conjunction with patchy effacement of bony walls of sinuses. Computed Tomography with contrast or magnetic resonance image (MRI) scan can demonstrate erosion or destruction of bone and help to delineate the extent of disease.[11] Potassium hydroxide smear of lesional area can reveal non septate fungal hyphae which was positive in our cases. Culture on sabouraud's dextrose agar is preferred but histological examination of biopsy specimen is conclusive with H&E and PAP stains. The H&E stained section of biopsy specimen demonstrates broad nonseptate fungal hyphae that branch at right angles. Tugsel et al observed that the initial culture of biopsy tissue may be negative and that histopathological examination is essential for early diagnosis.[12]

In all of our cases the diagnosis was confirmed by all the three methods. Successful treatment of mucormycosis consists of rapid accurate diagnosis of the condition followed by radical surgical debridement of infected necrotic tissue with systemic administration of antifungal drugs. Most commonly used drug is intravenous Iiposomal Amphotericin-B with 80% of cure rate.[13] A new triazole derivative posaconazole an oral antifungal agent has been used recently either alone or in combination with Amphotericin-B. The underlying systemic disease should be controlled immediately. Patients with localised invasive sinus disease without cerebral involvement can have the survival rates of about 50-80%. If the infection spreads to brain fatality rate exceeds more than 80%. Prognosis may improve with rapid diagnosis, early management and reversible underlying risk factors.[14] The cases represented here showed all the features of Rhino-orbital mucormycosis like swelling of the face and ulceration along with perforation of palate with underline diseases like diabetes and COVID-19 infection which were consistent with features described in the literature.

CONCLUSION

Mucormycosis, along with other deep fungal infections, should be considered as an important outcome of SARS-CoV-2 infection. Because COVID-19 is still under investigation, all possible associations with the disease should be reported. This condition gains increasing interest because of its initial manifestation in orofacial tissues. So, we emphasise that mucormycosis should be included in differential diagnosis whenever a patient with impaired immune response presents with spreading sinusitis, facial swelling, cellulitis and palatal ulcer. A degree of clinical suspicion, early histopathologic diagnosis and prompt aggressive surgical debridement of necrotic tissue along with systemic Amphotericin-B therapy can save lives.

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