Oral mucormycosis in post-COVID-19 patients: A case series

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ABSTRACT

The rise of mucormycosis in COVID-19 patients is predisposed by indiscriminate intake of corticosteroids, poorly controlled diabetes, injury, prolonged neutropenia, organ transplant, hematopoietic malignancies, prolonged stays in the intensive care unit, and due to nosocomial infection. Oral lesions seen in COVID-19 patients are more probably caused by co-infections, adverse reactions, and immunocompromised conditions instead of direct COVID-19 infection. We would like to report a case series of four patients who had oral mucormycosis after the COVID-19 recovery period.

Key words: Corticosteroid, COVID-19, Immunocompromised, Mucormycosis, Sinusitis

Mucormycosis is an emerging fungal infection worldwide, with destructive disease signs, symptoms, and diverse clinical manifestations [1]. Mucormycosis is an infection caused by fungi belonging to the order Mucorales. *Rhizopus oryzae* is the most common organism isolated from patients with mucormycosis and is responsible for mucormycosis in 70% of cases [2]. Although it is classically defined as an opportunistic infection, preferentially affecting patients with diabetes mellitus (DM), malignancy, chronic renal failure, neutropenia, acquired immunodeficiency syndrome (AIDS), and those who have undergone organ transplantation, or hematopoietic stem cell transplants, it can affect immunocompromised hosts as well (such as trauma patients) [3]. In general, these infections occur in immunocompromised individuals and progress locally through direct extension into adjacent tissues but rarely are angioinvasive or become disseminated [4]. Treatment includes the control of underlying risk factors, antifungal therapy, surgical debridement, supportive therapy, and prosthetic or surgical rehabilitation. It is essential to the restoration of quality of life in individuals to the premorbid state [5].

CASE SERIES

Case 1

A 61-year-old male patient reported to the outpatient department with complaints of pain and pus discharge for 4-5 days from the palatal side of the maxilla in relation to 11, 21, and 22 after COVID recovery. He received treatment of COVID-19 2 months back with hyperbaric oxygen therapy, steroid medication, and antiviral medicines (Remdesivir). Previously, the pain was in the anterior hard palate region which was moderate in nature and aggravated on mastication. The patient also complained of purulent discharge, paraesthesia, and foul odor. The patient had undergone extraction of maxillary anterior teeth 11, 21, 22, and 3 months earlier due to poor oral hygiene and periodontal health. Following extractions, the socket never healed completely. The patient had persistent pain and discomfort for the past 3 months.

Clinical examination revealed necrotic bone exposure on the anterior maxillary edentulous area and pus discharge from the mid-palatal area (Fig. 1a). The palate showed a necrotic bone of approximately 1–2 cm diameter in the mid-palatal region. Denuded mucosa with exposed necrotic grayish-white colored bone was seen from the mesial aspect of 11 to the distal aspect 22 involving alveolar ridge (Fig. 1b). Buccally and palatally involving alveolar ridge in the region of 14–17 region of teeth. Computed tomography shows mucosal thickening that obliterates the right maxillary antral cavity with soft-tissue mass that extends to sphenoid sinuses (Fig. 1c). It causes blockage of the right ostiomeatal complex, representing sinusitis of oral mucormycosis. The nasal septum deviated to the left side. A final diagnosis of mucormycosis of the palate was made on the basis of histological investigation.

Case 2

A 64-year-old male patient was reported to our department with complaints of headache, malodor, nasal obstruction, and

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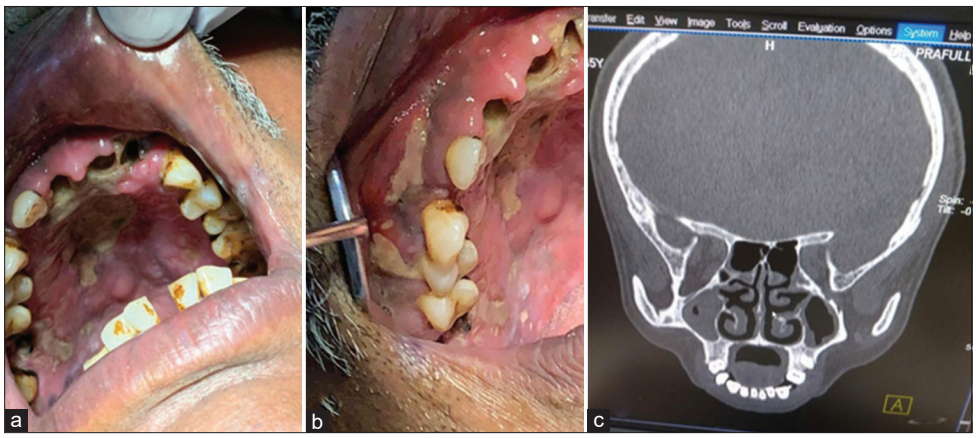

Figure 1: Showing denuded necrotic bone exposure in the (a) anterior maxillary edentulous area and pus discharge in the mid-palatal area; (b) right side of maxilla on buccal side and on palate; and (c) computed tomography scan image shows that hyperdense area in right paranasal sinuses (Case 1)

postnasal discharge for 2 months. He received treatment of COVID-19 3 months back with hyperbaric oxygen therapy and steroids. The patient was known to be hypertension and diabetic and on medication for the same for the past 9 years.

The systemic examination was unremarkable. The blood pressure was 160/100 mm of Hg. On oral examination, he had purulent and foul-smelling discharge from multiple draining sinuses from the maxillary arch (Fig. 2a). There was segmental right mobility in the maxillary arch region and grade II mobility with 13, 14, generalized attrition, and root stump with 25, 26. The radiographic finding shows a radiopacity in the right maxillary sinus suggestive of maxillary sinusitis (Fig. 2b). Generalized horizontal bone loss is suggestive of chronic generalized periodontitis. Based on fungal morphology demonstrated by using a special stain, a final diagnosis of oral mucormycosis was made.

Case 3

A 54-year-old male patient reported to the outpatient department with complaints of pain and mobility in the left side of the back region of the jaw for 5–6 days. He had a significant long-standing history of hypertension and myocardial infarction and was on medication of antihypertensive and anticoagulant drugs.

On clinical examination, the patient was in severe pain on the left side of the face with paresthesia of the lower left lip. Left submandibular nodes were tender on palpation. On intraoral examination, the mandibular left posterior region shows avascular denuded necrotic bone extending from the mesial side of the 37 to the distal side of the 38 region in the buccal side and on the lingual side, exposed necrotic bone seen with the 38 region (Fig. 3a and b). Magnetic resonance imaging (MRI) scan shows left maxillary sinusitis with mucosal plug obstructing the left ostiomeatal unit. The nasal septum was deviated. MRI shows left maxillary sinusitis with mucosal plug obstruction. Bilateral concha bullosa and hypertrophy of bilateral inferior nasal turbinates were also seen (Fig. 3c). A final diagnosis of oral mucormycosis of the mandible was made on the basis of histological investigation using potassium hydroxide staining.

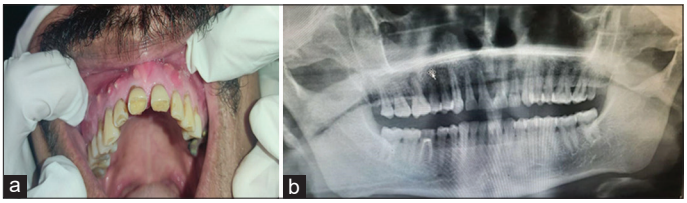

Figure 2: (a) Shows multiple draining sinuses in maxillary arch; and (b) OPG shows radiopacity in the right maxillary sinus (Case 2)

Case 4

A 54-year-old male patient reported to the outpatient department with complaints of pain and pus discharge from the palate region for 6–7 days. The patient was asymptomatic after COVID-19 recovery, and then he experienced pain in the palatal region which was not associated with any tooth. The patient experienced fluid discharge from the palate and nose. The patient also gives a history of pain and heaviness on bending down the head. He received treatment of COVID-19 2 months back with hyperbaric oxygen therapy, steroid medication, and antiviral medicine (Remdesivir). The patient had no history of DM before COVID but after COVID-19. The patient was detected with an increased blood sugar level.

The systemic examination was unremarkable and all vital signs were normal. On clinical examination, perforation was seen on the midpalatal region with fluid discharge and black crust with foul odor (Fig. 4a). Perforation shows exposed necrotic bone. MRI shows a mucosal thickening of all paranasal sinuses suggestive of pansinusitis (Fig. 4b). Mild inflammation was seen in superior orbital soft tissue, superior rectus muscle on the left side. A final diagnosis of mucormycosis of the palate was made on basis of histological investigation.

DISCUSSION

Mucormycosis is a highly destructive fungal infection with increased mortality rates despite recent advances in its diagnosis and treatment [3]. We presented a case series of four cases of mucormycosis who reported to the outpatient department of Oral

Figure 3: (a and b) Shows denuded necrotic bone in left mandibular posterior region in both buccal and lingual side; and (c) magnetic resonance imaging shows left maxillary sinusitis with mucosal plug obstruction (Case 3)

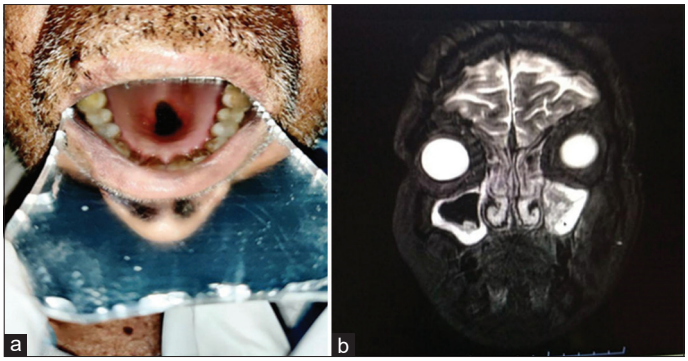

Figure 4: (a) Showing palatal perforation; and (b) magnetic resonance imaging image shows paranasal sinusitis on left side (Case 4)

Medicine and Radiology and are diagnosed based on clinical findings, radiographic findings, and laboratory investigations. In all the cases, patients developed mucormycosis after the recovery from COVID-19 disease. The cause of the sudden rise of mucormycosis in India is due to the COVID-19 infection which makes the patients immunocompromised [6]. The route of infection is through the spread of Mucorales spores through the inhalation route, which later gains entry into paranasal sinuses and then into the lungs [7]. Medical specialists also associated the rise of mucormycosis among patients with a history of COVID-19 occurring mostly due to the indiscriminate use of steroids and other antibiotics. Moreover, the use of other unproven medication for COVID-19 such as iron and zinc tablet supplements, which provide the right environment for the fungus to grow is also linked to the occurrence of mucormycosis [6].

According to the anatomic site, mucormycosis can be classified as rhinocerebral, gastrointestinal, pulmonary, cutaneous, and disseminated [8]. Other factors associated with the rise of mucormycosis due to the use of unhygienic masks and prolonged use of ventilators and humidifiers. However, a hypothesis that has been underreported by the global medical community but being debated by some experts in India is the use of industrial oxygen cylinders in COVID-19 patient are at high potential risk to rise in mucormycosis [6]. Mucorales are considered an opportunistic infection, requiring a breach in the immune system and breakthrough infections after prolonged exposure to antifungals (Table 1) [9,10].

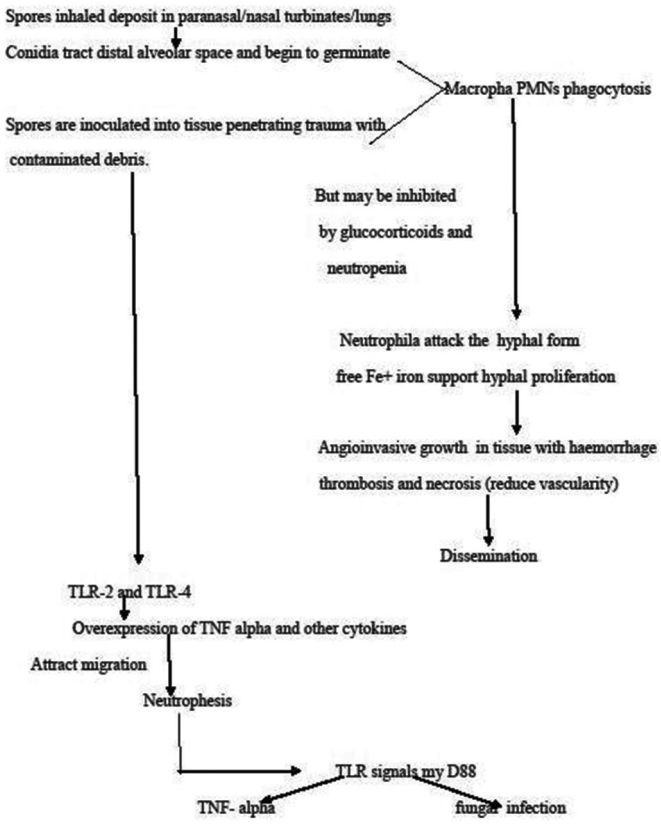

Figure 5: Flowchart of pathogenesis of mucormycosis

Clinical differential diagnosis of the lesion should include squamous cell carcinoma, chronic granulomatous infection such as tuberculosis, midline lethal granuloma, tertiary syphilis, and other deep fungal infections [11]. The occurrence of mucormycosis can probably be attributed to the consumption of glucocorticoids and suggests a need for their judicious use. The pathophysiology of mucormycosis is shown in Fig. 5.

Management includes surgical debridement and antifungal therapy. First-line anti-fungal treatment is included as an amphotericin-B derivative, preferably with liposomal amphotericin-B due to less nephrotoxicity [12]. Oral posaconazole treatment is considered either as salvage therapy or as step-down therapy [13]. Despite treatment with highly potent antifungals, mucormycosis still has increased mortality rates. Prompt diagnosis

Table 1: Relationship between predisposing condition and localization of infection [10]

Predisposing conditions	Predominant localization of infection
Diabetic ketoacidosis	Rhinocerebral
Neutropenia	Pulmonary and disseminated
Corticosteroids	Pulmonary, rhinocerebral or disseminated
Deferoxamine	Disseminated
Trauma, skin maceration, catheter/injection site,	Cutaneous/subcutaneous

and antifungal-surgical treatments play a key role in the management of mucormycosis [14,15].

CONCLUSION

Mucormycosis is an aggressive fulminant invasive fungal infection that can occur in patients with diverse precipitating factors such as uncontrolled diabetes, long-term corticosteroid, immunosuppressive therapy, cirrhosis of the liver, burns, renal failure, organ transplant, AIDS, and malignancies such as lymphomas and leukemia. The current COVID-19 pandemic wave has thrown up yet an extra challenge for the health care system, with some cases of an uncommon fungal infection mucormycosis being described, which are associated with increased morbidity and mortality. Further attempts should be made for the early diagnosis of this disease and prompt treatment of the patient and to reduce the side effects of drugs.

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