

Case report

Post COVID-19 Mucormycosis In Mandible- Case Report Of Two Rare Cases

ABSTRACT

Mucormycosis, also known as black fungus, is a fulminant fungal infection that is reported most often in diabetic and immunocompromised individuals is a life-threatening, invasive fungal infection. After the COVID-19 pandemic, there was a significant rise in the Mucormycosis cases reported in the Maxillofacial region which was attributed to the unbalanced use of steroids to avoid the cytokine storm in covid patients. The majority of the cases reported were of rhinocerebral/orbital or maxillary areas. Very few reports describing the Muromycosis involving mandible have been published on the online database. So here, in this case, report a brief of two cases of Mucormycosis involving the mandible have been described its clinical presentation and histopathologic features.

Keywords: Mandibular Mucor, COVID associated Mucormycosis, Diabetic, Maxillofacial infection.

UNDER PEER REVIEW

INTRODUCTION

The severe acute respiratory syndrome coronavirus type 2 (SARS-CoV2) is the cause of COVID-19, which is most frequently linked to a number of opportunistic bacterial and fungal infections. It may also be linked to pre-existing comorbidities, such as diabetes mellitus, lung disease, or any infections contracted in a hospital[1].

Aspergillus and Candida's species were the most commonly reported pathogens causing coinfection in COVID-19 patients. Additionally, there was a significant surge in cases of Mucormycosis patients involving the tissues of the Maxillofacial area in the Post-covid era[2].

In the immunocompromised host, the altered immunity causes the proliferation and invasion of Mucorales to reach the deeper tissues. As a component of the host's defensive mechanism, phagocytes play a major role in controlling mucormycosis infection. However, when a person is receiving corticosteroid medication, their capacity to inhibit the genesis of fungal spores is diminished[3].

The endothelium is invaded by the fungus' hyphae leading to thrombosis and infarctions, which causes progressive tissue ischaemia and necrosis of the afflicted tissues.

The six accepted clinical types of mucormycosis are as the following[4].

- (1) Rhinocerebral mucormycosis, often associated with diabetes mellitus.
- (2) Gastrointestinal mucormycosis
- (3) Pulmonary and disseminated mucormycosis
- (4) Burn wound mucormycosis.
- (5) CNS mucormycosis.
- (6) Endocarditis and vascular mucormycosis following cardiac surgery.

The maxilla is the most reported site of mucormycosis, while the mandible is very rarely affected. So to give highlight the clinical presentation and histopathological features of the infection at the such an unusual site, in this article we have described a Post-COVID Mucormycosis infection in 2 male patients, involving the Mandible.

CASE DESCRIPTION

Case report-1

A 50-year-old male patient reported to Government Dental College & Hospital, Ahmedabad with a chief complaint of pain, pus discharge, and swelling on the lower face region since one month. He was relatively asymptomatic before one month, then he noticed redness and swelling which slowly increased in size on the lower part of face, and was painful.

The patient had a history of covid-19 before 2 years and was admitted to the covid care center for 20-25 days, where systemic corticosteroids were given and oxygen support was administered till the systemic status was stabilized. He also reported a history of Type 2 diabetes mellitus since 4-5 years and consuming Metformin 500mg for the same. Also, a history of trauma before 7 years and a jaw fracture was reported which was managed without any complications.

Extraoral examination revealed diffuse swelling on the lower face region with mild tenderness on palpation and normal overlying skin(Fig-1). Intraoral examination revealed an edentulous mandibular alveolar ridge with an exposed necrotic bone of the alveolar crest region covering almost the arch of the lower jaw on both sides(Fig-2). The exposed bone was soft to firm in consistency. Pus discharge was present and the surrounding mucosa was inflamed and erythematous.

Radiographic investigation using an orthopantomogram (OPG), revealed missing all mandibular teeth, and a generalized decrease in bone density. The mixed radiopaque and radiolucent density of bone was present. Radiodensity with a moth-eaten appearance involving the whole mandible with the coronoid and condylar process was seen. On CT-Scan aggressive osteolytic changes with a permeative pattern of bone destruction were evident.(Fig-3)

Based on history, clinical examination, and radiographic findings a diagnosis of osteomyelitis was provisioned. The excised specimen was sent for histopathological examination. A gross examination of the specimen showed a single hard tissue measuring approximately about

3x2x1.8 cm³ in size, dark brown to black, soft to firm in consistency, and a few areas of necrotic bone.

On histological examination, H & E, as well as **Periodic Acid Schiff** staining of sections, revealed considerable necrosis with ribbon-like fungal non-septate hyphae, some of which branched at 90 degree with sparse inflammatory components in a bony background(Fig-4).

The patient was admitted to the ward of the Oral and Maxillofacial Surgery department. Full thickness mucoperiosteal flap was reflected and debridement of the necrotic tissue was done till that viable tissue margins appeared, followed by primary closure of the flap with sutures(Fig-5). The patient showed improvement after the treatment and is under regular follow-up.

Case Report 2

A 52-year-old male patient reported to the Government Dental College & Hospital, Ahmedabad with a chief complaint of pain and pus discharge on the lower face region since one month.

The patient had a past medical history of covid-19 before 1.5 years and was under treatment with corticosteroids. He also had a history of Type 2 diabetes mellitus since a year. The patient had a history of Mucormycosis in the mandible before a year and was treated by debridement and curettage of the involved segment and with antifungal therapy- Posaconazole 300mg as reported by the patient.

At present, on extraoral examination, there was no swelling and the overlying skin was normal and no tenderness, sinus, or fistula was there.

Intraoral examination showed exposed necrotic bone on both the right and left posterior alveolar ridge(Fig-6). The exposed bone was soft to firm in consistency. Multiple draining sinuses, pus discharge was present and the surrounding mucosa was inflamed and edematous.

On CT-Scan examination, there was cortical thickening and bony remodeling noted involving the entire mandible. Osteolytic destruction was noted involving rami, bilateral mandibular canal, body, and left condylar process. The left condylar process was deformed with lytic destruction and loss of normal curvature. Bony sequestrum was noted involving the ramus on the left side(Fig-7). Radiological features were suggested of Chronic Osteomyelitis or a lytic

lesion with sclerosis of the bone of the mandible. Based on history, clinical examination, and radiographic findings a provisional diagnosis of a recurrent case of Mucormycosis was made, and excised tissue was sent for histopathologic examination.

Gross examination of the specimen showed multiple hard tissues measuring approximately about 1.5 x 1.1 x 1.0 cm³ to 1.2 x 1.0 x 0.8 cm³ in size, dark brown to black. The consistency of bony fragments was firm to hard. On histological examination with H & E, considerable necrotic tissue with long non-septate hyphae, which branched at the right angle was seen. Chronic inflammatory cell infiltration was there in connective tissue(Fig-8).

The final diagnosis was made based on clinical, radiological, and histological examination as a recurrent case of post covid-19 mucormycosis involving mandible.

Debridement, Curettage, and removal of dead necrotic bone were done under local anesthesia followed by irrigation with physiologic saline and betadine.

Discussion

The word "mucormycosis" refers to any illness brought on by a fungus. It is typically an opportunistic infection of fungal origin that most frequently affects immunocompromised individuals, uncontrolled diabetes, lymphomas, leukemias, renal failure, organ transplant, corticosteroids, immunosuppressive therapy, and rare in healthy individuals.

Chakrabarti et al stated diabetes mellitus was the risk factor for 53.6%.(Prakash and Chakrabarti, 2021)[5]. Other common risk factors were chronic kidney disease, ketoacidosis, neutropenia, corticosteroid therapy, and other immune deficient conditions prevailing in the host.[6] Patients with the triad of SARS-COV 2, Diabetes, and Steroid therapy are at higher risk of contracting Mucormycosis.

The most frequent risk factor in the Indian context is diabetes mellitus, however, in other nations like the US and Europe, the risk factors include hematological cancers and organ transplants[7]. The most common factors that encourage the growth of fungi in COVID-19 patients include hyperglycemia, hypoxia, diabetic ketoacidosis, high iron levels, decreased phagocytic activity, steroid-mediated conditions, and other pre-existing comorbidities. Hyperglycemic status has been reported in individuals affected with COVID-19, SARS-CoV-1, and also in pneumonia unrelated to SARS-CoV-1[8].

A recent study by (Sen et al., 2021) of Rhinocerebral mucormycosis patients in COVID patients revealed that 78% had diabetes and 87% had a history of corticosteroid therapy which is in accordance with above described case reports[9].

Based on this participation, mucormycosis most frequently affects the sinus (39%), lungs (24%), and skin (19%); the transmission method might be either spore inhalation or direct injection. At present, the number of mucormycosis cases reported to affect the mandible is minimal accounting for its rarity[10].

On searching online databases including Pubmed and Google scholar only 20 articles describing the isolated mandibular mucormycosis were found. Out of which mandibular mucormycosis associated with COVID-19, reported were only a few (Aafiya Ambereen et al.)[11].

Most of the cases described in the published literature were of Mandibular Mucormycosis with the dentate mandible. In our case, both patients had an edentulous mandible. In the second case, improper or inadequate resection of the infected tissue margins during the previous surgery might have led to the recurrence of the infection.

While in the first case, as the patient had a history of being admitted for covid treatment and Supportive oxygen therapy for a long time in the hospital covid ward, this might have led to cross-infection or hospital-acquired infection or from the usage of an oxygen mask which creates a moist environment favorable for the growth of fungal spores in and around the orofacial area. Previous articles support that fungus invades the vasculature through the tissues and this angioinvasion leads to thrombosed vasculature and necrosis of the tissues supplied by the vessel. This might have lead to necrosis and disruption of the overlying mucosa of the alveolar process and exposure of the underlying necrotic tissues.

In H & E stained section, histopathology often reveals wide, atypically formed, nonseptate hyphae with right or obtuse angle branching, although **Periodic Acid Schiff** or silver stains make them clearly visible which is in accordance with the histopathological features described in both the above cases. The organism is usually found near the area of necrosis, especially close to the necrotic vessel walls.[12] **Periodic Acid Schiff** or Grocott's methenamine silver stains can be used for further confirmation and usually, they show broad, aseptate, irregular, and ribbon-like folding of fungal organisms and branching at an obtuse angle. PAS staining in our case showed ribbon-like filamentous organisms, and

magenta-colored hyphae at obtuse angles[13]. Similar features were also reported by Verma *et al.*[14]

CONCLUSIONS

In both case reports most of the clinical presentations were similar to the mucormycosis associated with the more common, maxillary bone. Radiographic and Histopathologic examination using the H&E and Fungal stains confirmed the diagnosis to be Mucormycosis of the mandible. So if any immunocompromised patient presents with features mimicking Osteomyelitis or necrotic infection of the lower jaw, Fungal detection through histopathology and culture should also be done. Inadequate investigation and management may lead to severe morbidity and may affect the lifestyle of the patient as Mucormycosis is an aggressive infection, that spreads and causes significant tissue destruction.

REFERENCES

1. Mehta S, Pandey A. Rhino-orbital mucormycosis associated with COVID-19. *Cureus* 2020;12:e10726.
2. Song G, Liang G, Liu W. Fungal co-infections associated with global COVID-19 pandemic: A clinical and diagnostic perspective from China. *Mycopathologia* 2020;185:599-606.
3. Waldorf AR. Pulmonary defense mechanisms against opportunistic fungal pathogens. *Immunol Ser* 1989;47:243-71.
4. L. Eisenberg, T. Wood, and R. Boles, "Mucormycosis," *Laryngoscope*, vol. 87, no. 3, pp. 347-356, 1977.
5. Prakash H, Chakrabarti A. Epidemiology of Mucormycosis in India. *Microorganisms*. 2021 Mar 4;9(3):523. doi: 10.3390/microorganisms9030523. PMID: 33806386; PMCID: PMC8000977.
6. Mandibular mucormycosis following SARS-CoV-2 infection – A case report and review of Aafiya Ambereen a, Sajjad A. Rahman a, Suhailur Rehman b, Kamran Zaidi a, S.H. Arif b

7. Montefusco L, Ben Nasr M, D'Addio F, Lorelli C, Rossi A, Pastore I, *et al.* Acute and long-term disruption of glycometabolic control after SARS-CoV-2 infection. *Nat Metab* 2021;3:774-85.
8. Mishra N, Mutya VS, Thomas A, Rai G, Reddy B, Mohanan AA, *et al.* A case series of invasive mucormycosis in patients with COVID-19 infection. *Int J Otorhinolaryngol Head Neck Surg* 2021;7:867-70.
9. Sen M, Honavar SG, Bansal R, *et al.* Epidemiology, clinical profile, management, and outcome of COVID-19-associated rhino-orbital-cerebral mucormycosis in 2826 patients in India - Collaborative OPAI-IJO Study on Mucormycosis in COVID-19 (COSMIC), Report 1. *Indian J Ophthalmol.* 2021;69(7):1670-1692. doi:10.4103/ijo.IJO_1565_21
10. Agarwal S, Anand A, Ranjan P, Meena VP, Ray A, Dutta R, *et al.* Case of mucormycosis of mandible after self-extraction of teeth incidentally detected to have chronic granulomatous disease: Case report and literature review. *Med Mycol Case Rep* 2020;28:55-9.
11. Oswal NP, Gadre PK, Sathe P, Gadre KS. Mucormycosis of mandible with unfavorable outcome. *Case Rep Dent.* 2012;2012:257940. doi: 10.1155/2012/257940. Epub 2012 Jun 20. PMID: 22779014; PMCID: PMC3388289..
12. Warris A, Henriët SS. Invasive fungal infections in the child with chronic granulomatous disease. *Curr Fungal Infect Rep* 2014;8:37-44.
13. Aggarwal P, Saxena S, Bansal V. Mucormycosis of maxillary sinus. *J Oral Maxillofac Pathol* 2007;11:66-9.
14. Verma M, Sharma R, Verma N, Verma K. Rhinomaxillary mucormycosis presenting as palatal ulcer: A case report with comprehensive pathophysiology. *J Oral Maxillofac Pathol* 2020;24:558-62.
15. Dalimot, J.J.; Smith, I.M.C.; Gerkrath, J.; Hartmann, S.; Cornely, O.A.; Lee, S.C.; Heitman, J.; Rickerts, V. Identification of Mucormycosis by Fluorescence In Situ Hybridization Targeting Ribosomal RNA in Tissue Samples. *J. Fungi* 2022, 8, 289. <https://doi.org/10.3390/jof8030289>

FIGURES



Fig-1 Extraoral swelling



Fig-2 Exposed necrotic mandibular alveolar bone

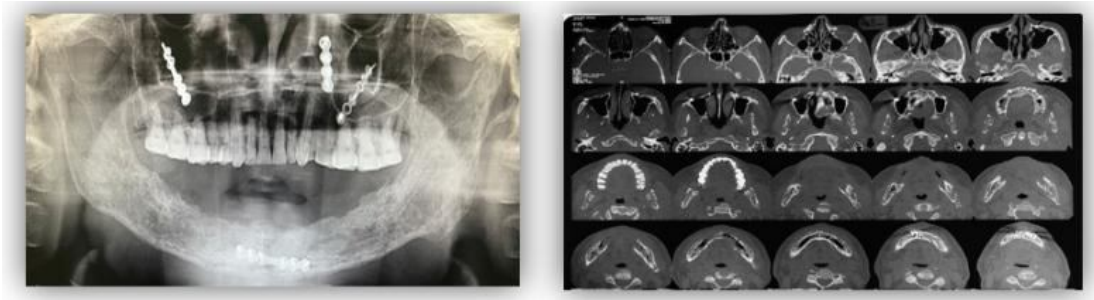


Fig-3 OPG and CBCT showing osteolytic changes

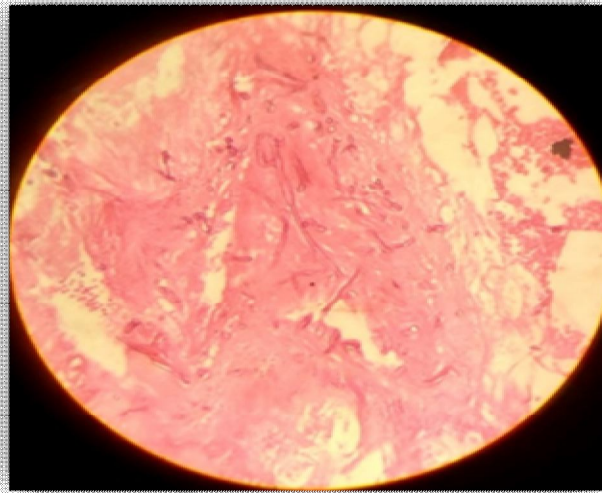


Fig-4 H&E stained section showing ribbon like fungal nonseptate hyphae



Fig-5 Primary closure after mandible debridement



Fig 6 Exposed bone in posterior right mandibular alveolar ridge



Fig-7 Osteolytic destruction noted involving rami, bilateral mandibular canal, body and left condylar process. Left condylar process appears deformed with lytic destruction and loss of normal curvature. Bony sequestrum noted involving ramus on left side.

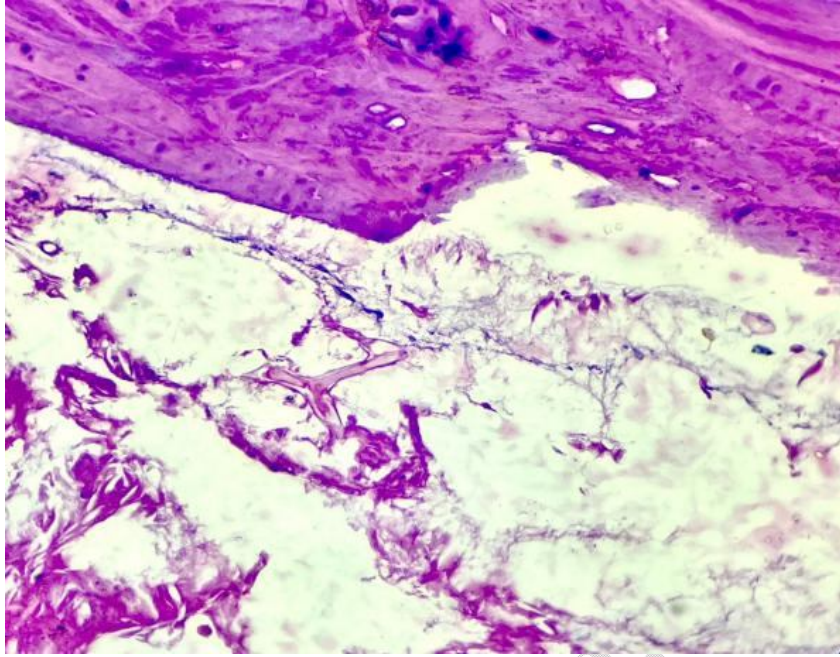


Fig-8 H&E stained section showing ribbon like fungal nonseptate hyphae

UNDER PEER REVIEW