Case Report

MUCORMYCOSIS OF THE MANDIBLE FOLLOWING SARS-COV-2 INFECTION – A CASE REPORT WITH A BRIEF REVIEW OF LITERATURE

Virender Gombra[1], Deepika Bablani Popli[2], Deborah Sybil[3], Shahnaz Mansoori[4]*

[1]*Department of Oral Medicine and Radiology, Faculty of Dentistry, Jamia Millia Islamia, New Delhi, India. vgombra@jmi.ac.in*
[2]*Department of Oral Pathology and Microbiology, Faculty of Dentistry, Jamia Millia Islamia, New Delhi, India.*
[3]*Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Jamia Millia Islamia, New Delhi, India.*
[4]*Faculty of Dentistry, Jamia Millia Islamia, New Delhi, India.*

https://doi.org/10.51847/mUdEYiBzJa

ABSTRACT

Mucormycosis is a rare fungal infection of the craniofacial region and lungs. An upsurge in the cases of mucormycosis was observed in the patients who had a history of SARS-CoV-2 infection.Infact in India, mucormycosis was declared an epidemic during the second wave of the COVID-19 pandemic. Rhino-orbital and cerebral regions were most commonly involved and very few cases of mandibular involvement have been reported in Post-COVID-19 Mucormycosis in India. Herewith, we report a case of isolated mandibular mucormycosis in a COVID- 19 patient. A 47-year-old patient who recently recovered from COVID-19 presented with typical symptoms of osteomyelitis which was confirmed by radiological findings. An incisional biopsy followed by histopathologic examination confirmed mucormycosis of the mandible. Mucormycosis is an aggressive fungal infection thatrequires prompt diagnosis and treatment. Judicious management of osteomyelitis with secondary fungal infections involving the maxilla or mandible in patients with a history of SARS-CoV-19 infection can improve prognosis.

Key words: Zygomycosis, Mandible, Fungus, COVID-19.

Introduction

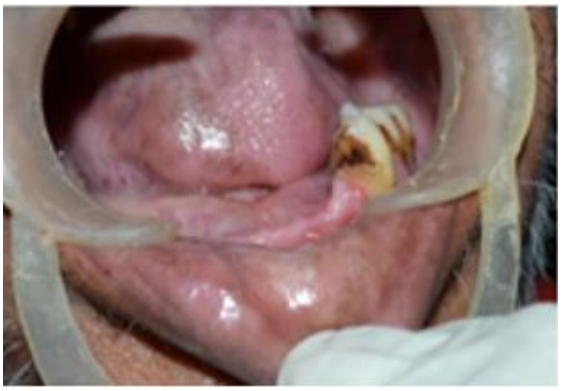
Mucormycosis is an opportunistic fungal infection caused by filamentous moulds, and it belongs to the Mucorales order and the Mucoraceae family [1, 2]. Mucorales can be present in the dirt, rotting plant matter, bread, and dust. Infection to Mucorales may occur by spores inhalation, infected meal absorption, or inoculation of the fungus at a traumatic surface or ulcerative lesion site [1]. Mucorales easily multiply in favourable conditions like immunocompromised state [3]. The organisms responsible for Coronavirus Disease (Covid-19) Associated Mucormycosis (CAM) are primarily R. arrhizus, Rhizopus spp., and Rhizopusmicro spores. The prevalence rate of mucormycosis in a five-decade analysis was 0.14 per 1000 which was 80 times more than in developed countries [4, 5]. Etiology for onset and progression of this disease is multifactorial. A breach in the mucosa or skin makes that site susceptible to spore inoculation and disease initiation. Low Ph, Hypoxia, hyperglycemia, and reduced chemotactic and phagocytic activity support fungal growth. Some factors associated with SARS Cov-2 infection, have also been shown to be linked with increased risk of fungal infection namely raised serum iron, increased endothelial GRP78, Cytokine storm, free radical, and lymphocytopenia [3, 6].

An alarming increase in mucormycosis cases was seen during the second wave of Covid-19 in India. The reported cases were around 47000 in three months duration, although the actual numbers are believed to be much higher [7]. The use of high doses of steroids for a long duration is a known causative factor responsible for the exacerbation of pre-existing diabetes mellitus, its complications such as diabetic ketoacidosis, and even the new onset of diabetes. Steroids which were used rampantly in the management of COVID-19were showed to be an independent risk factor for CAM [8]. Mucormycosis is sub classified as rhinocerebral (rhino maxillary), pulmonary, and cutaneous forms (superficial) and less commonly, gastrointestinal, disseminated, and miscellaneous forms. After the initial lesion at the breach site spreading of the lesions occurs through the haematogenous spread and direct invasion. Through the bloodstream, fungal infection can spread to distant organs such as the lungs or cerebrum which may result in mortal infection [2]. Mucormycosis patients may present facial pain, earache, sinus pain, or odontalgia, initially and dental treatment such as extraction and curettage wound makes oral cavity vulnerable site for fungal infection [9]. A literature search showed very few cases of mucormycosis involving the mandible. We present a rare presentation of CAM involving mandibles along with a brief review of the literature.

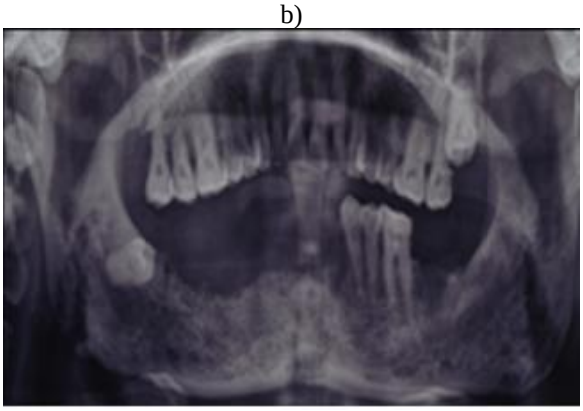
Case report

A 47-year-old male reported to the OPD, of Oral Medicine and Radiology with a complaint of pain and a gradual increase in swelling on the right side of the lower jaw for2

weeks. The patient gave a history of 15 days of hospitalization for COVID-19-associated severe pneumonia three months back. The patient was given supportive oxygen and steroid therapy and he developed steroid-induced hyperglycemia. Oral hypoglycemic drugs were prescribed to control raised blood glucose levels. He had no history of any other medical comorbidities. The patient developed gradual swelling in the right side mandible and extraction was performed, however, the swelling was progressive in size. He then noticed an insidious, moderate pain in the right side lower back teeth region. The pain was radiating to the right jaw and cheek region. Panoramic radiograph showed patchy radiolucencies, which were suggestive of moth-eaten appearance bilaterally in the body and angle of the mandible. Cortical bone appeared deficient in the right parasymphyseal region and right side posterior alveolar bone region **(Figure 1)**. A radiographic diagnosis of osteomyelitis was given and a differential diagnosis of intra-bony malignancy of the mandible was considered. An incisional biopsy followed by a histopathology examination was performed to confirm the diagnosis.KOH wet mount showed the presence of squamous epithelial cells and tissue debris surrounded by numerous broad, aseptate fungal hyphae **(Figure 2a)**. H & E stained sections showed fragmented non-vital bony tissue with empty osteocytic lacunae. Dense mixed inflammatory infiltrates and necrotic tissue fragments were present along with numerous broad, aseptate hyphae of variable thickness and right-angled branching **(Figures 2b and 2c)**. The fungal hyphae were PAS-positive **(Figure 2c)**. Surgical treatment and antifungal treatment were planned for the patient but unfortunately, we lost follow-up for the case.

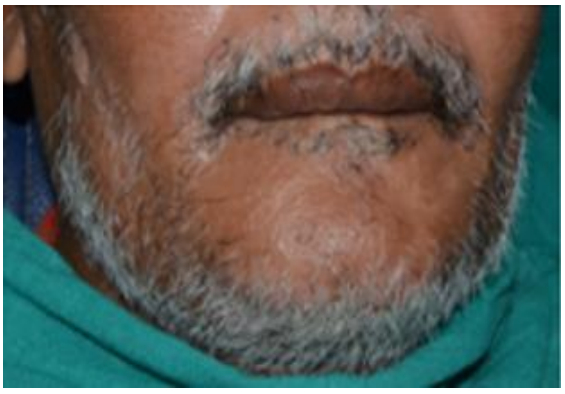


b)

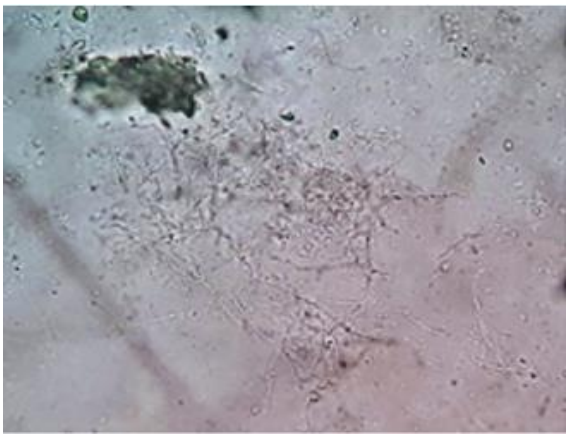


c)

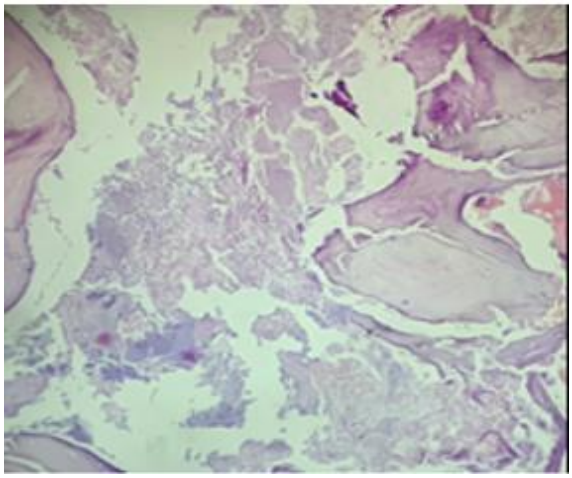
Figure 1. Extra oral (a) and intraoral (b) presentation of the mandible. OPG shows moth eaten appearance of the mandible (c).



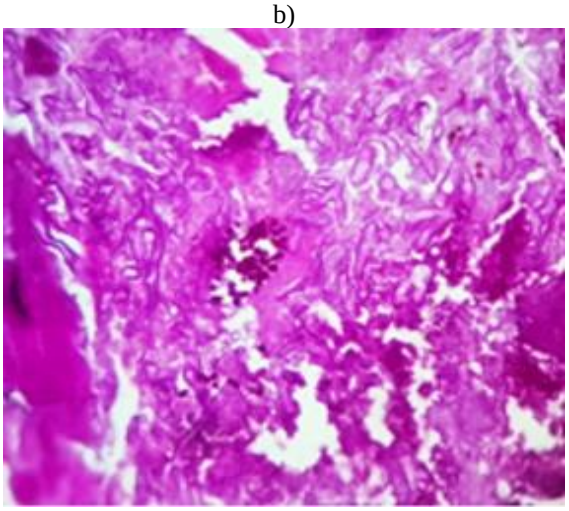
a)



a)



b)



c)

Figure 2. a) (KOH mount 100X), b) (H&E,100X), c) (PAS 400X)

Results and Discussion

Baker introduced the term mucormycosis in 1957 for severe Rhizopus infection. A sudden global increase in mucormycosis cases was seen in the 2021 COVID-19 pandemic and out of these 70% of the cases were reported in India, especially in diabetic patients (94%) or patients with pre-existing immunocompromised status. Mucormycosis is also known as black fungus due to the black appearance of the lesions and dying tissue [8, 10]. As per the study at a tertiary hospital in India, most of the mucormycosis patients during COVID-19 pandemic were male (74.7%), above 40 years (77.4%) with associated increased risk factor of diabetes mellitus (86.6%) and steroids use (44%). Most of the patients had mucormycosis within 1 month of the COVID -19 infection [11]. Clinically Mucormycosis can be seen in the following body areas of the Rhino-orbital-cerebra, pulmonary, gastrointestinal, burn, or skin wound. Disseminated type or kidney Mucormycosis is an aggressive and lethal infection. Mucorales spores inoculate into the host site, escape macrophage phagocytosis and germinate into fungal hyphae. Haematogenous spread of the Rhizopus infection is more due to its ability to attach endothelium via receptors CotH and endothelium GRP78 (Glucose regulatory protein). In addition to these increased levels of glucose, iron, and ketone bodies enhance the expression of CotH and GRP78 and these factors are seen in diabetic patients and Covid-19 patients treated with or without steroids. Resistance to antifungal agents such as amphotericin B, Posaconazole, itraconazole, and isavuconazole further contributes to the poor prognosis of mucormycosis. Platelets, Natural killer cells, B cells, and T cells play important role in the destruction of the fungal hyphae; which explains for increased severity in immunocompromised individuals [10]. Clinical presentation of the dental and orofacial involvement includes black purulent discharge from the nose, nasal blockage, facial swelling and erythema, orofacial pain, headache, proptosis, mobile teeth, black necrotic palate or palatal ulcer, oroantral communication, osteomyelitis, trismus, vision loss and loss of cranial nerve function [1, 2]. Localised infection of mucormycosis is rare but it has been reported in lesion occurrence in the tongue, palate, maxilla, mandible, orbitomaxillary and infraorbital region [10].

The differential diagnosis of mucormycosis include cocaine abuse, fasciitis, aspergillosis, herpes simplex, or herpes zoster [9].

In addition to conventional radiographs CBCT, CT scan and MRI can further help in the evaluation of the lesion. Contrast-enhanced MRI is the diagnostic modality of choice for rhino-orbital-cerebral mucormycosis. Imaging features may present as a classic black turbinate sign, non-enhanced lesions of the sinus and extrasinus region, Infarction of the internal carotid artery, central artery of the retina, and cerebral artery suggestive of angioinvasions, Devitalized orbital, maxillary, and ethmoidal sinus region and on contrast-enhanced fat-saturated MRI show cavernous sinus thrombosis. CT scan may show partial or complete opacification in para- the nasal region, demarcated region of healthy and necrotic bone, and sequestrum formation. Fat effacement in and around pterygoplatine fossa [10, 12]. Histopathology or microbiological culture is the mainstay for the diagnosis of mucormycosis. A simple chair-side test like KOH wet mount can prove beneficial when suspecting fungal infections like mucormycosis and helps initiate antifungal treatment early in the disease course for a more favorable outcome [13]. Histopathological findings confirm the diagnosis by reporting the presence of broad, ribbon-like hyphae, (10 to 20 micrometers) which are usually aseptate. The fungal hyphae are thin-walled and often collapse. The hyphae are irregularly branched and show wide angles and often 90-degree branching. The examination of morphology, width, branching angle and septation helps to differentiate mucormycosis from other similar fungal infections like aspergillosis. Cultures are also confirmatory in the diagnosis of mucormycosis but the slow-growing

nature of such fungi and falsely negative results in up to 50% of mucormycosis cases limit its use in regular clinical practice. Recently, immunohistochemistry using monoclonal antibodies is being used to identify the fungus to the genus or species level. Serum mucorales PCR is also a good diagnostic tool with high sensitivity [12, 14, 15]. Management of the mucormycosis includes prescription of Amphotericin B (first line of treatment),itraconazole, and posaconazole (prophylactic coverage or second line of treatment), Isavuconazole results are comparable to amphotericin B and can be used as the first line of therapy and Echinocandins, Deferasirox (combination therapy with amphotericin B). Side effects and contraindications of the therapeutic agents should be considered while prescribing these drugs. Surgical debridement is the mainstay and should be preceded as early as possible to prevent the spread of the disease. Adequate timely treatment of the lesion can help in a better prognosis of mucormycosis [3, 10].

Conclusion

Mucormycosis is a severe, aggressive, and lethal disease with a poor prognosis. An increased number of disseminated and localized orofacial lesions has been observed in post-COVID-19 recovery cases. Any suspected mucormycosis lesion should be promptly followed for diagnosis and early treatment to prevent mortality in the affected individual.

Acknowledgments: None

Conflict of interest: None

Financial support: None

Ethics statement: None

References

1. Sharma A, Goel A. Mucormycosis: risk factors, diagnosis, treatments, and challenges during COVID-19 pandemic. Folia Microbiol. 2022:1-25. doi:10.1007/s12223-021-00934-5
2. Afroze SN, Korlepara R, Rao GV, Madala J. Mucormycosis in a diabetic patient: A case report with an insight into its pathophysiology. Contemp Clin Dent. 2017;8(4):662-6. doi:10.4103/ccd.ccd_558_17
3. Dogra S, Aggarwal A, Passi G, Sharma A, Singh G, Barnwal RP. Mucormycosis amid COVID 19 crisis: pathogenesis, diagnosis and novel treatment strategies to combat the spread. Front Microbiol. 2022;12:794176. doi:10.3389/fmicb.2021.794176
4. Chakrabarti A, Singh R. Mucormycosis in India: unique features. Mycoses. 2014;57:85-90.
5. Chavan RP, Ingole SM, Nazir HA, Desai WV, Kanchewad GS. Mucormycosis in COVID-19 pandemic: study at tertiary hospital in India. Eur Arch Otorhinolaryngol. 2022;279(6):3201-10. doi:10.1007/s00405-022-07282-1
6. Jose A, Singh S, Roychoudhury A, Kholakiya Y, Arya S, Roychoudhury S. Current understanding in the pathophysiology of SARS-CoV-2-associated rhino-orbito-cerebral mucormycosis: a comprehensive review. J Maxillofac Oral Surg. 2021;20(3):373-80.
7. Muthu V, Rudramurthy SM, Chakrabarti A, Agarwal R. Epidemiology and pathophysiology of COVID-19-associated mucormycosis: India versus the rest of the world. Mycopathologia. 2021;186(6):739-54. doi:10.1007/s11046-021-00584-8
8. Yang JK, Lin SS, Ji XJ, Guo LM. Binding of SARS coronavirus to its receptor damages islets and causes acute diabetes. Acta Diabetol. 2010;47(3):193-9.
9. Papadogeorgakis N, Parara E, Petsinis V, Vourlakou C. A case of successfully treated rhinocerebral mucormycosis: dental implications. Int J Dent. 2010;2010. doi:10.1155/2010/273127
10. Janjua OS, Shaikh MS, Fareed MA, Qureshi SM, Khan MI, Hashem D, et al. Dental and Oral Manifestations of COVID-19 Related Mucormycosis: Diagnoses, Management Strategies and Outcomes. J Fungi. 2021;8(1):44. doi:10.3390/jof8010044
11. Chavan RP, Ingole SM, Nazir HA, Desai WV, Kanchewad GS. Mucormycosis in COVID-19 pandemic: study at tertiary hospital in India. Eur Arch Otorhinolaryngol. 2022;279(6):3201-10.
12. Riad A, Shabaan AA, Issa J, Ibrahim S, Amer H, Mansy Y, et al. COVID-19-associated mucormycosis (CAM): case-series and global analysis of mortality risk factors. J Fungi. 2021;7(10):837. doi:10.3390/jof7100837
13. Mohanty A, Gupta P, Arathi K, Rao S, Rohilla R, Meena S, et al. Evaluation of direct examination, culture, and histopathology in the diagnosis of mucormycosis: reiterating the role of KOH mount for early diagnosis. Cureus. 2021;13(11):e19455. doi:10.7759/cureus.19455
14. Hernández JL, Buckley CJ. Mucormycosis. [Updated 2022 Apr 30]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022. Available from: https://www.ncbi.nlm.nih.gov/books/NBK544364/
15. Skiada A, Pavleas I, Drogari-Apiranthitou M. Epidemiology and diagnosis of mucormycosis: an update. J Fungi. 2020;6(4):265. doi:10.3390/jof6040265