

A Case Report of Mucormycosis in a Patient with a Recent History of COVID-19 Infection in India.

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ABSTRACT

Introduction: Mucormycosis is an angio-invasive fungal infection that increased significantly during the 2nd wave of the Covid-19 pandemic in India. The rise of cases was attributed to inflammatory changes, poor quality oxygen, immune suppression, and corticosteroid therapy.

Case Presentation: This case study reports the history, treatment, and rehabilitation of a case of post-Covid-19 mucormycosis infection. The patient was admitted to the hospital following respiratory distress, at the beginning of the 2nd Covid-19 wave in India. Intravenous antibiotics, steroids, and moist O₂ were administered, intensive support was provided and the patient was discharged after 13 days. Following extraction of 17, the patient reported signs of oro-antral communication which was managed by performing antral lavage and buccal advanced flap closure. Histopathological investigation of tissue salvaged during the procedure revealed the presence of fungal hyphae.

Management and Prognosis: Following diagnosis, anti-fungal medication was prescribed, and a maxillectomy was performed to remove the affected tissue. On follow-up, the tissue healed with no further complications or symptoms, and rehabilitation was performed using an obturators and are movable complete denture. Histopathological investigations were carried out on the tissue salvaged during maxillectomy which confirmed Mucormycosis infection.

Conclusion: The importance of histopathological investigation in the diagnosis of any infectious disease is enumerated in this paper.

Keywords: Mucormycosis, Covid-19, Maxillary Antrum, Hyphae, Oxygen

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INTRODUCTION

Mucormycosis is an angio-invasive fungal infection caused by a fungus of the order Mucorales. It is reported, most frequently among diabetics, followed by patients undergoing haemodialysis and organ transplant or suffering from malignancies.¹ Corticosteroid therapy has been reported to be a significant predisposing factor.²

During the 2nd wave of the Covid-19 pandemic in India, a surge in Mucormycosis was reported among patients with a history of Covid-19 infections. Sars CoV-2 has a diverse clinical presentation ranging from asymptomatic cases to extremely severe cases requiring ICU admission and artificial respiratory support. In such severe patients, Covid-19 pneumonia has been linked to cytokine release syndrome and immune dysregulation. Additionally, many patients were under steroidal pharmacotherapy. Specifically, during the second wave, the use of industrial oxygen due to the lack of medical grade oxygen without optimal sanitation has also linked the fungal infection to post-Covid-19 cases.³

An increase of pro-inflammatory markers, for example, IL-1, IL-6, and TNF-alpha, and a decrease of CD4 interferon-gamma, CD4, and CD8 cells occur as a result of severe Covid-19 infections. This environment, coupled with poor quality oxygen, immune suppression and corticosteroid

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therapy creates an ideal platform for opportunistic pathogens to flourish and spread.⁴

Mucormycosis affects the sinus and brain, skin, gastrointestinal system, and lungs. Rhino-orbital-cerebral

mucormycosis is the most prevalent form, followed by cutaneous, pulmonary, and disseminated types. Diagnosis of the fungal infection is often difficult due to its nonspecific presentation. A final diagnosis is determined by closely examining the clinical features using EORTC/MSG (European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group) criteria, followed by histopathology and culture.¹

This case study reports the presentation, diagnosis, and treatment of a patient with a past history of Covid-19 infection who has developed rhino-orbital-cerebral mucormycosis.

CASE PRESENTATION

A 52-year-old Indian male was admitted to the hospital following respiratory distress, at the beginning of the 2nd Covid-19 wave in India. Covid-19 RTPCR investigation reports were negative. Intravenous antibiotics, steroids, and moist O₂ were administered due to acute symptoms. As oxygen saturation was unstable, the patient was shifted to the Intensive Care Unit for oxygenation with Non Rebreather Mask. The patient was discharged after 13 days, against medical advice, with ongoing oxygen support.

Two days following discharge, the patient sought dental care for pain and irritation in the upper right posterior teeth. Radiographic and clinical examination revealed decayed teeth number 17 which was extracted. Sutures were placed at the extraction site. Twenty-four hours post-operative, the patient complained of water draining from the nose and pus discharge from the palate. On examination, the nasal test

for oro-antral communication was positive. The infraorbital area and nasolabial fold were tender. Antral lavage was first performed, followed by a buccal advancement flap to manage the communication. Bone and sinus lining specimens were salvaged for histopathological and microbiology investigations. At this appointment, pustules were visible on the palatal and buccal surface in relation to 11–18 (Figure 1). Baseline workup showed normal levels of urea (27 mg/dl), creatinine (1.02 mg/dl), calcium (9.5mg/dl), potassium (4.0 mmol/dl), sodium (139 mmol/dl) and chloride (99 mmol/dl).

Differential blood count was normal; however, hemoglobin was reduced (8.7 gm/dl). Erythrocyte Sedimentation Rate (70) and C reactive proteins (72 mg/dl) were elevated. Glycated hemoglobin level was 5.7.

The Paranasal Sinuses radiograph revealed hazy maxillary sinus cavities with thickened sinus lining with questionable continuity of the right zygomatic buttress (Figure 2). Cone Beam Computer Tomography revealed mucosal lining thickening of both maxillary sinuses. Additionally, changes in bony architecture were evident in relation to teeth numbers 16, 17, and 18. Computer Tomography scan revealed space occupying lesion (Figure 3). Histopathological investigation of bone and soft tissue specimens from the right maxillary antrum during antral lavage revealed the presence of fungal hyphae (Figure 4).

More specifically, degenerated tissue infiltrated by pauciseptate broad fungal hyphae with irregular branching was visible after H and E and PAS staining (Figure 5, 6, 7, 8). Following the histopathological investigation, a provisional diagnosis of fungal infection, either Mucormycosis or Aspergillosis, was determined. Prior to treatment planning, the final diagnosis



Fig. 1. Pustule on buccal vestibule



Fig. 2. PNS view

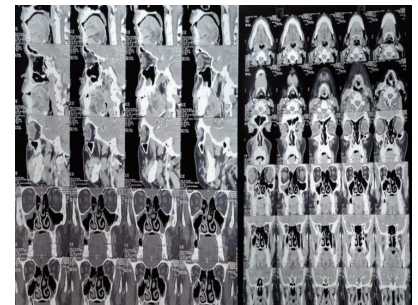


Fig. 3. CT scan image

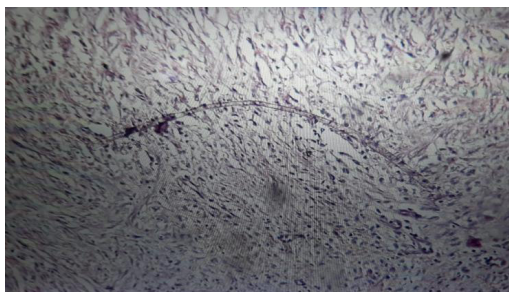


Fig. 4. Photomicrograph of H&E stain in 40X showing fungal hyphae

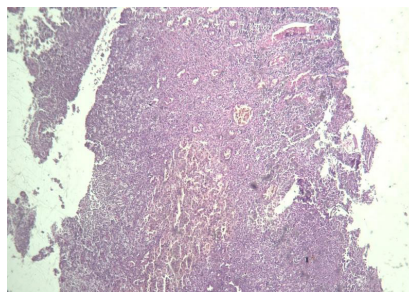


Fig. 5: Photomicrograph of H & E stain 4X

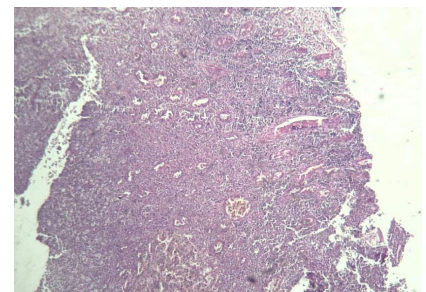


Fig. 6: Photomicrograph of H & E stain 10X

was conditional on the results of the microbiological analysis (potassium hydroxide preparation) of antral lavage fluid, which, however, revealed no trace of fungal elements. Following the diagnosis, anti-fungal medication Amphotericin B deoxycholate (D-AmB)-1.0-1.5 mg/kg/day for 3-6 weeks was prescribed, and a hemimaxillectomy was performed to remove the affected tissue (Figures 9). Histopathological investigations were carried out on the tissue salvaged during maxillectomy which confirmed mucormycosis infection (Figures 4). On follow-up, the tissue healed with no further complications or symptoms and rehabilitation was performed using obturators and removable complete denture (Figure 10,11).

DISCUSSION

Mucormycosis occurs in the oral cavity of immunocompromised patients as the fungal spores spread through inhalation, discontinuity of oral epithelium, ulcers, or an extraction socket.⁵ This case report sheds light on the diagnostic limitations of rhino-orbital-cerebral mucormycosis, the most prevalent type, in resource-limited settings. In comparing mucormycosis among patients with a past history of Covid 19 and patients without any such histories, mortality rates were similar. But rhino-orbital-cerebral or pulmonary types were associated with higher mortality rates. For successful treatment and better prognosis, combined medical and surgical management improved survival, especially in the rhino-orbital-cerebral mucormycosis.⁴ Research has identified that a triad of SARS CoV-2 in combination with corticosteroid use and uncontrolled diabetes mellitus results in an increase in the incidence of rhino-orbital-cerebral mucormycosis.²

The importance of histopathological investigations is

highlighted in this case which revealed fungal hyphae. The diagnosis was complicated further as the initial microbiological analysis revealed no fungal element, which would have helped in determining the final diagnosis. In such a situation where time is important and microbiology analysis could take several days, the definitive diagnosis was based on the hyphal structure. Hyphae are specific for the type of fungus. For example, mucor represents broad non-septate hyphae with right-angle branching, and Aspergillus shows septate hyphae that branch at 45° angles.⁶ This histopathological report clearly reveals non-septate hyphae (Figure 4), confirming Mucormycosis.

It is difficult to determine the time point at which the infection started and what triggered it. Reports revealed severe pneumonia and multi-organ involvement less than one month prior to Mucormycosis diagnosis. The severe infection could have predisposed the patient to the fungal infection resulting in oral pain due to Mucormycosis just a few days after discharge.

On the other hand, initial dental pain could be a result of typical periapical dental infections, and Mucormycosis infection may have been a complication of extraction.

The Covid-19 pandemic has resulted in an increase in the incidence of Mucormycosis cases, especially in India. Initiatives such as the Mycotic Infections in COVID-19 (MUNCO) registry⁷ in India have significantly helped in the surveillance of active cases and keeping the medical personnel updated. Additionally, physicians and dental care professionals, including dentists, should be vigilant while examining potential cases, especially in immunocompromised cases.

CONCLUSION

Mucormycosis is seen in immunocompromised patients.

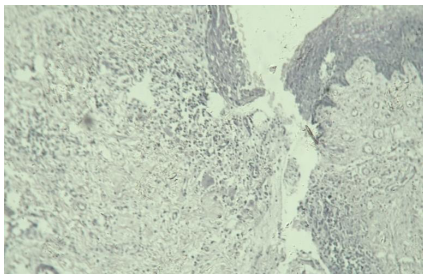


Fig. 7: Photomicrograph of PAS stain 4X

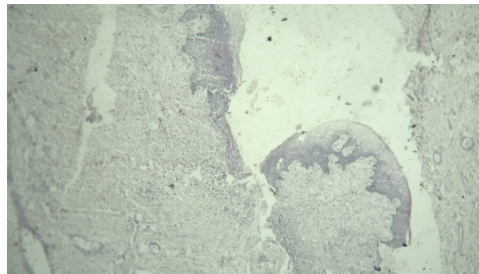


Fig. 8: Photomicrograph of PAS stain 10X



Fig. 9. Specimen Showing segment of maxilla



Fig. 10. Six (6) months follow-up



Fig. 11. Patient with prosthetic rehabilitation

The cases increased significantly during Covid-19 second wave when this case was recorded. In conclusion, this case study sheds light on the importance of microscopy in determining and diagnosing lesions and conditions caused by pathogens. Had the histopathological analysis been not undertaken, the final diagnosis and appropriate treatment of the disease could not be possible leading to further complications. Hence, it is advised to conduct such examinations whenever required.

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