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Case Report

Mucormycosis in immunocompetent COVID 19 patients: 2 case reports

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ABSTRACT

Mucormycosis is an uncommon but fatal fungal infection that usually affects patients with altered immunity and is caused by mold fungi of the genus Rhizopus.
The common mode of transmission of these fungal spores is inhalation, ingestion, or direct inoculation. COVID 19 infection caused an upsurge of this rare disease in the last year. It usually affects immunocompromised patients. In this article, we have discussed the clinical features, radiographic features and management of 2 cases of Mucormycosis affecting the maxilla, nasal and sinus cavities in immunocompetent individuals post covid-19 infection.

1. Introduction

In 2019, the worldwide outbreak of the coronavirus produced an unforeseen challenge for all healthcare givers to combat this deadly virus. One such treatment modality widely accepted was the use of corticosteroids as a means to modulate lung injury and reduce mortality in COVID-19 patients.[1] But unfortunately the widespread use of corticosteroids in patients with COVID 19 causes immunosuppresion which in turn paves the way for various opportunistic fungal and other viral infections. One such disease was mucormycosis, an angioinvasive disease caused by fungi of the order Mucorales like Rhizopus, Mucor, Rhizomucor, Cunninghamella and Absidia.[2] The prevalence of mucormycosis in India is approximately 0.14 cases per 1000 population, about 80 times the prevalence in developed countries.[3]

2. Case 1

Patient aged 41 years came with the chief complaint of swelling and pus discharge in the upper right back region of jaw since 25 days. Patient gave a history of dislodged prosthesis and history of tuberculosis 12 years ago, dengue one year ago, and history of covid one month ago treated with Remdesivir. Diffuse swelling was seen on right side involving the lower half of the face extending ala to external auditory meatus and 2cm from infra-orbital margin to body of the mandible. Intra-orally, erythematous soft, tender swelling with multiple draining sinus was seen in the buccal and lingual aspect of the right quadrant. All teeth in the quadrant were mobile. (Fig 1a,b)

OPG showed ill-defined radioluecency extending from distal aspect of 22 to mesial aspect of 18. Lesion is completely radioleucent in the region of 13-23 and in the region of 16. Mixed radio-opaque radioleucent region seen in the apex of 16, 15, 14. Discontinuity seen in the floor of maxillary sinus and opacification seen.(Figure 2)

CBCT findings: CBCT revealed ill defined moth eaten appearance of bone with effacement of buccal and lingual

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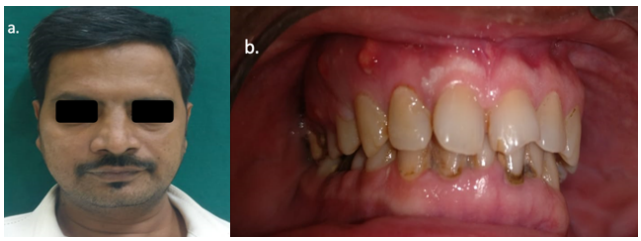

Fig. 1: a,b

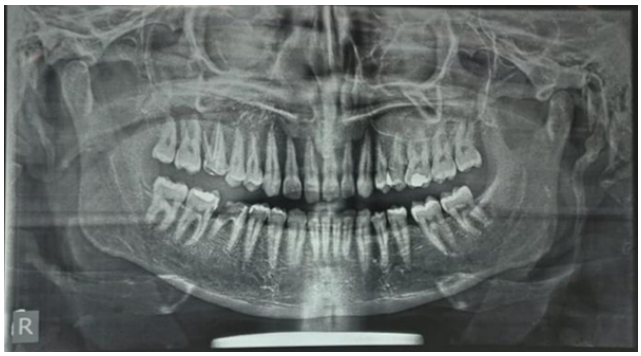

Fig. 2:

cortical plates, involving the maxillary sinus in the upper right quadrant. Moth eaten appearance in relation to 12, 13, 14, 15, 16- areas of radiolucency surrounded by areas of radio-opacity. (Fig 3)

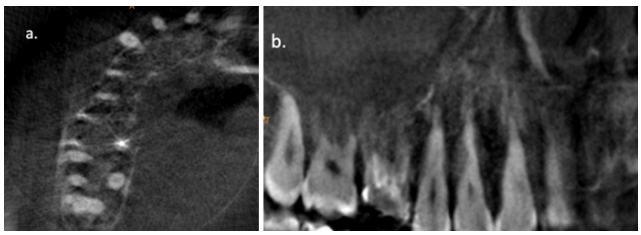

Fig. 3: a,b

CT scans showed similar findings of ill defined hypodensity in the right maxillary alveolus with destruction of bone and involvement of the maxillary sinus.(Figure 4a-d)

Histopath examination revealed areas of necrotic osseous tissue and adjacent fungal colonies, fungal hyphae with isolated , clamped, septae exhibiting branching at obtuse angle, occasional giant cells of hemorrhage. Patient was treated with subtotal hemimaxillectomy followed by liposomal amphotericin B.

3. Case 2: Case Report

A male patient aged 45 years reported with the chief complaint of pain and swelling in the upper left jaw since a fortnight. Patient also complained of pus discharge from

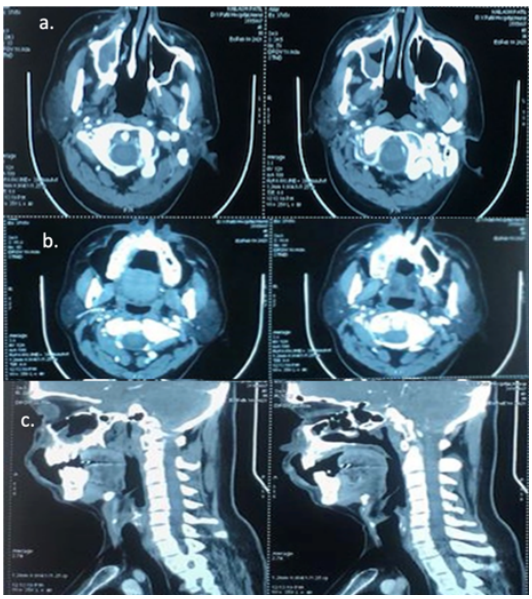

Fig. 4: a-c

multiple sites in the upper jaw and occasional spontaneous discharge from the throat and nose especially on coughing. The discharge appeared to be yellowish green in color and thick mucus like in consistency. This was accompanied with headache on lying down. Medical history revealed incidence of Covid infection a month ago, for which he was admitted to the hospital for about a week and received oxygen therapy in the ICU. No other relevant medical history noted. Maxillofacial examination revealed middle third swelling in the pre maxillary region extending from infra orbital margin to the ala tragus line and from ala of the nose to the outer canthus of the eye on both the right and left side of the face. On palpation, swelling was soft to firm and tender. Intra-orally multiple pustules were noted with pus discharge. All the teeth in the area were mobile. (Figure 5a-c)

Panoramic image revealed large diffuse radiolucent area involving the right maxillary quadrant and partly the left quadrant with effacement of right maxillary sinus floor. (Figure 6)

Axial section of CBCT scan revealed perforation of both the buccal and palatal cortical plate. Also speckled areas of radiolucency noted giving it a typical “Moth eaten” appearance or ground glass appearance.Few authors also refer to it as “salt and pepper” appearance. (Figure 7)

MDCT scans revealed mucosal thickening in left side paranasal sinuses with large defect in the middle wall of maxillary sinus. Focal thinning of nasal septum noted along with periantral fat stranding on left side thus indicating an invasive fungal sinusitis. There is soft tissue involvement on the left lateral border of the nose extending into the sphenoidal sinus. The left maxillary sinus showed partial obliteration with palatal destruction. (Figure 8)

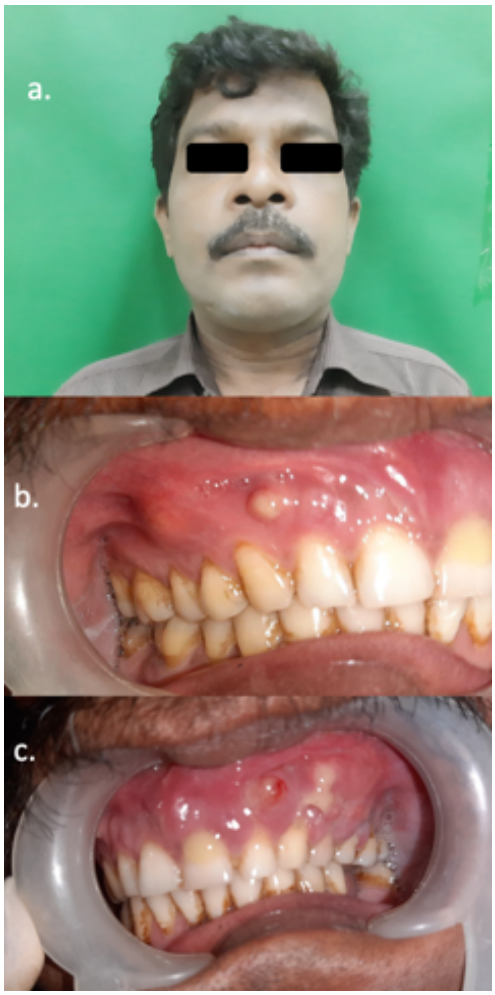

Fig. 5: a-c

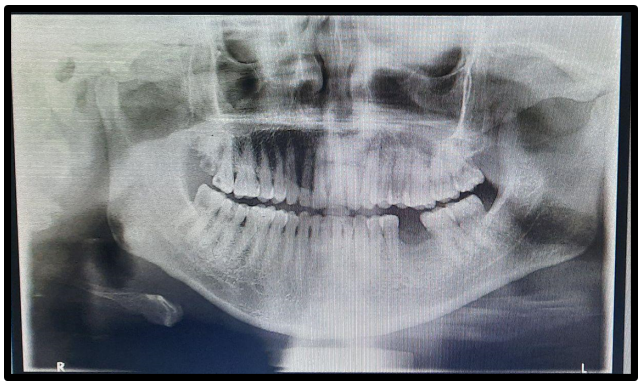

Fig. 6:

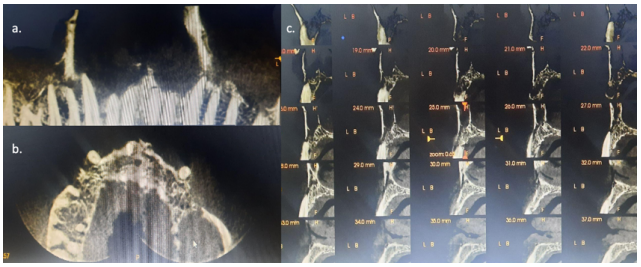

Fig. 7:

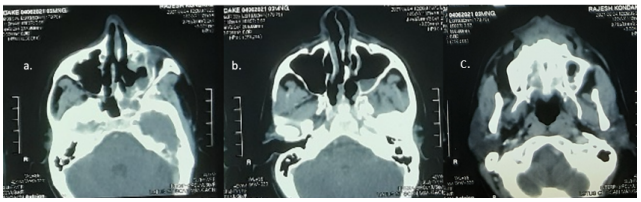

Fig. 8: a-c

3.1. Treatment

After complete evaluation and routine blood investigations the Patient underwent surgical intervention involving Functional Endoscopic Sinus Surgery followed by combination of piperacillin, tazobactum, metrogyl and amikacin. He was also administered liposomal amphotericin B 500 ml every 2 hours for the 14 days post-surgery. A month later he was given an obturator as part of rehabilitation.

4. Discussion

Mucormycosis or zygomycosis was first described in 1885 by Paltauf and later coined as Mucormycosis in 1957 by Baker, an American pathologist for an aggressive infection caused by Rhizopus.[4,5] Mucormycosis is an uncommon but a fatal fungal infection that usually affects patients with altered immunity. Mucormycosis is primarily caused by mold fungi of the genus Rhizopus, Mucor, Rhizomucor, Cunninghamella and Absidia of Order- Mucorales, Class- Zygomycetes.[6] These fungal spores enter the human organism by inhalation, ingestion or direct inoculation.

Mucormycosis is found to be common in the age group of 52.6 ± 13.9 years with males being at a 3.5 times higher risk than females. Diabetes mellitus with or without ketoacidosis was found to be associated in 85% of the cases (Type II diabetes 78%, Type I at 6% and newly diagnosed 16%). Diabetes mellitus has been a risk factor for Mucor infection as it increases free unbound iron in serum, increased IL6 in COVID infection causes further increase in serum ferritin causing excess intracellular iron that generates carboxyhydramine, causing death of hepatocytes. Other associated comorbidities are hypertension, Chronic kidney disease , End stage renal disease, obesity, asthma,

hypothyroidism, haematological malignancy, chronic liver disease and arterial fibrillation, prolonged neutropenia, corticosteroids, trauma, iron overload, illicit intravenous drug usage, neonatal prematurity and malnourishment.[7] Immunocompetent patients can also be affected, when the spores of the fungus are directly inoculated in the skin, as a result of trauma or burn. A 2019 nationwide multi-center study of 388 confirmed or suspected cases of mucormycosis in India prior to COVID-19, Prakash et al. found that 18% had diabetic ketoacidosis and 57% of patients had uncontrolled Diabetes mellitus.[8]

COVID-19 has been known to initiate a cytokine storm causing increased IL6, it infects and replicates in human islet cells causing B-cell damage and thereby decreases endogenous insulin secretion. The severity of the COVID 19 infection also acts as a major predisposing factor in the development of the disease with critically ill patients being affected as much as 37% and mild cases being affected as much as 7%. Oral glucocorticoids are administered to majority of these patients; use of glucocorticoids, Lopinavir, Iitonavir, Ramdesivir worsen the glucose control and predispose to mucormycosis. The patient in Case 1 had been given ramdesivir as treatment for COVID infection.[7]

Depending on clinical presentation, Mucormycosis is classified as rhinocerebral, pulmonary, cutaneous, gastrointestinal, disseminated or other, which includes uncommon rare forms, such as endocarditis, osteomyelitis, peritonitis, renal, etc[9] Patel et al. has shown that rhino-orbital presentation was the most common (67.7%), followed by pulmonary (13.3%) and cutaneous type (10.5%).[10]

Diagnosis is made on the basis of clinical suspicion, however this approach has low sensitivity and specificity. The hallmark of mucormycosis is tissue necrosis resulting from angioinvasion and thrombosis, the absence, however, of a necrotic eschar does not preclude the diagnosis.[9] The colonization in nasal mucosa, sinuses, and its spread to adjacent structures such as orbit, bone erosions and rarely intracranial manifestations can be visualized on CT. Necrotic cutaneous lesions in immunocompromised patients may be due to mucormycosis, but the differential diagnosis includes other pathogens, such as Aspergillus, Fusarium, Pseudallescheria and Scedosporium species. Corzo-Leon et al. proposed an algorithm for the diagnosis and treatment of rhino-orbito-cerebral mucormycosis in patients with diabetes mellitus. The “red flags/warning signs” as given by are cranial nerve palsy, diplopia, sinus pain, proptosis, periorbital swelling, orbital apex syndrome or a palatine ulcer. The finding of any of these signs should prompt immediate further testing, including blood tests, imaging, ocular and/ or sinus surgery or endoscopic revision and initiation of antifungal treatment.[11] In the present cases , we clinically noticed infraorbital swelling, sinus pain and tissue necrosis.

Diagnosis of mucormycosis remains challenging. Histopathology, direct examination and culture remain essential tools, although the molecular methods are improving.[9] New molecular platforms are being investigated and new fungal genetic targets are being explored. Molecular-based methods have gained acceptance for confirmation of the infection when applied to tissues, most accurate being the KOH stain or the cauliflower white stain.

The gold standard of all the imaging techniques is contrast enhanced computed tomography or gadolinium enhanced MRI.

Methods on detection of Mucorales DNA in blood have shown promising results for earlier and rapid diagnosis and could be used as screening tests in high-risk patients, but have to be validated in clinical studies. More, much needed, rapid methods that do not require invasive procedures, such as serology-based point-of-care, or metabolomics-based breath tests, are being developed and hopefully will be evaluated in the near future.[10]

The most widely used means for treatment of the disease is administration of antifungal drugs more specifically Amphotericin B. Results of various studies show that total amphotericin B has been given in 93% COVID 19 associated patients among which liposomal B had been given in 90% of patients. Both the cases in the article were also treated with liposomal amphotericin B. Surgical methods adopted include mechanical debridement majorly, orbital decompression and exenteration.[12]

In this article, we discussed 2 cases of immunocompetent individuals who developed mucormycois post COVID 19 infection. They presented with typical features of the disease and were treated successfully.

5. Source of Funding

No financial support was received for the work within this manuscript.

6. Conflict of Interest

None declared.

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