Mucormycosis coinfection post-COVID-19 recovery: Early suspicion and prompt action

ABSTRACT
Severe acute respiratory syndrome coronavirus 2 infection has resulted in a pandemic, the disease manifests itself as various conditions ranging from respiratory disorders to exacerbated inflammatory responses. The management in some cases involves immediate care in an intensive setup with the administration of various antibiotics and steroids which has resulted in the imposition of risk factors and growth of fulminant fungal infection. The present article addresses two such cases which presented with osteomyelitis secondary to mucormycosis in patients who had more than one episode of COVID-19 infection. The upsurge of existing manifestation and development of opportunistic infections has to be considered in patients who are suffering or recovering from COVID-19. The COVID-19 scenario brings up a possibility of many bacterial and fungal infections in its aftermath. This article brings out two such opportunistic aggressive fungal infections and comprehensive management of the same.

Keywords: COVID-19, mucormycosis, severe acute respiratory syndrome coronavirus 2

INTRODUCTION
COVID-19 pandemic has presented itself with a plethora of manifestations which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The manifestations may range from symptoms arising from lung damage or may be due to an exacerbated inflammatory response. The treatment plan may at times involve the use of one or more immunosuppressant drugs; either individually or in combination to ward off the adverse effects of the inflammatory response, thus leading to the imposition of risk factors and encouragement of the growth of fungal micro-organisms. The treatment also involves additional risk factors such as malnutrition, prolonged intubation, central and/or arterial venous access, and the need for a nasogastric tube that can increase the chances of mycosis infections in patients suffering from severe cases of COVID-19. There has been an emergence in the incidence of fungal infection which could be attributed to the outbreak of the pandemic; the present situation has indeed increased the incidence of invasive fungal infections especially in the systemically compromised individuals. Although fungal infections such as mucormycosis are ubiquitous in nature, the weakened immune system as mentioned earlier may cause the germination of spores and develop into hype which can spread and cause various infections such as orbitorhinocerebral infection, pulmonary, gastrointestinal, cutaneous, renal, and isolated central nervous system infections. The definitive treatment for the invasive fungal disease is surgical debridement because systemic medications cannot reach the infected tissue due to vaso-occlusion. Surgical management includes aggressive debridement of all necrotic tissue, sometimes requiring multiple debridements to...

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reduce the microbial load. It is important that debridement is carried out until healthy tissue is encountered. Reconstructive surgery should only be considered after complete recovery from infection.\(^\text{[6]}\) In the present article, we report two cases of osteomyelitis secondary to mucormycosis who were systemically compromised and had suffered more than one spell of COVID-19 disease along with other systemic manifestations.

**CASE REPORTS**

**Case 1**

A 54-year-old male patient reported to our tertiary level teaching hospital as a refer in case from the department of neurosurgery with chief complaints of foul smell and discharge from the mouth with a persistent headache and blurred vision in the right eye. Clinical examination revealed halitosis and pus discharge from the anterior part of hard palate. There were areas of exposed bone over the buccal vestibule and parts of hard palate. The exposed bone was nontender and mobile with brownish discoloration. The right eye had shown signs of proptosis. Ophthalmologic consultation revealed blurring of vision in the right eye [Figures 1 and 2]. Laboratory investigations revealed decreased hemoglobin level (8 g/dL) with increased levels of serum creatinine (2.4 g/dL) and lactate levels of 2.8 g/dL. Past history revealed the patient was a known case of chronic kidney disease and he had two episodes of flu-like symptoms and was tested positive for COVID-19 by reverse transcription-polymerase chain reaction. During his stay at the hospital for management of SARS-CoV-2, he was administered steroid drugs and other supportive treatment. The computed tomogram of the subject in question was suggestive of diffuse bony erosion and hyperdense mucosal thickening which involved the right maxillary, ethmoid, and bilateral sphenoid sinuses. A similar lesion was seen to be associated with the right side of the alveolus, hard palate, and right greater wing of sphenoid and also anterior part of the zygomatic arch [Figure 3]. A swab culture was sent for microbiologic analysis which did not show any growth in the first 48 h. Owing to the situation at hand, a decision was made to undertake complete removal of the necrotic bone and debridement of the maxillary antrum under general anesthesia, followed by further multiteam approach for rehabilitation of vision and reconstruction of the palate. The postoperative period involved copious irrigation of the surgical site and administration of titrated doses of amphotericin B and also having a close watch on the serum creatinine levels [Figure 4]. There were drastic improvements in the levels of blood sugar (fasting: 96 g/dL, postprandial = 134 g/dL) and serum creatinine (1.5). The patient has now been shifted back to oral antihyperglycemics for glucose control.

**Case 2**

Our second case was a 64-year-old male patient who presented with white patches over the oral cavity during
the time he was admitted to the hospital. The reason for his hospital stay was lobar pneumonia and was also tested positive for SARS-CoV-2 for more than one time. The individual was also a known case of Type II diabetes mellitus and was on oral antihyperglycemic. Local examination revealed exposed areas of necrotic bone over the hard palate and in relation to upper right back molars on the buccal side [Figure 5]. The associated teeth were mobile with signs of pus discharge. The computed tomogram of the subject in question showed hyperdense collection in the maxillary antrum right, suggestive of hemosinus (Hounsfield unit = 55) with a change in density at the borders suggestive of membrane thickening [Figure 6]. Laboratory investigations revealed blood sugar levels for 254 g/dL with increased serum creatinine at 1.8. The individual was taken up for complete excision of the necrotic mass and debridement of the maxillary antrum under general anesthesia. The necrotic bone was removed and the Schneiderian membrane was debrided and submitted for HPE along with excised maxilla segments [Figures 7 and 8]. The pus was aspirated and sent for culture and sensitivity. The individual was started on empirical antifungal therapy with Caspofungin, being relatively lesser nephrotoxic index.[7] The individual was taken up for continuous copious irrigation with amphotericin B and sterile vehicle as irrigant. Postoperative culture and sensitivity report revealed that the organism was resistant to multiple antibiotics [Table 1]. Hence, a plan was made to start; the patient was started on intravenous amphotericin B with continuous monitoring of serum creatinine, blood glucose, and serum potassium. The individual developed hyperglycemia (335 g/dL) during the postoperative period and was started on sliding scale insulin therapy, as per the recommendations of the medical specialist. The biopsy that was evaluated for histopathologic examination revealed angio-invasive mucormycosis [Figure 9]. The postoperative period involved continuous and copious irrigation and maintenance of meticulous oral hygiene. There was a drastic improvement of symptoms and the nasal floor showed adequate healing [Figure 10]. Postop splint administered to avoid regurgitation of fluids. The postoperative blood picture showed an improvement of hemoglobin (12.4 g/dL), blood sugar of 122 g/dL, serum creatinine, and potassium also returned to near-normal levels. The sequence of events of Case 1 [Figure 11] and Case 2 [Figure 12] is depicted in the form of a time-lapse chronology.
DISCUSSION

The increased incidence of fungal infections in patients affected by SARS-CoV-2 has been scantly reported in the literature. The early studies conducted by Wu and McGoogan reveal an increased incidence of invasive fungal disease in patients undergoing treatment for COVID-19. However, galactomannan testing and other fungal diagnostics for further differentiating these infections are rarely available in the Indian subcontinent which could help the clinician in early recognition of the fungal infection, which makes us to depend on early clinical signs and symptoms and further establish a favorable treatment plan.

The usual presentation in such individuals is the early involvement of the oral cavity as we saw in both of our cases; there are numerous studies to support the increased manifestation of the oral cavity to fungal diseases like mucormycosis which is in tandem with our cases. The choice of antifungal is always amphotericin B as shown in most of the studies; it provides a steady dose-dependent elimination of the fungus, we also started the same therapy in both the cases, but in the second case, it had to be stopped owing to increase in blood sugar (as the drug was delivered in conjunction with dextrose infusion) and also due to increased serum creatinine levels.

Surgical intervention with complete debridement is the mainstay for management which was done in both the cases as recommended by most of the studies. The various causes of fungal infection in COVID-19 patients have been studied by Cataldo et al., which suggests a higher incidence of fungal infection as a “collateral effect” and also points at three key drivers for such high incidence, namely (1) immune dysregulation, (2) extensive use of corticosteroids, and (3) less adherence of infection control and preventive measures. The challenge that is posed on the clinicians is that the
disease hardly gives time for establishing a suitable diagnosis; the manifestation is seen once it is disseminated to a greater degree, as seen in the first case where it posed as bigger lesion extending to the temporal region also, and the in the second case where the angioinvasion had already set in. The presence of COVID-19 as seen in both cases presents with extreme dilemma in rapid surgical management, the time required for the patient to become stable for a surgical procedure implies that vital time is lost which could have led to a disseminated spread of the infection as we saw in both the cases. The discoveries of recent time suggest that a
CONCLUSION

SARS‑Cov‑2 has taken a toll on the medical setup and has posed a lot of challenges by the emergence of existing and novel infections. The individual who requires intensive care is often in an immunocompromised state and also needs intubations, nasogastric tube feed which would further hamper the immune status of the individual. The manifestation of mucormycosis presenting as osteomyelitis of the maxilla could be attributed to the state of the host post recovery from COVID‑19 infection. There are various studies that indicate increasing incidence of fungal infection post‑COVID‑19; it hence becomes prudent that a protocol may be devised for the prevention or early diagnosis and prompt management of fungal diseases in such patients.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the legal guardian has given his consent for images and other clinical information to be reported in the journal. The guardian understands that names and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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