

Review Article

Mucormycosis—A potential aftermath post COVID-19: A brief review

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Abstract

The Corona virus pandemic and its continued streak along with numerous mutations have put forth a major challenge for the medical fraternity worldwide. Due to new disease entity with high infectivity rate and associated fatality, it is proving to be highly challenging by being associated with certain morbidities induced by novel therapeutic protocols. Some of the COVID-19 treated patients suffer with another fatal infection, mucormycosis, commonly called as black fungus and this has posed yet another challenge in fighting the COVID menace. The paper features mucormycosis as a preexisting entity in medical science along with its current hazardous trend with novel corona virus including its management.

Keywords: COVID-19, diabetes, management, mucormycosis

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INTRODUCTION

Mucormycosis is a lethal fungal infection in the order Mucorales that was formerly known as zygomycosis and now commonly identified as black fungus. The disease is caused by saprophytic aerobic fungi rhizopus, rhizomucor, and cunninghamella genera of order Rhidopodoceae.^[1] The disease transmission seems to occur predominantly via inhalation of spores from the environment.^[2] Mucormycosis colonizes the oral mucosa, nasal mucosa, and paranasal sinuses apart from being associated with lung, gastrointestinal tract, and skin.

Mucormycosis being a post COVID-19 complication is emerging as a subject of discussion on several academic groups, and print and media forums. The disease finds its

association with diabetes and other immune-compromised conditions such as human immune deficiency virus infection, malignant hematological disease, and solid organ transplantation, and rarely affects patients recovering with COVID-19 with no underlying disease.^[3] Having a humongous estimated 77 million diabetic cases in India with recent cross-sectional study depicting 47% Indians unaware of their diabetic status and consequent lack of proper glycemic control,^[4] India also bears an infamous distinction of being both the diabetes as well as mucormycosis capital of the world.^[5] Mucormycosis is one of the most fatal complications of uncontrolled diabetes with high mortality rates ranging between 40% and 80%. Early symptoms of the disease being sinus pain or nasal blockage, one-sided headache, toothache/loosening of teeth, blurred or double vision, chest pain, and blackening of nose, to name a few.

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With underlying comorbidity in patients contracting COVID-19 infection, the risk of severity of infections and hospitalization increases. Post COVID-19 sepsis is a common entity in critically ill patients, resulting in deranged immune response, ciliary dysfunction, cytokine storm, thromboinflammation, and final immune exhaustion.^[5] These patients when subjected to emergency invasive procedures (intubation, intravenous lines, and catheterization), mechanical ventilation, prolonged hospital stays, and poor nursing may be exposed to facilitation of secondary bacterial and fungal infections. A breach in the aseptic condition by not following the infection control measures in hospitalized patients, more so, in intensive care unit (ICU) predispose to bacterial and fungal infections. Usage of anti-interleukin-6 strategies and corticosteroid treatment in such susceptible hosts with environmental fungal spore counts provide a suitable setting for mold infections.^[5] Amidst the gravity of the existing complications in such patients, current guidelines suggest the use of steroids in admitted patients requiring oxygen support.^[6] This further emphasizes the possibilities and consequent disease formations in such opportunistic conditions. *Candida* as a normal resident in the human body and its expression in the form of candidiasis upon lowered immune state of body is a well-known information since many years. Recently, hospitalized COVID-19 patients with underlying complications were the high-risk group for fungal infections like aspergillosis and mucormycosis. COVID-19-associated pulmonary aspergillosis has garnered international eyes; Indian epidemiology of invasive mold infections in the ICU reveals significantly higher burden of invasive mucormycosis.^[7] There have been case reports of mucormycosis as a complication in post COVID-19 patients in several other countries, including the UK, the USA, France, Austria, Brazil, and Mexico, but the volume is greater in India.^[8]

Hallmark of mucormycosis is tissue necrosis that results from angioinvasion, leading to vascular thrombosis.^[1,9] Oral mucormycosis manifests as bone exposure and necrosis, demanding histopathological examination for confirmation of diagnosis due to its nonspecific features and much similar possibilities seen in traumas, iatrogenic infections, and osteomyelitis.^[9] Negative galactomannan and beta-D-glucan are useful to rule out other mold infections as there is no biomarker for mucormycosis. Biopsy, potassium hydroxide mounts, and calcofluor stain are rapid diagnostic methods.^[5] As *Mucor* is difficult to routinely culture, biopsy remains the most sought after diagnosis for it.^[5]

Documented cases of oral mucormycosis with other systemic diseases were reported in patients battling the

COVID-19 infection. In a Brazilian study conducted by Pauli *et al.*, a painful lesion on a hard palate of a 50-year-old Latin female patient was observed and the patient was subjected to biopsy. Histopathology diagnosis of oral mucormycosis was made after excluding the differential diagnosis of necrotizing sialometaplasia, malignant salivary gland neoplasm, and oral leishmaniasis. The patient had debilitating condition due to uncontrolled diabetes and acute inflammatory immune response due to COVID-19.^[10] Trauma resulting in mucormycotic osteomyelitis in the nasomaxillary zygomatic complex was reported by Srivastav *et al.* in a 42-year-old male patient with poorly managed diabetes.^[1] A combination of oral mucormycosis and aspergillosis in a patient with acute leukemia was reported by Vučićević Boras *et al.*^[11] An invasive form of oral mucormycosis on the tongue as a complication post orthotopic liver transplant with a history of hepatocellular carcinoma and hepatitis C cirrhosis was reported by Vahabzadeh-Hagh *et al.*^[12] A systemic review conducted by Rawson *et al.* reported that 8% of patients during their course of hospitalization suffer from a bacterial or fungal co-infection while recovering from COVID-19.^[13] A case of oral mucormycosis in a patient with diabetes after tooth extraction was reported by Rajashri *et al.*^[9]

The management of mucormycosis includes antifungal agents, surgical debridement, adjuvant therapy, and reversal of underlying predisposing factors. As per the global guidelines on treatment of mucormycosis by the European Confederation of Medical Mycology, amphotericin B, isavuconazole, and posaconazole remain the three molecules of choice in the anti-mucor drugs.^[14] For the mainstay treatment of mucormycosis, amphotericin B is a potent broad spectrum fungicidal agent and treatment should be initiated with its high dose. Liposomal amphotericin B (doses titrated to toxicity—initial test dose followed by 3–5 mg/kg/day) and conventional amphotericin B (doses titrated to toxicity—initial test dose followed by 1–1.5 mg/kg/day) was stated as per All India Institute of Medical Sciences, New Delhi, COVID-Mucor care team.^[15]

CONCLUSION

Oral lesions seen in patients with COVID-19 are most likely to be induced by co-infection, impaired immunity, and adverse reaction than direct severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections.^[16] Oral mucormycosis is best managed when diagnosed early along with the treatment of underlying predisposing risk factor if any; surgical debridement; and spontaneous

administration of active antifungal agents.^[11] Teledentistry and consultation is the optimum approach for the early diagnosis of the disease in socially isolated, quarantined COVID-19 patients. Other deep fungal infections along with mucormycosis should be considered as a possible association of SARS-CoV-2 infection because COVID is still under scrutiny and its association with any other disease entity should be documented for better research and evidence-based results.

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Conflicts of interest

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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