

Mucormycosis infection in COVID-19 patients in India: An emerging lethal threat.

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Abstract

Opportunistic fungal infections have been reported to be associated with COVID-19 disease. Mucormycosis, an invasive fungal disease is being increasing being reported from India in patients with covid-19 infection with comorbidities like diabetes and given corticosteroids for treatment of COVID-19 during the current wave of COVID-19 pandemic which is alarming owing to lethal sequels of the disease.

Keywords: Mucormycosis, COVID-19, Vision loss, Diabetic ketoacidosis.

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About the Study

The coronavirus disease 2019 (COVID-19) pandemic which started from Wuhan city of Hubei province, China since December, 2019 and was declared the Public Health Emergency of International Concern (PHEIC) by World Health Organization (WHO) continues to be a significant problem worldwide [1,2].

The clinical profile of COVID-19 infection can range from mild to life-threatening pneumonia with associated bacterial and fungal co-infections [3]. Due to the associated comorbidities (e.g., diabetes mellitus, chronic obstructive pulmonary disease) and immunocompromised conditions (e.g., corticosteroid therapy, ventilation, intensive care unit stay), COVID-19 patients are very susceptible to acquire and develop severe opportunistic infections. There are many reports of severe opportunistic infections such as oropharyngeal candidiasis, pneumocystis jiroveci pneumonia, pulmonary aspergillosis, bloodstream candida infections, etc., in patients affected with COVID-19 [4,5]. Among the various factors associated with morbidity and mortality among the COVID-19 patients, opportunistic bacterial or fungal infections could worsen the position of the patients and may lead to ARDS [6].

As of March, this year, 41 cases of COVID-19-associated mucormycosis had been documented globally, with around 70% from India only [7]. Reports also suggest that the number of cases is now going to be much higher, which is not surprising given the current wave of COVID infections in India.

In India, the prevalence of mucormycosis is approximately 0.14 cases per 1000 population which is about 80 times the prevalence found in the developed countries [8]. Infection with COVID-19 has been associated with many fungal infections. The disease of mucormycosis is more often found in immunocompromised individuals, and complications of orbital and cerebral involvement are more likely in case of diabetic ketoacidosis and with concomitant use of steroids. The most common risk factor associated with the disease of mucormycosis in India is diabetes mellitus [9].

Sen et al. [10] reported a series of six COVID-19 cases with rhino-orbital mucormycosis. One patient in this case series had concurrent COVID-19 and mucormycosis at the time of presentation, while five other patients developed mucormycosis during hospitalization in course of treatment with systemic steroids given for treatment of COVID-19. All the patients were known diabetics and the mean duration between the diagnosis of COVID-19 and development of mucormycosis was 15.6 ± 9.6 (3-42) days. All patients underwent endoscopic sinus debridement, whereas two patients required orbital exenteration. At the last follow-up, all six patients were alive, on antifungal therapy.

Patel et al. [11] in another case series reported 12 cases of Rhino-orbit cerebral mucormycosis seen at department of ENT, GMCH, Nagpur, Maharashtra from November, 2020 to February, 2021. Previous history of COVID-19 infection and treatment for the same was found in 41.67% cases, concomitant infection in 16.67% and asymptomatic undiagnosed covid (antibodies positive) was detected in rest 41.67% cases. Commonest presenting complaint was nasal obstruction (66.67%) followed by loss of vision (33.33%) and swelling around eye (25%). Diabetes mellitus was the commonest comorbidity (83.3%) with one patient (8.3%) having Pulmonary TB+CKD. At the end of 1 month, improvement in vision was observed in the 2 cases who had blurring of vision whereas all the 4(33.33%) cases with complete loss of vision did not show any improvement. Improvement in the general condition with reduction in nasal necrotic tissue and inflammation was noted in all cases (100%).

Similarly, Sarkar et al. [12] reported a cluster of 10 cases of clinically diagnosed orbital mucormycosis with concurrent COVID-19 illness seen between October and November 2020. All the patients presented with clinical features of orbital mucormycosis and COVID-19 was diagnosed later on routine screening. All the patients in the series were known diabetics. Diabetic ketoacidosis (DKA) was evident in four patients at admission while five more patients developed DKA after the initiation of corticosteroid therapy for COVID-19 disease. Four patients expired within 1 month of the diagnosis whereas five patients had satisfactory systemic outcomes, but with

irreversible vision loss, while only one of the patients had both ocular and systemic favorable outcome.

Mehta et al. [3] reported a case of rhino-orbital Mucormycosis associated with COVID-19 in a 60-year male patient. The patient was a longstanding diabetic, with a positive RT-PCR for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). He received parenteral meropenem and oral oseltamivir with parenteral methylprednisolone for treatment of his COVID-19 infection. Over the course of the hospitalization, he developed signs of orbital cellulitis. Magnetic Resonance Imaging (MRI) of the brain, orbits, and paranasal sinuses, revealed soft tissue swelling in the right pre-septal, malar, pre-maxillary and retro-bulbar regions with paranasal sinusitis. A nasal biopsy was performed which revealed broad aseptate filamentous fungal hyphae suggestive of mucormycosis, which was later confirmed on culture. The patient continued to deteriorate, required mechanical ventilation, and eventually required inotropic support. Despite all measures, he died on day six of his admission. The authors concluded that extensive use of steroids/monoclonal antibodies/broad-spectrum antibiotics may lead to the development/exacerbation of a pre-existing fungal disease.

A study by White et al. [13] from UK screened 135 adults with COVID-19 infection and reported incidence of invasive fungal infections as 26.7% among the COVID-19 patients (most commonly aspergillosis (14.1%) followed by yeast, usually candida (12.6%)). Patients with invasive fungal diseases had higher mortality (53% with v/s 31% without). Corticosteroid therapy and a past history of chronic pulmonary disease were found to be associated with a higher risk of the invasive fungal disease. The authors concluded that fungal disease occurs frequently in critically ill, mechanically ventilated COVID-19 patients.

Conclusion

In conclusion, mucormycosis is a, opportunistic, life-threatening infection and patients with moderate to severe COVID-19 are more susceptible to it. Uncontrolled diabetes mellitus and use of corticosteroids increase the risk of invasive fungal infection with mucormycosis in COVID-19 patients which can develop during the course of the illness or as sequelae. High index of suspicion, early diagnosis, and appropriate timely management can improve survival and reduce the morbidity. All physicians and surgeons including otolaryngologists and ophthalmologists should, therefore, be mindful of the probability of development of mucormycosis in patients with COVID-19 illness, especially in those with comorbidities and on immunosuppressive agents.

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