

COVID-19 associated mucormycosis (CAM): A tale of two pathogens

Dear Editor,

There have been many reports of a very high prevalence of mucormycosis among COVID-19 patients throughout the globe since the beginning of the pandemic, particularly among diabetics who have been administered glucocorticoids for COVID-19.^[1-3] This entity has been described as COVID-19 Associated Mucormycosis (CAM).^[3] CAM has been linked to high morbidity and mortality, as well as exorbitant medical expenses and a shortage of antifungal medicines, particularly in India.^[4]

Mucormycosis is a group of distinct potentially fatal mycoses caused by one of the widespread saprophytic fungi belonging to order Mucorales. These fungi are opportunist organisms that may be found in thorns, soil, and feces, as well as in the nasal and oral mucosa of healthy people. Infection to mucormycosis usually occurs following inhalation of spores. Due to unclear reasons, these fungi have a proclivity for blood vessels, and hyphal infiltration of blood vessels is the most distinguishing feature of them. This attack causes a variety of manifestations, like hemorrhage, thrombosis, infarction, or tissue necrosis.^[5]

The majority of cases of CAM are recorded in India, with the United States of America, Egypt, Iran, Brazil, and Chile following closely after.^[3] The increased incidence of mucormycosis since the emergence of novel coronavirus disease is most likely due to systemic immune modifications caused by SARS-CoV-2 infection or due to the drugs given for its treatment. COVID-19 patients who have a history of trauma, diabetes mellitus, glucocorticoid use, hemopoietic malignancy, prolonged neutropenia, or transplant are more prone to get mucormycosis.^[6] The reason being that these patients can have significantly elevated levels of inflammatory cytokines, which are coupled with compromised cell-mediated immune response, impacting the T cells. As a result, there is an increased susceptibility to fungal coinfections, even without a history of immunosuppressive therapy.^[7] Aside from that, many mechanisms have been proposed: As with any other serious infection, patients with COVID-19 are predisposed to DKA because angiotensin-converting enzyme-2-receptors are highly expressed in pancreatic islets, and SARS-CoV-2 may infect and proliferate in human islet cells leading to β -cell damage and reduced endogenous insulin secretion.^[8,9] Furthermore, increased insulin resistance owing to cytokine storm may be potential reasons for COVID-19's "diabetogenic condition."^[10]

Severe COVID-19 alters iron metabolism, which is a known independent risk factor for mucormycosis infection.^[11] Moreover, additionally, high zinc supplementation in COVID-19 patients may be a factor in mucormycosis infection.^[12] The spread of fungal spores through water used in oxygen humidifiers is another indirect link between the concurrent rise in cases of CAM.^[3] Apart from that, the treatment regimen, which comprises medications known to cause immunosuppression, such as steroids, remdesivir, and tocilizumab, predisposes the host to mucormycosis.

While other forms of mucormycosis are also reported, rhino-orbitocerebral mucormycosis (ROCM) is most reported in the literature concerning CAM. Mucormycosis is a fatal disease, with death rates ranging from 50% to 85%, especially in cases where the brain is involved.^[11,12] These kinds of infections by themselves are associated with the worst outcome, especially when the immune system response does not improve. However, opportunistic infections can be managed once the immune system recovers.

The detection of mucormycosis dissemination requires regular evaluation and imaging (CT and MRI). Wherever possible, early complete surgical treatment for mucormycosis should be performed when treating cases of mucormycosis. Amphotericin B lipid complex, liposomal Amphotericin B, and posaconazole oral suspension are first-line antifungal monotherapies, with isavuconazole reserved as a rescue drug.^[6] If no improvement in clinical symptoms is seen after a broad range of empirical therapy, and a compromised immune response caused by SARS-CoV-2 is suspected, opportunistic infections such as mucormycosis should be considered as a possible causative agent. Clinical suspicion and early surgical debridement are critical in minimizing morbidity in this potentially lethal disease. Controlling blood sugar, monitoring blood glucose levels, prescribing steroids judiciously (in terms of time/dose/duration), using safe, sterile water for humidifiers during oxygen therapy, and judicious use of antibiotics and antifungals are all implicated in COVID-19 and post-COVID-19 patients, especially diabetics and those treated with glucocorticoids.

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Conflicts of interest

There are no conflicts of interest.

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