Emerging cases of mucormycosis under COVID-19 pandemic in India: Misuse of antibiotics

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Abstract

COVID-19’s second wave had a significant impact on India, on May 7, 2021, the largest daily recorded case count was a little more than 4 million, and it has since fallen. Although the number of new cases reported has dropped, during the third week of May 2021, India accounted for about 45% of new cases identified globally and around 34% of deaths. As India maintains its present level of stability, a new urgent threat has emerged in the form of coronavirus-associated mucormycosis. Mucormycosis, an acute and deadly fungal infection caused by Mucorales-related fungal species, is a fungal emergency with a particularly aggressive propensity for contiguous spread, associated with a poor prognosis if not properly and immediately identified, and treated. Mucormycosis, sometimes referred to as the “black fungus,” has increased more rapidly in India during the second wave of COVID-19 than during the first wave, with at least 14,872 cases as of May 28, 2021. Uncontrolled diabetic mellitus (DM) and other immunosuppressive diseases such as neutropenia and corticosteroid treatment have traditionally been identified as risk factors for mucormycosis. Therefore, the use of glucocorticoids or high doses of glucocorticoids in mild COVID-19 cases (without hypoxemia) should be avoided. In addition, drugs that target the immune pathway, such as tocilizumab, are not recommended without clear benefits.

KEYWORDS
black fungus, COVID-19, mucormycosis, SARS-CoV-2, steroids
Infections in diabetes can affect the development of mucormycosis, a serious fungal infection. Studies have shown changes in the innate immune system in diabetic patients, with reduced phagocytic activity and cytokine secretion (Ahmadikia et al., 2021; Cornely et al., 2019; Salehi et al., 2020).

Although rare, the infection has been around for decades, but it only affects people whose health is compromised by the use of steroids and whose immune system is significantly weakened. Increased cases of mucormycosis in COVID-19 patients are prevalent, primarily due to reduced phagocytic activity and steroid use (Ahmadikia et al., 2021; Cornely et al., 2019; Salehi et al., 2020). Glucocorticoids are inexpensive and widely available and have been shown to reduce mortality in patients with COVID-19 hyperglycemia. Nevertheless, glucocorticoids can increase the risk of secondary infections. In addition, the combination of virus-induced immunomodulatory dysfunction and immunomodulatory drugs such as tocilizumab may further increase the risk of infection in patients with COVID-19 (Revannavar et al., 2021; Somasekharan Nair Rajam et al., 2020).

A case of COVID-19 infection with multiple infections of nasal orbital zygomycosis along with ketoacidosis has been identified in a newly diagnosed diabetic patient. Reduced phagocytic activity, transferrin replacement increases iron availability in diabetic ketoacidosis and fungal heme oxygenase enzyme that facilitates iron absorption for the fungal metabolism are the pathogenic pathways implicated in fungal aggression. In the case mentioned for extreme COVID-19 coinfection with fungi, cell count reveals a gradual decrease in lymphocytes while a progressive rise in the number of neutrophils and white blood cells. It has been hypothesized that infection with SARS-CoV-2 can have an effect on CD4+ and CD8+ T cells, to play a significant role in the pathophysiology of COVID-19 infection (Garg et al., 2021; Saldanha et al., 2021). In severe COVID-19 cases, the total number of T cells and lymphocytes decreases and has been linked to the most negative outcomes. T cells specific for Mucorales, like CD4+ and CD8+, produce cytokines such as IFN-γ and IL-4, IL-10, IL-17, and fungal filaments that cause damage. According to Sharma et al., such unique T cells are only present in patients with invasive mycosis, and that they may be useful surrogate diagnostic markers for invasive mycosis. Lymphopenia can raise the chance of transmitting invasive mucormycosis, although an increase in lymphocyte count can be beneficial to the adaptive immune system and induce T cell development specific for Mucorales, which can aid in the control of the invasive infection (Sarkar et al., 2021).

There are many reports showing changes in cell-mediated immunity involving phagocytosis, chemotaxis, and cytokine secretion in diabetic patients. Diabetes has been associated with changes in the components of the innate immune system. Diabetics have lower factors for mucormycosis. Inhalation of spores and/or seeding onto the airways or any susceptible epithelium required for the spread of mucormycosis; using host conditions such as hyperglycemia, ketoacidosis, iron overload, and neutropenia to germinate into angioinvasive hyphae that cause endothelial damage; resulting in local hemorrhaging, thrombosis, and necrosis, as well as eventual spread to numerous organs (Ahmadikia et al., 2021; Cornely et al., 2019; Salehi et al., 2020).

Glucocorticoids and perhaps remdesivir are the only drugs that have proven beneficial in COVID-19 (Jain et al., 2020; Rajendra Santosh et al., 2021). Glucocorticoids are inexpensive and widely available and have been shown to reduce mortality in patients with COVID-19 hyperglycemia. Nevertheless, glucocorticoids can increase the risk of secondary infections. In addition, the combination of virus-induced immunomodulatory dysfunction and immunomodulatory drugs such as tocilizumab may further increase the risk of infection in patients with COVID-19 (Revannavar et al., 2021; Somasekharan Nair Rajam et al., 2020).

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