Letter to the editor

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Mitigating the Emerging Threat of Mucormycosis in COVID-19

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Dear Editor,

There is a rising concern regarding the increasing incidence of rhino-orbital or rhino-cerebral mucormycosis in patients with severe COVID-19.[1–3] This invasive fungal infection has significant morbidity and mortality. Patients with a history of diabetes mellitus, organ transplantation, rheumatological diseases requiring long term use of immunosuppressive agents like corticosteroids, haematological malignancy, end stage renal failure, organ transplantation and acquired immune-deficiency syndrome, are at a higher risk. The fungus proliferates and spreads to the paranasal sinuses, with subsequent invasion to the orbits as well as intracranial invasion, leading to ischemia, necrosis and thrombosis.[4]

In patients with COVID-19, poorly controlled diabetes mellitus has been associated with increased morbidity and mortality. Furthermore, patients with severe COVID-19 are known to develop cytokine storm as well as impaired cell-mediated immunity. Critically ill patients admitted to intensive care units, requiring mechanical ventilation, have a prolonged duration of hospital stay. Extensive use of steroids, broad-spectrum antibiotics and monoclonal antibodies in treatment of these patients can further suppress immunity. These factors, in isolation or in combination, increase their susceptibility to supper-added fungal infections.

In patients with mucormycosis, uncontrolled diabetes has also been implicated as a major risk factor.[5] There is a high expression of angiotensin-converting enzyme 2 (ACE-2) receptors in pancreatic islets, Binding of SARS CoV-2 to these ACE- 2 receptors leads to damage of these pancreatic islets resulting in uncontrolled diabetes and diabetic ketoacidosis. Moreover, cytokine storm in patients with severe COVID-19 also leads to increased insulin resistance.[6] Interleukin 6 (IL-6) in severe COVID-19 leads to hyperferritinemic state, which combined with academia in these patients adds to the risk for development of mucormycosis. [7,8] Use of systemic corticosteroids is another significant risk factor for development of opportunistic fungal infections, including mucormycosis.[9]

The National Institute of Health as well as National Centre for Infectious Diseases, Singapore (NCID) recommends the use of corticosteroids (6 mg oral/intravenous dexamethasone or equivalent for up to 10 days) in patients with severe or critical COVID-19, especially those requiring supplemental oxygen or mechanical ventilation.[10,11] Also, NCID does not recommend the routine use of monoclonal antibodies outside of a clinical trial or monitored program.[11] Many patients who receive broad-spectrum antibiotics considering the risk of concomitant or super-added bacterial infection are also at a higher risk. The presence of multiple risk factors and co-morbid illnesses in patients with severe/critical COVID-19 patients, along with the additional immunosuppression caused by glucocorticoids and uncontrolled diabetes, predisposes them to a higher risk of mucormycosis.

Patients with severe or critical COVID-19 have a higher incidence of developing secondary bacterial or fungal infections, due to dysregulation of the immune system. Especially patients with uncontrolled diabetes mellitus and those on corticosteroid therapy have a higher risk of developing rhino-orbito-cerebral mucormycosis. They should be closely monitored for development of signs and symptoms of mucormycosis, as spread of this infection carries a high risk of morbidity and mortality. Physicians should strictly adhere to recommended guidelines, and indiscriminate use of steroids to treat patient with mild COVID-19 (without hypoxemia) or utilization of high doses of glucocorticoid should be avoided. Optimal glycemic control also plays a key role for prevention of mucormycosis.

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Not applicable.

Informed Consent

Not applicable.

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