Mucormycosis: A Challenge with COVID-19

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Summary

Mucormycosis is an aggressive opportunistic fungal infection caused by fungi of Phycomycetes class including Rhizopus species and Mucor species. The pathogen can be present in the environment, on the skin, and in orifices of the body. There are several types including Rhinocerebral, Pulmonary, Gastrointestinal, Cutaneous and Disseminated Mucormycosis.¹ The spores infect the paranasal sinuses and nasopharynx, extending to the orbit and brain cavity in persons who have reduced cellular and humoral defenses. During the ongoing COVID-19 pandemic, a surge in the cases of rhino-orbital mucormycosis has become a life-threatening combination. Early diagnosis and intervention in the only way to save the vision and life of the affected patient.

Clinical Presentation of Mucormycosis

- Edema on one side of the face, headache, nasal sinuses are clogged, blood-tinged nasal discharge. Ptosis, proptosis and ophthalmoplegia
- Fever is accompanied by black lesions on the bridge of the nose or the inside of the lips that quickly intensify.
- Pathologically it is characterized by giant cell invasion, thrombosis, and eosinophilic necrosis of the underlying tissue.

Factors predisposing Mucormycosis in COVID-19

*Source: The graph is reproduced from meta-analysis of Sing AK et al

Apart from COVID-19 some important risk factors are- **Diabetes mellitus:** Uncontrolled DM and DKA is the most common associated co-morbidity in RCOM. It is estimated in a meta-analysis that 80 percent of cases of mucormycosis was also suffering from DM.⁸

New onset hyperglycemia: Patient who had new onset hyperglycemia (mostly steroid induced) during COVID-19 treatment had higher risk.

Hematological malignancies and organ transplant: This is the major risk factor in the USA and European countries.⁹

Steroid use: This is probably the most significant risk factor during this pandemic.

Sex: Men are at higher risk of getting infected compared to women.

Others: Includes iron overload, deferoxamines treatment, severe burns, AIDS, malnutrition, IV drug abuse etc.

COVID-19 and Mucormycosis

Aspergillus and *Candida* are two main pathogens that are found to be infecting people with COVID-19.³ However, the rise of mucormycosis as a co-infection of COVID-19 particularly in India made it a global concern. This is mainly due to the aggressiveness of the Rhino-orbital-cerebral (ROCM) form of the disease.

Although, it is a rare disease globally, India has the highest number of patients with this disease (0.14/1000 people) in 2019-2020.³ Some studies pointed out this is due to high number of DM patients in the country.⁴

During this pandemic, steroids became the life saving drug. The link between use of steroid and opportunistic infection is well-established. From short term use of steroid to long term use, opportunistic infection like aspergillosis, candidiasis and mucormycosis were reported in several studies.⁵

In a recent meta-analysis by Sing AK *et al*; on COVID-19 and mucormycosis analyzing 101 cases from 10 countries where 82 patients were from India.⁶

The Mechanism of Mucormycosis in COVID-19

The relationship between COVID-19 and mucormycosis can be explained by connecting immunosuppression from COVID-19, DM and steroid use as evident by available data.

Both DM and hyperglycemia are risk factors. Due to intake of corticosteroids, uncontrolled hyperglycemia is a common side effect in COVID-19 patients. Steroids also decrease the WBC function and impairment of the macrophage activity. Moreover, acidic environment in DKA is a good growth factor for mucor.

COVID-19 itself causes endothelial damage and reduce T cell count leading to opportunistic infections.

Due to hyperglycemia, glycosylation of ferritin cause increased free iron which helps growth of mucor. Higher cytokine in COVID patients like IL-6 also increase free iron.

So, the combination of hyperglycemia, acidic environment, free iron, reduced capability of WBC, mucormycosis finds the perfect place for destruction.⁷

*Source: The graph is reproduced from the meta-analysis by Sing et el.

Conclusion

The outcome of the triple combination of COVID-19, DM with mucormycosis is deadly. Healthcare providers should do everything to manage optimal blood glucose levels, use steroids only when necessary and act fast to treat the disease at the earliest possible stage to save lives.

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