

An Epidemic of Mucormycosis - Known to Unknown

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What we know?

Rhino orbito cerebral Mucormycosis (ROCM) is a well known potentially lethal, fulminant fungal infection. It is caused by ubiquitous filamentous fungi belonging to the order of Mucorales. Predisposing factors as we know from pre COVID-19 era include a state of immunosuppression, such as Diabetes mellitus (DM), Diabetic ketoacidosis (DKA) hematologic malignancy, hematopoietic stem cell transplantation, solid organ transplantation, immunosuppressive drugs, iron overload and chronic renal failure. Infection is the result of inhalation of sporangiospores followed by angio-invasion and thrombosis of blood vessel which leads to tissue necrosis. Specific reactions of fungal hyphae with endothelial cells result in systemic dissemination of the disease.

There was an exponential increase in incidence of ROCM in association with second wave of COVID-19 in India and other places in May 2021 which had become a matter of concern. More than 14,000 cases of COVID-19 associated ROCM have been reported from all over India with many states declaring Mucormycosis as an epidemic and making it a notifiable disease. It became a major burden on the Health care system to handle as it claimed many lives.

Uncertainty!!

Many schools of thought have been put forward in relation to etiology of ROCM during COVID-19 era. Immune dysregulation, neutropenia & lymphopenia caused by COVID-19 infection, COVID-19 associated high blood glucose levels, uncontrolled DM, DKA, widespread use of steroids and broad spectrum antibiotics for treatment of COVID-19 may have led to rise in mucormycosis. Even after the first wave in 2020 we had an increase in the number of patients with ROCM but its association with COVID-19 remained uncertain.

The management of COVID-19 associated mucormycosis is challenging, especially because the radiology may not correlate with the actual extent of disease. Patients with ROCM underwent extensive radiological evaluation and surgical debridement followed by medical management with antifungal medication (Amphotericin B and Posaconazole) for a prolonged duration. A part of them lost their lives fighting it and a part of them became handicapped with loss of vision either due to disease or due to the extensive debridement which formed a part of the treatment protocol. Even among those who survived the quality of life took a toll. Many are still undergoing repeat debridements including maxillectomies and dental, prosthetic and psychosocial rehabilitation.

Many health care professionals are still uncertain regarding orbital exenteration and duration of antifungal medication since there are no standard guidelines for management.

What remains unexplained?

It was observed that in different groups of patients the same disease had varied presentation. In some it was acute onset fatal ROCM with rapid progression in contrast to isolated involvement of palate without involvement of nose or orbit in others. Few had loss of vision due to central retinal artery occlusion (CRAO)/central retinal vein occlusion (CRVO) and not due to fungal disease invading the orbit. Some had delayed subacute presentation of nasal symptoms lasting weeks to months wherein others had delayed onset isolated osteomyelitis of palate where post operative histopathological and microbiological examination confirmed invasive fungal etiology.

Following surgery and medical management only a small set of patients succumbed to disease with a reported death rate of about 1.15% in ROCM with COVID-19, whereas ROCM in pre COVID-19

times had a much higher case-fatality rate of about 50% or more. Though all these COVID-19 ROCM patients had high HbA1c and high blood glucose levels at presentation, in those newly diagnosed diabetics blood glucose values and HbA1c have normalized and medication has been discontinued. Hence we can assume it was a transient COVID-19 induced hyperglycemia.

Majority of patients with stable radiological intracranial disease with or without retroorbital involvement who had not undergone orbital exenteration are surviving without progression of disease or adverse events. So it is still not clear when to stop antifungal medication posaconazole. Patients who underwent orbital exenteration had increased morbidity due to multiple secondary bacterial infections and non-healing eye sockets. It was also observed that few patients with ophthalmoplegia and vision loss regained eye movements and vision in the follow up period. Hence it remains unexplained whether all these patients with vision loss and orbital involvement required exenteration or observed and planned for repeat debridement if required.

Many ROCM patients also had facial nerve palsy among whom few recovered and few have not but the cause for facial nerve palsy and the chances of recovery remain unexplained. However all patients with limited sinus/palatal disease have recovered completely.

With these observations, we have more unanswered questions. Are we looking at different stages of progression of the same disease i.e. rapidly progressive fatal ROCM requiring immediate aggressive management for better prognosis or is it different types of Invasive fungal mucormycosis i.e. acute/chronic stable inflammatory ROCM/Limited invasive fungal disease where adequate surgical debridement

With uncertainty of future COVID-19 waves and associated mucormycosis there is a dire need for long term multi-institutional studies on guidelines for management of Mucormycosis.

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