

Mucormycosis in Ebbing Covid-19: Bedevil Inflaming Misery

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Mucormycosis in the context of Covid-19 is one of the most horrendous fungal infection which is predisposed by unchecked diabetes mellitus, immunosuppression, iron overload, elevated deferoxamine, hematological malignancies, neutropenia. The causative organisms are from order Mucorales which includes *Mucor*, *Rhizopus*, *Rhizomucor* etc. In India, 28252 cases of Mucormycosis have been reported till 6th June 2021. It was associated with Covid 19 infection in 86% and Diabetes in 62.3% of patients in India. Steroids reduce inflammation in the lungs when used for Covid 19, albeit reduces immunity and increased blood sugar levels fosters mucormycosis. Also, low oxygen levels, high blood sugar levels (steroid-induced or new-onset diabetes or previously diabetics), high iron levels, immunosuppression along other factors lead to the development of mucormycosis in Covid 19 patients.

Mucormycosis is often referred to as black 'fungus' which is a misnomer as the fungus is not dematecious or pigmented but disseminates through angioinvasion, thrombosis and ischemic necrosis of tissues thereby causing black discoloration of tissues.

Depending upon the site of infection Mucormycosis can be classified into rhino-orbital cerebral (ROCM), pulmonary, cutaneous, gastrointestinal, and disseminated. The fungal spores make their way into the nasal and oral cavity subsequently involving paranasal sinuses. Infection spreads through laminapapyracea, inferior orbital fissure, apex of orbit and infratemporal fossa into orbit. The intracranial extension is through the cribriform plate of the ethmoid, supraorbital fissure, and perineural invasion. Thrombosis of cavernous and sagittal sinus, carotid artery occlusion, brain infarction, aneurysm, rupture of aneurysm leading to haemorrhage and brain abscesses are the perilous outcomes.

The warning symptoms and signs of ROCM raising alarm are nasal stuffiness, epistaxis, nasal discharge, nasal mucosa erythema, eschar, eyelid, periocular or facial edema, proptosis, sudden vision loss, facial paraesthesia, sudden ptosis, fever, altered sensorium, focal seizures. The management requires inter-departmental collaboration of ophthalmologist, otorhinolaryngologist, radiologist, neurosurgeon, microbiologist, and pathologist.

The surgical debridement (Functional Endoscopic Sinus Surgery) is indispensable in that it not only limits the spread of the disease but also allows intraoperative diagnosis by procuring samples from the necrotic area for histopathological and microbiological confirmation. The diagnosis of ROCM involves direct microscopic examination (90% sensitivity) of the nasal swab or under endoscopy-guidance swabs from paranasal sinus or orbital tissue using a potassium hydroxide mount and calcofluor white showing aseptate hyphae branching at wide angles > 90° and width of 6 - 25 µm. The fungal culture media such as brain heart infusion agar (BHI), Sabouraud dextrose agar (SDA) and potato dextrose at 25 to 30° shows the white, grey or beige fast growing colonies with older colonies becoming grey-brown due to sporangiospores. Molecular diagnostic kits such as qPCR, Multiplex Target: 18s, ITS, 28s, or rDNA immunohistochemical staining, show 75% sensitivity however are not widely available commercially.

Radiologically contrast-enhanced Magnetic resonant imaging is preferred over computer tomography scan. The mucosal thickening of paranasal sinuses with patchy enhancement is an early sign. On MRI, ischemia leading to non-enhancing turbinate is an early sign (black turbinate sign). The early orbital invasion is suggested by thickening of the medial rectus. Involvement of orbit with irregular patchy enhancement of the fat, lesion adjoining the superior and inferior orbital fissure and the orbital apex show advancement of disease. Optic nerve stretching and tenting of eyeball posteriorly show severe inflammatory edema following necrosis of tissue.

The cardinal element of treatment is Antifungals especially liposomal Amphotericin B. Intravenous Amphotericin B (liposomal) 5 - 10 mg/kg BW or Amphotericin B deoxycholate 1 - 1.5 mg/Kg with strict metabolic control is given. The latter has higher systemic toxicity as compared to liposomal Amphotericin B. If AMB is contraindicated because of impaired renal function, Isavuconazole iv 200 mg TDS for 2 days, then followed by 200 mg OD or Posaconazole iv 300 mg TDS for 1 day, then followed by 300 mg OD. The induction therapy with

IV AMB for a minimum of 4 weeks is followed by a step down the treatment of oral Isavuconazole 200 mg TDS for 2 days, then followed by 200 mg OD or oral Posaconazole 300 mg TDS for 1 day, then followed by 300 mg OD from day 2 for 3 to 6 months or at least 6 weeks following clinical stabilization or radiological regression.

The prevention of mucormycosis in Covid-19 patients includes judicious and monitored use of systemic corticosteroids and tocilizumab. There should be vehement monitoring and control of diabetes mellitus and new onset diabetes secondary to use of corticosteroids. Sterile water in humidifier, sterilized humidifier and tube, need to be changed daily. Personal and environmental hygiene should be encouraged. Saline nasal drops and betadine mouth gargle must be used in Covid 19 patients on oxygen therapy.

The rapidity of diagnosis, the reversal of underlying predisposing factors along with aggressive debridement of infected tissue, and appropriate antifungal therapy along with strict metabolic control are all critical factors in the management of Mucormycosis [1-3].

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