

Rhino-orbital-cerebral Mucormycosis in COVID Scenario - A Pathologic Perspective

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Since the first case of COVID-19 was reported in December 2019, there have been several additions to the already broad spectrum of its clinical manifestations. The SARS-CoV-2 being a respiratory virus has crucial significance in the otorhinolaryngologic specialty. ENT specific COVID symptoms range from minor cases of sore throat on the one hand to severe presentations of mucormycosis on the other hand. Mucormycosis is an atypical life threatening deep fungal infection with increased propensity of presentation in immunocompromised patients. COVID-19 being an immune-mediated disease has obvious implications in the pathogenesis of mucormycosis.

The infection is caused by a family of fungi belonging to the order Mucorales and class zygomycetes with the *Rhizopus oryzae* accounting for nearly 70% of the overall cases and 90% of the rhino-orbital-cerebral forms. Mucormycosis or as it was previously termed as zygomycosis, was introduced into pathology by Pattauf in 1885 while the term was coined by Baker in 1957. Though the incidence of mucormycosis is miniscule as it is reported to affect only 0.005 to 1.7 million people globally, yet the mortality of this angio-invasive disease is massive with more than 50% of the patients presenting with unsalvageable disseminations.

The primary pathologic link between mucormycosis and immunosuppression is neutropenia which explains the increased risk of hematological malignancies to acquire this mold fungal infection, especially in developed countries. In developing countries, the picture is slightly different with diabetes mellitus accounting for the major share of mucormycosis correlations. Corticosteroid therapy in diabetes mellitus has been implicated in the surge of opportunistic infections. It is well demonstrated that chances of

mucormycosis are proportional to the dysfunctional phagocytes. Hyperglycemic state and acidic conditions both of which are seen in uncontrolled diabetes, handicap the phagocytes leading to impaired chemotaxis.

Mucorales sporangiospores penetrate the body vasculature and metastasize to distant sites causing thrombosis and necrosis. Consequent ischaemia averts the delivery of leukocytes to the site of infection. The endothelial damage and hematogenous spread account for the severity of infection. Iron also plays a unique role in the pathogenesis of mucormycosis in diabetes through dual mechanism. In patients with diabetes ketoacidosis, iron availability is enhanced by intracellular transport by reductase permease system and also by chelatic release of ferrioxime. This host iron is utilized by Mucorales for imparting and spreading virulence, thus leading to widespread multisystem involvement.

In 1950, Smith and Krichner proposed the gold standard criteria for the identification of mucormycosis, such as the necrotic damage to the superior, middle and inferior turbinates that present the characteristic black appearance of the infection. Additionally, the rhinocerebral variant may be associated with nasal congestion, facial pain and swelling, paralysis, induration, and ulcers. Soft tissues opacifications are identified through computed tomography images while bony involvement in later stages of the disease can be appreciated via panoramic imaging. Histological identification is done using routine hematoxylin and eosin stained cytological smears or special stains such as periodic acid Schiff's reagent. KOH mounts can also be used to demonstrate the aseptate mucor with characteristic right angled branching of the fungal hyphae.

Treatment involves lipid formulations of amphotericin B or Posaconazole in advanced cases. Addition of echinocandin to the drug regimen has limited data while capsosfungin has proved to be efficacious in the rhino-cerebral-orbital forms. Most of the symptomatic cases require surgical debridement of the necrotic debris and hyperbaric oxygen can be used for the same.

Despite optimal care, mortality rate is quite high with mucormycosis especially in a COVID scenario. The head and neck is enigmatic in terms of management owing to the paucity of clinical signs. By the time the patient present with symptomatic disease, multisystem involvement is inevitable. Mucormycosis has the unique ability to disseminate at extraordinary rates and even a slight delay could be fatal. This necessitates the requisite for prompt diagnosis. Paradoxically, the laboratory facilities is below par in developing countries which share the largest burden of the pandemic associated mortality. Despite adequate interventional management, complete recovery is minimal. Therefore, any COVID associated sinusitis in a diabetic patient should be strictly scrutinized for probable causes. Overzealous use of corticosteroids should be discouraged. A holistic approach to disease management can halt the disease progression to the fulminant stage and maximize quality of life.

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