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Original Research Paper

Pathology

RHINO-ORBITAL MUCORMYCOSIS: COULD IT BE AN INDICATOR OF PAST COVID INFECTION

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ABSTRACT Mucormycosis cases following Coronavirus 2019 (Covid 19) disease are on rise in immunocompromised patients. Diagnosis and treatment of Mucormycosis is challenging. Many studies have postulated the role of fungal contamination of oxygen humidifiers and steroid treatment in Covid patients in pathogenesis of Mucormycosis. However we report a case of Mucormycosis in a poorly controlled diabetic patient who was never diagnosed and treated for Covid infection. However his Covid antibodies were reactive, indicating past Covid infection. The understanding of disease dynamics at molecular, cellular, humoral level will be key to developing personalised management strategies for patients.

KEYWORDS : Mucormycosis, Covid 19, Diabetes mellitus, Acute invasive fungal rhinosinusitis

INTRODUCTION:

The pandemic coronavirus 2019 (COVID-19) continues to be a significant problem worldwide. Infection caused by novel severe acute respiratory syndrome coronavirus-2 (SARS CoV-2) may be associated with a wide range of disease patterns ranging from mild to life threatening pneumonia and multiorgan dysfunction syndrome. Comorbid patients are prone to develop severe opportunistic infections such as oropharyngeal candidiasis, pneumocystic jiroveci pneumonia, pulmonary aspergillosis and rhino-orbital Mucormycosis etc.[1]Acute invasive fungal rhinosinusitis (AIFRS) is a rare, life threatening infection with a high risk of mortality[3].

CASE REPORT:

A 61 year old diabetic and hypertensive male patient presented with complaints of headache, right side eye and facial swelling and blood stained nasal discharge. Headache and swelling was gradually increasing since 10 days. He was taking insulin infusion since 20 years and antihypertensive drugs since 2 years respectively. As a part of preoperative workup SARS CoV-2 RTPCR was done and it was not detected. KOH mount of nasal scraping showed branched aseptate fungal hyphae. Anti-SARS-Cov2 antibodies significantly detected (98.79 -Reactive). He was not vaccinated. His random blood sugar was 27.63 millimoles per liter; HbA1C was 7.9%, C reactive Protein was 10.1mg/L. Ketones were detected in blood and urine during hospital stay. Renal and liver function tests were normal.

HRCT (High resolution computed tomography) Paranasal sinuses showed proptosis of right globe. There was marked soft tissue thickening in ethmoidal sinuses and sphenoid sinus. Diffuse ill-defined soft tissue thickening seen in the preseptal region across the bridge of nose to the left. MRI Brain and Orbit showed involvement of right orbital soft tissue, right maxillary sinus and posterior ethmoidal sinus. Right basifrontal parasaggital brain parenchyma was also involved with diffuse gyral swelling and mild surrounding edema.

After glycemic control, Functional endoscopic sinus surgery (FESS) was performed and local debridement was done. Nasal biopsy was performed and sent to the pathology lab for histopathological examination. Microscopy showed dense necro-inflammatory infiltrate. Broad aseptate fungal hyphae branching at 90^0 seen in the tissue as well as invading the vessel wall. Special stains Periodic Acid Schiff (PAS, Fig 1b) and Gomori methenamine silver (GMS) highlighted the fungal elements and angioinvasion (Fig 2a, b). The patient was started on intravenous meropenem (1gm thrice daily), injection liposomal amphotericin B (100mg once daily for 3 weeks), and intravenous methylprednisolone (20mg once daily for 2 weeks) in conformity with local protocol along with general supportive care. He was then transferred to a higher centre for neurosurgical management.

DISCUSSION:

Post COVID-19 sepsis is what occurs after SARS- CoV-2 infection. It leads to a dysregulated innate immune response, ciliary dysfunction, cytokine storm, thrombo-inflammation, microvascular coagulation and eventual immune exhaustion. This cascade of events facilitates secondary bacterial and fungal infections especially in critically ill patients. The use of corticosteroid treatment , anti-IL-6-directed strategies in these highly susceptible hosts , high fungal spore counts in the environment or oxygen humidifiers creates the perfect setting for mould infections.[3]There are shared risk factors for COVID-19 and invasive fungal sinusitis, including pre-existing immunosuppression from comorbidities such as diabetes mellitus.[4]

While many fungal species can cause AIFRS, it most commonly involves Rhizopus, Aspergillus, Mucor and Rhizomucor.[5] Mucorales are ubiquitous moulds, abundantly found in the environment on decaying organic matter. Various studies from hospitals across India have revealed heavy mould spore counts even in hospital air due to predominantly hot, humid conditions in our tropical climate.[6]Mucormycosis is one of the most devastating complications in uncontrolled diabetics with mortality rates ranging between 40-80%. India contributes to 40% of the global burden of mucormycosis with an estimated prevalence of 140 cases per million population.[7,8]SARS CoV-2 binds to angiotensin-converting enzyme 2 receptors in pancreatic islets possibly causing hyperglycemic state.[9]

Mucormycosis is characterized by extensive angioinvasion that leads to vessel thrombosis and tissue necrosis.[10] It could be explained as acidemic states and hyperglycemia induce the endothelial receptor glucose-regulated protein (GRP 78) and the Mucorales adhesion spore coat protein homologs

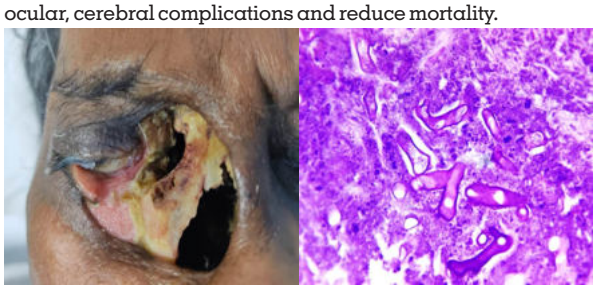
(CotH), which create a "perfect storm" for increased adhesion and penetration of Mucorales to the endothelium. Of interest, GRP 78 has been postulated as one of the receptors responsible for SARS-CoV-2 entry.[11] Angioinvasion results in hematogenous dissemination of the organism, whereas necrosis of the affected tissues prevents penetration of immune cells and antifungal agents to the infection focus.[12]

This case is unique because Mucormycosis was detected initially and on further work up Covid antibodies were detected. The patient had not received any treatment for COVID. Steroids and ventilation support was not given. This patient was long-standing poorly controlled diabetic and hypertensive . He never had any opportunistic infection in the course of 20 years but now only.

All these factors tend to facilitate fungal co-infection, along with any possible COVID-19 pathophysiological mechanisms Diagnostic methods include KOH mount , Calcofluor stain, biopsy and special stains like PAS, GMS. Mucor is difficult to routinely culture. Biopsy remains the mainstay of diagnosis and the benefits of the procedure outweigh the risk, even in a 'difficult to access' location or in the presence of coagulopathy. Screening in ENT and Ophthalmology OPD is important not only in detected cases of covid but also in all immunosuppressed patients .This is because asymptomatic cases of COVID may not be tested and diagnosed but they are also at risk of developing secondary fungal infection. Diagnosis of mucormycosis should raise suspicion of past covid infection. Awareness, high degree of suspicion and screening for secondary fungal infection is essential for timely diagnosis and treatment of fungal disease.

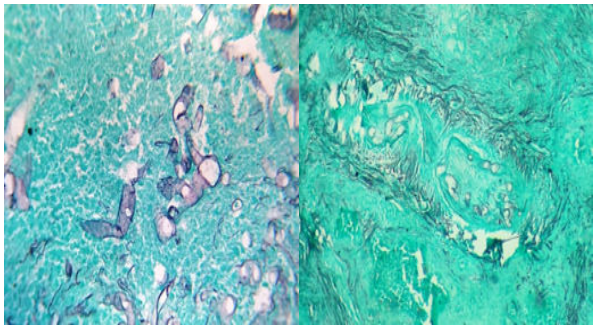
CONCLUSION:

Histopathology is the gold standard for diagnosis of Mucormycosis. Diagnosis of Mucormycosis should raise suspicion of past COVID infection. All immunosuppressed cases must be actively screened for any evidence of fungal infection especially in pandemic period. Timely diagnosis of Mucormycosis will help to initiate timely treatment, prevent ocular, cerebral complications and reduce mortality.



1 (A) 1 (B)

Fig 1: a) Celluilitis and Black eschar in orbit, proptosis; b) Necrosis, broad, aseptate, irregular fungal hyphae branching at 90^0 angles. (PAS, 40x)



2 (A) 2 (B)

Fig 2a: Fungal hyphae in the tissue and, b) invading the vessel (GMS 40X).

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