



## Covid 19 triggered Palato-Rhino-Orbital Mucormycosis in a susceptible patient: A case report

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### ABSTRACT:

Mucormycosis is a life-threatening infection that occurs in patients who are immunocompromised because of diabetic ketoacidosis, neutropenia, organ transplantation, and/or increased serum levels of available iron. Because of the increasing prevalence of diabetes mellitus, cancer, and organ transplantation, the number of patients at risk for this deadly infection is increasing.<sup>[1]</sup> Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been associated with a wide range of opportunistic bacterial and fungal infections.<sup>[2]</sup>

Both Aspergillus and Candida have been reported as the main fungal pathogens for co-infection in people with COVID-19.<sup>[3]</sup>

Here I am going to present in detail a case of palato-rhino-orbital mucormycosis with clinical, radiographic and histopathological details along with evidences from the microbiology.

**KEYWORDS:** rhino-orbital, mucormycosis, COVID 19, diabetes mellitus, swelling, rhizopus, aseptate hyphae.

### I. INTRODUCTION

Phycomycosis or zygomycosis was first described in 1885 by Paltauf and later coined as Mucormycosis in 1957 by Baker an American pathologist for an aggressive infection caused by Rhizopus.<sup>[2]</sup> Mucormycosis is an uncommon but a fatal fungal infection that usually affects patients with altered immunity.

Mucormycosis is an angioinvasive disease caused by mold fungi of the genus Rhizopus, Mucor, Rhizomucor, Cunninghamella and Absidia of Order- Mucorales, Class- Zygomycetes.<sup>[4]</sup>

The Rhizopus Oryzae is most common type and responsible for nearly 60% of mucormycosis cases in humans and also accounts for 90% of the Rhino-orbital-cerebral (ROCM) form.<sup>[5]</sup> Mucormycetes mould can invade in the susceptible host via nostrils, mouth or burned/disrupted skin which results in rhino-orbito-

cerebral, gastrointestinal or cutaneous wound infections. Mucormycosis also results in vascular thrombus and may lead to tissue necrosis.

Studies suggested that Rhino cerebral Mucormycosis is most common among all other cases of Mucormycosis. It is most common in the patients with uncontrolled diabetes and leukemia. Sometimes progression of rhino-cerebral Mucormycosis may leads to central nervous system and it becomes fatal. The second most preferred site of infection could be lungs and sinuses. Mortality rate associated with lungs infection may be over 60%.<sup>[6]</sup>

Recently, several cases of mucormycosis in people with COVID-19 have been increasingly reported world-wide, in particular from India. The primary reason that appears to be facilitating Mucorales spores to germinate in people with COVID-19 is an ideal environment of low oxygen (hypoxia), high glucose (diabetes, new onset hyperglycemia, steroid-induced hyperglycemia), acidic medium (metabolic acidosis, diabetic ketoacidosis [DKA]), high iron levels (increased ferritins) and decreased phagocytic activity of white blood cells (WBC) due to immunosuppression (SARS-CoV-2 mediated, steroid-mediated or background comorbidities) coupled with several other shared risk factors including prolonged hospitalization with or without mechanical ventilators.<sup>[2]</sup>

In severe Covid-19 situation patient could develop dysfunction of immune system with decrease in lymphocyte counts and exponentially rise in inflammatory cytokines such as IL-6, IL-1 $\beta$ , IFN-  $\gamma$ , MCP-1, IP-10, IL-4, IL-10 and Tumor necrosis factor (TNF) that leads to hyper inflammation in the lungs and in some patients it may lead to death.

Due to the severity of hyper inflammation or viral load physicians preferred use of immunosuppressant or steroids as a life saving treatment in critically severe patients. A steroid reduces inflammation in the lungs besides these



steroids also reduce immunity of the body and increases blood sugar level in both diabetic and normal patients.

According to the physicians immunosuppressed patients are more likely to be affected with Mucormycosis or Black fungus.<sup>[6]</sup>

## II. CASE PRESENTATION

### CLINICAL PRESENTATION

A 69 year old female patient reported to the outpatient department with tooth ache in the upper right jaw side since 7 days. The patient is a known case of type 2 diabetes mellitus. There was an associated swelling around the teeth which was followed by facial edema and swelling which is subsiding. Patient developed deviation of angle of the mouth 5 days back. History of vomiting and retching present. No history of blurring of vision/peri orbital edema/ proptosis/nasal discharge.

Patient had a history of Type 2 diabetes mellitus and is on insulin for 8 years and a history of hypertension and dyslipidemia which are under treatment.

She was reported as COVID positive on 07/08/21, and became negative as on 18/08/21, category C Covid Bronchopneumonia.

No relevant family and personal history.



### CLINICAL EXAMINATION

General and systemic examination are within normal limits.

Local examination:

Nose- external frame work- shows slight deviation to right

Anterior rhinoscopy- No blackish discharge, crusting

Right maxillary/ frontal/ ethmoid sinus tenderness (+)

Here, I am going to present a case of palato-rhino-orbital mucormycosis associated with COVID- 19 infection. Along with the clinical and radiographical features, histopathological features are also provided with supporting microbiological evidences.

### CT IMAGING OF PARANASAL SINUSES

There is soft tissue density lesion within the right maxillary sinus with near complete opacification of the lumen.

Permissive pattern of bone destruction noted in posterolateral wall and floor of right maxillary sinus with involvement of almost entire right half of the maxillary alveolar process, right side of the hard palate and right zygoma.

Erosions in floor of right orbit around the infraorbital canal with minimal extension into the inferior extra coronal space noted. There is invasion to the retro maxillary fat with involvement of right lateral pterygoid muscle origin.

Soft tissue density lesion with calcification, involving right frontal sinus causing erosions in bony walls with a focal defect ( about 6x3 mm) in posterior wall and probable intracranial extension.

Post surgical defect noted in medial wall of maxillary sinuses bilaterally and there is evidence of bilateral internal ethmoidectomy.

Moderate inflammatory mucosal thickening in left frontal sinus and anterior ethmoidal air cells.

Minimal inflammatory mucosal thickening in left sphenoidal sinus with sclerosis of bony walls. No erosions noted.

Deviation of nasal septum to right. The nasal cavities are bilaterally symmetrical.

Partial middle turbinectomy noted bilaterally.

Visualized parts of rests of the orbits and visualized bony skull appear normal.

### IMPRESSION

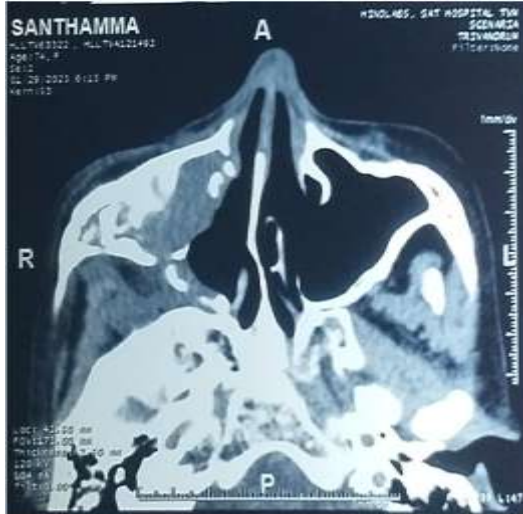
Residual/ recurrent right maxillary invasive fungal sinusitis with permissive type bone destruction involving posterolateral wall, right zygoma, entire side maxillary alveolar process and right side of the hard palate.

Erosions in floor of right orbit around infra orbital canal with minimal extension into the inferior extra conal space noted. There is invasion to the right retro maxillary fat with involvement of right lateral pterygoid muscle origin.

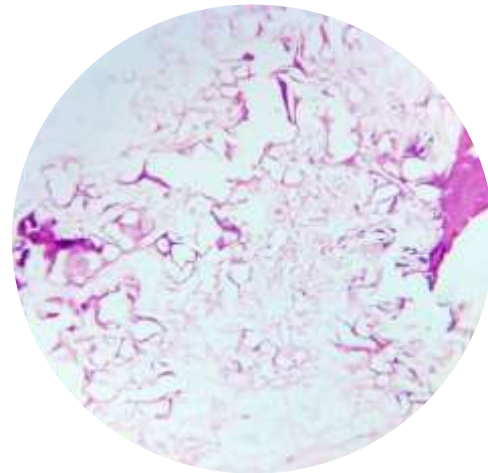
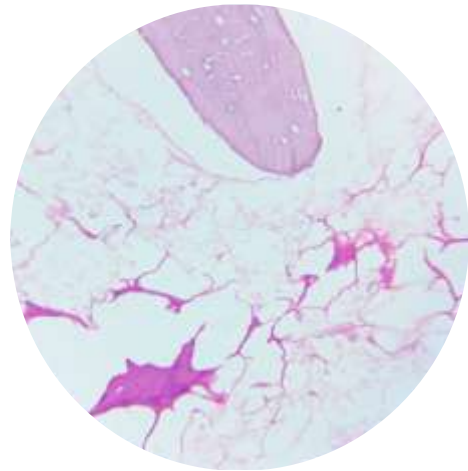
Right frontal chronic fungal sinusitis with erosions in bony walls with a focal defect in posterior wall and probable intra cranial extension. Mild left sphenoid chronic sinusitis without any bony erosions. Minimal inflammatory mucosal



thickening in left frontal sinus and anterior ethmoidal air cells.



## HISTOPATHOLOGY



Periodic Acid Schiff stained sections highlighting the presence of broad based, irregularly branching non septate hyphae characteristic of mucor within the connective tissue. The hyphae tend to branch at 90 degree angles.

## MICROBIAL CULTURE

Fungalstain (10 % KOH) - aseptate hyphae seen.  
Fungal culture and sensitivity- Rhizopus species isolated from culture.

## III. DISCUSSION

DM is the most common risk factor predisposing patients to mucormycosis. Up to 85% of mucormycosis cases are associated with uncontrolled DM. Previously reported HbA1c among these patients was approximately 10%. India has reported the highest number of mucormycosis cases in the world, which might be partially explained by the high incidence of DM in



India, as it constitutes 15% of the diabetic population globally.<sup>[2]</sup>

There are a significant number of reports showing alterations in cell-mediated immunity, such as chemotaxis, phagocytosis and cytokine secretion in both type 1 and type 2 diabetics.

Individuals with diabetes have been described to have alterations in innate immune system components. Natural killer cell activity is reduced in individuals with diabetes, and more pro-inflammatory M1 macrophages are present. Furthermore, T-cell activity is skewed. Disease severity in patients is due to not only the viral infection but also the host response. Elevated glucose levels may also suppress the antiviral response.

In the context of COVID-19, severe disease progression is described by a delay in IFN- $\gamma$  response with a prolonged hyperinflammatory state and lower CD4 and CD8 cell numbers.

Regardless of the involvement of the endothelial cells, the initial delay in IFN- $\gamma$  response together with the hyperinflammatory response in individuals with diabetes may exacerbate the 'cytokine storm' and increase COVID-19 severity.<sup>[7]</sup>

Pathogenic mechanisms involved in fungal aggressiveness include decreased phagocytic activity, accessible amounts of iron due to the displacement of protons by transferrin in diabetic ketoacidosis and fungal heme oxygenase, which promotes iron absorption for its metabolism.<sup>[8]</sup>

Early diagnosis of mucormycosis is the key for survival. A multidisciplinary team approach is required to optimize management of mucormycosis cases. Strictly controlling hyperglycemia and avoiding DKA play an important role in preventing progression of the disease.

High-dose steroids, especially in poorly controlled patients with DM, even if indicated in patients with severe COVID-19, should be used cautiously, and unjustified corticosteroid treatment of patients with non-hypoxemic COVID-19 should be avoided.<sup>[9]</sup>

#### IV. CONCLUSION

Mucormycosis is a rare disease, but during the second wave of the COVID-19 pandemic in India, it was unfortunately widespread and associated with significant morbidity and mortality. With recent history of COVID-19 infection, uncontrolled diabetes mellitus, and high-dose steroid supplementation are the most

important risk factors for the development of mucormycosis.

The essential elements for successfully managing this fatal infection are controlling the predisposing factors, early detection with a high index of suspicion in patients with contributing factors, anti-fungal drugs, and surgical debridement of the involved tissues.

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