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Case Series

A case series of mucormycosis, post COVID-19 in a tertiary care centre

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ABSTRACT

In the 3rd wave of COVID-19 especially in India, an associated angio-invasive opportunistic infection with mucormycosis is emerged. The clinical, imaging and treatment data of 22 patients with mucormycosis was analyzed. Clinical features observed are periorbital swelling, facial pain, swelling of cheek, nasal discharge, dental pain associated with loose tooth. Imaging demonstrated PNS, orbital and intracranial extension in 100%, 55%, 20% patients respectively. All received ampho-B and underwent endoscopic debridement, 20% orbital decompression and 5% maxillectomy, 2 patients died. The association of hyperglycemia and steroid intake warrants judicious use of corticosteroids and optimal glycemic control. Good clinical outcome is achieved by aggressive surgical debridement and antifungal medication with optimal glycemic control.

Keywords: Mucormycosis, Hyperglycemia, Steroid intake

INTRODUCTION

Mucormycosis, a fatal fungal infection, caused by ubiquitous environmental molds, was being reported from all over India as a COVID-19 associated infection. Mucormycosis mainly affects people who are immunocompromised, or patients already infected with other diseases.

High risk groups include people with diabetes (especially diabetic ketoacidosis), solid organ transplantation, neutropenia, long-term systemic corticosteroid use, and iron overload (hemochromatosis). The risk is high in people living with HIV, and in those using immunomodulating drugs, and the anti-fungal voriconazole.

Unlike Aspergillus and Candida, which targeted critical patients in the ICU, mucormycosis was observed even in mild or asymptomatic COVID-19 cases. We studied the profile of 22 patients of COVID-19 associated mucormycosis presented to ENT OPD.[1]

CASE SERIES

Informed consents were obtained from the patients were taken. A total of 22 patients of mucormycosis who were diagnosed after recovery from COVID-19, were included.

The data was prospectively collected from patients presenting in the (June 2021 to October 2021) the second COVID-19 wave in a tertiary care centre.

Almost all cases presented with symptoms of periorbital swelling, pain and swelling of cheek area, loose tooth.

Inclusion criteria

Patients of age group above 35 years, post COVID-19 patients, and KOH mount positive were included.

Exclusion criteria

Patients who had mucormycosis during COVID-19, KOH mount negative, and recurrence of mucormycosis were excluded.

All cases were subjected to a detailed history, (a) the day of mucormycosis symptom onset from post COVID-19 symptom, (b) presence of comorbidities, (c) detection of new onset diabetes, (d) receipt of corticosteroids, its duration, and dosage, (e) receipt of other immunomodulators, (f) details of imaging (CT/MRI) of paranasal sinuses, orbit and brain, with emphasis on the number of sinuses involved, bony erosions, orbital, palatal and cerebral involvement, and (g) microscopy, culture and histopathology reports.

Computed tomography (CT-PNS) was done in all patients. Microscopic examination was done.

Table 1: Results of number of patients and the sinuses involved in CT/MRI scans.

CT/MRI	Percentage (%)
Maxillary sinus	100
Pansinusitis	55
Orbital involvement	12.1
Bone erosion	45.5
Cerebral involvement	4.4

Note: Maxillary sinus is the most common sinus involved and cerebral involvement is the least involved.

Table 2: Total number of patients and type of treatment.

Surgery	Percentage (%)
Amphotericin-B and surgical debridement	100
Orbital decompression	20
Maxillectomy	5

Note: All patients received ampho-B and underwent endoscopic surgical debridement, 20% orbital decompression, and 5% maxillectomy.

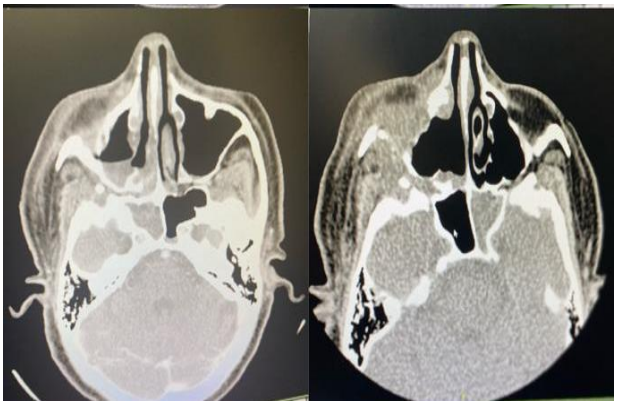

Figure 1: CT PNS Axial view showing pre-op and post-op of a patient.

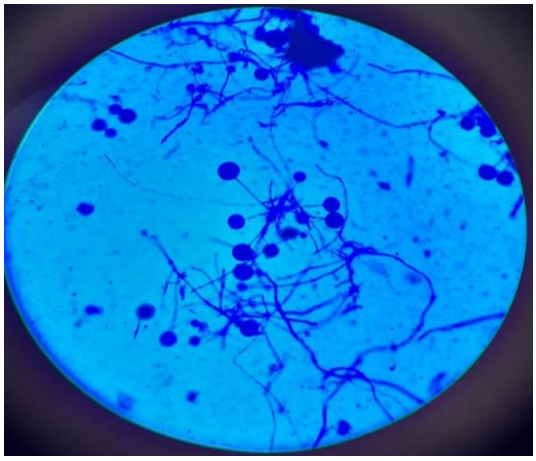

Figure 2: Rhizopus inoculated on microscopic examination.

Figure 3: Pre-op and post-op pictures of patients who underwent ampho-B and surgical debridement and orbital decompression.

DISCUSSION

There are increasing case reports of rhino-orbital cerebral mucormycosis in patients with COVID-19, especially from India. COVID-19 infection, its treatment, resultant immunosuppression, and pre-existing comorbidities have made the patients vulnerable to secondary infections including mucormycosis.

All the symptomatic COVID-19 patients developed mucormycosis symptoms, between 8 to 15 days (average 12.5 days) of COVID-19 symptoms.Diabetes mellitus (DM) was the commonest comorbidity observed in our study, similar to other studies. Thirteen (59.09%) had pre-existing long standing DM and 9 (40.90%) had new onset

diabetes. Approximately 70% of cases of rhinocerebral mucormycosis occurs in patients with uncontrolled diabetes mellites.[2] While long term use of corticosteroids have often been associated with several opportunistic fungal infection including aspergillosis and mucormycosis, even a short course of corticosteroids has recently been reported to link with mucormycosis especially in people with DM.[2] The rampant misuse of steroids in COVID-19 has aggravated the already existing hyperglycemia and fuelled the fungal infection.[6]

Glucocorticoids can increase the risk of secondary infections. Moreover, the immune dysregulation caused by the virus and the use of concurrent immunomodulatory drugs such as tocilizumab could further increase the risk of infections in COVID-19 patients.[9] Both long term and short term use of corticosteroids have been associated with several opportunistic fungal infections, especially in people with DM. The concurrent use of immunomodulatory drugs possibly added to the immunosuppression caused by steroids.

This is concerning and highlights, firstly, the major contribution of hyperglycemia due to SARS-CoV-2 and the stress of infection. Secondly, hyperglycemia induced availability of free iron, which is an ideal resource for mucor. Furthermore, interleukin 6 also increases free iron by increasing ferritin levels.[3]

There are reports implicating the use of industrial oxygen in CAM in the study by Patel et al, 55.6% of the patients were hypoxic in their study and 59.09% in our study.[4] Uncontrolled hyperglycemia and precipitation of DKA is often observed due to corticosteroid intake. Low pH due to acidosis is a fertile media for mucor spores to germinate. Moreover, steroid use reduces the phagocytic activity of WBC (both first line and second line defense mechanism), making a diabetic patient exceptionally vulnerable to mucormycosis.[2] High glucose, low pH, free iron, and ketones in presence of decreased phagocytic activity of WBC, enhances the growth of mucor. Endotheliatis, thrombosis, up-regulation of GRP 78 (glucose receptor protein-78), a receptor that facilitates fungal invasion, fungal ligand spore coating homolog (CotH) protein facilitating fungal angioinvasion, hepcidin activation by SARS-CoV-2 glycoprotein leading to dysregulation of iron homeostasis and iron overload are some of the other mechanisms that explain the increased predisposition of COVID-19 patients to mucormycosis.[7]

Traditional risk factors that increase the chances of acquiring mucormycosis include diabetes mellitus, haematological malignancies, stem cell transplant, organ transplant, iron overload, treatment with deferoxamine, malnutrition, burns, extensive use of broad-spectrum antibiotics, critical care admissions.[9] Both microscopy and histopathology showed aseptate and septate hyphae in 1 patient, though culture grew only Rhizopus in 5 out of 20 (25.00%) patients in whom the culture reports were available. Mucorales are fragile and any mishandling or grinding of the specimen, may destroy the hyphae and cultures may also be negative due to unviable organism in necrotic tissues.[5]

Studies have shown that amphotericin B is generally well-tolerated and can be safely administered in subjects undergoing dialysis (even with the older deoxycholate and colloidal dispersion formulations of amphotericin).[10] The ideal duration of therapy, the ideal route of antifungals, the role of combination therapy, the number of surgical debridements were needed.

CONCLUSION

All efforts should be made to maintain optimal hyperglycemic index and only judicious use of corticosteroids in patients with COVID-19 is recommended in order to reduce the burden of fatal mucormycosis. Early diagnosis and aggressive treatment (by medical and surgical) can be life-saving.

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