



A CASE SERIES OF HISTOLOGICALLY DIAGNOSED MUCORMYCOSIS IN POST COVID-19 PATIENTS IN A TERTIARY CARE HOSPITAL

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ABSTRACT **Introduction:** Prevention of mucormycosis in COVID-19 patients involves reducing exposure to fungi in the environment and careful management of underlying health conditions. Healthcare professionals should maintain a high index of suspicion for mucormycosis in COVID-19 patients presenting with symptoms suggestive of fungal infection, particularly in those receiving high-dose corticosteroids. **Objectives:** To determine histopathological findings in mucormycosis cases and correlate them with prognosis and risk factors. **Results:** Out of the 25 patients with mucormycosis studied in post COVID-19 patients, age ranged from 24-76 years, of which 16 were men and 9 were women. Diabetes was present in 22 patients and hypertension in 16 patients. On histopathological examination, fungal load was severe in 3 patients, angioinvasion was present in 8 patients, perineural invasion was present in 3 patients. The number of patients discharged after surgery was 23, whereas 2 died. **Conclusion:** Histopathological features of mucormycosis such as vascular invasion, perineural invasion, heavy fungal load and extensive necrosis are proportional to mortality. Thus, histopathologists can help assess prognosis at the time of tissue diagnosis so that clinicians can optimize treatment accordingly. Diabetes mellitus and a history of taking corticosteroids for the treatment of COVID-19 are the two most common predisposing factors for the development of mucormycosis.

KEYWORDS : COVID-19, mucormycosis, diabetes, corticosteroids

INTRODUCTION

Mucormycosis, also known as zygomycosis, is a rare but serious fungal infection that has recently been reported with increased frequency in patients with COVID-19. COVID-19 is a viral illness caused by SARS-CoV-2 that primarily affects the respiratory system. The infection can cause severe respiratory distress and systemic inflammation, particularly in individuals with underlying health conditions or weakened immune systems.

Mucormycosis can occur as a complication of COVID-19, particularly in individuals with uncontrolled diabetes, prolonged use of corticosteroids, or other factors that impair the immune system. The use of high-dose corticosteroids to manage severe COVID-19 infection has been associated with increased risk of mucormycosis.

The clinical presentation of mucormycosis in COVID-19 patients can vary, depending on the location and extent of the infection. Common symptoms include facial pain, swelling, fever, headache, and visual disturbances. The infection can progress rapidly, leading to tissue necrosis, organ failure, and death.

Early diagnosis and prompt treatment of mucormycosis are essential to prevent severe complications. Treatment typically involves antifungal medication, surgical removal of infected tissue, and management of underlying conditions. However, mucormycosis has a high mortality rate, and even with treatment, the prognosis can be poor, particularly in individuals with advanced disease or underlying health conditions.

Prevention of mucormycosis in COVID-19 patients involves reducing exposure to fungi in the environment and careful management of underlying health conditions. Healthcare professionals should maintain a high index of suspicion for mucormycosis in COVID-19 patients presenting with symptoms suggestive of fungal infection, particularly in those receiving high-dose corticosteroids. Further research is needed to better understand the risk factors and mechanisms underlying the development of mucormycosis in COVID-19 patients and to develop more effective treatments and preventive measures for this serious fungal infection.

Materials and Methods

A prospective observational study was conducted at our department of pathology, Gajraraja Medical College, Gwalior over a period of 2 months in April-May 2021.

Tissue biopsy samples of 25 post COVID-19 patients were included in the study who developed mucormycosis symptoms.

Received specimens were processed histologically with H&E & PAS stain. Microscopic findings were observed and correlates with prognosis and clinical findings.

Results

A total of 25 post COVID patients who were clinically diagnosed as mucormycosis were confirmed with histopathology. Out of these 16 (64%) patients were men and 9 (36%) patients were women. Male to female ratio was 1.7:1. Age of the patients ranged from 24 to 76 years, with higher incidence in 35-45 years of age in both sexes. Youngest age was 24 years in men and 27 years in women. Oldest age was 76 years in men and 52 years in women. Diabetes and hypertension were seen in 22 and 16 patients respectively.

Out of the 25 patients studied, the characteristic fungal hyphae were broad, aseptate, and ribbon like, with wide angled branching. Fungal load was mild in 10 (40%), moderate in 12 (48%) and severe in 3 (12%) patients.

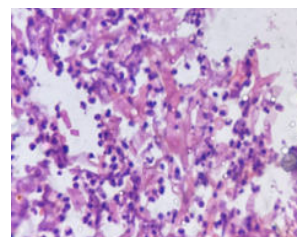


Figure: H and E stained slide showing broad aseptate wide angled branched hyphae suggestive of mucormycosis (400x)

Corticosteroids were used for treatment of COVID in 23 patients (86%). Number of patients discharged after surgery were 23 (92%), and 2 (8%) died.

DISCUSSION

Mucormycosis is an opportunistic fulminant fungal infection that occurs in post-COVID-19 patients. Precipitating conditions were uncontrolled diabetes with or without diabetic ketoacidosis, hematological and other malignancies, organ transplantation, neutropenia, immunosuppressive and corticosteroid therapy, and acquired immune deficiency syndrome (AIDS).

Histopathological evaluation of mucormycosis is the most important diagnosis, showing broad banded fungal hyphae without septa (10-20 microns). In our study, patients with severe fungal burden had a worse

prognosis in terms of survival compared to mild and moderate fungal burden. Therefore, as the fungal load increased, the survival rate decreased. Patients with a high fungal load have conditions conducive to fungal growth and a relatively high degree of immunosuppression. Ashina Goel et al showed a similar association in non-COVID patients in their study on the role of histopathology in the prognosis of rhino-orbital-cerebral zygomycosis.¹

In our study, invasion of fungal hyphae into blood vessels (vascular invasion) was observed in 8 patients (32%), and these patients died, indicating a poor prognosis. Thus, vascular invasion is directly proportional to mortality, a similar result was noted in a study by Ashina Goel et al.¹

Three (12%) patients had perineural infiltration. Histopathology revealed fungal hyphae combined with vascular and perineural invasion showing high mortality. In a study of non-covid patients by Sravani et al., perineural infiltration was found to be associated with late infiltration by mucormycosis.²

Fungal hyphae are observed in the subcutaneous tissue of cutaneous mucormycosis. In our study, patients with post-COVID mucormycosis had a strong association with diabetes. Most patients receive corticosteroid therapy to treat COVID-19, and the combination of corticosteroid therapy and diabetes increases the risk of mucormycosis-mediated hyperglycemia-induced immunosuppression.⁴ John et al⁵, Kumar et al⁶ and Sharma et al³ concluded that there is a strong relationship between the presence of diabetes and the use of corticosteroids for the treatment of COVID-19 and the development of mucormycosis.

Possible mechanisms for increased mucus growth were uncontrolled hyperglycemia and precipitated diabetic ketoacidosis due to corticosteroid intake, freely available iron, high blood sugar, and low pH reducing leukocyte phagocytic activity.⁷ Therefore, efforts should be made to maintain optimal blood glucose levels and the use of corticosteroids should be approached with caution.

CONCLUSION

Histopathological features of mucormycosis show that severe fungal load, extensive necrosis, and the presence of vascular and perineural invasion are associated with poorer prognosis and reduced survival. Thus, histopathologists can help assess prognosis at the time of tissue diagnosis so that clinicians can optimize treatment accordingly.

The relationship between diabetes and the use of corticosteroids to treat COVID-19 are also two major disease-aggravating factors and need to be properly investigated. Therefore, optimal blood glucose levels and careful use of corticosteroids should be maintained to reduce the burden of mucormycosis in post-COVID-19 patients. Early diagnosis and treatment can slow disease progression and reduce mortality.

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