

Clinical, Morphological and Histopathological Staining Characteristics of Mucormycosis in COVID 19 Patients

Aswathy P^{1*}, Jaseela T. K², Sankar Sundaram³

¹Junior Resident, Department of Pathology, Government Medical College Kottayam, Kerala, India

²Senior Resident, Department of Pathology, Government Medical College Kottayam, Kerala, India

³Professor and Head, Department of Pathology, Government Medical College Kottayam, Kerala, India

DOI: [10.36348/sjpm.2022.v07i03.011](https://doi.org/10.36348/sjpm.2022.v07i03.011)

| Received: 05.02.2022 | Accepted: 12.03.2022 | Published: 23.03.2022

*Corresponding author: Aswathy P

Junior Resident, Department of Pathology, Government Medical College Kottayam, Kerala, India

Abstract

COVID 19, caused by severe acute respiratory syndrome – corona virus -2 (SARS – CoV 2), is a pandemic that affected millions of people worldwide. During the second wave of COVID -19 pandemic in India, an unprecedented surge in cases of mucormycosis was observed. This study was carried out to describe the clinical, morphological and histopathological staining characteristics of mucor mycosis in 16 covid patients in a tertiary care setting. Older patients with comorbidities like diabetes mellitus are commonly affected. The most common site of involvement was sinonasal tract (68.75%) followed by sinonasal tract and orbit (37.5%). Out of the 16 patients, 2 were partially vaccinated whereas others were not vaccinated. Histopathological examination of specimens revealed broad aseptate fungi in all cases. Tissue necrosis was present in all cases. Suppuration being the most common tissue reaction. 43.75% showed angioinvasion and 37.5% had bone invasion. All the cases were GMS positive with variable intensity. Treatment given in all cases were liposomal amphotericin B injection and surgical wound debridement. On follow up, 40 % of the patients died inspite of aggressive clinical management. Hence this fatal fungal infection should be kept in mind in covid 19 recovered patients especially those who are immunocompromised.

Keywords: COVID 19, Mucormycosis, Tissue reactions, liposomal Amphotericin B, fungus.

Copyright © 2022 The Author(s): This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC BY-NC 4.0) which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited.

INTRODUCTION

COVID 19, caused by severe acute respiratory syndrome – corona virus -2 (SARS – CoV 2), is a pandemic that affected millions of people worldwide. It has diverse clinical presentations ranging from fever to serious systemic involvement. It is associated with wide range of opportunistic bacterial and fungal infections. Mucormycosis, being an opportunistic fungal infection, has shown to affect those patients who have recovered from COVID 19. Mucor is a member of zygomycetes family and are found in soil, dung and dust. It can cause ulcerated and destructive lesions. Nasal sinuses, lung and gastrointestinal tracts are the three primary sites of mucormycosis (Garg D *et al.*, 2021). The serious complication is spread of infective agent through paranasal sinus to orbit and brain resulting in rhinocerebral mucormycosis. The treatment modality available now is intravenous liposomal amphotericin B with surgical wound debridement.

MATERIALS AND METHODS

Study sample included 16 covid patients who developed secondary mucormycosis infection who were treated at government medical college kottayam. Biopsy specimens was taken from affected area were received in our department. Samples were received in 10 % neutral buffered formalin solution, processed for light microscopy and stained with hematoxylin and eosin. Gomori Methanamine silver special stain was also done in all cases.

RESULTS

DEMOGRAPHY

The study was conducted among 16 post covid patients who developed secondary mucormycosis infection. The clinical, morphological and staining characteristics of mucormycosis infection was analysed. The median age group of the affected population was 56.53 years with a male to female ratio of 0.7: 1. Majority patients suffer from a combination of

comorbidities in which diabetes mellitus was the most common risk factor. In our study, 2 patients were partially vaccinated against COVID 19 infection. The most common site affected was sinonasal tract alone (62.5%) followed by sinonasal tract and orbit (37.5%). Other rare site identified was appendix. All patients contracted mucormycosis within six weeks of covid 19 infection. All of them were hospitalized during covid 19 infection in which 62.5% required oxygen therapy.

LIGHT MICROSCOPY FINDINGS

Broad aseptate fungi with right angle branching and extensive tissue necrosis was identified

in all cases. Different types of tissue reactions were observed which include suppuration, granulomatous inflammation and foreign body giant cell reaction. The most common tissue reaction identified was suppuration (68.75%). Mucor is notorious for tissue destruction, angioinvasion and bone invasion. In the present study, 43.75% cases showed angioinvasion and 37.5% showed bone invasion. The presence of mucor was confirmed by identifying black fungal elements on Gomori Methanamine Silver Stain (GMS). All cases were found to be GMS positive but with variable intensity. Two case each of coexistent fungal infection of candida and aspergillus was also observed.

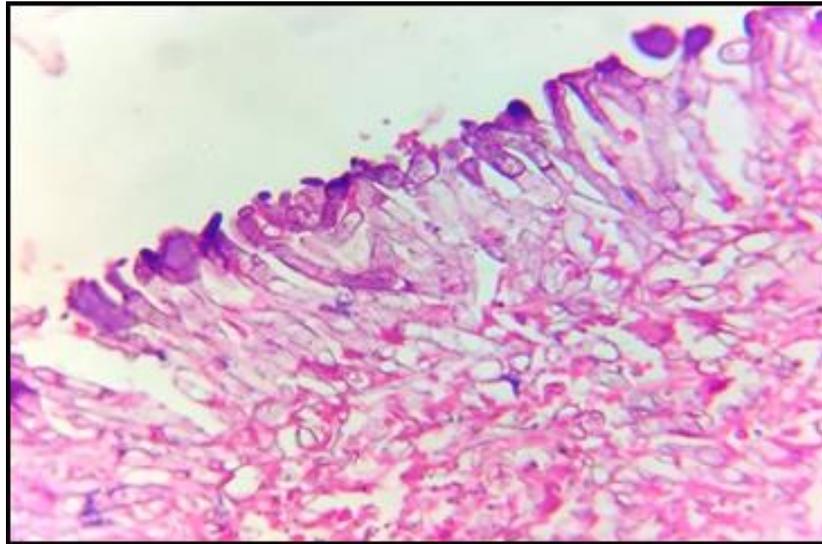


Figure 1: H & E (40X) – broad aseptate fungi of mucor with right angle branching

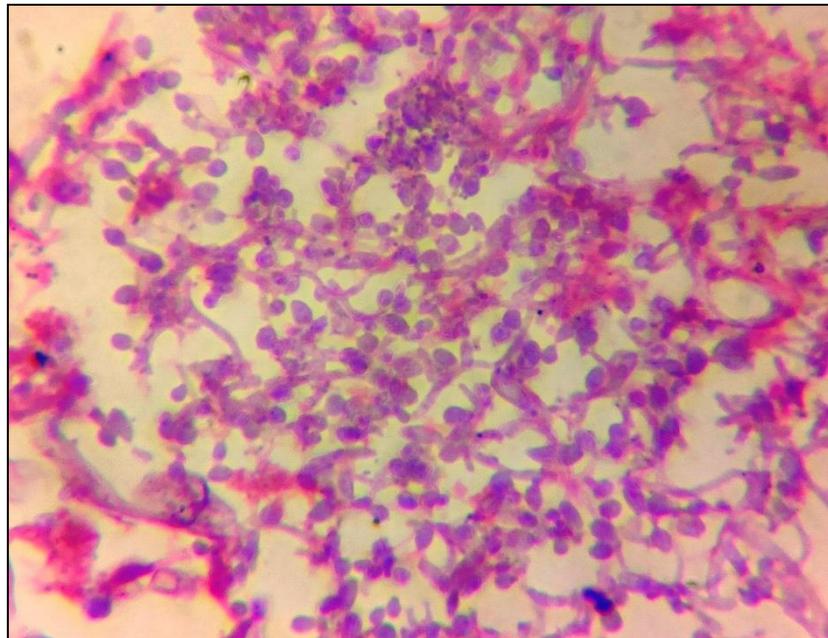


Figure 2: H & E (40X) coexistent candida spore and pseudohyphae in mucormycosis cases

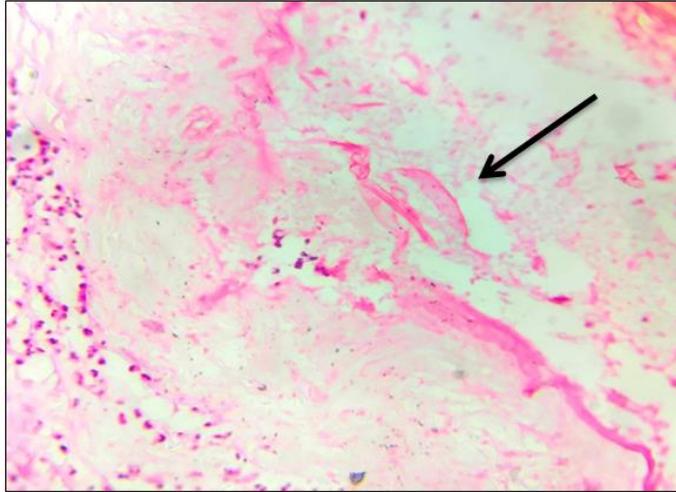


Figure 3: H & E (40X) – angioinvasion (arrow – fungalelement)

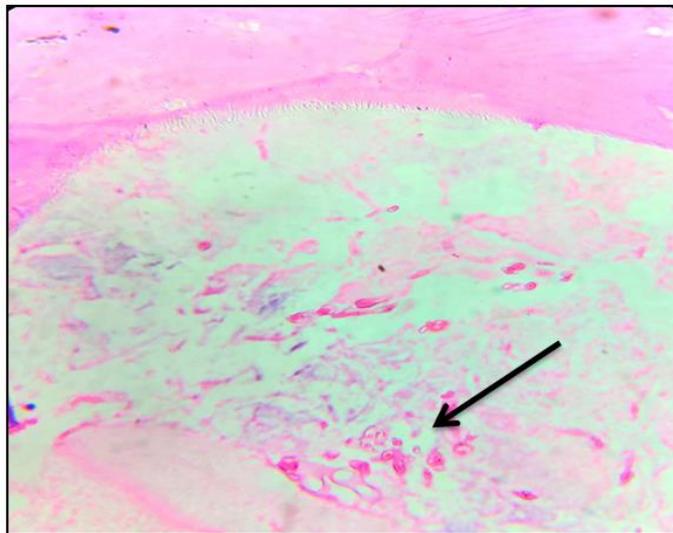


Figure 4: H & E (40X) – bone invasion (arrow – fungal element)

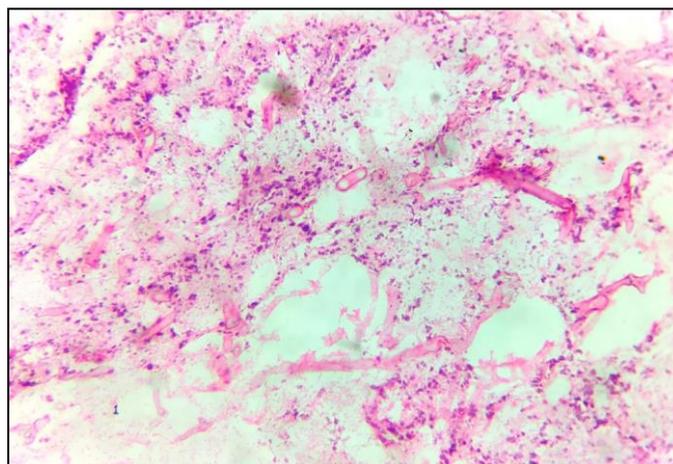


Figure 5: H & E (40X)- mucor detected in wall of appendix

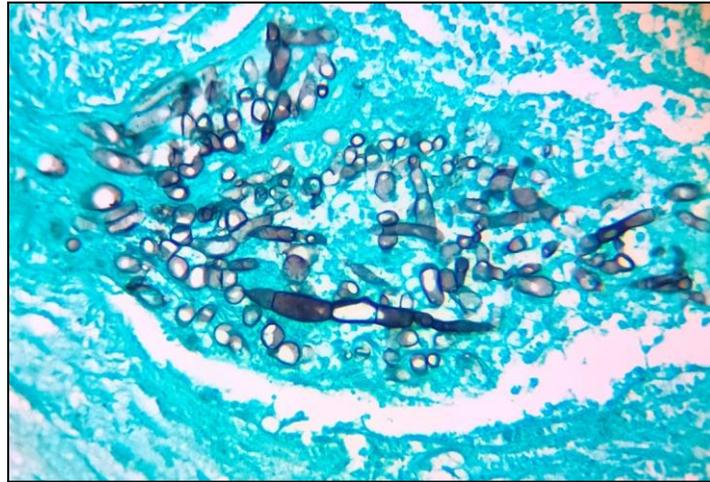


Figure 6: Special stain GMS (40 x) – fungi stained black TREATMENT AND FOLLOW UP

All patients underwent surgical wound debridement accompanied by intravenous liposomal amphotericin B injection with careful monitoring for the development of nephrotoxicity. On follow up, 40% of the patients died in spite of aggressive clinical management. Rest of the patients were asymptomatic.

DISCUSSION

Mucor is a saprophytic fungus that resides in soil, dung and dust. Mucormycosis is an extremely rare infection in healthy individuals. Most researches on post covid mucormycosis revealed that elderly immunocompromised individuals are prone to develop this opportunistic infection. According to study by (Maini *et al.*, 2021), most common comorbidity associated with mucormycosis is diabetes mellitus which is comparable with the present study. Most common site of involvement is rhino-orbital region. Rare sites include appendix. The evidence on relationship between covid vaccination status and severity of post covid mucor mycosis is minimal. In majority of covid related mucormycosis studies, vaccination status of the study population was not analysed. Rapid growth of fungus, ability to utilize the host iron for growth, ability to adhere to the endothelial surface and downregulation of host defense genes responsible for immune defense are considered to be responsible for the virulence and pathogenesis of mucor infection (Jose A *et al.*, 2021). According to the study by Choksi *et al.*, on outcomes of rhinoorbital mucormycosis following COVID 19 infection, 36% of patients were died on follow up. It was comparable with the present study where 40 % patients died on follow up.

Microscopic identification of the hyphae based on diameter, presence or absence of septae, branching angle and positive staining for fungal stains like GMS differentiate it from other fungal infections. Most common coexistent fungal infections are candida and aspergillus (Pakdel F *et al.*, 2021). The associated

different tissue reactions like suppuration, chronic granulomatous inflammation and foreign body giant cell reactions were not analysed in other studies. Tissue destruction, angioinvasion and bone invasions are characteristic of mucor infection. In our literature search, it was found that all patients were managed with either intravenous amphotericin B injection or surgical debridement of affected site.

Despite of these aggressive clinical management, a significant proportion of patients succumbed to death. That may be due to complications associated with mucormycosis especially intracranial spread. However, histopathological examination of the tissue sections have a significant role in early identification which aids in appropriate clinical management.

CONCLUSION

Mucormycosis is a rare but fatal fungal infection that should be kept in mind in covid 19 recovered patients especially those who have uncontrolled diabetes and treated with corticosteroids. Timely diagnosis by histomorphological assessment supported with special stains is the cornerstone to prevent an adverse clinical outcome.

ACKNOWLEDGEMENT

I express my sincere gratitude to all my teachers in the Department of Pathology, as well as fellow post graduate students and my friends for their whole hearted co-operation, help and encouragement for completing this work.

Conflicts of Interest: Nil

REFERENCES

- Garg, D., Muthu, V., Sehgal, I. S., Ramachandran, R., Kaur, H., Bhalla, A., ... & Agarwal, R. (2021). Coronavirus disease (Covid-19) associated mucormycosis (CAM): case report and systematic

review of literature. *Mycopathologia*, 186(2), 289-298.

- Maini, A., Tomar, G., Khanna, D., Kini, Y., Mehta, H., & Bhagyasree, V. (2021). Sino-orbital mucormycosis in a COVID-19 patient: A case report. *International Journal of Surgery Case Reports*, 82, 105957.
- Jose, A., Singh, S., Roychoudhury, A., Kholakiya, Y., Arya, S., & Roychoudhury, S. (2021). Current understanding in the pathophysiology of SARS-CoV-2-associated rhino-orbito-cerebral mucormycosis: a comprehensive review. *Journal of maxillofacial and oral surgery*, 20(3), 373-380.
- Pakdel, F., Ahmadikia, K., Salehi, M., Tabari, A., Jafari, R., Mehrparvar, G., ... & Khodavaisy, S. (2021). Mucormycosis in patients with COVID-19: a cross-sectional descriptive multicentre study from Iran. *Mycoses*, 64(10), 1238-1252.