

Original Research

Assessment of histopathologic findings of patients with COVID complications

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ABSTRACT:

Background: COVID-19-associated mucormycosis, an opportunistic fungus that invades rhinal, occipital and cerebral areas, come to light as the pandemic proceeds. Mucormycosis is caused by the fungus *Mucor* (class *Phycomycetes*, order *Mucorales*) that is capable of reaching craniofacial compartments such as paranasal sinuses, pharynx, orbita and intracranial cavity via the spore spread. Hence; the present study was conducted for assessing the histopathologic findings of patients with COVID complications. **Materials & methods:** A total of 20 patients who had past history of COVID-19 infection and reported with presence of post-COVID Mucormycosis were enrolled. Complete demographic and clinical details of all the subjects were obtained. Biopsy specimens were obtained and histopathologic examination was carried out. Histopathologic findings were analysed and correlated. **Results:** A total of 20 patients with presence of post-COVID Mucormycosis were enrolled. Mean age of the patients was 52.3 years. Histopathologic findings revealed non-septate hyphae invading blood vessels in 13 cases while it revealed minimally septated broad, ribbon-like hyphae in 7 cases. **Conclusion:** Mucormycosis is a life-threatening fungal infection, with very high mortality.

Key words: Histopathologic, COVID, Complication

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INTRODUCTION

The novel severe acute respiratory syndrome coronavirus-2 (SARS CoV-2) first reported in Wuhan, China on 21 December 2019. Thereafter, the virus has spread rapidly and affected millions across the globe, and on 11 March 2020, it was finally declared a pandemic. As of June 2021, 172 million people have been affected by this virus with 3.69 million deaths worldwide. The most common presenting complaints of this disease include cough, fever, and dyspnea. Extra pulmonary manifestations comprise alteration of taste, olfactory changes, erythematous rashes and urticaria, and even severe neurologic complications like altered consciousness, dizziness, and cerebrovascular events. Like SARS-CoV and MERS-CoV, the virus causes lower respiratory tract infection leading to acute respiratory distress syndrome, and eventually ground-glass opacity of the lungs. Due to

the severe inflammatory reaction and diffuse alveolar damage, COVID-19 patients experience a decline in their CD-4+ and CD-8+ T cell count, making them susceptible to a wide range of infections, particularly fungal infections.¹⁻³

Specially, COVID-19-associated mucormycosis, an opportunistic fungus that invades rhinal, occipital and cerebral areas, come to light as the pandemic proceeds. Mucormycosis is caused by the fungus *Mucor* (class *Phycomycetes*, order *Mucorales*) that is capable of reaching craniofacial compartments such as paranasal sinuses, pharynx, orbita and intracranial cavity via the spore spread. Thus, the invasion is highly lethal and rapidly progressive, requiring a multidisciplinary approach and fast actions in treatment. *Mucor*-derived angioinvasion presents as diverse signs and symptoms including nasal stuffiness; mucoid, purulent, bloody or black nasal

discharge; epistaxis; facial, nasal or periocular edema and discoloration, speaking defects, vision impairment and excruciating headache. Predisposing factors were known to be consisting of conditions such as diabetes mellitus, corticosteroid usage and immunosuppression, immunodeficiency, malignancies (especially hematologic) and cell/tissue/organ transplant treatments. However, COVID-19, which requires a comprehensive and multi-organ-based treatment in varying severities, is unfortunately added to the list of risk factors for the opportunistic Mucor infection.⁴⁻⁶ Hence; the present study was conducted for assessing the histopathologic findings of patients with COVID complications.

MATERIALS & METHODS

The present study was conducted for assessing the histopathologic findings of patients with COVID complications. A total of 20 patients who had past history of COVID-19 infection and reported with presence of post-COVID Mucormycosis were enrolled. Complete demographic and clinical details of all the subjects were obtained. Biopsy specimens were obtained and histopathologic examination was carried out. Histopathologic findings were analysed and correlated. All the results were recorded in Microsoft excel sheet and were analysed by SPSS software. Univariate regression curve were used for evaluation of level of significance.

RESULTS

A total of 20 patients with presence of post-COVID Mucormycosis were enrolled. Mean age of the patients was 52.3 years. Out of these 20 patients, 12 were males and 8 were females. Out of these 20 patients, 13 were having uncontrolled diabetic. 3 patients were having grade II hypertension while remaining 4 patients were of geriatric age group. Physical examination revealed an ulcerated lesion in majority of the patients. A scraping from the lesion was collected and sent for potassium hydroxide (KOH) preparation and bacterial / fungal cultures. Histopathologic findings revealed non-septate hyphae invading blood vessels in 13 cases while it revealed minimally septated broad, ribbon-like hyphae in 7 cases.

Table 1: Demographic

Variable	Value
Mean age (years)	52.3
Males (n)	12
Females (n)	8

Table 2: Co-morbid status

Variable	Number	Percentage
Uncontrolled diabetes	13	65
Grade II hypertension	3	15
Geriatric age group	4	20

Table 3: Histopathology

Variable	Number	Percentage
Non-septate hyphae	13	65
Minimally septated broad, ribbon-like hyphae	7	35

DISCUSSION

The pandemic coronavirus disease 2019 (COVID-19) continues to be a significant problem worldwide. While several treatment options have been evaluated, none except systemic glucocorticoids have been shown to improve survival in COVID-19. Unfortunately, the widespread use of glucocorticoids can lead to secondary bacterial or fungal infections. Invasive pulmonary aspergillosis complicating the course of COVID-19 is widely recognized; however, mucormycosis is uncommonly suspected or diagnosed. Herein, we report a case of pulmonary mucormycosis in a patient with severe COVID-19.⁷⁻¹⁰ Hence; the present study was conducted for assessing the histopathologic findings of patients with COVID complications.

A total of 20 patients with presence of post-COVID Mucormycosis were enrolled. Mean age of the patients was 52.3 years. Out of these 20 patients, 12 were males and 8 were females. Out of these 20 patients, 13 were having uncontrolled diabetic. 3 patients were having grade II hypertension while remaining 4 patients were of geriatric age group. Physical examination revealed an ulcerated lesion in majority of the patients. Garg D et al described a case of probable pulmonary mucormycosis in a 55-year-old man with diabetes, end-stage kidney disease, and COVID-19. The index case was diagnosed with pulmonary mucormycosis 21 days following admission for severe COVID-19. He received 5 g of liposomal amphotericin B and was discharged after 54 days from the hospital. They also performed a systematic review of the literature and identified seven additional cases of COVID-19 associated mucormycosis (CAM). Of the eight cases included in their review, diabetes mellitus was the most common risk factor. Three subjects had no risk factor other than glucocorticoids for COVID-19. Mucormycosis usually developed 10–14 days after hospitalization. All except the index case died. In two subjects, CAM was diagnosed postmortem. Mucormycosis is an uncommon but serious infection that complicates the course of severe COVID-19. Subjects with diabetes mellitus and multiple risk factors may be at a higher risk for developing mucormycosis.¹¹

In the present study, histopathologic findings revealed non-septate hyphae invading blood vessels in 13 cases while it revealed minimally septated broad, ribbon-like hyphae in 7 cases. Mucormycosis is a life-threatening infection that most commonly occurs in patients with uncontrolled diabetes mellitus and/or immunocompromised status. Patients with severe to critical coronavirus disease 2019 (COVID-19) infection have been recently identified as an at-risk

population for mucormycosis with reports of COVID-19-associated mucormycosis (CAM) from many countries.^{12, 13} Dilek A et al described a patient with COVID-19-associated mucormycosis and, searched and analyzed current medical literature to delineate the characteristics of COVID-19-associated mucormycosis. They reported a patient developed mucormycosis during post-COVID period. They described a 54-year-old male, hospitalized due to severe COVID-19 pneumonia. He was given long-term, high doses of systemic steroids. He developed maxillo-fascial mucormycosis and died of sepsis. Our literature search found 30 publications describing 100 patients including present case report. The majority (n = 68) were reported from India. 76% were male. The most commonly seen risk factors were corticosteroid use (90.5%), diabetes (79%), and hypertension (34%). Also, excessive use of broad-spectrum antibiotics were noted in cases. Most frequent involvements were rhino-orbital (50%), followed by rhino-sinusal (17%), and rhino-orbito-cerebral (15%). Death was reported as 33 out of 99 patients (33,3%). Steroid use, diabetes, environmental conditions, excessive use of antibiotics, and hypoxia are main risk factors.

CONCLUSION

Mucormycosis is a life-threatening fungal infection, with very high mortality. Interprofessional management typically consists of infectious disease, otolaryngology, hematology/oncology, endocrinology, microbiology, specialty-trained nursing, and pharmacist assistance of therapeutic drug administration and monitoring, all collaborating across disciplines to achieve optimal patient results.

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