

CASE REPORT

Rhizopus microsporus as Causative Agent of Mucormycosis in COVID-19 Patient

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SUMMARY

Background: The pandemic of coronavirus disease (COVID-19) emerged as a fatal infection, especially in immunocompromised patients. Currently, this infection is managed with systemic corticosteroids. Co-infection of COVID-19 with opportunistic fungi is increasingly recognized.

Methods: We describe a case of rhino-cerebral mucormycosis 12 days following severe COVID-19 in a diabetic patient.

Results: He received 50 mg amphotericin B and surgical debridement. The patient's symptoms improved following medical and surgical intervention.

Conclusions: 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. (Clin. Lab. 2022;68:xx-xx. DOI: 10.7754/Clin.Lab.2022.220232)

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KEYWORDS

mucormycosis, rhino-cerebral, diabetes

INTRODUCTION

The pandemic of coronavirus (COVID-19) remains a global problem and spreads rapidly. So far, despite many studies, definitive treatment of this disease has not been determined [1]. However, the diagnosis in the early stages of the disease has a good outcome for the patients. Secondary or co-infections following the disease, such as bacterial, fungal, and other respiratory infections, have also been reported in patients with COVID-19 [2,3]. The prevalence of these secondary infections in hospitalized patients is higher than in outpatients and is estimated to be between 10 and 30% [4]. Fungal infections are the most common in hospitalized patients with COVID-19. Risk factors for secondary infection with these agents include broad-spectrum use of corticosteroids such as dexamethasone to reduce pulmonary inflammation in COVID-19 patients. These drugs



Figure 1. Ulcerative black lesion.



Figure 2. PNS CT scan revealed mucosal thickening and involvement of both maxillary and right ethmoid sinuses (coronal view).

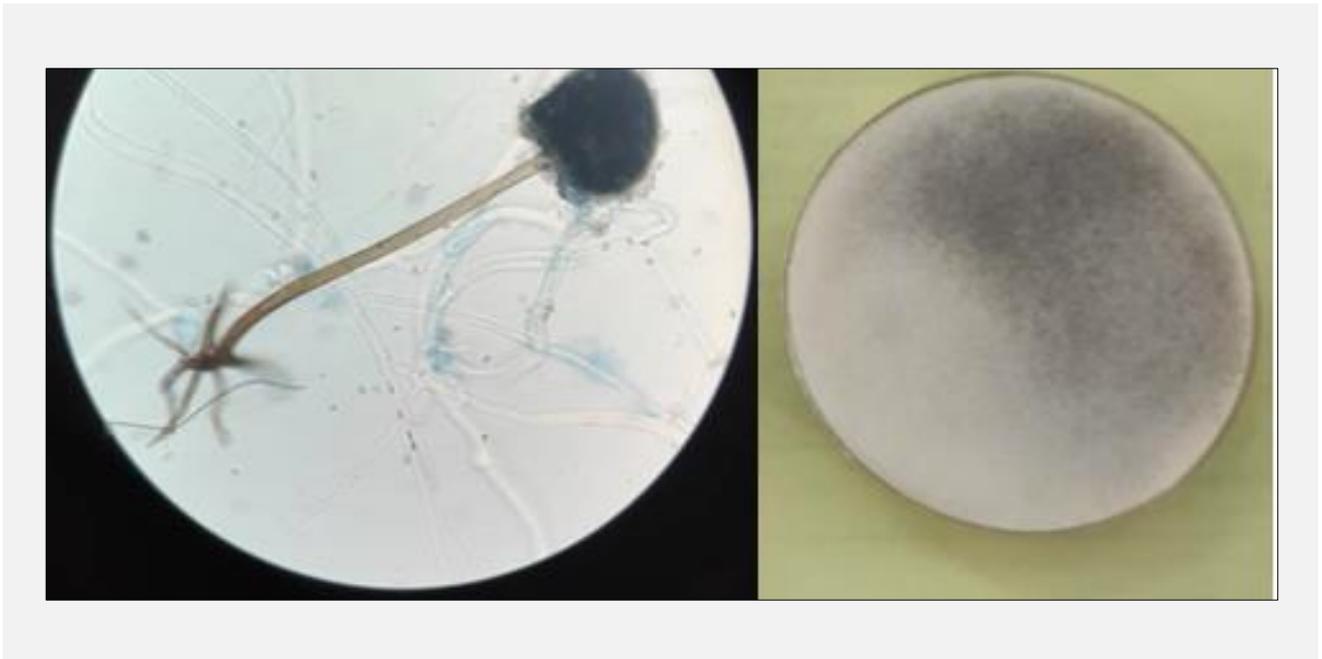


Figure 3. Microscopic and macroscopic feature of *Rhizopus*.

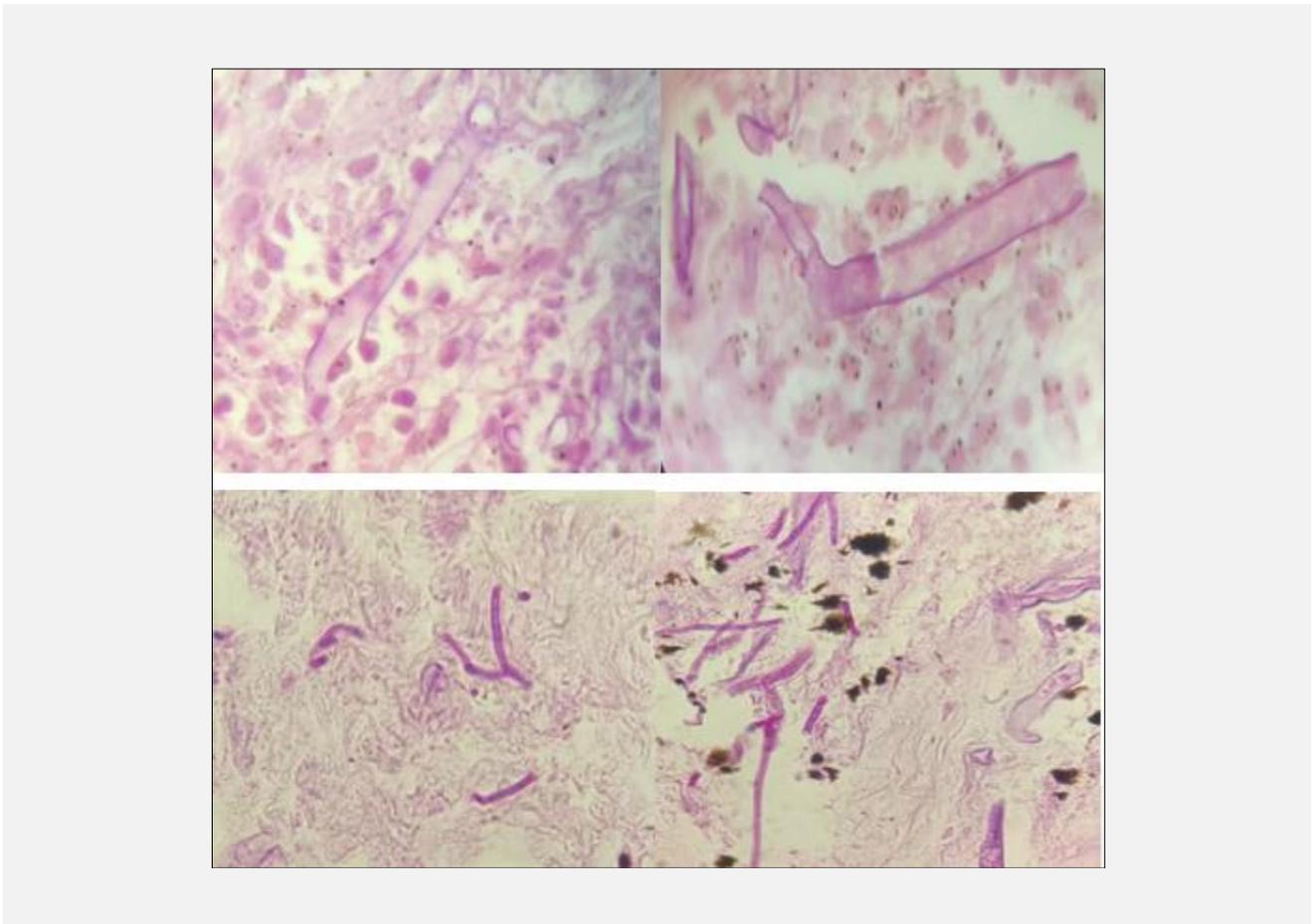


Figure 4. Periodic acid Schiff stained section showing typical aseptate, branching fungal hypha in necrotic tissue.

have many side effects including increased secondary infections, immune modulation, manifestation of latent diabetes mellitus, dizziness, weight gain, mood changes, insomnia, and muscle weakness [5].

Mucormycosis is an opportunistic fungal infection caused by non-septated fungi belonging to the phylum Zygomycota. This infection has a poor prognosis and is lethal if the infection occurs in immunocompromised or diabetes mellitus patients [6,7].

Herein, we report a case of rhinocerebral mucormycosis in a patient with COVID-19. This report aims to alert clinicians to be aware of mucormycosis as one of the common side effects of COVID-19 infection.

MATERIALS AND METHODS

Presentation of case

A 57 years old male diabetic and hypertension patient was presented to outpatient with the chief complaint of an ulcerative growth in the hard palate with pain. In addition, the patient had a headache and swelling of the right eye. The medical history of the patient showed that he had had COVID-19 and received dexamethasone, remdesivir, amoxicillin, and penicillin 12 days ago. The general intraoral examination revealed a necrotic ulcerative lesion in the center of the hard palate, measuring approximately 5 x 5 cm in diameter (Figure 1).

Management and follow up

PNS CT scan revealed mucosal thickening and involvement of both maxillary and right ethmoid sinuses (coronal view). The medical regime was planned using amphotericin B 50 mg and surgical debridement. Fortunately his symptoms improved with medical and surgical intervention.

Microbiology

For the microbiological survey, a tissue biopsy (in normal saline) was divided into two parts. Direct smear was prepared with potassium hydroxide 10%. Then, the rest of the specimen was inoculated on Sabouraud dextrose agar (SDA) and incubated at 37°C. The fungal agent that grew was examined macroscopically and microscopically. We saw the special structure of *Rhizopus microsporus* after staining with lactophenol methylene blue (Figure 2).

For accurate identification, molecular identification was performed based on PCR-sequencing of the ITS₁- 5.8-ITS₂ region. Genomic DNA was extracted from mycelia grown in Sabouraud dextrose broth. Briefly, mycelia were homogenized with 300 µL lysis buffer (100 mM Tris-HCl [pH 8.4], 1.4 M NaCl, 25 mM EDTA) and 300 µL glass bead suspension. After that, DNA of the homogenized suspension was extracted by phenol-chloroform protocol and used for PCR amplification. The PCR amplification was done using ITS1 and ITS4 primers [8]. The PCR product was sent to the Kadiogenic company for sequencing analysis and the result was de-

posited in Gene Bank. Finally, *R. microsporus* was identified and confirmed.

Histopathology

Figure 4 shows periodic acid Schiff stained necrotic tissue. Aseptate, branching broad-based fungal hyphae from areas of necrosis along with epithelioid cell granulomas comprising of epithelioid cells, multinucleated giant cells and chronic inflammatory cell infiltrate were seen.

DISCUSSION

Mucuracea is the largest family of saprophytic fungi with diverse habitats. These fungi can be localized in different sites of the body and cause mucormycosis [9]. Severe mucormycosis with the necrotic lesion is often fatal. Several conditions and risk factors including diabetes mellitus, immunosuppressive therapy, leukemias, and neutropenias have been introduced as the underlying cause of this disease [10]. Also, the high rate of invasion of the disease to the nose and sinuses can lead to thrombosis and infarction. COVID-19 infection creates special conditions for the invasion with Mucorales species [11]. The first condition is hyperglycemia especially in diabetic patients which occurred during COVID-19 infection. Besides, corticosteroid therapy in these patients can prepare the initial condition for invasion with opportunistic fungi [4,12].

CONCLUSION

It seems that the presence of diabetes mellitus with the use of corticosteroids, especially in intensive care units, is an alarming observation of mucormycosis. Therefore, physicians caring for critically ill COVID-19 patients must be aware of opportunistic fungal infections, especially mucormycosis.

Declaration of Interest:

The authors have declared that no conflict of interest exists.

References:

1. Liu M, Wang T, Zhou Y, Zhao Y, Zhang Y, Li J. Potential role of ACE2 in coronavirus disease 2019 (COVID-19) prevention and management. *J Transl Med* 2020;8(1):9-19. (PMID: 32435607)
2. Bhansali A, Bhadada S, Sharma A, et al. Presentation and outcome of rhino-orbital-cerebral mucormycosis in patients with diabetes. *Postgrad Med J* 2004;80(949):670-4. (PMID: 15537854)
3. Al-Tawfiq JA, Alhumaid S, Alshukairi AN, et al. COVID-19 and mucormycosis superinfection: the perfect storm. *Infection* 2021; 1-21. (PMID: 34302291)

4. Koumpa FS, Forde CT, Manjaly JG. Sudden irreversible hearing loss post COVID-19. *BMJ Case Reports CP*. 2020;13(11):e238419. (PMID: 33051251)
5. McNulty JS. Rhinocerebral mucormycosis: predisposing factors. *Laryngoscope* 1982;92(10):1140-3. (PMID: 7132514)
6. Patel A, Agarwal R, Rudramurthy SM, et al. Multicenter epidemiologic study of Coronavirus disease-associated mucormycosis, India. *Emerg Infect Dis* 2021;27(9):2349-59. (PMID: 34087089)
7. Garg D, Muthu V, Sehgal IS, et al. Coronavirus disease (Covid-19) associated mucormycosis (CAM): case report and systematic review of literature. *Mycopathologia* 2021;186(2):289-98. (PMID: 33544266)
8. Nagao K, Ota T, Tanikawa A, et al. Genetic identification and detection of human pathogenic *Rhizopus* species, a major mucormycosis agent, by multiplex PCR based on internal transcribed spacer region of rRNA gene. *J Dermatol Sci* 2005;39(1):23-31. (PMID: 15978416)
9. Manjunatha BS, Das N, Sutariya RV, Ahmed T. Mucormycosis of the hard palate masquerading as carcinoma. *Clin Pract* 2012; 2(1):e28. (PMID: PMC3981330)
10. Tugsel Z, Sezer B, Akalin T. Facial swelling and palatal ulceration in a diabetic patient. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2004;98(6):630-6. (PMID: 15583532)
11. Pathak K, Karadwal A, Nayak P, Nayak S. Mucormycosis in Post Covid Patient-A Case Report. *Indian J Forensic Med Toxicol* 2021;15(3):241-4. DOI: <https://doi.org/10.37506/ijfmt.v15i3.15311>
12. Kyrmizakis DE, Doxas PG, Hajjiannou JK, Papadakis CE. Palate ulcer due to mucormycosis. *J Laryngol Otol* 2002;116(2):146-7. (PMID: 11827594)