



**A CASE REPORT ON COVID-19 ASSOCIATED RHINO-ORBITAL
MUCORMYCOSIS (CAROM)****AMALU S¹, JOSHUA JM¹ AND MATHEWS SM^{2*}****1:** Department of Pharmacy Practice, Pushpagiri College of Pharmacy, Thiruvalla**2:** Department of Pharmaceutics, Pushpagiri College of Pharmacy, Thiruvalla***Corresponding Author: Dr. Santhosh M Mathews: E Mail: drmathews63@gmail.com****Received 23rd June 2022; Revised 26th Aug. 2022; Accepted 4th Dec. 2022; Available online 1st Sept. 2023****<https://doi.org/10.31032/IJBPAS/2023/12.9.7289>****ABSTRACT**

Coronavirus disease 2019 (COVID-19) infections may be associated with a wide range of bacterial and fungal co-infections. There has been a rapid rise in the number of COVID-19-associated rhino-orbital mucormycosis cases to an extent that it has been considered an epidemic among the COVID-19 patients in India. Here, we report a case of rhino-orbital-cerebral mucormycosis (ROCM) in a patient recovered from COVID-19 infection with uncontrolled Diabetes mellitus (DM). A 53 year old diabetic patient was admitted with a diagnosis of covid-19 based on positive RT-PCR and CT of lungs. He was treated with corticosteroids. Then the patients was readmitted to hospital due to right sided facial pain, swelling and vision loss of right eye after several days of discharge. A right endoscopic pansinus disease clearance was done and specimens sent for biopsy. The nasal biopsy showed mucormycosis. The patient was treated with IV antifungals and antibiotics. Our reports highlights that all physicians including ophthalmologists should, therefore, be mindful of the probability of development of fungal infections such as mucormycosis in patients with COVID-19 illness, especially in those with comorbidities and on immunosuppressive agents in the coming future.

Keywords: COVID-19, Rhino-orbital mucormycosis, diabetes, corticosteroids, antifungals**INTRODUCTION**

The coronavirus disease 2019 (COVID-19) respiratory syndrome coronavirus 2 infection caused by the novel severe acute (SARS-CoV-2) may be associated with a

wide range of disease patterns, ranging from mild to life-threatening pneumonia [1]. A wide range of bacterial and fungal co-infections may exist and may be associated with preexisting morbidity (diabetes mellitus, lung disease) or may develop as a hospital-acquired infection such as ventilator-associated pneumonia. India has a high prevalence rate of type 2 diabetes mellitus (8.9% of adults, 77 million patients), which is a well-known risk factor [2].

Mucormycosis, a fungal infection caused by ubiquitous environmental molds, such as *Rhizopus arrhizus*, *Rhizomucor pusillus*, *Apophysomyces variabilis* and *Lichtheimia corymbifera*, is surging as a COVID-19-associated infection at unprecedented rates throughout India and raising alarm bells around the world. Prior to the COVID-19 pandemic, the prevalence of mucormycosis in India was approximately 0.14 cases per 1000 population, about 80 times the prevalence in developed countries [3, 4].

Reports of COVID-19-associated mucormycosis have been increasing in frequency since early 2021, particularly among patients with uncontrolled diabetes [5]. Patients with diabetes and hyperglycemia often have an inflammatory state that could be potentiated by the activation of antiviral immunity to SARS-CoV2, which might favor secondary

infections [6]. Here, we report a case of rhino-orbital-cerebral mucormycosis (ROCM) in a patient recovered from COVID-19 infection with uncontrolled DM. To the best of our knowledge, this is the first case report of CAROM from South Kerala.

CASE PRESENTATION

A 53-year old man with known case of type 2 diabetes mellitus was diagnosed with covid-19 on positive RT-PCR and CT scan of lungs. After several days of discharge, the patient was readmitted due to right sided facial pain. He also had swelling and outward displacement of the right eye, associated with visual loss – rapidly progressive and also foul smelling nasal discharge and crusting inside the nose. On examination – right eye proptosis, no vision in right eye. CT PNS – right pansinusitis with branch of right periorbital region. KOH fungal test was done and shows mucormycosis. The operative procedure – right endoscopic pansinus disease clearance was done. Nasal decongestion done, right middle turbinate was necrosed and removed, right uncinectomy done, fungal debris cleared from sinus, anterior and posterior ethmoidectomy done. Diseased periorbital fat noted in the region of orbital apex. The patient was post operatively managed with IV antifungal and antibiotics. The patient was discharged with Inj. Amphomul 200 mg once daily with Inj

Dexa 4 mg in 250 ml and Syp Posaconazole 10 ml twice daily for 7 days. At time of discharge, the condition of the patient was stable and satisfactory.

DISCUSSION

A composite interplay of certain aspects including comorbidities such as diabetes mellitus, previous respiratory infections, risk of nosocomial infections, immunosuppressive therapy, and systemic immune alterations of COVID-19 infection itself may lead to secondary infections [7].

Current guidelines in India recommend intravenous methylprednisolone 0.5-1 mg/kg/day for three days in moderate cases and 1-2 mg/kg/day in severe cases [8]. National Institute of Health recommends the use of dexamethasone (6 mg per day for a maximum of 10 days) in patients who are ventilated or require supplemental oxygen but not in milder cases [9, 10]. The guidelines specifically mention the risk of developing a secondary infection [11].

Various pathophysiologic features of COVID-19 which might allow secondary fungal infections, including a tendency to cause extensive pulmonary disease and the subsequent alveolar-interstitial pathology that may augment the risk of invasive fungal infections [12]. Second, several case reports postulated that the SARS-CoV-2 infection may affect CD4+ and CD8+ T cells, with a reduction in the absolute number of lymphocytes and T cells

associated with creation of a temporary state of compromised immunity [13].

Diabetes mellitus has been associated with severity in COVID-19. It has been seen that diabetics are at increased risk of dying than those without this and a high mortality rate with CAM remains the main concern [14]. Mucormycosis represents a complex and challenging clinical entity, both from a diagnostic and management standpoint [15]. Rhino-orbital-cerebral-mucormycosis (ROCM), previously referred to as orbital zygomycosis, refers to the presentation of pathologic symptoms in the orbit as a result of fungal infections caused by fungi in the order Mucorales, most commonly by the species *Rhizopus oryzae* [16]. ROCM usually occurs in an immunocompromised host and presents with initial symptoms such as vision loss, ptosis, diplopia, and external ophthalmoplegia. Left untreated, ROCM can progress to acute vision loss, metastasis (brain, sinuses) and death. Orbital involvement results from the spread through the medial orbital wall and nasolacrimal duct as in our case. The fungi invade the adjacent blood vessels causing thrombosis and infarction, as well as dissemination to the brain parenchyma [17].

The patient we describe here with COVID-19 was a long-standing uncontrolled diabetic patient. The signs of orbital infection were noticed after several days of

admission for COVID-19 infection during which time he was treated with both broad-spectrum antibiotics and steroids. All these factors tend to facilitate fungal coinfection, along with any possible COVID-19 pathophysiological mechanisms. However, patient was post operatively managed with IV antifungal and antibiotics and discharged.

CONCLUSION

To sum up, clinicians must be aware of the risk of mucormycosis in patients suffering as well as recovering from COVID-19 especially those with inappropriate steroid therapy and with uncontrolled diabetes mellitus. A high index of suspicion should be there while managing COVID-19 patients as mucormycosis is potentially treatable if diagnosed early, unlike COVID-19 which has only anti-inflammatory therapies available as of now. Also, there is a need to stress the sensible use of steroids. Where there is no oxygen requirement and no evidence to suggest a florid inflammatory response, it would be prudent to avoid steroid and immunosuppressive use for COVID-19. Early and overzealous antibacterial use may also be harmful. Key to the management of mucormycosis remains early diagnosis and starting of appropriate antifungal treatment, and if required timely surgical intervention.

Acknowledgement

The authors would like to thank Prof. Dr. Santhosh M Mathews, Principal, Pushpagiri College of Pharmacy for motivation in publication of this work in a reputed journal.

REFERENCES

- [1] Sarkar S, Gokhale T, Choudhury SS, Deb AK. COVID-19 and orbital mucormycosis. *Indian Journal of Ophthalmology*, 2021; 69(4): 1002.
- [2] Bhatt K, Agolli A, Patel MH, Garimella R, Devi M, Garcia E, *et al*. High mortality co-infections of COVID-19 patients: mucormycosis and other fungal infections. *Discoveries (Craiova)*, 2021; 9(1): e126.
- [3] Prakash H, Chakrabarti A (2019) Global epidemiology of mucormycosis. *J Fungi*, 2019, 5(1): 26.
- [4] Skiada A, Pavleas I, Drogari-Apiranthitou M. Epidemiology and diagnosis of mucormycosis: an update. *Journal of fungi*, 2020; 6(4): 265.
- [5] Hoenigl M, Seidel D, Carvalho A. The emergence of COVID-19 associated mucormycosis: a review of cases from 18 countries. *Lancet Microbe*, 2022; 3(7): e543-e552.
- [6] Lim S, Bae JH, Kwon HS, Nauck MA. COVID-19 and diabetes mellitus: from pathophysiology to

- clinical management. *Nature Reviews Endocrinology*, 2021; 17(1): 11-30.
- [7] Singh AK, Singh R, Joshi SR, Misra A. Mucormycosis in COVID-19: a systematic review of cases reported worldwide and in India. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*, 2021; 15(4): 102146.
- [8] Mehta S, Pandey A. Rhino-Orbital Mucormycosis Associated With COVID-19. *Cureus*. 2020; 12(9).
- [9] Group TR. Dexamethasone in hospitalized patients with Covid-19—preliminary report. *The New England journal of medicine*, 2020 Jul 17.
- [10] COVID-19 Treatment Guidelines Panel. Coronavirus disease 2019 (COVID-19) treatment guidelines. National Institutes of Health. 2020; 2020.
- [11] Zhang H, Zhang Y, Wu J, Li Y, Zhou X, Li X, *et al.* Risks and features of secondary infections in severe and critical ill COVID-19 patients. *Emerging microbes & infections*, 2020; 9(1): 1958-64.
- [12] Ahmed OF, Al-Neaimy S, Kakamad FH, Mikael TM, Hamasaeed AG, Salih RQ, *et al.* COVID-19 associated with pulmonary mucormycosis; a case series. *Annals of Medicine and Surgery*, 2022; 76: 103434.
- [13] Urra JM, Cabrera CM, Porras L, Ródenas I. Selective CD8 cell reduction by SARS-CoV-2 is associated with a worse prognosis and systemic inflammation in COVID-19 patients. *Clin Immunol*, 2020; 217: 108486.
- [14] Hussain A, Bhowmik B, do Vale Moreira NC. COVID-19 and diabetes: Knowledge in progress. *Diabetes Res Clin Pract*, 2020; 162: 108142.
- [15] Nayak N, Khan E, Panigrahi D. COVID-19 and Mucormycosis Coinfection: How Challenging It Is. *Canadian Journal of Infectious Diseases and Medical Microbiology*. 2022; 2022.
- [16] Gamaletsou MN, Sipsas NV, Roilides E, Walsh TJ. Rhino-orbital-cerebral mucormycosis. *Current infectious disease reports*, 2012; 14(4): 423-34.
- [17] Patnaik A, Sharma B, Ahmad R, Kumar A, Chitrotpala R, Gupta M. A Case of Bilateral Central Retinal Artery Occlusion in a Post-COVID Rhino-Orbital-Cerebral Mucormycosis Patient. *Cureus*, 2021; 13(11).