



Black Fungus Goes Viral: A Case Series of Rhino-Orbital Mucormycosis Associated with COVID-19 from an Academic Hospital in North India

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Clinical Image

While rhino-orbital mucormycosis seen among patients with Diabetes Mellitus (DM), neutropenia, chronic use of steroids and other immunosuppressive agents, and stem cell or solid organ transplant, it has been recently recognized in those with Coronavirus Infection Disease-2019 (COVID-19) [1-3]. We report six cases of rhino-orbital mucormycosis in COVID-19 patients who presented to the medical emergency of our academic hospital in north India from May 17th through May 24th, 2021. All the patients in this series were COVID-19 positive with nasopharyngeal swab testing. Five out of six cases had severe COVID-19 pneumonia, for which they were receiving steroid treatment, interleukin-6 inhibitors or other immunomodulatory therapy not used in any patient. The typical predisposing comorbid illness was type-2 DM in all patients, with poor glycemic control indicated by high plasma glucose levels and elevated glycosylated hemoglobin. Further, diabetic ketoacidosis is seen in two patients at admission and diabetic ketosis in one patient.

The first symptoms of the rhino-orbital syndrome were unilateral facial pain or swelling, periorbital swelling, orbital pain, and blurred vision. Two patients had cerebral involvement at presentation. The interval between the onset of symptoms of COVID-19 and the first symptoms of rhino-orbital mucormycosis ranged from 1 to 14 days. Computed tomography of paranasal sinuses and orbit was obtained in four cases. Severe unilateral thickening of the sinonasal mucosa with or without underlying bone erosions had been the most consistent finding (Figure 1). The intraorbital disease was evident in three patients, two patients had bilateral sinus involvement, and intracerebral invasion was present in two patients. For a prompt diagnosis, microscopic examination of the specimens (scrapings from the nasal cavity or destructive palatal lesion) using the potassium hydroxide-calcofluor white method was performed, which yielded aseptate broad-branched hypha suggestive of mucor in three patients, and in the rest three, remained inconclusive. All the patients treated with intravenous amphotericin, and one patient underwent surgical debridement. Hyperglycemia managed with insulin infusion to achieve a glycemic target of 140 mg/dL to 180 mg/dL. Of the six patients, only two patients improved clinically and discharged successfully. Two patients died, and two left against medical advice.

Poorly controlled DM is a common and significant predisposing condition for both severe COVID-19 and mucormycosis [2-4]. The increased reporting of COVID-19 associated mucormycosis cases from India compared to the rest of the world might reflect a higher prevalence of DM in India [3]. Moreover, unhygienic practices, including the frequency of changing or washing face masks coupled with a tropical environment with high humidity, might also be a contributing factor. Only two out of six patients used to change or clean their masks daily according to the World Health Organization recommendation [5].

A potential diabetogenic effect of COVID-19 and the use of steroid or other immunosuppressive therapy for treatment exponentially increases the risk of invasive and relentlessly progressive fungal disease [2,4,6]. In this case, series, the doses of steroids used were variable; i.e., the usual recommended dose for COVID-19, higher than recommended, or lower than recommended [7]. These findings support the previous observation that a short course of steroids may predispose to severe fungal infections [8].

COVID-19 per se postulated to be independently associated with the occurrence of Mucor infection because of direct epithelial cell damage, widespread micro-thrombosis with subsequent

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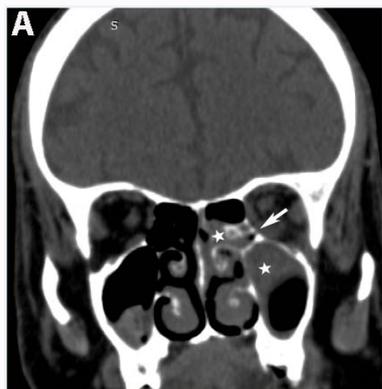


Figure 1: High resolution computed tomography of the paranasal sinus (coronal, soft window image) in patient no. 2 showing the presence of soft tissue involving left maxillary and ethmoid sinuses (stars) and rarefaction of the orbital rim (arrow).

stagnant blood supply, dysregulated immune response, and lymphopenia [3,6]. Lymphopenia (absolute lymphocyte counts <1000 per μL) noted in all patients, including five having a count <500 per μL . Elevated serum ferritin associated with the dysregulated inflammatory response in severe COVID-19 disrupts typical iron sequestration, supporting *Mucor* growth. Serum ferritin was available in five cases in our series. All had elevated levels, including a level >1000 ng/ml in four patients. Because the reported incidence of mucormycosis during the current wave is seemingly higher than previously observed, an increased association with the increased circulation of emerging new strains of COVID-19 might also remain possible.

The predisposition with uncontrolled diabetes and first symptoms of mucormycosis are similar to that occurs without COVID-19 [1-4]. Although based on this observational series involving six cases, it is not possible to determine the exact etiopathogenesis of COVID-19-associated mucormycosis, the potentially modifiable risk factors such

as strict glycemic control in the diabetic population and improved preventive measures for secondary infection should be urgently addressed. We could not determine that prognosis is similar or worse; however, overall, COVID-19 associated mucormycosis is a devastating disease, and the increasing cases are regarded as a parallel pandemic. A comprehensive strategy including awareness about preventive measures is required to reduce the risk of this life-threatening condition.

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