

An Unusual Orbital Presentation of COVID-19-Associated Mucormycosis

Santosh Kumar Swain

Department of Otorhinolaryngology and Head and Neck Surgery, IMS and SUM Hospital, Siksha "O" Anusandhan University, Bhubaneswar, Odisha, India

Abstract

Coronavirus disease 2019 (COVID-19) is an ongoing pandemic that spreads mainly through close contact and tiny respiratory droplets. The ocular surface is a potential site for transmission, whereas the ophthalmologists are highly potential to acquire infection. Because of the presence of the angiotensin enzyme 2 in different ocular tissues and cytokine storm results in vasoconstriction, ischemia, hypercoagulopathy, and thromboembolic phenomenon, this virus easily binds and in different ocular manifestations such as conjunctivitis, retinal vascular occlusion, diabetes retinopathy, ocular nerve palsies, and orbital mucormycosis. Mucormycosis is a life-threatening infection that often affects patients with diabetes mellitus and other immunocompromised patients. The diagnosis of mucormycosis is usually done by microbiological tests and radiological investigations. Proper ocular care and awareness among clinicians need the hour for prompt management of orbital mucormycosis. Here, we are presenting a case of COVID-19-associated mucormycosis with subconjunctival involvement of mucormycosis.

Keywords: Amphotericin-B, coronavirus disease 2019, mucormycosis, orbit

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2).^[1] This pandemic started in December 2019 at the seafood market in Wuhan city, China presenting with fever, cough, fatigue, and diarrhea.^[2] Acute invasive fungal rhinosinusitis with orbital involvement is an uncommon and life-threatening infection with a greater risk for mortality in COVID-19 patients. It often affects immunocompromised persons including diabetes mellitus, hematological malignancy, and organ transplantation.^[3] COVID-19 infection is a global pandemic caused by SARS-CoV-2 which may progress to acute respiratory distress syndrome, a condition where the patient is susceptible to pulmonary fungal infections.^[4] A sudden exponential increase in mucormycosis in patients with COVID-19 is a matter of concern. Mucormycosis is a fatal fungal infection that characteristically presents with angioinvasion.^[1] This fungal infection is caused by a fungus that belongs to the order Mucorales of the class Zygomycetes.^[5] Here, we are presenting a case of COVID-19-associated mucormycosis (CAM) with unusual orbital involvement, particularly subconjunctival mucormycosis.

CASE REPORT

A 28-year-old man diagnosed with COVID-19 infection presented with dark lines in the conjunctiva of both eyes [Figure 1] following 10 days of the infection. He had no nasal secretion and nasal obstruction. He had no history of diabetes mellitus or any other debilitating diseases with no relevant family history. During the COVID-19 infection, he was monitored at the intensive care unit (ICU) days where he was administered with injection remdesivir IV with a loading dose of 200 mg, followed by 100 mg daily for 10 days. He had also taken corticosteroids (methylprednisolone) during the treatment period of COVID-19 infections. The patient had no history of trauma to the eye, exposure to the soil, or other vegetable materials. Clinical examination showed no chemosis, orbital cellulitis, or vision loss. Visual acuity was

Address for correspondence: Dr. Santosh Kumar Swain, Department of Otorhinolaryngology and Head and Neck Surgery, IMS and SUM Hospital, Siksha "O" Anusandhan University, K8, Kalinga Nagar, Bhubaneswar - 751 003, Odisha, India.
E-mail: santoshvoltaire@yahoo.co.in

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6/6 in both eyes. Because of the appearance of the cornea, the infection with mucormycosis was suspected. Eyeball movements on both sides were within the normal limit. Nasal discharge and conjunctival secretion with lactophenol cotton blue staining were positive for broad aseptate hyphae with 90° branching [Figure 2]. He was confirmed for mucormycosis infection in the eye, particularly at the subconjunctival region. Computed tomography (CT) scan of the nose and paranasal sinuses showed no sinonasal pathology and no bony erosion in the sinonasal tract and has an intact bony orbital wall. Magnetic resonance of imaging (MRI) of the brain and orbit showed no pathology in the brain and thickening in the corneal region of both orbits. This is an uncommon clinical presentation of CAM during the pandemic. He was immediately administered with liposomal amphotericin B (L-Amb) (5 mg/kg/day) diluted in 200 ml 5% dextrose over 2–3 h infusion with a total cumulative dose of 3 g. The blackish changes or mucormycosis lesions in the subconjunctival and corneal region of both eyes were disappeared after 1-month treatment with L-Amb.

DISCUSSION

The COVID-19 patients who have a history of prolonged hospital stay or required mechanical ventilation and taking systemic steroids for a prolonged period are likely to get a cofungal infection like mucormycosis, called CAM.^[6] Mucormycosis is a rare but most aggressive systemic fungal infection which affects patients with diabetes mellitus and immunocompromised conditions.^[6] Hyperglycemia and acidic pH-mediated leukocyte dysfunction result in more free iron because of the disruption of the binding with transferrin. As *mucor* is a ferrophilic organism, this event enhances the susceptibility of this organism.^[7] Angioinvasion, a higher propensity for arteries than veins, is another important feature that results in thrombosis and hemorrhage followed by tissue necrosis infarction and necrosis.^[1] COVID-19 patients often show higher levels of inflammatory cytokines (interleukin [IL]-2R, IL-6, IL-10, and tumor necrosis factor-alpha) and deranged cell-mediated immune response, affecting both CD4+ T and CD8+ T cells.^[8] Hence, the patients with COVID-19 infection are susceptible to fungal infections like mucormycosis.^[4] Mucormycosis may result in orbital and cerebral complications by infarction and necrosis

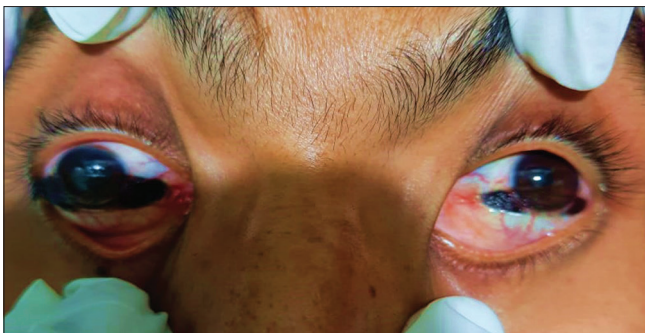


Figure 1: Subconjunctival mucormycosis in both orbits

of the host tissue through invasion of the blood vessels by hyphae.^[4] Prone positioning of the COVID-19 patients in the ICU facilitates increased lung expansion and perfusion, decreasing ocular perfusion by increasing venous pressure and intraocular pressure.^[9] Prone position can aggravate acute angle-closure glaucoma. Different comorbidities of the patients such as diabetes mellitus, hypertension, and atherosclerosis also result in ocular hypoperfusion by enhancing vascular resistance. Dryness of the eye can be found because of the positive pressure ventilation and the use of different types of oxygen masks. The ocular complications of the COVID-19 can be reduced by avoiding the prone position for a short period. Positive pressure ventilation and prone positioning can lead to a subconjunctival hemorrhage.^[10] Subconjunctival hemorrhage may confuse with mucormycosis. Eye drops, viscous lubricants, and ointments can be useful to decrease dryness. If patients with lagophthalmos, tape tarsorrhaphy, or surgical tarsorrhaphy can be undertaken to avoid exposure keratitis, otherwise it can aggravate endophthalmitis or panophthalmitis in sepsis cases. Ocular complications are more in COVID-19 patients in ICU and especially in patients of invasive mechanical ventilation, and health-care workers should be aware of this. External ophthalmoplegia reduced visual acuity, and proptosis is common orbital manifestations. Very rarely, endophthalmitis is found in rhino-orbital mucormycosis. Mucormycosis rarely cause endophthalmitis and eyelid gangrene.^[11]

In the case of COVID-19 patients, clinical suspicion for sinonasal and ocular mucormycosis are supported by warning signs such as nasal stuffiness, nasal discharge, foul smell, epistaxis, perifacial edema, periocular and eyelid edema, discoloration or pain, sudden loss of vision, proptosis, and restricted ocular movements.^[1] These features need immediate investigations such as diagnostic nasal endoscopy, fungal smear, contrast-enhanced CT scan, and contrast-enhanced MRI to rule out orbital involvement.^[12] Diagnostic nasal endoscopy can be performed, and tissue sent for histopathological examination for confirmation of the diagnosis. *Mucor* is often

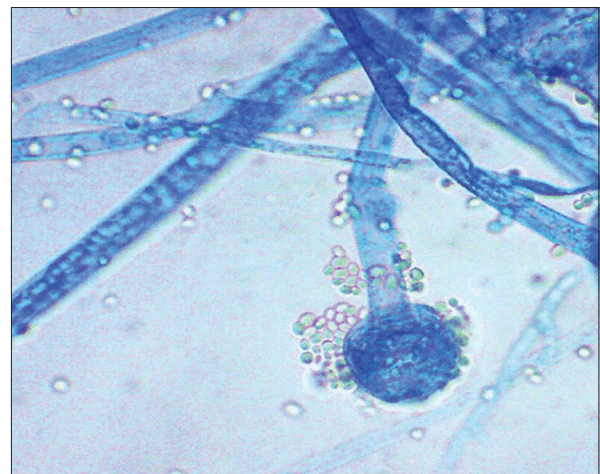


Figure 2: Lactophenol cotton blue staining shows mucor as broad aseptate hyphae with the extension of columella into sporangium (×400)

demonstrated by biopsy and subsequent culture. Tissue is often sent for histopathological examination and KOH mount for confirmation of the mucormycosis.^[13]

In this case, nasal secretions and conjunctival fluid with lactophenol cotton blue staining show *mucor* as broad aseptate hyphae with the extension of columella into sporangium. The antifungal agent is often insufficient to cure mucormycosis as angioinvasion and thrombosis of the blood vessels prevent maximum penetration of the antifungal drugs to the site of infection. Hence, surgical debridement of the infected necrotic tissues is needed along with systemic antifungal agents.^[13] Endoscopic debridement should be done promptly after confirmation of the CAM. The medical treatment with amphotericin should be started without delay. L-Amb is the preferred medical treatment.^[13] Amphotericin B deoxycholate (D-Amb) can be given if the cost and availability of L-Amb are an issue. In this case, L-Amb was administered for 1 month.

CONCLUSION

Mucormycosis of the head-and-neck region are rare life-threatening infections where patients need prompt diagnosis and immediate intervention for survival. Patients of COVID-19 infection with diabetes mellitus, immunosuppressive medications, or taking systemic steroids are at a greater risk for mucormycosis. The established treatment for mucormycosis is amphotericin B along with surgical debridement. The subconjunctival mucormycosis is an extremely rare lesion in CAM which needs prompt diagnosis and immediate treatment.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published

and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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