

## Rhino-orbital mucormycosis in COVID-19 (Corona Virus Disease): A case report

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### ABSTRACT

**Background:** Mucormycosis, often referred to as black fungus is being recognized as post treatment complication in COVID-19. A complex interaction of immune compromised state may lead to secondary fungal infections. Rhino-orbital mucormycosis, a rare fungal disease, involves the orbit, nose, and sinuses. If not intervened early it might progress with a fatal outcome. The present case report is a Rhino-orbital mucormycosis presenting as a secondary infection in COVID-19 patient and its management. A 51-year-old male patient diagnosed with COVID-19, developed periorbital edema of the left eye along with tooth pain. Nasal endoscopy, computed tomography, and Magnetic Resonance Imaging suggested Rhino-orbital mucormycosis. Surgical debridement followed by intravenous Amphotericin B was prescribed. After a week of follow-up, complete resolution of symptoms was noticed. **Conclusion:** An early diagnosis and prompt management is the key to reduce morbidity and mortality in these patients. Prophylactic measures and judicious use of drugs may reduce the incidence of this opportunistic infection.

**Keywords:** Black fungus, Corona virus, COVID-19, mucormycosis, pneumonia, fungal infections

### Introduction

Coinfections in patients with COVID-19 disease is an emerging concern globally because of the complex course of the disease. A myriad of complicated clinical presentations ranging from mild to life-threatening pneumonia have been delineated so far and new symptoms are showing up.<sup>[1]</sup> Mucormycosis belongs to the fungi group mucormycetes which lives in soil and decaying matter. It is transmitted by direct contact to fungal spores in the environment. There has been a rise in mucormycosis cases in patients with COVID-19 due to various underlying conditions like hypoxia, high glucose levels due to diabetes

or steroid-induced hyperglycaemia, high ferritin levels due to inflammation, decreased activity, and count of white blood cells, these promote favorable environment for spores to grow.<sup>[2,3]</sup>

Globally, the prevalence varies from 0.005 to 1.7 per million population, where as in India, it is 0.14 per 1000. Similarly, the fatality rate globally is 46% but the involvement of intracranial and orbital regions and irreversible immune suppression have increased it to as high as 50% to 80%. The diagnosis solely depends on clinical features, pathological findings, and imaging. The difficulty in diagnosing has hindered the outcome and prognosis of the condition. Thus, the primary care physician's role assumes a vital aspect who may be the primary contact for the patient. Hence, early detection of symptoms and initiation of treatment or prompt referral plays a prominent role.<sup>[4]</sup>

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We report a case of Rhino-orbital mucormycosis in patient recovered from COVID-19.

## Case Report

A 51-year-old male patient was referred by a primary care physician with a complaint of pain and swelling on the left side of the face for the past 3 days. The patient was apparently asymptomatic and subsequently developed pain in the upper left back teeth. The patient gave no history of recent dental treatment or any type of trauma. The patient gave a history of positive reverse-transcriptase polymerase chain reaction for severe acute respiratory syndrome corona virus 2 and reported that he was hospitalized for 4 days and the discharge summary revealed that COVID-19 infection was managed with 200 mg (loading dose) of Inj.Remdesivir IV, followed by 100 mg of the injection daily for 12 days, 80 mg/day Methylprednisolone IV in 240 mL saline for 15 days, and 4 mg of Inj.Dexamethasone twice daily for 12 days. The post-treatment of HbA1c was 12.3%.

On the 18<sup>th</sup> day, the patient reported unilateral left periorbital edema and erythema with restricted eye movements [Figure 1a]. On intraoral examination, the maxillary molars were tender [Figure 1b]. Mucormycosis was provided as a preliminary diagnosis, with osteomyelitis, persistent granulomatous infection, and deep fungal infections as differential diagnoses. Orthopantomogram showed thickened left maxillary sinus walls with no signs of dental abnormalities. Nasal endoscopy revealed crusting along the inferior turbinates and conchae [Figure 2]. A computed tomography scan revealed hyperdensity of the maxillary antrum with erosive changes of sinus wall and the left inferior orbital rim [Figure 3]. MRI brain and orbit (T1W-imaging) revealed an ill-defined hypointense mucosal thickening of left maxillary sinus, anteriorly displaced left eye ball due to Retrobulbar fat stranding, and odema encroaching left optic nerve [Figure 4]. Surgery, under general anesthesia was planned for debridement of the necrotic tissue.

At admission, oral intubation was done with debridement of the necrotic tissue by Caldwell–Luc approach, inferior turbinectomy, and orbital decompression was done [Figure 5]. Postoperatively, the patient was kept under follow-up and was advised systemic antifungal treatment with lipolyzed Inj.Amphotericin B 300 mg/day for 7 days.

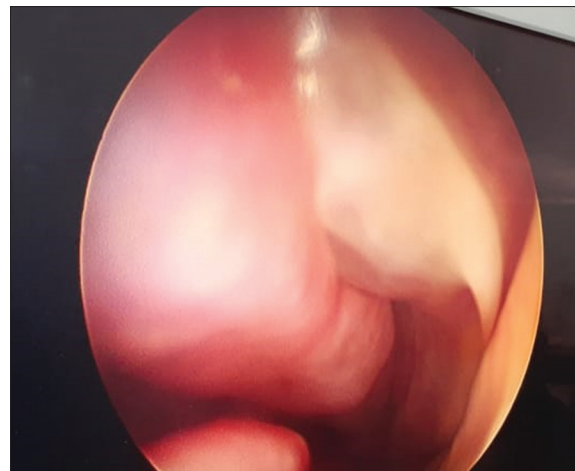
Histopathological examination of necrotic tissue specimen, showed broad, hyphae with right-angle branching and chronic inflammatory cell infiltrate [Figure 6]. Based on radiological and histopathological findings, a final diagnosis of rhino-orbital mucormycosis was given. On the 7<sup>th</sup> day follow-up, the eye movements were relatively better on medial and lateral movement and the swelling has reduced.

## Discussion

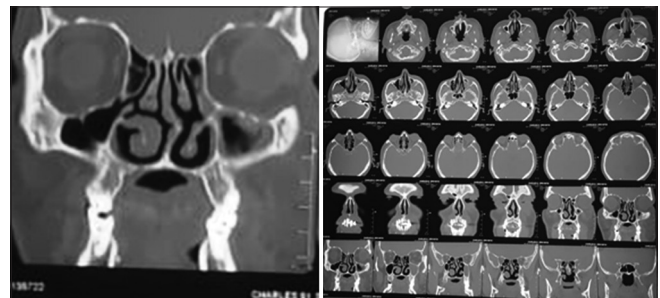
COVID-19, a worldwide pandemic caused by a novel corona virus (SARS-CoV-2) is associated with significant secondary



**Figure 1:** (a) Periorbital odema and drooping of the eyelids on left side of face. (b) Left maxillary 1st molar gingival inflammation



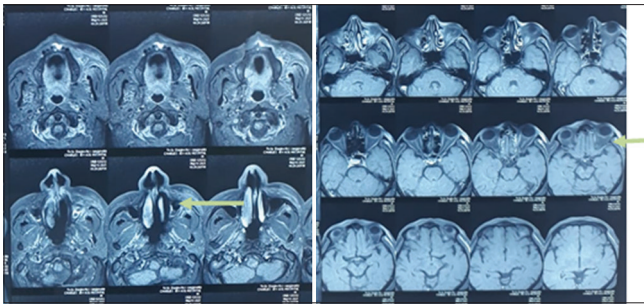
**Figure 2:** Endoscopic view showing eschars on inferior turbinates



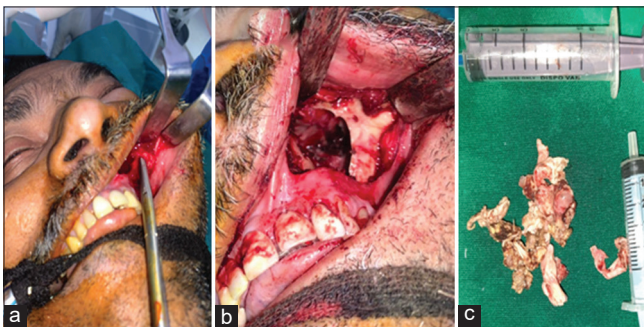
**Figure 3:** CT image of axial sectional view showing hyperdense mucosal thickening of left maxillary sinus

infections like bacterial and fungal.<sup>[2]</sup> Fungal infection being more common than other secondary infections leading to hospitalization and also in severely ill COVID patients.<sup>[4]</sup>

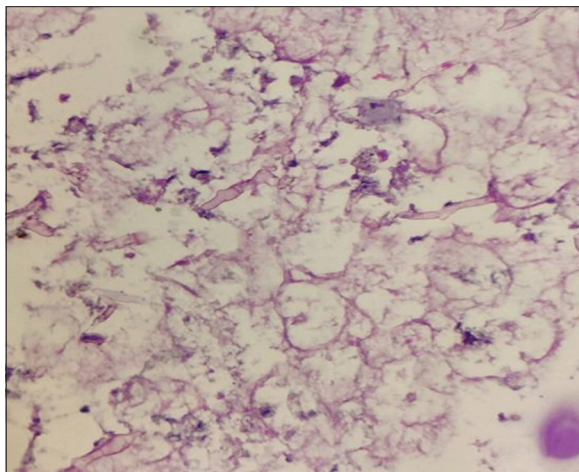
Mucormycosis, a rare opportunistic fungal infection is caused by saprophytic aerobic fungi *Rhizopus*, *Rhizomucor*, and *Cunninghamella* belonging to order Mucorales. The zygospores are airborne and may settle on the oral, nasal mucosa, and paranasal sinuses of humans.<sup>[2]</sup> Immunocompromised



**Figure 4:** MRI [T1 W image] of axial view showing hyperdense mucosal thickening of left maxillary sinus and proptosis of the left eyeball can be noted



**Figure 5:** (a) Caldwell–Luc approach for necrotic tissue debridement, (b) intraoperative view of left maxillary sinus; (c) surgically removed necrotic specimen



**Figure 6:** Lactofuchsin stained section under 10× magnification showing mycelium with typical aseptate branching at right angle with broad base and chronic inflammatory cell

individuals or debilitated patients having uncontrolled diabetes mellitus with ketoacidosis, other metabolic acidosis, hematologic malignancies, neutropenia, solid organ/stem cell transplant, and treatment with immunosuppressants and corticosteroids are more vulnerable and helps in establishing the infection.<sup>[5,6]</sup>

Mucormycosis is thought to be acquired via the inhalation of fungal spores into the paranasal sinuses followed by pulmonary, cutaneous/subcutaneous, and disseminated diseases. Tissue necrosis, resulting from angioinvasion leading to vascular

thrombosis, is the hallmark of the disease.<sup>[5]</sup> Most commonly involved sites are nose, sinuses, orbit, central nervous system, lung, gastro-intestinal tract (GIT), skin, jaw bones, joints, heart, kidney, and mediastinum (invasive type).<sup>[7]</sup> Based on a study by Jeong *et al.*,<sup>[8]</sup> Rhino-orbital-cerebral mucormycosis was commonly observed (34%) than pulmonary (20%) and cutaneous mucormycosis (22%).

ROCM is a rare life-threatening invasive fungal infection involving the nose, orbit, and brain. The orbital spread makes the prognosis poor as the surrounding bone and soft tissue gets infiltrated and destroyed by the fungus through vascular thrombosis and subsequent tissue infraction and lead to fatal complications after reaching the brain.<sup>[9]</sup> Initial symptoms may be fever, headache, nausea, and generalized weakness. Later course may follow purulent discharge with or without epistaxis along with sinusitis, congestion, and decreased sensation in nose. When orbital region and brain are involved, there may be inflammation and odema of the orbital tissues, ophthalmoplegia, proptosis, partial/complete loss of vision, and signs of meningoencephalitis. Grey/reddish nasal or palatine mucosa are seen which undergoes necrosis to progress into black areas of eschar.<sup>[10]</sup>

Oral manifestations of mucormycosis usually include tissue necrosis and bone exposure. A thorough examination of the involved area along with investigations is mandatory as the symptoms may overlap with other conditions such as osteomyelitis, chronic granulomatous infections, and other deep fungal infection.<sup>[5]</sup>

Patients with diabetes or defects in phagocytic function seem to be the direct targets for this disease. Diabetic ketoacidosis enhances fungal survival because of iron disassociation and use of corticosteroids also causes further hyperglycaemia leading to upregulation of mammalian cell receptor binding to Mucorales.<sup>[11-13]</sup>

The National Institute of Health recommends the use of dexamethasone (6 mg per day for a maximum of 10 days) in patients who require supplemental oxygen and intravenous methylprednisolone 0.5 to 1 mg/kg/day for 3 days in moderate cases of COVID-19 infection with the risk of secondary infection on long-term use.<sup>[14]</sup>

Oral mucormycosis occurs infrequently when there is no other underlying systemic condition.<sup>[8]</sup> In our case, the patient had debilitating condition resulting from poorly controlled diabetes, corticosteroid therapy, and acute inflammatory immune response due to COVID-19 infection resulting in this fatal fungal disease. At present, very few studies have been reported investigating the possible correlation between COVID-19 and mucormycosis [Table 1]. The key to reduce morbidity and mortality in COVID-19 patients lies in follow-up and early diagnosis of invasive fungal infections. The timely diagnosis in our patient prevented disease progression. The red flags in mucormycosis aid in early diagnosis and timely management. The surgical debridement along with antifungal medications most probably contributed to the favorable outcome in our patient.

**Table 1: Summary of previously reported cases of rhino-orbito-cerebral mucormycosis in patients with COVID-19**

Research group	Age, gender	Diagnosis of Diabetic mellitus	Discussion/Case presentation	Outcome
Werthman-Ehrenreich <i>et al.</i> <sup>[8]</sup>	33/F	New-onset diabetes and diabetic ketoacidosis	proptosis, rhino-orbital-cerebral mucormycosis	death
Waizel Haiath <i>et al.</i> <sup>[6]</sup>	24/F	New-onset diabetes and diabetic ketoacidosis	facial pain, swelling, proptosis, and hypoesthesia.	death
Mekonnen ZK <i>et al.</i> <sup>[9]</sup>	60/M	Diabetes mellitus	facial pain, eye swelling, and conjunctival chemosis .	death
Pauli AM <i>et al.</i> <sup>[10]</sup>	51/F	type 2 diabetes mellitus	COVID-19 associated oral mucormycosis with palatal lesion	
Mehta S <i>et al.</i> <sup>[11]</sup>	60/M	longstanding diabetic (>10 years) on oral antihypoglycemic tablets	COVID-19 associated rhino-orbital mucormycosis (bilateral lid edema, thickening of frontal, maxillary, and ethmoidal sinus)	death
Tabars P <i>et al.</i> <sup>[12]</sup>	50/F	uncontrolled diabetes	COVID-19 associated rhinosinusitis mucormycosis with facial swelling and numbness	Alive
Maini A <i>et al.</i> <sup>[13]</sup>	38/M	New onset diabetes mellitus	COVID-19 associated Sino-orbital mucormycosis with facialodema, proptosis, and periorbital cellulites	patient recovered with minimal residual deformity
Revannavar SM <i>et al.</i> <sup>[14]</sup>	Middle aged/F	newly detected diabetes mellitus	COVID-19 associated Rhino-orbital mucormycosis left eye ptosis, facial pain, fever, and sinusitis.	no resolution of ptosis or ophthalmoplegia until she was discharged.
Sen <i>et al.</i> <sup>[15]</sup>	1) 46/M 2) 60/M 3) 73/M 4) 72/M 5) 62/M 6) 47/M	diabetes mellitus diabetes mellitus diabetes mellitus diabetes mellitus diabetes mellitus diabetes mellitus	with ptosis, periocular swelling, and loss of vision ptosis, pain, and limited eye movement ptosis, pain, and restricted eye movements with periorbital odema, and loss of vision ptosis, fixed gaze, and loss of vision proptosis and ophthalmoplegia	Alive Alive Alive Alive Alive Alive (loss of vision)

## Conclusion

Outlining the characteristics of patients with invasive mucormycosis associated with COVID-19 may help to better evaluate the course of fungal infection in patients with COVID-19 to reduce morbidity and mortality.<sup>[15]</sup> Evidence-based advisory in the time of COVID-19 has been suggested by Indian council of medical research (ICMR) to guide the health care workers to manage this debilitating opportunistic infection.<sup>[16]</sup> It is, thus, important to be aware of the course of invasive fungal infections in patients with post COVID-19 discharge.

## Highlights

- Mucormycosis and specific rhino-orbital is an epidemic and an opportunistic infection in COVID-19 pandemic
- Early diagnosis and management reduces morbidity and mortality
- Primary care physician's role is vital for reducing morbidity of the disease.

## Declaration of patient consent

The authors certify that they have obtained all appropriate consent forms from the patient. In the form, the patient(s) has given their consent for images and other clinical information to be reported in the journal.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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