

**ORIGINAL RESEARCH**

# Transforming Lives: A Formidable Challenge in Black Fungus Spurt

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**ABSTRACT**

**Background:** As a sequelae to the severely complicated second wave of covid-19 pandemic in India, an outburst of an opportunistic invasive fungal disease involving maxillofacial-rhino-cerebro-orbital region was observed in covid-19 recovered or recovering patients. 'Mucormycosis' or black fungus were umbrella terms used for this fulminant disease. **Aims and Objectives:** A retrospective analysis of demographic profiles and management modalities of 77 patients suffering from mucormycosis or 'black fungus' who were admitted in mucor ward especially assigned to manage black fungus cases in Shyam Shah Medical College from April 2021 to February 2022. This paper reviews our role in precise management of 15 cases who underwent maxillectomy with intensive antifungal medication with special emphasis on 2 cases and their follow-up. **Results:** 52 patients out of 77 cases had undergone endoscopic debridement of fungal hyphae and infected nasal tissue via Rigid nasal endoscope '0', '30', '70' degree 4 mm of 2.7 mm nasal endoscope. 15 cases had to undergo partial, segmental and hemi maxillectomy. 3 cases reported with aggressive ascending infection and, hence, had to undergo extenteration of eye ball. However, we could not save lives of 16 admitted patients due to rapidly spreading infection in patients with severe comorbidities. **Conclusion:** Mucormycosis was a form of rapidly spreading opportunistic infection which invited fatal consequences due to cerebral involvement. We endorse mass awareness of the symptomatology and step-wise management protocol for management of black fungus cases.

**Key words:** Pandemic, Mucormycosis, Black fungus, Maxillectomy.

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**INTRODUCTION**

The health status of the later part of 2019 and whole of 2020 and 2021 had been affected all over the world by a novel strain of severe – acute respiratory syndrome corona virus 2 (SARS-COV-2) <sup>1</sup>. In the backdrop of COVID-19, during the second wave in India, a serious angio-invasive, opportunistic fungal infection, mucormycosis has been increasingly found in COVID-19 recovered patients. <sup>2, 3</sup> Rhino-cerebral mucormycosis is the most frequent form of this disease in the craniofacial area which causes high morbidity and mortality. <sup>4</sup> The fulminant spread of this fatal disease ensured Indian Health Ministry to declare mucormycosis an epidemic. <sup>3</sup> and colloquially, it was termed as 'black fungus' in social media and various press release.

The use of corticosteroids in comorbid individuals and use of non-sterile tap water in humidifier bottles of oxygen support equipments are common risk factors leading to opportunistic infections manifesting as mucormycosis. <sup>4</sup> Fungal hyphae actually infiltrate the vascular lamina, causing infarction and necrosis as well as inflammation. <sup>5</sup> Mobility of teeth, gingival abscess,

and history of dental extractions were the common presentations of dental patients as the common sites of involvement were nose, paranasal sinuses, orbit, facial bones and cranial cavity. <sup>6</sup> Additionally, COVID 19 is known to cause hyperglycemia in suffering patients, which could predispose to promote fungal growth by damaging endothelial lining of vessels resulting in vascular insufficiency and leading to bony necrosis and fungal osteomyelitis. <sup>6, 7, 8</sup>

The pathophysiology behind the rapid spread is associated with micro-organism virulence factors and host immunity status in a determinate microenvironment. <sup>9</sup> The infection begins in the nose and paranasal area. <sup>10</sup> It spreads to orbital and intracranial structures by direct invasion or through blood vessels. <sup>11</sup> As already discussed it infiltrates the vascular lamina, causing infarction and necrosis as well as inflammation. <sup>5, 11</sup> Rhinocerebral mucormycosis in bone marrow may promote fungal growth by damaging the endothelial lining of vessels, resulting in vascular insufficiency and leading to bone necrosis. <sup>12</sup>

The fatality rate is 46% globally. <sup>13</sup> However, factors like intracranial or orbital involvement and irreversible

immune suppression increases fatality to as high as 50% to 80%.<sup>13</sup> In severe infections this rate can be close to 100%, despite various active treatments.<sup>4</sup> The main stay of treatment is the use of amphotericin B and surgical debridement. Thus, this fatal disease needs a prompt and early definitive diagnosis, aggressive surgical therapy and a high dose of antifungal therapy. Taking all official developments seriously, Madhya Pradesh government also proposed prompt protocol for eradication of black fungus. In Rewa, an institutional multidisciplinary team was organized to transform lives of affected cases in April 2021 which comprised of representatives from departments of ENT, Dentistry, Medicine, Surgery and Ophthalmology departments at Shyam Shah Medical College (S. S. M. C), Rewa.

### MATERIALS AND METHODS

During a span of 10 months, we dealt with a manifold increase in the referrals to our mucor ward. Keeping in mind the alarming spread and prognosis of this disease, we aimed to promptly analyze, treat and record our experience of managing mucor mycosis patients at S. S. M. C, Rewa. We collected information such as age,

gender, associated comorbidities like hypertension, diabetes mellitus status, time duration for reporting of symptoms after COVID-19 treatment, vaccination history, use of oxygen and/or ventilator support and steroid, multivitamin and zinc medications. The data was tabulated and examined for presence of any common risk factors. Thus, this retrospective observational study of rhino-cerebral-orbital mucormycosis cases treated at our institute between April 2021 and February 2022 was planned in department of dentistry.

### RESULTS

77 patients were admitted in mucor ward. 52 patients underwent endoscopic debridement of fungal hyphae and infected nasal tissue via Rigid nasal endoscope '0', '30', '70' degree 4 mm of 2.7 mm nasal endoscope. 15 cases underwent partial, segmental and hemi maxillectomy. 3 cases reported with aggressive ascending infection had to undergo extenteration of eye ball. However, we could not save lives of 16 admitted patients due to rapidly spreading infection in patients with severe comorbidities.

**TABLE 1: Distribution of patients according to gender**

(n= 77)

Total No. of patient	Gender	
77	Male	Female
	54	23

**TABLE 2: Correlation of patients with coronainfection and Diabetes Mellitus**

(n=77)

Total No. of patient	COVID Status	Diabetes
77	Previously positive -66 Positive on admission - 11	Diabetic-70 Non-Diabetic-07

**TABLE 3: Distribution of patients according to management modalities**

(n=77)

Total No. of patient	Procedure		
77	Endoscopic Debridement	Partial, Segmental, & Hemi maxillectomy	Extenteration
	52	15	03

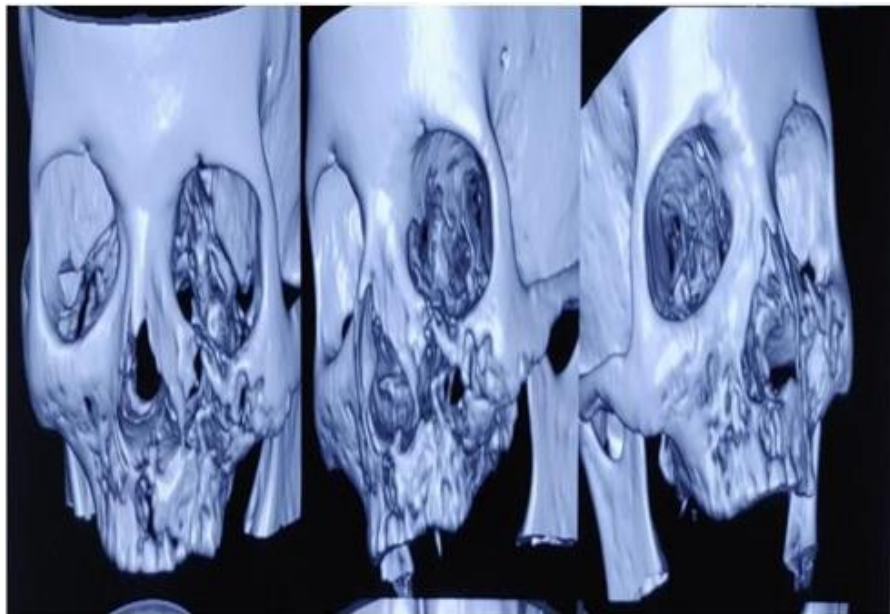
### CASE OBSERVATION CASE NO. 1

#### CLINICAL FEATURES

- An 86 years old lady with upper and lower edentulous ridges presented with complete vision loss in left eye.
- Perforating black discolored non healing palatal and vestibular ulcerations were present intraorally.
- H/O corona infection 50 days ago.
- RBS= 450 mg/dl.



**Fig 1: Preoperative clinical view**



**Fig 2: Radiological findings (3DCT Face): showing Necrosis of left maxilla**

### **RADIOLOGICAL FINDINGS**

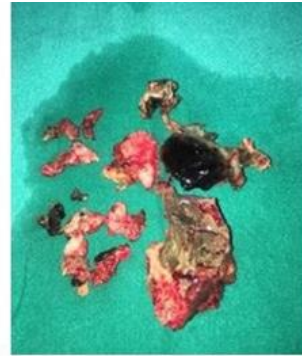
- Erosion of anterior, lateral and posterior walls of left maxillary sinus.
- Erosion of antero-lateral wall of right maxillary sinus.
- Perforation of hard palate.
- Perforation of left infra-orbital rim.
- Thickening of left maxillary sinus lining.



**(3a) Intraoperative incision line (WEBER)**



**(3b) Intraoperative (full skin thickness flap)**



**(3c) Resected necrosed left maxilla**



**(3d) Post-operative wound closure**

**Surgical management: Fig 3**

**CASE NO. 2**

**CLINICAL FEATURES**

- 43 years old male.
- Diffuse edema involving left half of face.
- Blurred vision in left eye.
- Discharging palatal sinus on left palatal sinus.
- H/O corona infection 24 days ago.
- RBS= 320mg/dl.



**Fig:4: Preoperative frontal view**



**Fig:5: Preoperative intraoral view**



**RADIOLOGICAL FINDINGS**

- Erosion of antero-lateral wall of left maxillary sinus.
- Erosion of entire left alveolar process.
- Obliteration of maxillary sinus and thickening of sinus lining.
- Perforation of hard palate.



**Fig6: Radiological findings (3DCT Face): showing Necrosis of left maxilla, permeative destruction of alveolar process left maxilla**



**(7a) Intraoperative incision line (WEBER FERGUSON)**



**(7b) Intraoperative (full skin thickness flap raised)**

**(7c) Resected necrosed left maxilla****(7d) Post-operative wound closure (Intraoral)****(7e) Post-operative wound closure (Extraoral)****Surgical management: Fig: 7****DISCUSSION**

We have found that mucormycosis is a very rapidly progressive disease which may prove fatal if timely making liver resistant to insulin.<sup>(17)</sup> They are also known to cause diabetes mellitus in patients without prior history of hyperglycemia, prior to initiation of glucocorticoids therapy. Higher blood sugar levels create a fertile broth for fungi to thrive and flourish thereby causing increased risk of secondary infections.<sup>(18)</sup> Diabetes mellitus, when combined with COVID-19 infection in patients on pathophysiology of hyperglycemia and immunosuppression which resulted in secondary fungal colonization.<sup>(15, 16, 20)</sup> It manifested in the form of rhinocerebral mucormycosis during diagnosis and treatment are not given. During the second wave of COVID-19, supportive medical therapy with glucocorticoids played a vital role as steroids are inexpensive and widely available drugs which proved to reduce mortality in hypoxemic corona

positive patients.<sup>(14, 15, 16)</sup> However, steroids caused hyperglycemia in immunocompromised individuals by COVID-19 recovery period. As per our survey, mucormycosis commonly encountered in patients after 10-15 days of COVID-19 infection which was similar to many other studies.<sup>16,19</sup> Diabetes mellitus is a key risk factor for mucormycosis in India, accounting for around 73% of all cases.<sup>20</sup> However, our study revealed a higher rate of involvement of hyperglycemia in nearly 89% of all the in-ward patients admitted in mucor ward of our centre. Infection enters the immunocompromised individuals through inhalation, ingestion and open wounds.<sup>20</sup> The clinical manifestations comprised of fever, headache, nasal or sinus congestion, swelling on one side of face, black lesions on nasal bridge, hard and soft palate ulcerations, loose teeth, gingival abscess, tenderness extending till ipsilateral temple region.<sup>12</sup> The common complaints of patients admitted in our institute

consisted of facial pain, unilateral swelling involving midface region, palatal ulcerations, black necrotic discharging extraoral and intraoral lesions of varying sizes which coincided with various other studies.<sup>21</sup> Delayed approach of patients led to orbital and cerebral spread leading to visual loss, sepsis and multiorgan failure due to dissemination of fungus into the lungs and other organs which thereby increase the morbidity and fatality.<sup>22</sup> Patients usually presented with advanced maxillary and nasal involvement and hence were advised computed tomography (CT) scans and magnetic resonance imaging (MRI). Radiographically, scans revealed erosion of sinus lying, mucosal thickening of sinuses paranasal sinus obliteration, perforation of alveolar process and hard palate. (Fig 2 and 6), which was similar to the findings of various case series.<sup>8, 11, 23</sup>

However, the diagnosis was confirmed on histological examination to tissue involved by lesion showing varying amounts of necrosis infiltrated with non-septate thin walled hyphae of large size (5-15 microns) branched at right angles appearing as ribbons. All these findings were seen in biopsy specimens from different parts of the world also.<sup>21, 24</sup> Special stains for fungus and microbiological culture from involved tissue confirmed the diagnosis and thus helped us in assessing prognosis at the time of diagnosis.<sup>21, 24, 25</sup> like it was used as a critical factor by clinicians all over India to optimize the treatment modality accordingly.<sup>25</sup>

As soon as the diagnosis was confirmed from the virology lab from our institute, the multimodal therapy was initiated which started with alleviation of preexisting morbidity conditions with glucocorticoids simultaneously with remdesivir for management of COVID-19 symptoms. Invasive mucormycosis patients were subjected to intensive antifungal therapy comprising of Amphotericin B. This drug was widely chosen as most efficacious parenteral antifungal agent in mucor cases by Ahmed and Al Thobaiti<sup>26</sup> and many others.<sup>27, 28</sup>

Injection Amphotericin B with a dose of 5mg/kg/day in 200 cc of 5% dextrose over 2-3 hours infusion were given to all 77 patients admitted in mucor ward at our center. This drug was provided by the vigorous steps of initiatives taken up by M. P. State government to all the mucor management centres throughout our state. However, the consistent supply of doses was hampered sometimes due to financial constraints and thus oral antifungal drugs like tablets of Posaconazole with a daily dose of 300 mg BD were given to all patients. Orbital involvement in 20 patients were subjected to transcutaneous retrobulbar Amphotericin B (TRAMB) injections with a dose of 1ml of 3.5 mg/ml for 3-5 days at the ophthalmological department at our centre. A recent study by Muthu et al<sup>27</sup> emphasized the importance of liposomal Amp-B given at 3mg/kg/day has similar efficacy and safer than 10 mg/kg/day dose of Amphotericin B drug as it is vaso occlusive in nature.<sup>26, 27</sup> However, liposomal variant was not available for our patients. At present, a novel drug

regimen consists of liposomal Amphotericin B in combination with either an Intraconazole or Echinocandin.

Surgical care is critical and should include debridement of all diseased and necrotic tissues as soon as possible depending on the disease progression. During our survey, functional sinus endoscopic debridement was performed in 52 patients. Combination of partial or total maxillectomy with surgical curettage was performed in 15 patients after raising full thickness flap using modified and extended Weber Fergusson incision (Fig.3 a and 7 a). Three of our patients had to undergo eye extenteration due to extensive orbital involvement. All these aggressive surgical modalities coincide with other world-wide studies.<sup>29, 30</sup> Hyperbaric oxygen therapy and iron chelating agents were started to all cases during post-surgical care. However, it was also reported to be beneficial in other surveys as they are known to aid in granulation tissue formation and rapid bone healing.<sup>31, 32</sup>

## CONCLUSION

Post Covid-19 era was associated with high incidence of secondary infections due to immune dysregulation. Rhino-orbital mucormycosis was one of the most aggressive and invasive fulminating fungal secondary infection encountered in Covid-19 patients after the second wave. The first case of Covid-19 related mucormycosis was reported in Chile.<sup>33</sup> This retrograde survey was thus planned in our department to make dental surgeons aware of the significance of early diagnosis and prompt treatment for managing cases of mucormycosis and henceforth subsequent reduction of mortality and morbidity due to cerebral involvement.

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## CONFLICTS OF INTEREST

None declared

## ETHICAL APPROVAL

Not required

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