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## Case Series

# The threat of fungus in the era of virus – Mucormycosis and Covid 19

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### ABSTRACT

As India faced a combined threat from mucormycosis and COVID 19 early diagnosis and appropriate treatment played an important role in reducing the morbidity and mortality due to the fungal infections. The current case study helped us in understanding the need to confirm the diagnosis before starting the antifungals which are highly nephrotoxic and they also helped us in the follow-up of the patient post-surgery.

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## 1. Introduction

As a human-to-human transmitted disease, coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was an emergency amidst global public health events. Besides, the diffuse alveolar damage with severe inflammatory exudation, COVID-19 patients have immunosuppression. Critically ill patients, especially those admitted to the intensive care unit (ICU) and required mechanical ventilation, or those that had a longer duration of hospital stays, even as long as 50 days, were more likely to develop fungal co-infections. COVID-19 patients with trauma, diabetes mellitus, corticosteroid use, prolonged neutropenia, also-hematopoietic stem cell implant, and organ transplant were more likely to develop mucormycosis.<sup>1</sup>

The occurrence of mucormycosis, a rare disease, in the general population was previously cited as 0.005 to 1.7 per million population. However, the incidence of mucormycosis in India was reported to be 0.14 per 1000 diabetic patients which are 80 times higher than that

reported in other parts of the world. There are multiple case reports describing mucormycosis in COVID-19 and most of these case reports were from India, especially in diabetic COVID-19 patients and those in whom corticosteroids were administered injudiciously for controlling the severity of COVID-19, leading to a higher fatality and complicated the pandemic scenario.<sup>2</sup>

Early diagnosis and accurate classification of fungal rhinosinusitis helped in deciding the treatment protocol and preventing multiple surgical procedures, and leading to effective treatment.<sup>3</sup>

In this case series, we elaborated on the KOH (potassium hydroxide) and histopathological report which helped us to treat mucormycosis patients in our clinical setup.

## 2. Case Series

As the world is experiencing COVID-19 and India had a huge surge of COVID cases with an added fear striking the Indian population – the black fungus. Mucormycosis is a normally occurring commensal and in normal times it was a rare case but during the COVID pandemic, it became an endemic of its own. In this study, we observed

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30 patients who presented to our hospital with sinusitis-like features post-COVID infection. In this series, we explain the intraoperative endoscopic features which helped us to differentiate mucormycosis from sinusitis, and the importance of tools that helped us substantiate the diagnosis such as KOH and histopathological report.

In the majority of the patients, the common feature that we encountered was that 90-95% of the patients were COVID positive and had associated co-morbidities like diabetes mellitus, cardiac complications, etc. Patients presented with symptoms similar to fungal sinusitis and were initially subjected to Diagnostic Nasal Endoscopy. They were then assessed with MRI & CT PNS to look for the involvement of sinuses and plan the operation accordingly.

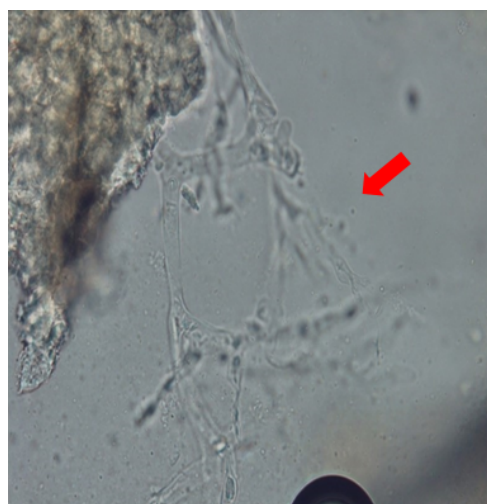
Intraoperatively majority of the patients had middle and inferior turbinate necrosis with sinus involvement, and mucopurulent discharge, two-thirds of patients had septal involvement and a third of the patients had hard palate involvement like necrosis and granulomatous lesions of the hard palate. Amongst sinus involvement most common to least are maxillary, anterior & posterior ethmoids, and sphenoids.

After debridement, the samples were sent for KOH, histopathological report (HPR), and fungal culture. KOH was positive for all the samples and HPR showed features of sinusitis and fungal filaments under a microscope. The number of patients involved in the study and their KOH & histopathological reports are displayed in a table. (Table 1), (Figure 3) according to our observation mucormycosis is more predominantly present in males who were COVID positive or recovered with associated co-morbidities which made them immunosuppressed.

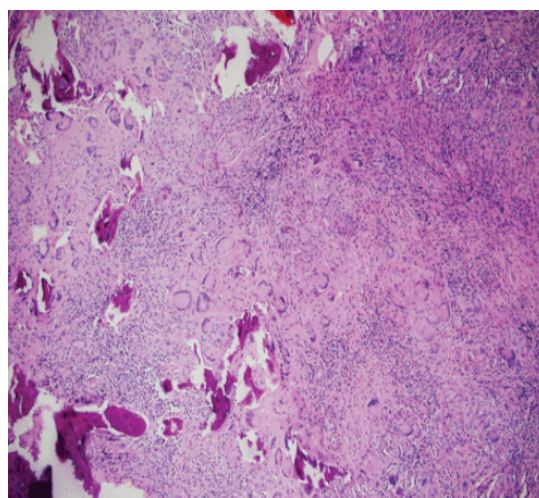
For a rapid presumptive diagnosis of mucormycosis, KOH wet mounts can be used for direct microscopy. It is used as a primary screening tool; it detects fungal elements present but may not necessarily identify the species of the fungi. Mucormycosis in KOH presents with features of aseptate hyphae. (Figure 1)

All the samples sent to histopathological examination tissue sections were fixed and stained with hematoxylin and eosin (H&E) or specialized fungal stains and appeared as ribbon-like, non-septate hyphae with wide-angle branching (approximately 90°). Tissue histopathology was dominated by inflammation which may be neutrophilic or granulomatous; inflammation seemed to be absent in a few cases, particularly in immunosuppressed patients. Invasive disease is characterized by prominent infarcts and angioinvasion. (Figure 2)

Patients were initially treated with medical management like Amphotericin B, Posaconazole, Isavuconazole, etc. Patients needed repeated debridement and after 2 negative KOH patients were discharged and followed up regularly.



**Fig. 1:** Aseptate hyphae seen in KOH wet mount as indicated by the red arrow.



**Fig. 2:** Prominent infarcts and angioinvasion of Mucormycosis.



**Fig. 3:** Inferior turbinate necrosis with sinus involvement, mucopurulent discharge.

**Table 1:** The number of patients involved in the study and their KOH & histopathological reports

<b>Patient no</b>	<b>Age</b>	<b>Gender</b>	<b>Intraoperative findings</b>	<b>KO H</b>	<b>Histopathological report</b>
1	51 year	Male	<ul style="list-style-type: none"> <li>• Left side middle turbinate blackish discoloration was present</li> <li>• In the left middle meatal region mucopurulent discharge was noted</li> </ul>	Positive	Features suggestive of mucormycosis
2	42year	Male	<ul style="list-style-type: none"> <li>• Hard palate ulcer proliferative lesion was noted</li> <li>• Left middle turbinate and inferior turbinate blackish discoloration noted</li> <li>• Middle meatal region mucopurulent discharge noted</li> </ul>	Positive	Features suggestive of mucormycosis
3	34year	male	<ul style="list-style-type: none"> <li>• Right middle meatal region mucopurulent discharge noted</li> <li>• Posterior part of the septum – discoloration +</li> <li>• Bulla ethmoidal–</li> <li>• Discoloration on +</li> </ul>	Positive	Features suggestive of mucormycosis
4	48year	Male	<ul style="list-style-type: none"> <li>• Bilateral middle turbinate discoloration was noticed</li> <li>• Posterior portion of the septum discoloration was noticed</li> <li>• Mucopurulent discharge noted in the left sphenoidal region</li> </ul>	Positive	Features suggestive of mucormycosis
5	60year	Male	<ul style="list-style-type: none"> <li>• Pale polypoidal growth noted in the left middle meatal region</li> <li>• Polypoidal growth was seen on the bilateral superior meatus and posterior part of the septum</li> </ul>	Positive	Features suggestive of mucormycosis
6	31year	Male	<ul style="list-style-type: none"> <li>• Bilateral middle meatal discharge was noted and mucopurulent discharge + in the bilateral maxilla</li> <li>• Discolouration noted over the mucosa of the hard palate</li> </ul>	Positive	Features suggestive of mucormycosis
7	40year	Female	<ul style="list-style-type: none"> <li>• Bilateral middle meatal region mucopurulent discharge noted</li> <li>• Mucopurulent discharge noted at the right sphenoidal recess</li> <li>• Discoloration noted over the mucosa of the hard palate</li> </ul>	Positive	Features suggestive of mucormycosis

Continued on next page

<i>Table 1 continued</i>						
8	37year	Male	<ul style="list-style-type: none"> <li>• Pale polypoidal growth noted in the left middle meatal region</li> <li>• Polypoidal growth was seen on the bilateral superior meatus and posterior part of the septum</li> </ul>	Positive		Features suggestive of mucormycosis
9	45year	Male	<ul style="list-style-type: none"> <li>• Hard palate ulcer proliferative lesion was noted</li> <li>• Left middle turbinate and inferior turbinate blackish discoloration noted</li> </ul>	Positive		Features suggestive of mucormycosis
10	60year	Male	<ul style="list-style-type: none"> <li>• Right middle turbinate discoloration noted</li> <li>• Posterior part of the septum – discoloration +</li> <li>• Right Middle meatal region – mucopurulent discharge noted</li> </ul>	Positive		Features suggestive of mucormycosis
11	50year	Female	<ul style="list-style-type: none"> <li>• Right Polypoidal tissue present, does not bleed on touch in the middle meatus</li> <li>• Polypoidal change in the right maxillary sinus</li> </ul>	Positive		Features suggestive of Aspergillus species
12	62year	Male	<ul style="list-style-type: none"> <li>• Right Maxillary and ethmoid sinus polypoidal tissue present</li> <li>• Mucopurulent discharge present in the right sphenoid sinus</li> </ul>	Positive		Features suggestive of mucormycosis
13	68year	Male	<ul style="list-style-type: none"> <li>• Posterior end of the septum necrosed</li> <li>• Right maxillary sinus mucopurulent discharge was present and in the ethmoid region polypoidal growth was noted</li> </ul>	Positive		Features suggestive of mucormycosis
14	65year	Male	<ul style="list-style-type: none"> <li>• Left maxillary sinus necrotic debris +</li> <li>• Right side maxillary sinus Mucopurulent discharge, necrotic tissue over the anterior wall</li> <li>• Left side maxillary sinus mucopurulent discharge +</li> </ul>	Positive		Features suggestive of mucormycosis

*Continued on next page*

<i>Table 1 continued</i>					
15	48year	Female	<ul style="list-style-type: none"> <li>• Right middle meatal region – devitalised tissue present</li> <li>• Right maxillary sinus polypoidal tissue present; necrotic debris present in the lateral wall</li> <li>• Left middle turbinate – black turbinate sign +</li> </ul>	Positive	Features suggestive of mucormycosis
16	60year	Male	<ul style="list-style-type: none"> <li>• Right inferior turbinate posterior end was devitalised; middle turbinate devitalised and slough +</li> <li>• Right maxillary sinus – fungal ball +</li> </ul>	Positive	Features suggestive of mucormycosis
17	51year	Male	<ul style="list-style-type: none"> <li>• Devitalised and polypoidal change present on both sides of the middle turbinate</li> </ul>	Positive	Features suggestive of mucormycosis
18	48 year	Male	<ul style="list-style-type: none"> <li>• Posterior end of the septum perforation +</li> <li>• Bilateral middle meatal and turbinate region – polypoidal growth +</li> <li>• Mucopurulent discharge +</li> </ul>	Positive	Features suggestive of mucormycosis
19	55year	Male	<ul style="list-style-type: none"> <li>• Right inferior turbinate – necrotic tissue +</li> <li>• Left middle turbinate – polypoidal tissue +</li> <li>• Left sphenoid- mucopurulent discharge +</li> <li>• Left ethmoid region inflammatory changes +</li> </ul>	Positive	Features suggestive of mucormycosis
20	38year	Male	<ul style="list-style-type: none"> <li>• Inflammatory and polypoidal mucosa present in the right middle meatal region</li> </ul>	Positive	Features suggestive of mucormycosis
21	52 year	Male	<ul style="list-style-type: none"> <li>• Polypoidal mucosa with mucopurulent discharge present in the left middle meatal region</li> </ul>	Positive	Features suggestive of mucormycosis
22	31year	Male	<ul style="list-style-type: none"> <li>• Bilateral middle meatal region – mucopurulent discharge +</li> </ul>	Positive	Features suggestive of mucormycosis
23	40 year	Female	<ul style="list-style-type: none"> <li>• Right maxillary region- necrotic tissue present</li> <li>• Left maxillary region – polypoidal changes and necrotic tissue present</li> </ul>	Positive	Features suggestive of mucormycosis

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Table 1 continued

24	60 year	Male	Posterior end of the septum and floor of the right nasal cavity necrotic tissue present	Positive	Features suggestive of mucormycosis
25	51year	Male	<ul style="list-style-type: none"> <li>• Mucopurulent discharge + in the left maxillary and sphenoid region</li> </ul>	Positive	Features suggestive of mucormycosis
26	42year	Male	<ul style="list-style-type: none"> <li>• Posterior end of the septum necrotic tissue present</li> <li>• Devitalised tissue presents in the right middle turbinate and</li> </ul>	Positive	Features suggestive of mucormycosis
27	60year	Female	<ul style="list-style-type: none"> <li>• Polypoidal mucosa present in the right middle meatal region and left middle meatal region mucopurulent discharge present</li> </ul>	Positive	Features suggestive of mucormycosis
28	70 year	Female	<ul style="list-style-type: none"> <li>• Bilateral mucopurulent discharge + in the middle meatal region</li> <li>• Anterolateral wall of the left maxillary sinus necrotic tissue present</li> </ul>	Positive	Features suggestive of mucormycosis
29	62year	Male	<ul style="list-style-type: none"> <li>• Posterior end of the septum necrosed</li> <li>• Right maxillary sinus mucopurulent discharge was present and in the ethmoid region polypoidal growth was noted</li> </ul>	Positive	Features suggestive of mucormycosis
30	49 year	Female	<ul style="list-style-type: none"> <li>• Left maxillary sinus necrotic debris +</li> <li>• Right middle meatal region mucopurulent discharge noted</li> <li>• Posterior part of the septum – discoloration +</li> <li>• Bulla ethmoidal – discoloration +</li> </ul>	Positive	Features suggestive of mucormycosis

### 3. Discussion

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been associated with a wide range of opportunistic bacterial and fungal infections. Recently, several cases of mucormycosis in people with COVID-19 have been increasingly reported worldwide, in particular in India. Mucormycosis is extremely rare in healthy individuals, but immunocompromised conditions predispose it. This includes uncontrolled DM with or without DKA, hematological and other malignancies, organ transplantation, prolonged neutropenia, immunosuppressive and corticosteroid therapy, iron overload or hemochromatosis, and deferoxamine therapy, severe burns, and acquired immunodeficiency syndrome (AIDS), intravenous drug abusers, malnutrition and open wound following trauma. Mucormycosis can involve the nose, sinuses, orbit, central nervous system (CNS), lung (pulmonary), gastrointestinal tract (GIT), skin, jawbones, joints, heart, kidney, and mediastinum (invasive type), but ROCM (rhino-orbit-cerebral mucormycosis) is the commonest variety seen in clinical practice worldwide.

The diagnosis and treatment of mucormycosis are challenging. Clinical approach to diagnosis lacks sensitivity and specificity as it can mimic sinusitis. Microscopic examination of the specimens either KOH or HPR aids in confirming the diagnosis to start the patient on appropriate antifungal medication and also help to follow up.<sup>4</sup>

### 4. Source of Funding

None.


### 5. Conflict of Interest

None.

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