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## RESEARCH ARTICLE

# DEMYSTIFYING POST COVID RHINO-MAXILLARY MUCORMYCOSIS FOR GENERAL DENTISTS

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### ABSTRACT

Mucormycosis, caused by saprophytic fungi is a rare opportunistic fungal infection, which has a rapidly progressive and fulminant course with fatal outcome. The most common form of mucormycosis is rhino-cerebral and is usually seen in uncontrolled diabetes mellitus or in immunocompromised patients. Recently it has been linked with the COVID 19 infection and the rapidly rising cases are alarming. It's the need of the hour to diagnose and treat the increasing cases urgently. This article deals with a clinical workflow for general dentists dealing with patients of mucormycosis. The aim of this article is to draw attention to the clinical presentation and pathogenesis of mucormycosis and to highlight the need for high degree of suspicion in its diagnosis and management.

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## INTRODUCTION

Mucormycosis is a rare opportunistic fulminant fungal infection caused by saprophytic fungi. It becomes pathogenic when associated with predisposing factors such as immunocompromised states, most commonly diabetes mellitus.<sup>1</sup> Other predisposing factors are malignancies like lymphomas and leukaemias, renal failure, organ transplant, long term immunosuppressant therapy, cirrhosis, burns and acquired immunodeficiency syndrome. And now in this COVID era it is associated with COVID 19 infection and the treatment for the same.<sup>2</sup>

**RELATION BETWEEN COVID 19 AND MUCORMYCOSIS:** COVID-19 disease has a propensity to cause extensive pulmonary disease and sub sequentialveolo-interstitialpathology. This by itself may

<sup>3</sup>Furthermore, there is an alteration of the innate immunity due to COVID-19-associated immune dysregulation characterized by decreased T cells, including CD4 and CD8 cells.<sup>4</sup> Secondly the use of medications like steroids, immunomodulators, antibiotics to treat COVID 19 infection makes the patient prone to the fungal infections.<sup>5</sup> Thirdly long term hypoxia induced by COVID 19 severely affects the immune system by suppressing its response making the host more immunocompromised. Lastly the mucorales flourish more in the state of hyperglycemia and acidosis. COVID causes hyperglycaemia due to drugs prescribed for the treatment of COVID 19 like- Tocilizumab, Steroids, etc. Also viral pancreatic involvement and stress of COVID illness along with high doses of Vitamin C can cause a state of hyperglycemia and acidosis.<sup>6</sup> Therefore judicious use of these medications is advisable.

**TYPES OF MUCORMYCOSIS:** Based on anatomic localization, mucormycosis can be classified as one of 6 forms:

- Rhinocerebral,
- Pulmonary,
- Cutaneous,
- Gastrointestinal,
- Disseminated, and
- Uncommon presentations<sup>7</sup>.

Rhinocerebral is the most common and most fatal manifestation, which is further divided into three subtypes: rhino-maxillary, rhino-orbital, and rhino-orbitocerebral. It is encountered in 60 to 80 percent of mucormycosis cases. In isolated rhinomaxillary infections, the survival rate is 82 percent, whereas prognosis is markedly poor in cerebral involvement, with a survival rate of 38 percent. The rhino-maxillary type primarily involves palate, maxilla, nasal turbinates and lateral nasal wall along with the paranasal sinuses. This article is focused predominantly on the rhino-maxillary mucormycosis.<sup>7</sup>

**COMMON CLINICAL FINDINGS:**

Rhinocerebralmucormycosis is the most distinctive form of mucormycosis.<sup>8</sup> The initial symptoms are nonspecific (e.g., headache, malaise, and lethargy). However, the characteristic features of rhino cerebralmucormycosis are summarized in

Type	Region	Clinical findings
RHINO-MAXILLARY	Intra oral findings:	Halitosis/ Intra oral pus discharge/ Ulceration & Blackening of mucosa/ Exposed palatal bone/ Sinus tract/ Loosening of teeth/ Unhealed tooth socket/ Mobility of maxilla
	Face	Facial swelling / Paresthesia / Sinus tract on face/ Discolouration of skin (necrosis)/ Infection in dangerous area of face
	Nasal findings:	Foul smelling nasal discharge/Nasal congestion/ Sinusitis/ Erythematous to violaceous to black necrotic eschar in nasal cavity
RHINO-ORBITAL + Nasal findings	Orbital findings:	Vision loss/ Peri orbital cellulitis/ Chemosis/ Exophthalmos(Proptosis)/ Ophthalmoplegia
RHINO-ORBITO-CEREBRAL + Nasal findings +Orbital findings	CNS findings:	Headache/ Cranial nerve involvement/ Rapidly progressive neurological deficit

**DIAGNOSIS OF MUCORMYCOSIS:** A clinician must think of this entity in the appropriate clinical setting and pursue invasive testing in order to establish a diagnosis as early as possible. Along with that a proper history is also important to establish the diagnosis. Specific points to be observed in history like-history of COVID infection (Immunosuppressive drugs/ Ventilatory care, etc.), Co morbid conditions: Diabetes mellitus/ Malignancy/ HIV/ Chronic kidney disease / Obesity/

Other systemic illness and local factors (H/O tooth extraction or any other oral/surgical procedure/ Head injury)<sup>9</sup>. Timely diagnosis is paramount in cases of mucormycosis. Persons with suspected rhinocerebral disease should undergo imaging of the paranasal sinuses and an endoscopic examination of

their nasal passages with biopsies of any suggestive lesions. The diagnosis of mucormycosis is established by obtaining a biopsy specimen and fungal culture of the involved tissue, and frozen tissue samples should be immediately evaluated for signs of infection.

Following investigations should be considered<sup>10</sup>

Examination	Test Type
Radiographic Examination:	CBCT, CT-PNS/Face, MRI
Direct Microscopy - KOH wet mounts	Direct microscopy of the deep nasal swab or paranasal sinus, using a KOH mount for rapid diagnosis
Lab parameters:	CBC/ ESR/ FBS, PPBS, HbA1C/ LFT/ RFT with electrolytes/ HIV, HbsAg
Biopsy in Oral cavity	Biopsy from deeper portion of extrac ted tooth socket/exposed bone
Other investigations	Nasal endoscopic examination, CSF (if indicated)

**TREATMENT:** Mucormycosis is a medical emergency. Currently a 3 pronged approach is recommended for treating mucormycosis 1. Surgical debridement 2. Antifungal therapy along with supportive medical therapy 3. Elimination or control of predisposing factors.<sup>7,11</sup>

**Surgery:** Surgical management of Rhino-maxillary mucormycosis should be initiated early in the course of treatment by an Oral and Maxillofacial surgeon along with ENT and ophthalmic surgeon when needed. Aggressive surgical debridement of involved tissues should be considered as soon as the diagnosis of any form of mucormycosis is suspected. In the case of rhino-maxillary infection, debridement to remove all necrotic tissue can often be disfiguring, requiring removal of the palate, nasal cartilage, and the orbit. In some cases, radical resection may be required, which can include partial or total maxillectomy, mandibulectomy, and orbital exenteration. However, more recent experience shows that endoscopic debridement with limited tissue removal can also be accomplished.<sup>14</sup>

**Antifungal Therapy:** For the medicinal therapy, Amphotericin B is the antifungal agent of choice. Early initiation of antifungal therapy improves the outcome of infection with mucormycosis. Amphotericin B is a polyene antifungal agent that acts by binding to sterols (primarily ergosterol) in the fungal cell membrane with a resultant change in membrane permeability. Posaconazole or isavuconazole is used as step-down therapy for patients who have responded to amphotericin B.<sup>12,13</sup> Following dosage can be given-

**Control of Predisposing Factors:** It is imperative to the treatment of mucormycosis to keep the predisposing factors under tabs. Proper control of blood sugar levels with control of electrolyte disturbance and regular renal function tests must be done. Control of other mentioned predisposing factors should also be considered.

**PROGNOSIS:** Rhinocerebralmucormycosis, as the most frequent form of mucormycosis, accounts for more than 75% of the cases.<sup>7</sup> Overall mortality from rhino-orbital-cerebral mucormycosis ranges from 25 to 62 percent, with the best prognosis in patients with infection confined to the sinuses. In isolated rhinomaxillary infections, the survival rate is 82 percent. Prognosis involves high morbidity and mortality;

survival depends on reversibility of underlying risk factors and early surgical intervention.

## SUMMARY

Early diagnosis of the disease process is crucial for the success of subsequent treatment and this is true for the post COVID mucormycosis. It will be prudent in our day today practice to look out for unusual tooth mobility, pain in jaws with no odontogenic cause, unusual swelling, etc. Making a diagnosis or proper referral during the incipient stage of a systemic disease will help in reducing the mortality and morbidity rate drastically.

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