

# Mucormycosis in Head, Neck and Face Region

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## ABSTRACT

*Mucormycosis is an opportunistic, rare fungal infection which majorly affects immune competent individuals especially in uncontrolled diabetics. Rarely, this condition affects healthy individuals. Rhizopus oryzae is the major causative organism. Cutaneous, gastrointestinal, disseminated, pulmonary, rhino cerebral are various types of mucormycosis. Rhino cerebral mucormycosis accounts for approximately half of all the newly reported cases. There have been increases in rhino cerebral mucormycosis cases in patients suffering from Coronavirus disease 2019.*

*Mucormycosis in the oral cavity manifests as palatal ulcers or the necrosis of the jaw bones. Many cases of oral mucormycosis following the tooth extraction have been observed in the patients having low immunity. Clinical observation, radiographic details, by cultivating the organism and by histologic examination of specimens is some of the factors used in making a proper diagnosis. Antifungal therapy with amphotericin B deoxycholate is suggested. Surgical debridement is needed in major cases. Bone grafting is advised if the disease causes necrosis of the jaw bones. Aggressive surgical treatment, including recurrent debridement and amphotericin B therapy increases the survival rate of these patients.*

**Key words:** Mucormycosis, Coronavirus disease 2019, Opportunistic, Fungal infection

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## INTRODUCTION

Mucormycosis is a rapidly progressive and life threatening type of fungal disease that commonly starts in the nose and paranasal sinus [1]. The organism infiltrates the arteries, forming emboli in the blood vessels which obstructs the flow of blood and followed by necrosis of organ tissues [2]. After aspergillosis and oral thrush, mucormycosis is the most common fungal infection [3]. It is responsible for nine percent of all invasive fungal infections in immune compromised individuals and 4% of all mycoses in immune competent people [4].

Some of the major predisposing factors for mucormycosis are uncontrolled diabetes mellitus, prolonged corticosteroid therapy, any organ transplantation, low neutrophil count in blood, trauma, hematologic disorders, forms of metabolic acidosis and use of deferoxamine therapy in haemodialysis patients [5,6]. Mucormycosis is rare among healthy individuals.

Histologic examination shows mucormycosis as broad, non septate hyphae with obtuse or perpendicular branching. Diagnosis is made by identifying

the distinctive hyphae in the haematoxylin and eosin dyed tissue slices, or periodic acid Schiff stain. The organisms can be grown on Sabouraud dextrose agar media.

Due to the rapid progression and high death rate, an early detection of the disease and implementation of suitable therapy is crucial for the patient's survival. A dentist may be the first practitioner to diagnose mucormycosis since the most common form of the illness affects tissues of the head, neck and mouth.

## LITERATURE REVIEW

### History

Paltauf initially described phycomycosis or zygomycosis in 1885. Baker [7,8], a pathologist named this highly aggressive *Rhizopus* infection as "mucormycosis" in 1957. In the late 1980s and 1990s, mucormycosis became more common among immune compromised people [9].

**Causative agents:** These organisms are the members of order *Mucorales* which comes under *Mucoromycotina* subphylum of the phylum *Glomeromycota* [10]. The term mucormycosis represents infection which is caused by members of family *Mucorales*. *Rhizopus oryzae* is the most common causative organism, accounting for approximately 70% of all cases [11] *Mucor*, *Apophysomyces*, *Rhizomucor* and *Cunninghamella* are the other etiological agents [12].

**Mode of spread:** The organism can enter the body through:

- Inhaling the spores
- Intake of contaminated food
- The wounded skin from trauma, injury or burns
- Through the skin by contaminated needles or catheters [5].

### Classification of mucormycosis

**Cutaneous mucormycosis:** This type of infection occurs when the organism enters the body through the skin breach that can occur following a cut, scratch, surgery, burn or other types of trauma to the skin. Characteristically, lesions begin as indurated plaques that range in colour from red to purple. These undergo necrosis and may turn into an eschar [13]. Cutaneous mucormycosis is the type of mucormycosis which is mostly observed in individuals having a healthy immune system.

**Pulmonary mucormycosis:** This type of infection arises when the fungal spores are inspired into the individual's respiratory system, which usually results in the rapid progression of pneumonia or an endobronchial illness. Mucormycosis affecting lungs is the common type of infection seen in cancer patients.

**Gastrointestinal mucormycosis:** This type of infection is comparatively rare [14]. Young children are more likely than adults to develop gastrointestinal mucormycosis. Antibiotics, surgeries, or drugs that impair an ability of the body to fight sickness put premature and poor weight new-borns under the age of a month at danger [15].

**Disseminated mucormycosis:** This develops when the disease spreads from one body part to another through the blood. The infection is mostly seen in brain; however it can even cause damage to other organs such as heart, spleen, liver and skin.

**Rhino cerebral mucormycosis:** This type of infection initially develops in the nasal sinuses when infected spores are inhaled. It can even spread to the brain. Incidence of this type of mucormycosis is approximately 30-50 percent. *Apophysomyces elegans* is thought to be the causative agent [16]. Individuals with uncontrollable increased blood glucose level and those who have undergone a renal transplant are most likely to get infected by this condition [17].

Rhino cerebral mucormycosis is categorised into two types:

- An extremely lethal invasive form that can affect the internal carotid and ophthalmic arteries.
- A less lethal rhino maxillary form that affects the greater palatine and sphenopalatine arteries, causing thrombosis and necrosis of palate [18,19].

Its clinical manifestations begin with necrosis of the palate and sinuses, then the infection progresses to the orbit before affecting intracranial structures. The patients commonly exhibits symptoms like headache,

cellulitis of face, palatal ulcer, lethargy, fever, loss of vision, difficulty in mastication, swallowing and nasal stiffness [20].

In cases of sinus inflammation in immune compromised individuals or diabetic patients, regardless of the status of control, rhino cerebral mucormycosis should be suspected [21]. Because of rapid progression of the disease, early diagnosis is very critical. Diagnosis is based on clinical findings, by growing the organism on Sabouraud's Dextrose Agar (SDA), radiographic evaluation and histological study of the specimen taken by biopsy. In the radiograph, rhino cerebral mucormycosis demonstrates as sinus thickening which has undergone tissue death, sinus inflammation and spot like sinus destruction [22,23]. A CT scan combined with an MRI scan can reveal bone damage, which can aid in determining the severity of the condition [22,24]. Sabouraud dextrose media is preferred for the culture, but histological inspection of the tissue specimen showing broad, long, and non septate hyphae, is mostly the conclusive factor [25]. The diagnosis should be confirmed by histopathological examination of specimen using various stains such as H and E, and PAS. Later done using GMS stain.

### Oral mucormycosis

Infected spores or contamination of an open wound in oral cavity are the most common causes. The clinical manifestations of mucormycosis in the oral cavity are ulcers or mucoperiosteum necrosis following an infection in the nasal cavity. Mucormycosis can enter the maxillofacial region through a mucosal ulcer or an extraction site in the mouth, especially if the person is immune compromised. Oral mucormycosis is more common in people in their fourth to sixth decades of life [26].

Although maxillary mucormycosis is more common, the source of infection is difficult to predict because these organisms were also seen cultivated from the oral cavity of healthy humans or can infect the maxilla during any minor or major surgical procedures, such as exodontia, any periodontal surgery, or abscess drainage [27]. Huang, et al. described a patient who reported with mucormycosis and necrosis of the upper jaw after a tooth extraction [28].

Even though the occurrence of mucormycosis in the mandible is rare, the cases have been reported in people having low body immunity. Bakathir reported a case of mandibular mucormycosis of an elderly patient who was newly diagnosed with diabetic mellitus and underlying lymphoblastic cancer [29].

Patients may seek preventive treatment immediately due to uncommon symptoms such as face pain, ear ache, odontalgia or pain in the sinuses.

Dental procedures may also contribute to the onset of an infection by causing a post-extraction or post curettage wound that is vulnerable to fungal infection [30].

If not treated appropriately, the infection spreads into the orbit, further into the brain causing cavernous sinus thrombosis can lead to further complications. In severe cases, it can also result in death.

## DISCUSSION

### Treatment

Early identification, treatment of the underlying predisposing factors, immediately performing excisional surgery of affected tissues, and treating patient with aggressive anti-fungal therapy are all key components of successful mucormycosis management. There are currently no established treatment regimens for mucormycosis. Amphotericin B deoxycholate is the recommended anti-fungal drug for mucormycosis, which has a maximum tolerable dose of 1 to 1.5 mg/kg/day [31]. Renal toxicity is generally always a complication of the amphotericin B treatment. The toxicity is mostly reversible and it is directly proportional to the serum concentration and overall drug dosage. If the blood creatinine level exceeds above normal level, most practitioners suggest holding of drug. Alternate day therapy has been indicated to minimise the severity of azotemia. Duration and the drug dosage of amphotericin B should be personalized for every case. The response of the patient to treatment is considered to be the most crucial factor.

A study compared survival rates of patients with and without wide surgical debridement which concluded rise in survival rate up to 78 percent in patients undergoing surgical debridement whereas 57.5% in patients not undergoing surgical debridement [32]. According to Pillsbury and Fischer [33], surgical debridement and early amphotericin B therapy increased survival rate of a patient up to 85%.

Similarly, Blitzer, et al. [32] reported an 89% survival rate among diabetics treated with amphotericin B and radical surgery. Early in course of mucormycosis, tissue necrosis is common. High susceptibility to necrosis should be managed early with surgical removal of the infected tissues. The debridement may sometimes require radical approaches, including surgeries such as maxillectomy, mandibulectomy, and the orbital surgery. Mucormycosis causing necrosis of the jaw bones or palatal perforation usually needs bone grafting [34] or flap surgeries [26]. The fungus thrives in necrotic tissue and amphotericin B is unable to reach the fungus in these tissues due to arterial thrombosis. Thus, surgical debridement eliminates the source of infection that cannot be properly treated by anti-fungal therapy alone.

### Mucormycosis and COVID-19

An increasing number of cases of rhino cerebral mucormycosis have been observed in individuals suffering from coronavirus disease 2019, particularly in India. Both COVID-19 [35,36] and mucormycosis have diabetes mellitus as a key risk factor. According to a recent study done in year 2019-2020, occurrence of

mucormycosis ranged from 0.005 to 1.7 per million people worldwide, with a prevalence roughly 80 times greater in India than in other developed countries [37,38]. Prolonged usage of corticosteroids has been linked with various fungal infections such as candidiasis, mucormycosis, and aspergillosis, even a short term treatment of corticosteroid therapy has lately been observed to link with mucormycosis mainly in individuals who are systemically involved with systemic diseases like diabetes mellitus, leukemia, and lymphoma, AIDS, hypertension and others. 46% of the patients had received corticosteroids within a month before the diagnosis of mucormycosis in the European confederation of medical mycology study [39].

## CONCLUSION

Rhino cerebral mucormycosis is a disease that dentists should be aware of, especially in immune competent patients. Unusual presentation such as pain of sinus and face, or tooth ache of the healthy teeth must alarm the clinician. Early systemic amphotericin B therapy combined with extensive surgical surgery prevents infection from spreading to key organs and improves patient's survival rate. Anyone with an underlying medically compromised condition with osteomyelitis of the jaw bones must be checked for fungal infections. In these patients, treating underlying conditions and early identification, as well as using an intensive treatment approach increases their chances of survival.

Early detection of oral mucormycosis is very crucial. Further studies needs to be done to determine the source of oral mucormycosis occurring after tooth extraction.

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