



MUCORMYCOSIS IN DENTISTRY

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ABSTRACT

Mucormycosis is a fungal infection, caused by mucorales which are filamentous molds, found predominantly in the immune-compromised patients. Mucorales have a natural susceptibility which are killed by human phagocytes, that eventually exaggerates its virulent power. Some belonging genera of mucorales are rhizopus, lichtheimia mucor, cunninghamella, rhizomucor. This article will dwell into the classification, signs & symptoms, oral manifestations, risk factors, pathogenesis, stages of mucormycosis, early diagnosis and treatment which will reduce the mortality and morbidity of fatal fungal infection. The prevalence of the disease states that about 70-75% higher cases are recorded in India in comparable to all the other countries globally. It is also seen that only 6 to 10 % of the cases occur in the subjects with no underlying disease or cause as in contrast it usually affects immunocompromised human bodies with poorly controlled diabetes and hypertensive patients. The fungi invades the blood vessels leading to thrombosis, necrosis and infarction of the tissue. Mucormycosis can progress rapidly and it may delay the initiation of the treatment in even few days and may lead to worst consequences. The primary line of treatment is amphotericin B, the newer triazoles, posaconazole and isavuconazole can be effective in patients who are resistant towards the amphotericin B. Early surgical excision plays a pivotal role in the management of the mucormycosis.

KEYWORDS : COVID-19, dentists, maxillary sinus, diabetes mellitus, opportunistic infections

INTRODUCTION

Mucormycosis, also known as black fungus,⁽¹⁾⁽²⁾ is a serious fungal infection that comes under fulminant fungal sinusitis,⁽³⁾ usually in people who are immunocompromised⁽⁴⁾⁽⁵⁾ It is curable only when diagnosed early.⁽³⁾ Symptoms depend on where in the body the infection occurs.⁽⁶⁾⁽⁷⁾ It most commonly infects the nose, sinuses, eyes and brain resulting in a runny nose, one-sided facial swelling and pain, headache, fever, blurred vision, bulging or displacement of the eye (proptosis), and tissue death.⁽⁸⁾⁽⁹⁾ Other forms of disease may infect the lungs, stomach and intestines, and skin.⁽⁹⁾

It is spread by spores of molds of the order Mucorales, most often through inhalation, contaminated food, or contamination of open wounds.⁽¹⁰⁾ These fungi are common in soils, decomposing organic matter (such as rotting fruit and vegetables), and animal manure, but usually do not affect people.⁽¹¹⁾ It is not transmitted between people.⁽⁷⁾ Risk factors include diabetes with persistently high blood sugar levels or diabetic ketoacidosis, low white blood cells, cancer, organ transplant, iron overload, kidney problems, long-term steroids or use of immunosuppressants, and to a lesser extent in HIV/AIDS.⁽¹²⁾⁽⁴⁾

Classification

Generally, mucormycosis is classified into five main types according to the part of the body affected.⁽⁷⁾⁽¹⁴⁾ A sixth type has been described as mucormycosis of the kidney,⁽⁸⁾ or miscellaneous, i.e., mucormycosis at other sites, although less commonly affected.⁽¹⁴⁾

- Sinuses and brain (rhinocerebral); most common in people with poorly controlled diabetes and in people who have had a kidney transplant.⁽⁷⁾
- Lungs (pulmonary); the most common type of mucormycosis in people with cancer and in people who have had an organ transplant or a stem cell transplant.⁽⁷⁾
- Stomach & Intestines (gastrointestinal); more common among young, premature, and low D

Sign & Symptoms

Signs and symptoms of mucormycosis depend on the location

in the body of the infection.⁽⁹⁾ Infection usually begins in the mouth or nose and enters the central nervous system via the eyes.⁽¹⁵⁾

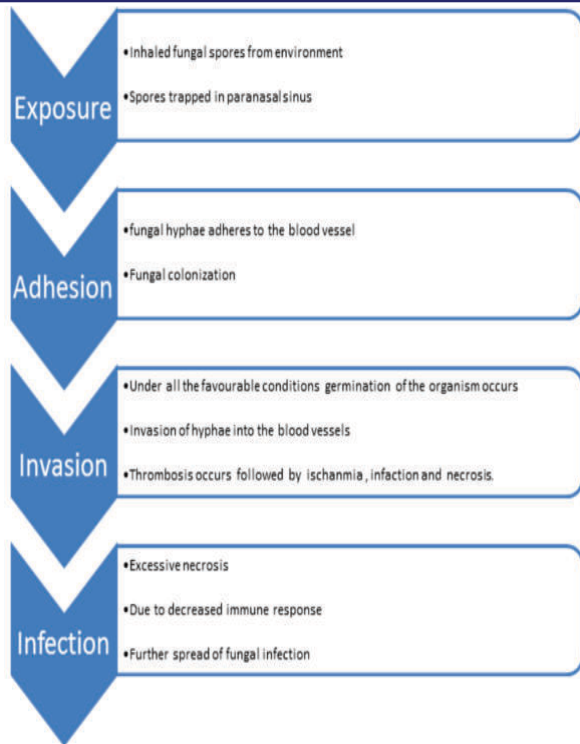
If the fungal infection begins in the nose or sinus and extends to brain, symptoms and signs may include one-sided eye pain or headache, and may be accompanied by pain in the face, numbness, fever, loss of smell, a blocked nose or runny nose. The person may appear to have sinusitis.⁽¹⁶⁾ The face may look swollen on one side, with rapidly progressing "black lesions" across the nose or upper inside of mouth. One eye may look swollen and bulging, and vision may be blurred.⁽⁹⁾⁽¹⁶⁾⁽¹⁷⁾

Fever, cough, chest pain, and difficulty breathing, or coughing up blood, can occur when the lungs are involved.⁽⁹⁾ A stomach ache, nausea, vomiting and bleeding can occur when the gastrointestinal tract is involved.⁽⁹⁾⁽¹⁸⁾ Affected skin may appear as a dusky reddish tender patch with a darkening centre due to tissue death.⁽⁵⁾ There may be an ulcer, and it can be very painful.⁽¹⁵⁾⁽¹²⁾⁽⁵⁾

Invasion of the blood vessel can result in thrombosis and subsequent death of surrounding tissue due to a loss of blood supply.⁽¹²⁾ Widespread (disseminated) mucormycosis typically occurs in people who are already sick from other medical conditions, so it can be difficult to know which symptoms are related to mucormycosis. People with disseminated infection in the brain can develop changes in mental status or lapse into a coma.⁽¹⁹⁾⁽²⁰⁾

Predisposing Factors¹³

- Renal failure
- Diabetes mellitus
- Liver failure
- Leukemia
- Organ transplant
- AIDS/HIV
- Tuberculosis
- Prolonged treatment with immunosuppressive therapy
- Trauma
- Untimely use of steroids.



Pathogenesis¹³

Oral Manifestation¹³

- Halitosis
- Intra oral pus discharge
- Palatal eschar
- Exposed palatal bone
- Sinus tract formation
- Unexplained loosening of teeth
- Mobility of maxilla
- Ulcerations on palate
- Erythematous lesion on tonsillar region
- Blisters and nodule formation on lips
- Desquamative gingivitis with sudden onset

STAGES OF MUCORMYCOSIS¹³

STAGE 1- INVOLVEMENT OF NASAL MUCOSA

- limited to middle turbinate
- Involvement of inferior turbinate
- Involvement of nasal septum
- Bilateral nasal mucosal involvement

STAGE 2- INVOLVEMENT OF PARANASAL SINUSES

- One sinus involvement
- Two ipsilateral sinuses
- More than two ipsilateral sinuses
- Bilateral paranasal sinuses involvement or involvement of zygoma or mandible

STAGE 3- INVOLVEMENT OF THE ORBIT

- Nasolacrimal duct ,medial orbit and vision is unaffected
- Diffuse orbital involvement with vision unaffected
- Central retinal artery or ophthalmic artery occlusion or superior ophthalmic vein thrombosis, involvement of superior and inferior orbital fissure, loss of vision
- Bilateral orbital involvement.

STAGE 4- INVOLVEMENT OF THE CNS

- Focal or partial involvement of cavernous sinus and cribriform plate
- Invasion beyond cavernous sinus, involving skull base ,internal carotid artery occlusion and brain infarction.
- Multifocal and diffuse CNS disease.

Diagnosis As seen in Table 1.1¹³

Investigations	Diagnostic features
Imaging Techniques	
Radiograph	Opacification in sella in case of mucormycosis. Aspergillus shows radiological coarctation in radiograph. ¹⁸
Computed Tomography (CT) Lung	Mucormycosis shows reverse halo sign (RHS) - an area of ground glass opacity surrounded by a ring of consolidation on thoracic CT, or vessel occlusion on CT pulmonary angiography. ^{19,14}
CT Cerebral	Involvement of sinuses and extent of bony destruction can be examined. ¹⁴ Foci of hyperdensity in the affected sinus on CT scans are highly suggestive of fungal disease. CT is 100% sensitive and 78% specific in the diagnosis of sinusoidal mycosis. ¹⁸
Magnetic Resonance Imaging (MRI) Cerebral	Involvement of Brain and orbit ¹⁴
Cone Beam Computed Tomography (CBCT) [Figure 2]	In CBCT the mucormycosis is depicted as erosion due to osteolysis of bone, perforation of palate to the maxillary sinus and extent of mushrooming of the infection can be seen in three-dimensional view. ^{14,17}
Laboratory Techniques	
Culture and Microscopy	Mycocoles in potato dextrose agar and Sabouraud grown upto 3-7 days when incubated at 25° ¹⁸
Serology	Impressions: Creamy white or greyish black colour. ¹⁴ Galactomannan, 1,3-β-D-glucan in Pointe for mucormycosis ELISA assays immunoblot and immunodiffusion tests are sensitive towards Mycoales and mucormycosis. ¹⁸
Biopsy	
Direct Microscopy	Stained with fluorescent brightener calcofluor white or bluishophor. ¹⁴
Histopathology	Hematoxylin-eosin (HE), periodic acid-Schiff stain (PAS) or Gomori-Gomori's methenamine-silver staining shows broad, non-septate type of hyphae with the pathognomonic nature of hyphae branching at right angles. ^{19,14} The 90° branching angle of Mycoales in tissue versus 45° branching angle of septate mould aspergillus can be difficult to differentiate due to interstitial pressures exerted on the fungi by the tissue during processing. Thus the wider and angular (oblong like) nature of the hyphae are more reliable distinguishing characteristics than septations and angle of branching. Acute lesions: Hemorrhagic infarction, coagulation necrosis, angioinvasion, infiltration by neutrophils and perivascular invasion are characteristic features. Chronic lesions: Presence of giant cells, and deeply eosinophilic material surrounding the pathogen is seen (Splendore-Hoeppli phenomenon) ¹⁴
Molecular staining	Immunohistochemical staining using specific antibodies to distinguish between Mycoales and Aspergillus. Polymerase Chain reaction on either fresh or formalin-fixed paraffin-embedded tissue shown to be highly specific, although it requires in-house validation. ^{18,19} AND PRIMARY CARE

Differential Diagnosis

Other filamentous fungi may however look similar.^[21] It may be difficult to differentiate from aspergillosis.^[22] Other possible diagnoses include anthrax, cellulitis, bowel obstruction, ecthyma gangrenosum, lung cancer, clot in lungs, sinusitis, tuberculosis and fusariosis.^[23]

Prevention

Preventive measures include wearing a face mask in dusty areas, washing hands, avoiding direct contact with water-damaged buildings, and protecting skin, feet, and hands where there is exposure to soil or manure, such as gardening or certain outdoor work.^[24] In high risk groups, such as organ transplant patients, antifungal drugs may be given as a preventative.^[24]

Comprehensive Management As seen in Table 1.2¹³

Speciality	Role in management
Role of Oral Physician and Radiologist	Administration of systemic antifungal medication is the first line of treatment. Amphotericin-deoxycholate and lipid complex which are polyenes are primary therapeutic agents for mucormycosis, however it is prudent to monitor electrolyte levels as polyenes causes imbalance in potassium levels. ¹² Posaconazole which is structurally similar to itraconazole, has generally been considered the second line or salvage therapy for patients intolerant to amphotericin B. ¹⁸
Role of Oral and Maxillofacial Surgeon	Although antifungal medications are administered, surgical debridement necessary in many cases to prevent further progression. ^{12,18} Functional endoscopic sinus surgery (FESS) under general anesthesia for resection/reconstruction of maxilla, total curectomy, and complete debridement of the maxillary antrum are the surgical procedures performed by Oral and Maxillofacial Surgeons. ^{19,20} Recently, Hyperbaric oxygen therapy is employed that suppresses fungal growth by reducing tissue hypoxia and acidosis, which are ideal growth factors for the fungus and also have found to increase the survival rate by 34%. ¹⁸
Role of Periodontist	Role of Periodontist in diagnosis and management of mucormycosis is significant as most of the systemic and immunocompromised conditions are reflected in the groups of the oral cavity. Diabetes Mellitus, Leukemia, drug induced gingival hyperplasia due to immunosuppressants are all reflected in the periodontium. McDermott et al. ²⁵ have reported a case on periodontal mucormycosis in a leukemic patient, which was diagnosed and treated appropriately thereby preventing its spread to the palate and adjacent structures.
Role of Prosthodontist	Surgical avulsion despite being a life saving procedure can cause large defects over the affected areas, and hampers the individual's lifestyle due to cosmetic and functional concerns. Surgical reconstruction is necessary to rehabilitate the defects, however Prosthetic rehabilitation is widely practiced due to various advantages. The inherent advantages of Prosthetic rehabilitation are that it is an ideal treatment for aged and medically compromised patients, which reveals multiple sagittal, insurmountable, easy to cover large defects and with predictable outcomes. ²⁶ Mandibular defects without orbital involvement is rehabilitated with Hollow Ball Obturator. Complex facial defects involving the orbit are corrected using the hollow ball obturator with orbit. Retention of the obturator involving the orbit is gained using a spectacle (eyeglass) frame, extensions from the obturator, magnets and buttons, engaging tissue undercut, adhesives or osseointegrated implants. ²⁶ At times, using magnets and buttons may cause movement of the prosthesis if these are multiple mandibular defects and in such cases, heat cylinders and button are used to retain the defect. In case of dentulous patients, the sagittal focuses on using as many teeth as possible for the purpose of retention of the prosthesis. ²⁶ Complete submaxillary resection is done in cases involving bilateral maxilla and sinus. In these cases, the patient becomes completely edentulous with an open communication between the oral and the nasal cavity thereby affecting function, phonetics, and esthetics. Operative, Flip-operative, and post-operative prosthesis are fabricated in these cases. A surgical obturator is fabricated to be used during surgery as a certain obturator is fabricated and utilized during the wound healing phase and finally a definitive obturator is constructed after 2-3 months. A palatal/lingual labial obturator can be used if the patient is edentulous. ²⁶ AND PRIMARY CARE

CONCLUSION

Mucormycosis is a rapidly spreading disease caused by mucorales, well spring of highly resistant species. It needs to be diagnosed as soon as possible to prevent the consequence of the involvement of vital organs which can be proven fatal to the life. A multispeciality team of doctors needs to be there for the proper eradication and elimination of the damaged tissue or organ from the body and thus saving the life and decreasing the mortality rate. A group of triazoles are the most potent antifungal agents that eases the pain and pressure and offers patients much needed and timely therapy options. Simple procedures such as saline nasal irrigation and anti fungal solvents are effective in stopping the further spread and improving quality of life in least affected individuals. The healthcare workers should focus on early detection and rapid management of the mucormycosis. So, that the society can live free from the deadly infections.

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