

Mucormycosis: From Bench to Bedside....

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Introduction:

Mucormycosis is a rapidly progressive, often fatal, opportunistic infection caused by fungi belonging to the class Zygomycetes/ Phycomycetes, order mucorales; which usually begins in the nose and paranasal sinuses[1]. Mucormycosis was first described by Paltauf in 1885 in human beings.

From past two decades the condition is being reported with increasing frequency. In dentistry, this condition gains increasing interest because of its first manifestation in the facial and oral tissue. It remains the challenge for the dentist to diagnose and treat the lesions of mucormycosis in the dental chair. The fungi are ubiquitous. Usually harmless and become pathogenic in man under certain conditions.

Etiology

Mucormycosis is caused by organisms that belong to order Mucorales. Five genera in the order Mucorales are rhizopus, absidia, mucor, cunninghamella and saksenaea². These fungi are typically found in the soil and in association with decaying organic matter such as leaves, compost piles or rotten wood, bread molds, decaying fruits and vegetables.

Historical facts:

Mucormycosis was first described by Paltauf in 1885 in human beings. From past two decades the condition is being reported with increasing frequency. In dentistry, this condition gains increasing interest because of its first manifestation in the facial and oral tissue. Mucormycosis generally occurs in people with weakened immune

systems but it can occur (rarely) in people who are otherwise healthy.

Risk factors

Risk factors for developing mucormycosis includes³:

- Uncontrolled diabetes
- Cancer(MALIGNANCY)
- Organ /hematopoietic stem cell transplant (HSCT),
- Neutropenia (low white blood cells)
- Skin trauma (cuts, scrapes, punctures, or burns)
- Malnutrition

Spread of mucormycosis

Organisms enter through the nose or mouth from inhaled dirt particles and occasionally invade the orbit or open wounds. Infection usually begins in nasal mucosa or palate and spreads into the paranasal sinuses, skin of the face, cribriform plate and brain, either by direct extension or through vascular channels[4]. The fungi A invades the arteries, leading to thrombosis that subsequently causes necrosis of hard and soft tissues.

Different forms of mucormycosis

Mucormycosis usually presents as an acute infection and manifests as different forms as rhinocerebral (most common), pulmonary, gastrointestinal, cutaneous or disseminated form⁵.

Types of Rhinocerebral Forms:

1. A highly fatal rhino-orbito-cerebral form which is invasive and may involve the ophthalmic and internal carotid arteries.

A less fatal rhino-maxillary form which involves the sphenopalatine and greater palatine arteries, resulting in thrombosis & necrosis of the turbinate & palate[6].(fig.1)

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Fig.1: Rhino-maxillary mucormycosis

Oral manifestations

Oral manifestations are usually in the palate where ischemic necrosis of the mucoperiosteum with bony denudation. The ulcers of mucormycosis have also been reported on the gingiva, lips, alveolar ridge, cheeks, tongue and mandible⁷.

How do I know if I have mucormycosis ?

If you have symptoms of the infection, you should see your health care provider. A health care provider can diagnose mucormycosis by taking a sample of infected tissue and sending it to a laboratory. There, the sample will be examined under a microscope.

Treatment of mucormycosis

Mucormycosis needs to be treated with antifungal medication. These medications are given by mouth or through a vein. Skin infections with the fungus may require surgery to cut away the infected tissue. The successful treatment of mucormycosis requires 4 steps³:

- (1) Early diagnosis;
- (2) Reversal of underlying predisposing risk factors, if possible;
- (3) Surgical debridement where applicable;&
- (4) Prompt antifungal therapy

(1) Early diagnosis²

Various methods of early diagnosis are as follows:

- Diagnosis from direct examination and histological sections of clinical material.
- Isolation & Culture requirements
- PCR
- CT scan
- MRI

Diagnosis from direct examination in 10% KOH:

Scrapings taken from the suspected lesion shows the presence of thick-walled, aseptate, and refractile hyphae 6 to 15 μ m in diameter, with some hyphae being swollen and distorted, is indicative of the presence of Mucorales fungi^[2].(fig.2)

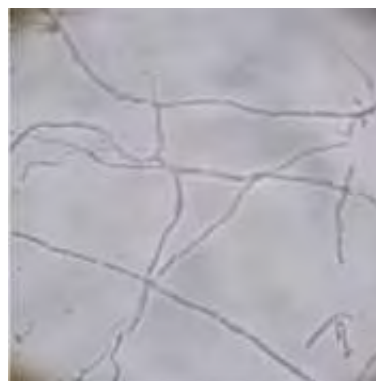


Fig.2 : Thick-walled, aseptate and refractile hyphae

Histopathology of mucormycosis

Histological sections shows acute suppurative inflammation with focal areas of granulomatous inflammation. There are aseptate hyphae 6 to 50 μ m in diameter, branching at 90°. The hyphae invade the adjacent blood vessel walls, producing thrombosis and infarction^[1]. Routinely Hematoxylin & eosin (H&E) stains can be used. thus Histopathology remains the gold standard.(fig.3)

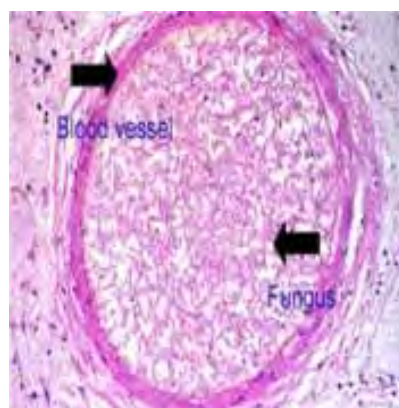


Fig.3 mucormycosis involving the blood vessel. (H&E) stains

Importance of Special stains in diagnosis of mucormycosis:

Staining with Grocott-gomori Methenamine Silver is best,(fig.4) though Periodic Acid-schiff (PAS)(fig.5) & Calcofluor white can give better results¹.

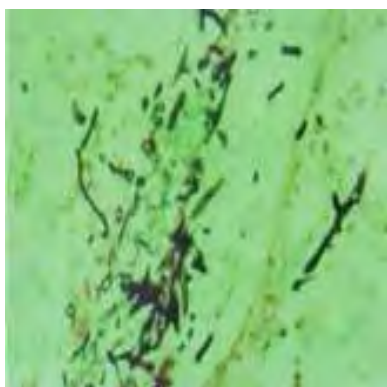


Fig.4 Non septate mucormycotic hyphae observed under Grocott's modified silver methenamine staining technique.

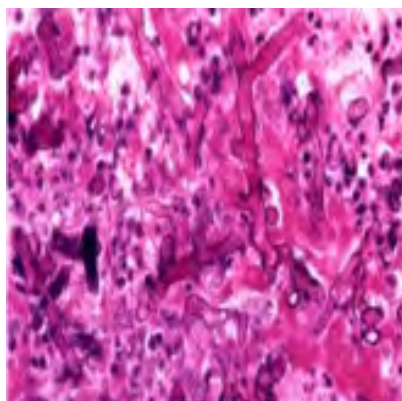


Fig.5 large, non-septated hyphae with 90 degree angle-branching and non-parallel walls(PAS)

- CT & MRI may demonstrate erosion or destruction of bone and may help to delineate the extent of the disease.(fig.6)



Fig.6 : Patient with rhinocerebral mucormycosis showing extensive skeletal defects.

(2) Reversal of underlying predisposing risk factors,if possible;

- By lowering or stoppage of immunosuppressants drugs such as corticosteroids.

(3) Surgical debridement may be critical for complete eradication of mucormycosis. where applicable as,

- Blood vessel thrombosis and resulting tissue necrosis during mucormycosis can result in poor penetration of antifungal agents to the site of infection.
- with high dose intravenous amphotericin B therapy (5mg/kg IV daily).

(4) Prompt antifungal therapy[8]

- Lipid formulations of amphotericin B (LFAB) have evolved as the cornerstone of primary therapy for mucormycosis.
- Posaconazole may be useful as salvage therapy,
- Combination LFAB- echinocandin therapy may improve survival during mucormycosis.

Differential Diagnosis[3]

Differentiation from *Aspergillus* and *Candida* must be made on histological section.

1. *Aspergillus* and *Candida* do not take H&E stain. *Aspergillus* has septate, narrow, acutely branching hyphae with smooth, parallel walls.
2. *Candida* has septate, narrow hyphae in tissue, with club-shaped pseudohyphae and yeast forms present.
3. Spreading sinusitis or
4. Facial cellulitis with palatal ulcer
5. Squamous cell carcinoma,
6. Chronic granulomatous infection,
7. Wegener's granulomatosis and
8. Other deep fungal infection.

Future directions

New radiographic, molecular, and antigenic tools are required to improve early detection and therapeutic monitoring. New antifungal agents and combinations of existing agents should be further explored in the laboratory and in clinical trials.

Conclusion

Death is a common outcome of the disease (30-50%). As the diagnosis to treatment interval increases & survival

rate decreases, so early and prompt diagnosis is must. Hence early, aggressive & with all modalities of treatment remains the goal and challenge for the dentist in treating the patients with mucormycosis.

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