Content available at: https://www.ipinnovative.com/open-access-journals

The Journal of Dental Panacea

Journal homepage: https://www.jdentalpanacea.org/

Review Article

Mucormycosis-"The deadly fungal disease" and its prosthodontic management

Rohit Raghavan[1], Shajahan PA[1], Shilpa RS[1,*]

[1] *Dept. of Prosthodontics, Royal Dental College, Palakkad, Kerala, India*

ARTICLE INFO

Article history:
Received 08-03-2022
Accepted 05-04-2022
Available online 20-06-2022

Keywords:
Mucormycosis
Clinical forms
Antifungal therapy
Prosthodontic Rehabilitation
surgical obturator

ABSTRACT

Coronavirus Disease 2019 (COVID-19), during the second wave in early 2021 has created devastating chaos. Adding more burden to such a challenging situation, mucormycosis an angioinvasive, fulminant fungal infection has seen a sudden surge in patients with COVID -19. Mucormycosis commonly affects immunocompromised patients. Early diagnosis, elimination of the predisposing factor, and surgical debridement, along with antifungal therapy, are the key factors responsible for successful treatment and patient survival. Mucormycosis is presented by various clinical forms. The present paper reviews about the clinical presentation, diagnosis and various treatment modalities for managing mucormycosis-"the deadly fungal disease".

1. Introduction

Mucormycosis is an aggressive fungal infection caused by saprophytic aerobic fungi-Mucorales which belongs to the class Phycomycetes.[1] Hence it is also called as Phycomycosis or black fungal disease. Nose and paranasal sinuses of the head and neck region are the commonly involved sites.[2]

This fungal disease has been a widespread in COVID outbreak.[3] It is an opportunistic infection associated with immunocompromised condition and becomes significant when the body defense mechanism becomes weaker.

Mucormycosis is an angioinvasive infection. Immunocompromised patients are highly prone to develop this disease and its complications, where in the spores of the fungi colonize in upper respiratory tract, germinate, develop hyphae and invade blood vessels and surrounding tissues.[2] The devitalized tissue due to thrombosis and tissue necrosis leads to continued fungal growth thus making it aggressive and fateful.

* *Corresponding author*.
E-mail address: rsshilpa123@gmail.com (Shilpa RS).

2. C linical forms of Mucormycosis

The various clinical forms of mucormycosis are– rhinocerebral, pulmonary, gastrointestinal, cutaneous, and disseminated.[4]

1. **Rhinocerebral**: The infections spread from sinus to the brain in rhinocerebral mucormycosis. It is seen in patients with renal transplants or uncontrolled diabetic patients.
2. **Pulmonary**: The lung or pulmonary mucormycosis is observed in the organ transplant or cancer patients.
3. **Gastrointestinal**: The gastrointestinal mucormycosis is affected more common in children than adults. The clinical situations that compromise the immune response of children by the extensive use of antibiotics or surgeries are affected by gastrointestinal mucormycosis.
4. **Cutaneous**: The skin or cutaneous mucormycosis occurs due to the outbreak in skin or cutaneous tissues.
5. **Disseminated**: The disseminated mucormycosis occurs through the infection spreading through the bloodstream. The brain and the other vital organs such

https://doi.org/10.18231/j.jdp.2022.014

as heart and spleen are the primary organs affected by this variant.

The population who are under risk involve diabetes, organ transplants, long-term corticosteroid use, excessive iron, and conditions that decrease immunity. The disease is developed due to the contact with the spores and weaker immune responses which can increase the widespread possibility of the disease.[3] These organisms proliferate rapidly, as they gain access to the mucous membranes and invade the nearby blood vessels causing vascular thrombosis and subsequent necrosis, thereby leading to tissue destruction and non-healing necrotic ulcers with underlying bony destruction.[5]

Therefore, it demands maximum attention in patients who are previously infected with COVID-19, for early diagnosis and surgical intervention in order to cease the propagation of infection to the vital organs of the body. Mucormycosis is diagnosed with the symptoms, history, examination, and laboratory investigations. The supportive investigations includes computed tomography scan of sinus, fungal culture, and tissue biopsy. The treatment required the control of any metabolic diseases, antifungal medications, and surgical resection of affected tissues.

3. Clinical Manifestations

Although, patients infected with mucormycosis are not encountered frequently in general dental practice, they may consult dentists during the early stage of the disease when the symptoms overlap with that of dental origin like dental pain, periorbital cellulitis or mucosal sloughing.[6] Sometimes, palatal ulceration alone may be the pathognomonic sign, that leads to the diagnosis of mucormycosis.[7]

Therefore, it demands consideration of mucormycosis as a differential diagnosis, when a patient shown with unilateral proptosis, swelling of the periorbital and perinasal tissues, dilation and fixation of the pupil, paranasal sinusitis, and cranial nerve involvement.

Considering the various clinical forms of mucormycosis, rhinocerebral is the most predominant one. It accounts for the one third to half of the reported cases. It is again divided as rhinoorbitalcerebral (Type 1) (more fatal) and rhinomaxillary form (Type 2) (less fatal), involving ophthalmic with internal carotid arteries and sphenopalatine with greater palatine arteries respectively.[8]

In 1950, Smith and Krichner have introduced certain criteria for the clinical diagnosis of mucormycosis that are yet found to be the gold standard and are as follows.[9]

1. Dark colored, blood-tinged, nasal discharge on the side where facial pain is elicited, of brief duration.
2. Soft periorbital or perinasal swelling that progresses to induration and discoloration. (With progressive vascular occlusion).
3. Proptosis of the globe and ptosis of the lid, fixation and dilation of the pupil, limitation of global mobility.
4. Progressive lethargy, in spite of good response to diabetic therapy.
5. Black necrotic turbinates, easily mistaken for dried blood.
6. Loss of corneal reflex and onset of facial weakness, usually observed, late in the course of invasion.

Nithyanandam et al., in 2003 put up three distinct clinical stages based on the signs and symptoms and degree of disease progression. Those clinical stages are as follows.[10]

Clinical stage 1: Signs and symptoms of Sino-Nasal disease.

Clinical stage 2: Signs and symptoms of Rhino-Orbital disease.

Clinical stage 3: Signs and symptoms of Rhino-Orbito-Cerebral disease.[10]

Clinical classifications aid in suitable surgical as well as prosthetic rehabilitative treatment planning to provide comprehensive medical care to the patient.[11]

Table 1:

Clinical stage	Nomenclature	Symptoms	Signs
Stage 1	Sino-nasal	a. Headache b. Nasal discharge c. Facial pain and swelling d. Fever	a. Nasal crusting b. Necrosis of turbinates c. Palatal necrosis and perforation
Stage 2	Rhino-orbital	a. Loss of vision b. Diplopia	a. Conjuntival chemosis b. Proptosis, ptosis and opthalmoplagia
Stage 3	Rhino-orbito cerebral	a. Facial and other palsy b. Altered sensorium	a. Cavernous sinus thrombosis b. Altered mental functions c. Hemiplegia

4. Radiographic Examination

Radiographic examination discloses a wide range of findings, from thickening of the mucosal lining and cloudiness of the sinuses to extensive bone destruction. Nodular thickening of the sinus mucosa, focal bone destruction and absence of fluid levels in erect radiographs are considered to be the diagnostic features of mucormycosis.[11] The maxillary and ethmoid sinuses are always involved, but the frontal and sphenoid sinuses are rarely involved in the disease process. Mucormycosis can be differentiated from the carcinoma by the multiple

sinus involvement. The disease is usually unilateral but occasionally it can involve both ethmoid sinuses. Although radiography can sometimes be suggestive but the definitive diagnosis is made only by biopsy of the affected tissues and by the identification of the organism.[12]

5. Diagnosis

Early diagnosis of mucormycosis is considered very important for providing appropriate treatment for the patient. Histopathological examination of surgical specimens can confirm the clinical diagnosis with the presence of right-branching aseptate hyphae, which are observed typical for mucor species, along with angioinvasion and tissue necrosis. Fungal cultures can also provide further confirmation. However, many false negative results have also been reported compared to direct histopathological examination.[13]

Other laboratory diagnostic modalities include molecular detection of zygomycetes and cerebrospinal fluid analysis. However, the results so far have been less promising.

Imaging methods are also helpful during the early stages of rhinocerebral mucormycosis with thickening of the sinus mucosa or extraocular muscles, which is considered as an early sign of the disease. CT scans can be used to assess the development of disease although correlation with the clinical findings may not always be correct. MRI scans may be more accurate in evaluating the extent of disease due to fungal invasion of soft tissues soft tissues.[13]

6. Differential Diagnosis

The differential diagnosis involves carcinoma, sinusitis, and cavernous sinus thrombosis. The symptoms are even complicated by predisposing conditions, such as renal dialysis, and in some instances by the more chronic, less explosive spread of the disease.[12] Other entities for the differential diagnosis includes retro-orbital abscess, uremic frost, gangrenous stomatitis, bacterial sepsis, diabetic polyneuritis, and abscessed tooth.[12] Due to the peak in the incidence reported in the literature has led to a heightened degree of suspicion toward mucormycosis. Diagnosis and progression of treatment are made on the basis of clinical findings and have resulted in a more favorable outcome.

7. Treatment

Therapy for rhinocerebral mucormycosis involves an integrated approach that includes,

1. Antifungal agent's mainly intravenous amphotericin B, Posaconazole, Isavuconazole
2. Surgical debridement, and
3. Control of the underlying disease that may often leads to infection[12,14]

Amphotericin B (Fungizone) is the antifungal agent which is known to control mucormycosis. Amphotericin B is a broad-spectrum antifungal antibiotic which was first isolated from a strain of Streptomyces in 1955. Intravenous administration of amphotericin B has been effective in treating histoplasmosis, eoccidioidomycosis, North American blastomycosis, cryptomycosis, and mucormycosis.[15] Irrigation of the paranasal sinuses with amphotericin B has been recommended but this approach is not considered to be effective in controlling the organism.

The major side-effects of this form of chemotherapy include chills, fever, nausea, vomiting, hypokalemia, anemia, and uremia. The side-effects can be controlled by adjusting the level of amphotericin B on a daily basis or administering it on an alternate-day basis.[15]

As the disease progresses, the affected tissues become necrotic, necessitating surgical debridement. Serial debridement procedures are often needed until the patient's metabolic and immunologic conditions are improved and the systemic amphotericin B level is sufficient to contain the invading organism. Surgery is indicated for the removal of necrotic tissue, not containment of the organism.

8. Prosthodontic Considerations

The post-surgical defects of mucormycosis are different from those defects that developed from tumor resection due to the unpredictable, indefinable advancement of the fungus which necessitates additional debridement procedure. The surgical modifications done for the prosthetic rehabilitation of tumor cases cannot be followed in case of mucormycosis.

Therefore, provision of prosthodontic rehabilitation is compounded in mucormycosis patients especially when they are also edentulous, as the resultant defect often cannot be utilized effectively to retain, support, or stabilize the obturator prosthesis. These defects are allowed to epithelialize spontaneously, generally resulting in a non-keratinized mucous membrane that provides a poor stress-bearing surface.[12]

The needs of the patient, both physical and psychologic, are best served if an immediate surgical obturator is provided to the patient. An immediate surgical obturator allows normal speech, deglutition, and protection for the surgical site during the phase of healing. Because of the uncertain spread of the disease, preparation should be made for modification of the immediate surgical obturator at surgery and even after subsequent debridement procedures.[12]

Proper clasping should be provided if teeth are present because, after the surgical packs and sutures are removed, retention is dependent on the teeth. The obturator is modified with a soft liner treatment after the surgical packs are removed. The patient is seen weekly after debridement procedures for evaluation of fit. Close tissue adaptation of the prosthesis is important for the stability of the

prostheses.[12]

In edentulous patients, the obturator prosthesis may exhibit varying degrees of movement based on the outline and amount of the residual hard palate, the contour, size and mucosal lining of the defect, the approachability of the undercuts, and the support areas that can be engaged within and peripheral to the defect. Engaging the defect extensively maximizes stability support and retention of the prosthesis.[11]

After debridement procedures are done, modification of the prosthesis should be made immediately. Definitive prosthodontic treatment should be considered only when healing is complete because the configuration of the permanent defect will be decided by the healing process and scar contraction.[12]

8.1. Implants

The implants which is one of the advanced treatment modality is less reported in the literature for the management of mucormycosis. The reason for this could be due to the lesser prevalence of the disease in past years. The use of implant and other treatment modalities is planned with fundamental principles that can help in improving the quality of life of patients.[3]

The decision whether to place implants or not should always be critically evaluated especially in mucormycosis patients as they are systemically immunocompromised and may not be willing for another psychological burden due to surgical intervention.

Therefore, the decision making should involve a comprehensive team comprising of a general surgeon, a physician, a maxillofacial surgeon, a prosthodontist along with the patient attendees.

In a nutshell.....

Table 2: Mucormycosis is a fungal infection which is aggressive in nature

Cause	**Rhizopus oryzae (Mucorales spp)**
Patients in risk	Diabetic patients, Neutropenic patients, Patients having hematologic malignancies, patients with Increased serum iron levels
Clinical presentation	Initially sinusitis / orbital cellulitis. Characteristic necrotic eschars of hard palate or nasal cavity
Diagnosis	Diagnosis is clinical. Histopathologic examination of biopsy specimens for confirmation of the disease.
Treatment	Amphotericin B based treatment with surgical debridement and reversal of underlying disease.
Prognosis	Good prognosis in localized disease. Spread of disease, especially if there is CNS involvement it worsen the prognosis significantly.[13]

9. Conclusion

As mucormycosis is a fatal fungal infection, it necessitates early diagnosis and treatment planning through a collaborative approach, in which the maxillofacial prosthodontist plays a vital role to improve the patient's quality of life. The defects that occur after surgical debridement, in mucormycosis, are different from those that occur otherwise. Therefore, it demands thorough knowledge about the course and nature of the disease, to critically evaluate the anatomic structures and prostheses designs to obtain maximum retention, stability, and esthetics. Maxillofacial prosthesis not only rehabilitates the defect but also recreates the self-confidence of the patient, which lead life to the fullest.

10. Conflict of Interest

The authors declare no relevant conflicts of interest.

11. Source of Funding

None.

References

1. Inbarajan A, Natarajan S, Thangarajan ST, Seenivasan M, Banu F, Kumar VA, et al. Impact of Prosthodontic Treatment on the Oral Health-related Quality of Life in Mucormycosis Patient: A Case Report. *Cureus*. 2018;10(10):e3493. doi:10.7759/cureus.3493.
2. Gowda M, Shashidhar MP, Prakash P, Sahoo NK. Rehabilitation of a defect secondary to sino-orbital mucormycosis-A prosthodontic challenge. *IP Ann Prosthodont Restor Dent*. 2021;7(1):41–5. doi:10.18231/j.aprd.2021.008.
3. Chander NG. Mucormycosis and prosthodontic management. *J Indian Prosthodont Soc*. 2021;21(4):317–8.
4. Mantadakis E, Samonis G. Clinical presentation of zygomycosis. *Clin Microbiol Infect*. 2009;5:15–20. doi:10.1111/j.1469-0691.2009.02974.x.
5. Oh WS, Roumanas E. Dental implant-assisted prosthetic rehabilitation of a patient with a bilateral maxillectomy defect secondary to mucormycosis. *J Prosthetic Dent*. 2006;96(2):88–95.
6. Ramon Y, Oberman M, Horowitz I, Freedman A. Extensive maxillary sequestration resulting from rhinocerebral mucormyocosis. *J Oral Surg*. 1977;35(12):989–91.
7. Ballester DG, González-García R, García CM, Ruiz-Laza L, Gil FM. Mucormycosis of the head and neck: report of five cases with different presentations. *J Cranio-Maxillofas Surg*. 2012;40(7):584–91.
8. Verma M, Sharma R, Verma N, Verma K. Rhinomaxillary mucormycosis presenting as palatal ulcer: A case report with comprehensive pathophysiology. *J Oral Maxillofac Pathol*. 2020;24(3):558–62. doi:10.4103/jomfp.JOMFP_145_20.
9. Smith H, Kirchner JA. Cerebral mucormycosis: a report of three cases. *AMA Arch Otolaryngol*. 1958;68(6):715–26.
10. Nithyanandam S, Jacob MS, Battu RR, Thomas RK, Correa MA, D'Souza O, et al. Rhino-orbito-cerebral mucormycosis. A retrospective analysis of clinical features and treatment outcomes. *Indian J Ophthalmol*. 2003;51(3):231–6.
11. Kumar PR, Kalavathy N, Shetty MM, Sanketh AK, Venkataramani A, Ramyashree SV, et al. Prosthodontic Perspectives in Mucormycosis: A Review. *RGUHS J Dent Sci*. 2021;13(4):293–302.
12. Kurrasch M, Beumer IJ, Kagawa T. Mucormycosis: Oral and prosthodontic implications. A report of 14 patients. *J Prosthetic Dent*. 1982;47:422–9.

13. Mallis A, Mastronikolis SN, Naxakis SS, Papadas AT. Rhinocerebral mucormycosis: an update. *Eur Rev Med Pharmacol Sci*. 2010;14(11):987–92.
14. Carlo PD, Pirrello R, Guadagnino G, Richiusa P, Casto AL, Sarno C, et al. Multimodal surgical and medical treatment for extensive rhinocerebral mucormycosis in an elderly diabetic patient: a case report and literature review. *Case Rep Med*. 2014;p. 527062. doi:10.1155/2014/527062.
15. Andriole VT, Kravetz HM. The use of amphotericin B in man. *JAMA*. 1962;180(4):269–72.

Author biography

Rohit Raghavan, Professor and Head

Shajahan PA, Professor

Shilpa RS, Post Graduate Student

Cite this article: Raghavan R, Shajahan PA, Shilpa RS. Mucormycosis-"The deadly fungal disease" and its prosthodontic management. *J Dent Panacea* 2022;4(2):70-74.