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Review Article

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CORONAVIRUS DISEASE (COVID-19) ASSOCIATED MUCORMYCOSIS

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ABSTRACT

Severe coronavirus disease (COVID-19) is currently managed with systemic glucocorticoids. Opportunistic fungal infections are of concern in such patients. Post-Covid mucormycosis has emerged massively in the second wave in India. A Covid survivor who has already suffered the brunt of a disease which affects almost all the systems of human body has to also face the deadly fungal disease. Most common type of mucormycosis being rhino-maxillary disease patients might report primarily to general dental practitioner for oral cavity related complains. So, this article gives a detail of Sign, Symptoms & treatment planning of the disease.

INTRODUCTION

'Mucormycosis - The Black fungus has emerged as a new challenge for doctors. Covid-19 pandemic has been creating havoc among the general population and health care system of world. Post-Covid mucormycosis has emerged massively in the second wave in India and we are getting large number of cases daily in OPD. A Covid survivor who has already suffered the brunt of a disease which affects almost all the systems of human body has to also face the deadly fungal disease. This is like a frying pan to fire scenario for the patient. Most common type of mucormycosis being rhino-maxillary disease so, patients might report primarily to general dental practitioner for oral cavity related complains.

Mucormycosis (MCM) is a devastating infection with high mortality rates despite recent advances in its diagnosis and treatment. It is caused by the filamentous fungi of the Mucorales order of the class of Zygomycetes.[1] Although it is classically defined as an opportunistic infection, preferentially affecting patients with diabetes mellitus (DM), neutropenia, malignancy, chronic renal failure, and acquired immunodeficiency syndrome and those who have received organ or hematopoietic stem cell transplants, it can affect immunocompetent hosts as well (such as trauma patients).[1,2] The incidence of MCM worldwide appears to be increasing, particularly now in Covid 19 patients and those with DM.[3]

Since the pandemic coronavirus disease 2019 (COVID-19) continues to be a significant problem worldwide. While several treatment options have been evaluated, none except systemic glucocorticoids have been shown to improve survival in COVID-19. Unfortunately, the widespread use of glucocorticoids can lead to secondary bacterial or fungal infections. So, the biggest risk factors for the black fungus infection are **uncontrolled diabetes, and steroids**, which are known to suppress immunity & increase blood glucose level, but are also being used to treat COVID-19 patients.

Despite aggressive surgical and polyene antifungal therapy, overall mortality for MCM infection remains high, with figures ranging from 20 to 50%.[4–6] Depending on patient characteristics (such as critically ill or immunocompromised patients as in Covid 19) and site of infection, mortality rises markedly, nearing 70–90% for cases of disseminated mucormycosis.[4–6] After nasal inoculation it takes a rapidly progressive course extending to neighboring tissues, including the orbit, sinuses and sometimes to the brain.

To eliminate this infection, it is important to quickly diagnose the patient as it can be aggressive and life-threatening.

SIGN & SYMPTOMS

- Pain and redness around eyes and/or nose
- Mobile Teeth

- Halitosis
- Dental Pain
- Palatal Ulceration
- Intra oral Draining Sinuses
- Para- sinusal pain
- Nasal stuffiness
- Nasal Discharge with epistaxis, black purulent discharge
- Erythema of nasal mucosa
- Facial Erythema
- Black Discoloration of Skin
- Periorbital erythema and edema
- Orbital Pain, Ptosis, Diplopia
- Fever

Fig. 1: Palatal Ulceration secondary to Mucormycosis.

Fig. 2: Upper Lip Edema with Black Nasal Discharge.

Fig. 3: Orbital Cellulitis.

Fig. 4: Orbital Cellulitis.

Radiographic Diagnosis of Mucormycosis

Early imaging is helpful in assessing the extent of involvement of this lethal disease which requires prompt and aggressive treatment.

General

It Can show varying degree of sinus opacification with most having a tumefactive nature. They generally demonstrate a rim of soft-tissue thickness along the paranasal sinuses. Complete sinus opacification, gas-fluid levels and obliteration of the nasopharyngeal tissue planes can also occur

Features on Contrast enhanced CT PNS

1. Mucosal Thickening
2. Inflammation of Nasal Turbinate
3. Bony Erosion
4. Fluid Filled Sinus
5. Sequestered Bone

MRI

Reported signal characteristics on MRI of the sinuses and brain include:

- **T1**: isointense lesions relative to brain in most cases (~80%)
- **T2**:
- Variable with around 20% of patients showing high T2 signal
- Fungal elements themselves tend to have low signal on T2
- **T1 C+ (Gd)**: the devitalised mucosa appears on contrast-enhanced MR imaging as contiguous foci of non-enhancing tissue, leading to the black turbinate sign.

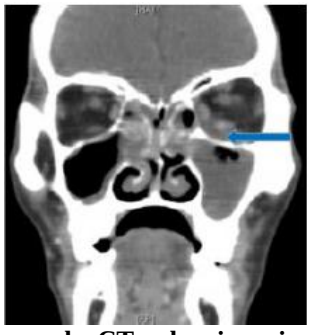

FIG. 5: Coronal CT showing involvement of Maxillary and Ethmoid Sinus.

FIG. 6: Black turbinate sign.

Protocol for prevention of Mucormycosis in admit Covid -19 patient
7 step approach
Step 1-Diagnosis of glycemic control on admission using glycocated hemoglobin
Step 2-Judicious use of Steroid and Toclizumab
Step 3-Blood Sugar level monitoring and maintainace (110-180 mg/dl)
Step 4-Hygiene maintenance of O2 delivery system and use of distill water in Humidifiers
Step 5-ENT/OMFS evaluation of patient on day 3, day 7 and before discharge.(Nasal endoscopy, Biopsy, Deep nasal swab for fungal culture can be taken in suspected cases)
Step 6-Nasal Saline Spray twice daily
Step 7-Application of Amphotericin B gel intranasal for high risk patients.

Protocol for prevention of Mucormycosis in post-covid patient 7 step approach
Step 1-Maintenance of Oral hygiene and Use of 2% povidone Iodine Gargles.
Step 2-Steam inhalation to improve ciliary function and sinus health.
Step 3-Use of 0.5% Betadine Nasal Irrigation
Step 4-Patient education regarding early symptoms and signs of mucormycosis leading to early reporting.
Step 5-Strict Glycemic control
Step 6-Defer non-emergency invasive oral or dental procedure for 3 months after covid 19 infection.
Step 7-Use of Tablet Vitamin E 1000IU6,Tablet Vitamin A 6000IU7 and B-complex tablets and high protein low sugar diet,

Treatment of Rhino-Orbito-Maxillary Mucormycosis
Medical Management
First Line Antifungal Therapy- Amphotericin B Therapy (Inj.Liposomal Amphotericin B,Inj. Amphotericin B lipid complex, Inj Amphotericin B Deoxycholate)

Second Line Antifungal Therapy- 1.Isavuconazole(Injection/Tablet) 2.Posaconazole(Tablet)

Combined team approach of ENT Surgeon, Maxillofacial Surgeon, Ophthalmologist, Neuro surgeon and Infectious Disease Specialist is required.

SURGICAL TREATMENT
Aim of Surgery-Aggressive clearance of pathologic tissue to make healthy tissue bed for perfusion of anti-fungal therapy.

ENT surgeon-Endoscopic sinus surgery for Sphenoid, Ethmoid and Maxillary Sinus. FESS or Denkers Operation can be done.

Maxillofacial Surgeon-Dual role of maxillofacial surgeon in clearance surgery as well as post-mucormycosis reconstruction and dental rehabilitation.

Resection of involved jaw bone by maxillectomy/Mandibulectomy.

Cadwell-Luc operation for maxillary sinus debridement, resection of zygomatic bone.

Use of free vascular grafts/regional soft tissue flaps for reconstruction and use of zygomatic implants for dental rehabilitation in indicated cases.

Ophthalmologist: Orbital exentration in indicated cases.

Neurosurgeon: Debridement of anterior table, posterior table of frontal bone and osteomyelitic skull bone and involved cerebral parenchyma.

CONCLUSION

In conclusion, MCM is a life-threatening infection that is most commonly affecting immunocompromised individuals and that despite aggressive multimodal treatment carries a significant risk of mortality. A high index of suspicion is required in order to begin the appropriate diagnostic workup and treatment. Cases most commonly involves the rhino-orbitocerebral cavities, and the main underlying disease is Diabetes Melitus patients with Covid 19 with ongoing/history of steroid therapy.

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