

MUCORMYCOSIS

Current Scenario

- There are reports that there has been a significant increase in in number of cases of Mucormycosis in Covid-19 patients during treatment in hospitals and after discharge in different parts of the country.

The scope of this document

- To provide a guidance to clinicians (physicians/ respiratory physicians/intensivists/ ENT surgeons etc.) to detect Mucormycosis at an early stage in patients who are hospitalized for treatment of Covid-19 (as well as those discharged after treatment) and treat such patients optimally.



BACKGROUND

- Mucormycosis is a potentially lethal, angioinvasive fungal infection predisposed by diabetes mellitus, corticosteroids and immunosuppressive drugs, primary or secondary immunodeficiency, hematological malignancies and hematological stem cell transplantation, solid organ malignancies and solid organ transplantation, iron overload, etc
- Mucor is a fungus which is normally present in the environment and in soil. It causes disease only when immunity is critically low.
- Mucormycosis is not a new disease. It is known to occur in patients with low immunity such as in uncontrolled diabetes, post-transplant, and some cancer treatments
- It is a rare but serious infection which can be life threatening.
- Mucor infection may occur during active COVID-19 infection or a few weeks after recovery from Covid-19.
- **It is not a contagious disease**



Causative Agents

- Mucormycosis (previously called zygomycosis) is a serious but rare fungal infection caused by a group of molds called mucormycetes.

RISK FACTORS

1. COVID-19 infection (Active or Post COVID)
2. Steroid therapy: High dose and early initiation of therapy in treatment of COVID
3. Uncontrolled Diabetes
4. Irrational use of broad-spectrum antibiotics
5. Chronic Kidney Disease
6. Immunodeficiency conditions: Neutropenia, hematological malignancies, stem cell transplants, and organ transplant patients on immunosuppressants.
7. Elevated free iron levels, deferoxamine
8. Inappropriate use of immunosuppressants like Tocilizumab
9. Living in dusty and damp area, stagnant area without proper ventilation
10. Dehydration

PRESENTATION

- Any age or sex but commonly middle-aged people
- Usually 2-4 weeks of Covid-19 symptom onset. However, can appear at 10-60 days or during active covid infection

SYMPTOMS AND SIGNS

Rhino-orbito-cerebral Mucormycosis

Common Early Symptoms

- Unilateral facial pain; Focal in cheek, retro- orbital pain
- Swelling, redness around the eyes and nose: progressive anesthesia felt over cheek region or nasal mucosa
- Nasal congestion
- Bloody/black nasal discharge
- Blurring of vision, double vision
- Fever, malaise
- Dental pain or loosening of teeth



Symptoms in later stage

- Facial swelling
- Ptosis (closure of eyelids)
- Proptosis (swelling of the eyeballs)
- Diplopia, Restricted eye movements
- Chemosis
- Facial skin discolouration
- Palatal blackish discolouration or ulcer
- Other neurological symptoms, Seizure, altered sensorium , Hemiplegia (Contralateral)

Pulmonary mucormycosis

- Refractory fever, non-productive cough, progressive dyspnea, pleuritic chest pain.

Gastro-intestinal mucormycosis

- Fever, Bleeding per rectum, mass like lesion, perforation (late stage)

Cutaneous and soft tissue:

- Erythema, induration, then black eschar, muscle pain with deeper involvement

Disseminated mucormycosis:

- Symptoms vary as per site of involvement, mostly associated with pneumonia

SAMPLING FOR LAB:

- Histopathology (In 10%Formalin) – for presence of fungus
- KOH mount (in Normal Saline) – for presence of fungus
- Fungal culture (in Normal Saline) – for type of fungus

TREATMENT

1. All mucormycosis cases should be managed in a separate ward.
2. In any immunocompromised patient with suspected mucormycosis, immediate treatment initiation is strongly recommended.
3. Treatment of comorbid illness/ blood sugar control & of Covid illness

The two mainstays of treatment:

Medical treatment with Amphotericin B and aggressive surgical debridement is the mainstay of treatment.



Antifungal:

- Injection Liposomal Amphotericin B is the drug of choice and to be started after the diagnosis is confirmed because it is effective and less nephrotoxic.

Liposomal Amphotericin B (L-AmB)

- Rhino-orbital -5 mg/kg/ day given as infusion in 5% Dextrose over 2 hours
- Intracranial - 10 mg/kg/ day

➤ **Amphotericin B deoxycholate (D-AmB)**

- 1 – 1.5 mg/kg/d to a total dose of 2 to 4 g (Maximum cumulative dose is 5-7 gm)
- Minimum 10-14 days weeks post debridement but may need to be given for up to 6 weeks if progressive
- Step down to oral Posaconazole 300mg BD on day 1 and then OD for at least 3 months

Note: Watch for toxicity: Serum creatinine, potassium and magnesium need to be monitored. In renal impairment cumulative dose needs to be reduced. Total cumulative dose: 5-7 gm) *No role of Fluconazole, voriconazole, and itraconazole as primary treatment or as prophylaxis

SURGICAL DEBRIDEMENT

(Functional endoscopy and sinus surgery and/or orbital clearance) at the earliest possible

- reduces the disease burden,
- allows better penetration of intravenous drugs,
- limits further spread of the disease
- allows intraoperative diagnosis with characteristic necrotic tissue and provides sample for histopathological and microbiological confirmation
- Glycemic control should be urgently undertaken in Diabetics.

Treatment duration:

- Mucormycosis usually requires long term treatment therapy ranging from weeks to months. If an immune defect is resolved e.g. diabetes is controlled, neutropenia definitively resolved, immunosuppression can be tapered or stopped, therapy can be continued until resolution of signs and symptoms and improvement in radiological signs.



PREVENTIVE MEASURES

At home during isolation

- Use dry clean mask and do regular hand washing or use of sanitizers
- Don't use dirty mask /reuse disposable masks
- Personal hygiene, long sleeves while working outdoor or in dirty areas
- Avoid dusty and damp areas like construction sites for isolation
- Nasal cleaning with saline water and oral gargle with povidone iodine for high risk cases

At HOSPITAL

- Decrease dust and damp in isolation, quarantine and treatment center
- Regular cleaning of the air ducts
- Maintain hygiene constantly of the equipment used for oxygenation - nasal prongs, nasal cannula, masks for ventilation. Equipment not used for long will have dust particles along with fungus spores.
- Skin abrasion, injury should be cleaned with soap and water and antiseptics

OXYGEN ADMINISTRATION

- Change oxygen tubing after every case when possible
- Humidification during oxygenation.
- Use distilled or sterile water, never use tap water or mineral water
- Fill upto about 10mm below the maximum fill line, check the water level regularly
- All the components of the humidifier should be soaked in a mild antiseptic solution for 30 minutes, rinsed with clean water and dried in air - once a week for the same patient and in between patients

During TREATMENT

- Control Diabetes – VERY IMPORTANT, regular monitoring of blood sugar with target Fasting = 110 mg/dl & PP = 140 mg/dl. HbA1C above 8 is high risk.
 - Judicious use OF ANTIBIOTICS AND STEROID in treating COVID patients
 - Steroids to be stopped or tapered if cannot be stopped
- In the absence of a clear benefit, drugs targeting immune pathways such as tocilizumab should be discouraged.

