



Mucormycosis Management Protocol

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Mucormycosis Management Protocol

A. INTRODUCTION:

Mucormycosis is a disease caused by fungus of Mucorales species. These fungi are present in the environment in soil or decaying organic matter.

In COVID 19 a three pronged assault make the patients susceptible:

- **COVID19** : immune dysregulation, ciliary dysfunction thrombo-inflammation
- **Hyperglycemia** : polymorphonuclear neutrophils (PMN) dysfunction, impaired chemotaxis and intracellular killing
- **Corticosteroid** : impairment in the neutrophil migration, ingestion, and phagolysosome fusion. Also exacerbates hyperglycemia.

B. PRESENTATION:

- **Rhino-orbito-cerebral mucormycosis (ROCM)**
- **Pulmonary**
- Gastrointestinal
- Cutaneous
- Disseminated

C. RISK FACTORS-

- a) **Hyperglycemia** in undiagnosed or uncontrolled diabetic.
- b) **Ketoacidosis**
- c) **Corticosteroid** and **anti-IL-6-directed** strategies in COVID patients
- d) Cancer or post-transplant patient
- e) Neutropenia, on chemotherapy
- f) Patients on Immunomodulators
- g) Voriconazole therapy

D. HOW TO SUSPECT:

Classical hallmark of mucormycosis is rapid onset of tissue necrosis with and without fever, associated with features of involvement of blood vessels and thrombosis.

RHINOCEREBRAL MUCORMYCOSIS

1. Black discoloration in patches over the skin of the nose
2. Necrotic skin lesions(eschar)
3. Black coloured discharge from the nose.
4. Nasal ulcers

5. Persistently stuffy nose on one side particularly
6. Facial swelling
7. Vision impairment associated with eye swelling, restricted eye movements.
8. Sinus infection
9. Non remitting febrile illness in association with any of the above symptoms should make one think about the possibility of Mucormycosis.

PULMONARY MUCORMYCOSIS

Non-specific including fever, cough, chest pain, and dyspnoea. At times, cavitation and/or haemoptysis.

E. DIAGNOSIS

Clinical examination is the key.

Presence of black crusts/discoloration over turbinates or palate or facial skin are quite diagnostic.

Simple tests like pupillary reaction, ocular motility, sinus tenderness and palatal examination should be a part of routine physical evaluation of a COVID-19 patient.

Fungal culture & staining can help but they take time & the treatment must start on an urgent pace even empirically to begin with when the clinical suspicion is strong.

Once clinically suspected:

1) **Routine laboratory tests:** CBC, ESR, FBS, PPBS, HbA1C, LFT, KFT with electrolytes, Viral markers (HIV/HBV/HCV)

2) **Diagnostic procedures**

a) RCOM- Diagnostic nasal endoscopy

b) Pulmonary- Broncho-alveolar lavage (BAL), Mini BAL, non-bronchoscopic lavage, transbronchial biopsy, CT guided biopsy from lung

3) **Imaging:**

RCOM: CECT Nose and PNS, CEMRI Brain Orbit and Face

Pulmonary: Chest X-ray and/ or HRCT

4) **KOH staining & microscopy** : Direct microscopy using fluorescent brightener and histopathology with special stains (e.g. PAS and GMS): **non-septate/pauci-septate**.

5) **Histopathology** :. haemorrhagic infarction, coagulation necrosis, angioinvasion

6) **Fungal culture** : Routine media at 30°C and 37°C

Typical findings: cotton white or greyish black colony

7) Repeated negative galactomannan & beta-D-glucan tests- if facility available

Sample collection and transportation:

Test (all endoscope assisted)	Sample to be collected in	To diagnose
KOH	Saline	Presence of Fungi
Fungal Culture	Saline	Type of Fungi
Histopathology	10% Formalin	Fungus/ Bony lesions/ Malignancy
<ul style="list-style-type: none">• Specimens should be collected aseptically in sterile containers and transported to the laboratory within 2 hours• Avoid sending swabs if pus or sterile body fluid can be aspirated or when tissue can be obtained. Swabs may give false negative reports• Never use dry swabs to collect specimen		

F. MANAGEMENT

- Strict control of blood sugar levels.
- Treat Diabetic ketoacidosis, if present
- Reduce steroids (if patient is still on) with aim to discontinue rapidly
- Antibiotics only if there is evidence of superadded infection.
- Surgical debridement: Extensive, to remove all necrotic material. Early extensive debridement of all the structures involved with disease is essential otherwise the disease will progress and may ultimately prove fatal. Images from the MRI scans help defining extent of the surgery but a fresh ooze from normal tissues in all directions of disease involvement at time of debridement is the goal. This may lead to extensive disfigurement, but one needs to remember that life is more important.

MEDICAL MANAGEMENT

ANTIFUNGAL THERAPY:

Available preparations with dose and duration:

1. Amphotericin B deoxycholate (**D-AmB**)- 1.0-1.5 mg/kg/day for 3-6 weeks
2. Inj. Amphotericin B Lipid Complex (ABLC- 5mg/kg/day for 3-6 weeks
3. Liposomal amphotericin B (L-AmB) - 5-10mg/kg/day for 3-6 weeks

Which preparation to use when:

Routinely use D-AmB. Avoid it in case of pre-existing severe renal failure or if creatinine clearance less than 30 ml/minute. Use ABLC/L-AmB in those situations.

ABL C to be used preferably for pulmonary mucormycosis.

L -AmB to be used preferably for CNS involvement.

GENERAL INSTRUCTIONS:

Maintain adequate hydration. Monitor renal function and serum potassium on alternate days or daily if necessary. Supplement potassium if required. Maintain monitoring chart.

Instructions for use for each preparation:

Amphotericin B deoxycholate (D-AmB)

- Consider giving one litre of normal saline solution with 20mEq of potassium chloride (1 amp KCl) over two hours before each controlled infusion of amphotericin B.
- Reconstitute each vial (50 mg) with 10 ml water for injection and shake immediately to produce a 5mg/ml colloidal solution.
- Dilute further in 500 ml of 5% dextrose to a concentration of 100 micrograms/ml.
- Infuse over 2-4 hours or longer if not tolerated (*initial test dose 10 ml i.e. 1mg over 20-30 minutes*).
- Begin infusion immediately after dilution and protect from light (cover with black sheet).
- It is incompatible with sodium chloride solution. Flush existing intravenous line with glucose 5% or use separate line.

ABL C

- Allow suspension to reach room temperature, shake gently to ensure no yellow settlement.
- Withdraw requisite dose (using 17 to 19 gauge needle) into one or more 20 ml syringes.
- Replace needle with a 5 micron filter needle provided (fresh needle for each syringe) and dilute to a concentration of 1 mg/ml (2 mg/ml can be used in fluid restriction and in children).
- Preferably give via an infusion pump at a rate of 2.5 mg/kg/hour (initial test dose of 1 mg given over 15 minutes).
- An inline filter (pore size no less than 15 microns) may be used.
- Do not use sodium chloride or other electrolyte solutions, flush existing intravenous line with 5% dextrose or use separate line.

L-AmB

- Reconstitute contents of vial (50mg) with 10ml water for injection, shake well for 2-5 minutes to generate liposomes.
- Once you reconstitute all the vials, fill 10 ml syringe with the reconstituted L-AmB.
- Remove needle, apply 5-micron filter to the syringe nozzle and empty content in to 200 cc 5% dextrose.
- Infuse L-AmB rapidly over 2-3 hours (initial test dose 1 mg over 10 minutes).
- It is incompatible with sodium chloride solutions, flush existing intravenous line with 5% dextrose or use separate line.

Amphotericin Monitoring Chart (To be filled daily)											Patient name :				
Sr. No.	Name of the drug	Date	Starting time	Ending time	Dose given	Cumulative dose	Serum Electrolytes					Premedication	Complications	K+ correction	
							Urea	Creatinine	Na	K	Mg				

e GFR may be calculated by CKD-EPI or MDRD formula (app available).

4. Patients who are intolerant to Amphotericin B:

Posaconazole (300mg twice on day 1, followed by 300 mg daily for 3-6 months

5. After 3-6 weeks of Amphotericin B therapy, **consolidation therapy** (Posaconazole) for 3-6 months

G. PREVENTION

1. Environmental cleanliness to have **NO exposure to decaying organic matters** like breads/fruits/vegetables/soil/compost/excreta/etc.
2. **Control hyperglycemia.**
3. Glucose monitoring in COVID-19 patients requiring steroid therapy.
4. **Optimally steroid usage** -right timing of initiation, right dose, and right duration.
5. Use clean distilled water for humidifiers during oxygen therapy.
6. Use antibiotics/antifungals **only and only when indicated.**
7. **Do not consider** all the cases with blocked nose as cases of bacterial sinusitis, particularly in the context of immunosuppression and/or COVID-19 patients on immunomodulators.
8. During discharge of the patients, advice about the early symptoms or signs of mucormycosis.