



**Department of Health and Family welfare
Govt. of West Bengal**

Mucormycosis in COVID Scenario

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Introduction

- Mucormycosis is a fungal infection caused by a ubiquitous mould **mucor myecetes**, found in the environment in soil/decaying organic matter.
- **Heavy mould spore counts in hospital air due to hot, humid conditions in our tropical climate.**

Case 1

- 65y/lady presented with
 - Eye swelling proptosis
 - Lid drooping
 - No vision in the eye for 3 days.
- History of
 - Admission in hospital for COVID infection
 - Diabetes on irregular medication



Case 1

- On investigations-
 - Hb- 9.7 g/dl,
 - Creat- 0.7 mg/dl
 - CRP-32.6 (N<6.0),
 - D- dimer- 0.65 (N<0.50)
- NCCT Brain-
 - Hypointensities in bilateral basifrontal lobes
 - Differential Diagnosis
 - Fungal sinusitis with frontal lobe involvement



Case 1

- On further investigation-
CEMRI PNS and Orbit-

Soft tissue attenuation nonenhancing hypointense lesion in left maxillary (antero-superiorly)& bilateral ethmoid sinuses extending in to both cavernous sinus and orbit with swollen extraocular muscles and inflammatory stranding in retro orbital fat with swollen enhancing bilateral optic nerve as described above-

-Likely Fungal infection with orbital invasion , optic neuritis and cavernous sinus thrombosis.

Medium size ill-defined abnormal altered signal in bilateral basifrontal lobe , showing patchy restriction on DWI and peripheral enhancement on post GAD images with adjacent thickened enhancing dura-

-Likely intracranial fungal infection.

Case 1

- Microscopic Examination of the debrided tissue revealed-

M/E: Aseptate Filamentous Hyphae

- It was diagnosed as Mucormycosis and treatment has been initiated with Amphotericin B deoxycholate

Case 2

- 50y/M presented with
 - Left sided Facial tenderness and swelling with dimness of vision for 5 days.
- History of
 - Admission in hospital for COVID infection 14 days
 - Diabetes controlled on OHA



Case 2

- On investigations-
 - TLC- 12,700
 - Creat – 1.0 mg/dl
 - CRP-11.0 (N<6.0),
 - D- dimer- 1.0 (N<0.50)
 - Procalcitonin- Normal
- NCCT Brain-
 - Hypo intensities in bilateral frontal lobes
 - Differential Diagnosis
 - Fungal sinusitis with frontal lobe involvement
 - Bilateral frontal lobe contusion

Case 2

- On CEMRI PNS and Orbit-
 - Ill defined iso to hypointense soft tissue in the orbit extending to left maxillary and ethmoidal sinuses, likely fungal invasion with orbital involvement

Case 2

- Microscopic Examination of the debrided tissue revealed-

M/E: Aseptate Filamentous Hyphae

- It was diagnosed as Mucormycosis and is currently being treated with Amphotericin B deoxycholate

Predisposing factors

- **Hyperglycemia** in undiagnosed or uncontrolled diabetic.
- **Ketoacidosis**
- **Corticosteroid** and **anti-IL-6-directed** strategies in COVID patients
- Cancer /post transplant
- Neutropenia, on chemotherapy
- Voriconazole therapy

Vulnerable people

- Critically ill patients subjected to emergency invasive procedures, mechanical ventilation, CRRT, ECMO, poor nursing ratios, **prolonged ICU** stays and breaches in asepsis.
- **After COVID 19 infection with DM / high dose/long duration steroid**

Three pronged assault

- **COVID-19:** immune dysregulation, ciliary dysfunction thromboinflammation
- **Hyperglycemia:** PMN dysfunction upregulation of GRP78, glycation of Fe sequestrating protein
- **Corticosteroids:** impairment in the neutrophil migration, ingestion, and phagolysosome fusion. Also exacerbates hyperglycemia

How to suspect

Classical hallmark of mucormycosis is **rapid onset of tissue necrosis** (*manifested as a necrotic lesion, eschar or black discharge in the nasal or oral cavity*) with and without fever and associated with features of involvement of blood vessels and thrombosis

Presentation

- **Rhino-orbito-cerebral**
- **Pulmonary**
- Gastrointestinal
- Cutaneous
- Disseminated

Rhino Orbito Cerebral mucormycosis

- Black discoloration in patches over the skin of the nose
- Necrotic skin lesions(eschar)
- Black coloured discharge from the nose.
- Nasal ulcers
- Persistently stuffy nose on one side particularly
- Facial swelling
- Vision impairment associated with eye swelling, restricted eye movements.
- Sinus infection
- Non remitting febrile illness in association with any of the above symptoms should make one think about the possibility of Mucormycosis.





Pulmonary Mucormycosis

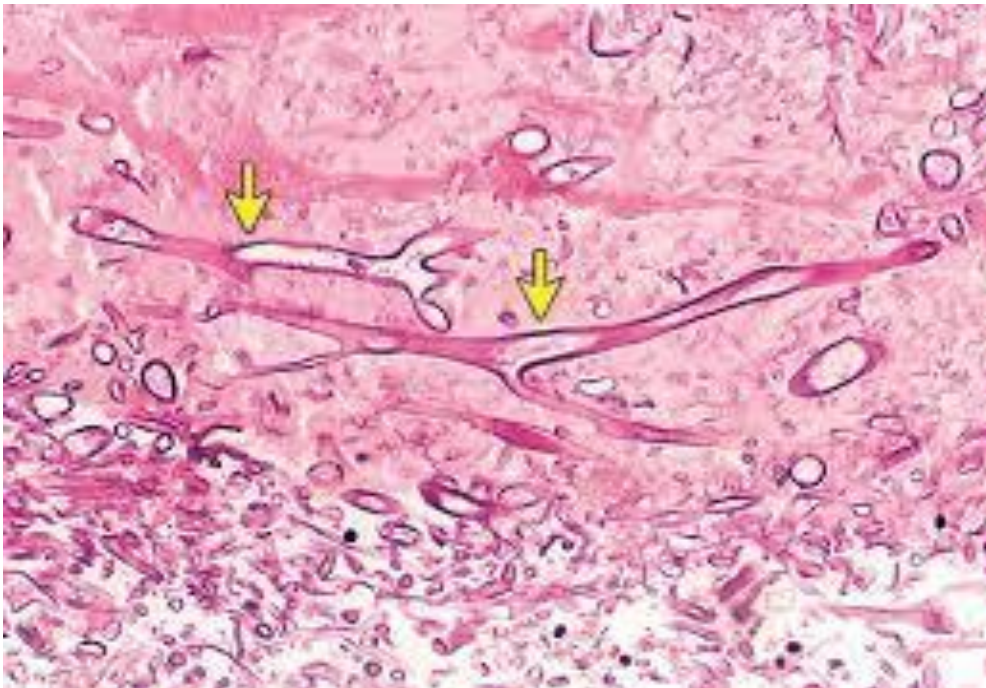
- Fever, cough, chest pain, pleural effusion, hemoptysis
- Worsening of respiratory symptoms

Rhino-orbito-cerebral diagnosis

- **MRI - PNS** with brain contrast study for ROCM
- **Endoscopic collection of debrided tissue/ biopsy**
 - a. microscopy, culture
 - b. histopathology

KOH, LPCB, PAS staining - nonseptate or pauciseptate ribbon like hyphae frequently occlude the vessel

- **M/E: Aseptate Filamentous Hyphae**

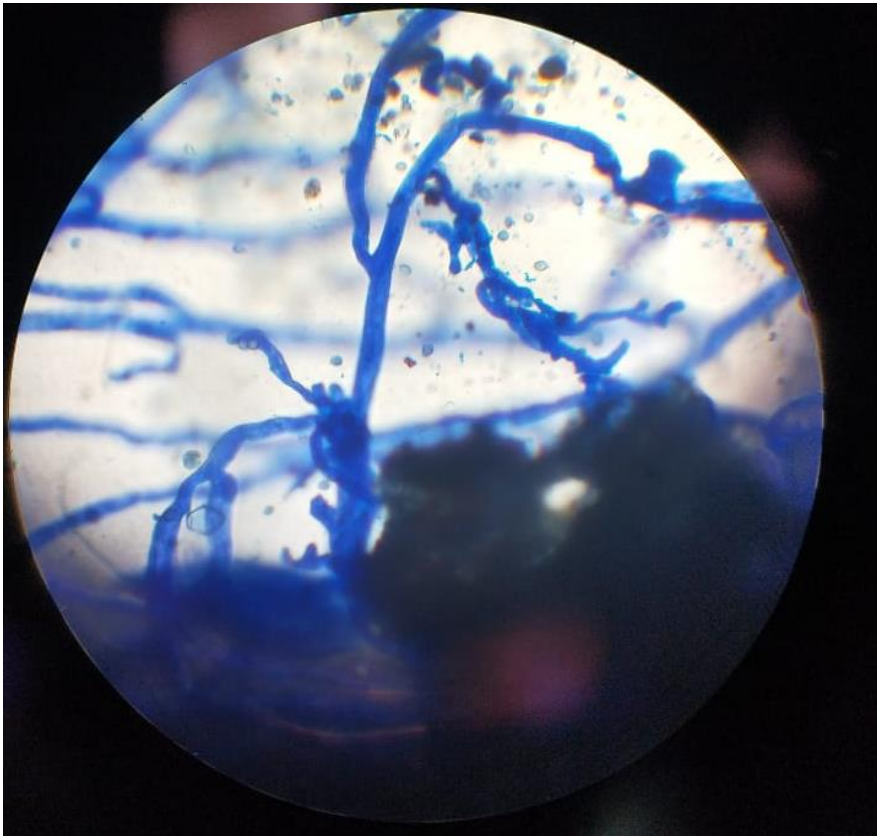


Mucor is difficult to routinely culture.

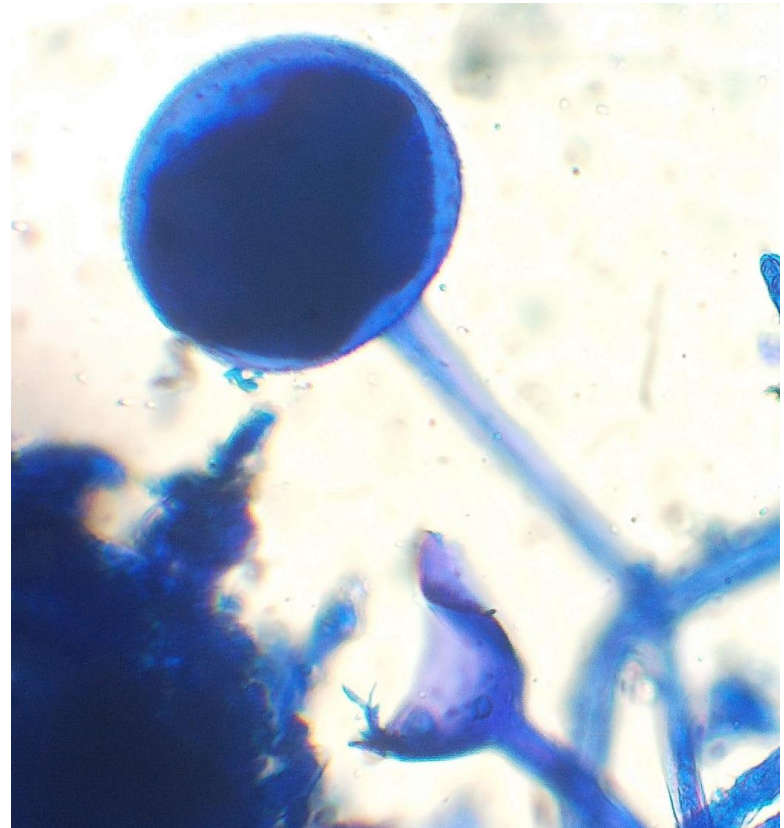
Biopsy remains the mainstay of diagnosis and the benefits of the procedure outweigh the risk

LPCB staining after culture growth

No rhizoid at node and thin wide aseptate hyphae.



LPCB mount showing Mucor isolated from a nasopharyngeal sample



Pulmonary mucormycosis diagnosis

- **Chest X-ray and/ or HRCT:**

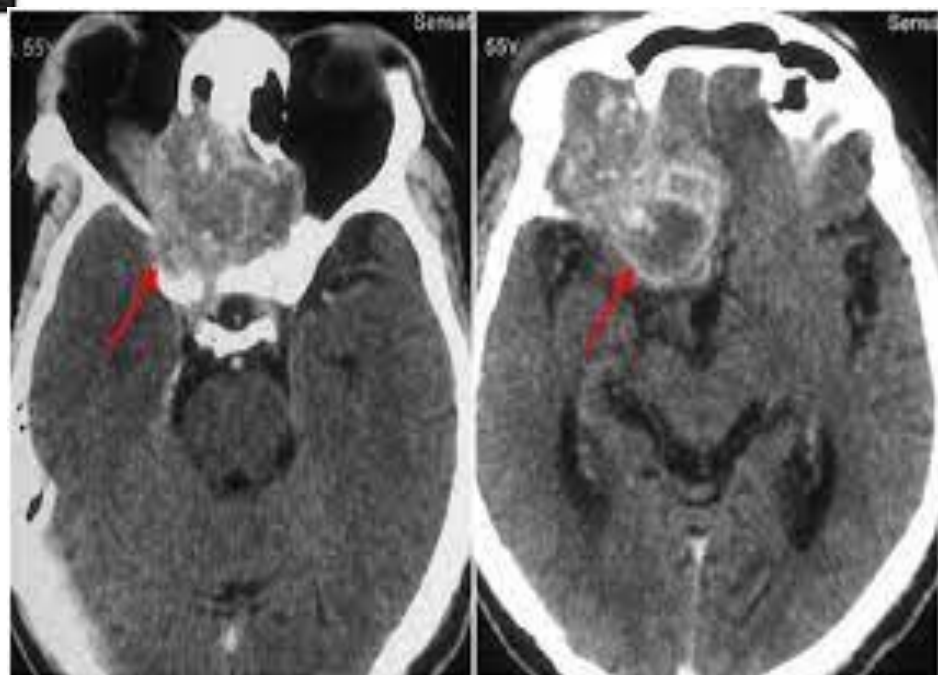
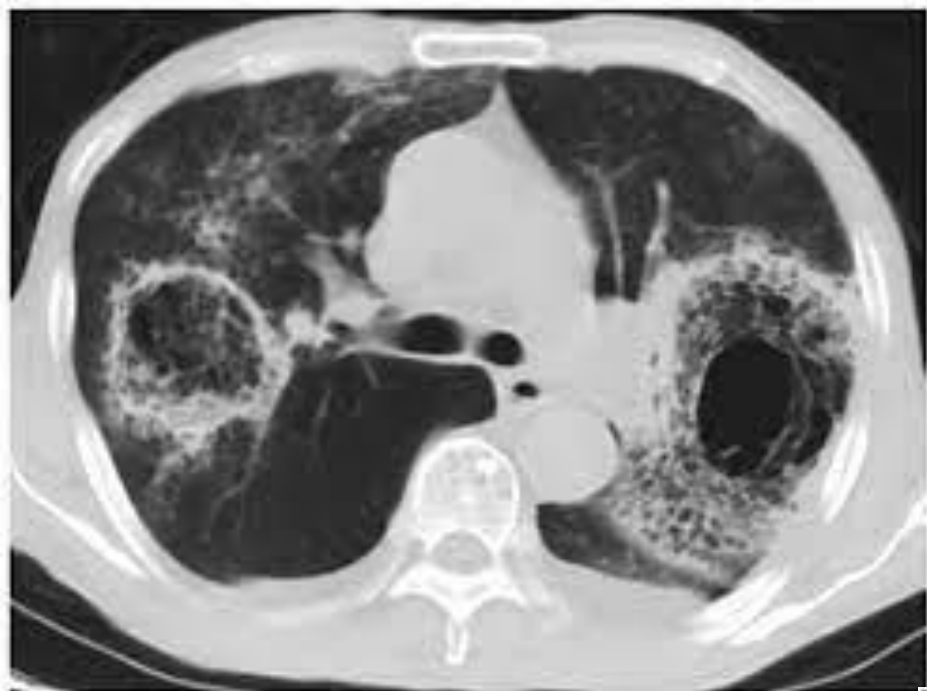
REVERSE HALO SIGN

THICK-WALLED CAVITY (need to differentiate from Covid associated pulmonary aspergillosis)

MULTIPLE NODULES

PLEURAL EFFUSION

- Repeated negative galactomannan & beta-D-glucan tests
- Broncho-alveolar lavage (BAL) fluid M/E
- Transbronchial biopsy
- CT guided biopsy from lung



Treatment

- Control of diabetes & diabetic ketoacidosis.
- Reduce steroids (if patient is still on) with aim to discontinue rapidly.
- Discontinue other immunomodulating drugs. Surgical debridement, the earlier the better, is pivotal in the management of mucormycosis.
- Surgical debridement: Extensive, to remove all necrotic material;
- if eye involved, exenteration of eye;
- in pulmonary, if the lesion is localized or in one lobe.

Medical Management

1. Amphotericin B deoxycholate (D-AmB)- 1.0-1.5 mg/kg/day
2. Liposomal amphotericin B (L-AmB) (preferred treatment)- 5-10mg/kg/day
3. Inj. Amphotericin B Lipid Complex- 5mg/kg/day

Adequate hydration

Monitor renal function and serum potassium

Inj Liposomal amphotericin B (LAmB):

Test dose

- Inj. Liposomal Amphotericin- B 1 vial (50 mg) to be diluted in 12 ml of the diluent and 0.25ml (1 mg) of solution made, to be mixed in 100ml Dextrose and to be infused in 30 minutes.
- Observe for fever and reactions

Pre-hydration

- 500 mL NS over 30 minutes
- To reduce the risk of renal toxicity and hypokalaemia :- 500ml Normal Saline + 1 Amp (20mmol) KCL

Therapeutic dose

- 5mg-10 mg /kg/day Amphotericin B in 500 mL D5 with 10 Units HIR over 3 hrs (To be covered in black sheet)

Post Hydration

- 500 mL NS over 30 minutes

Post dose

- KFT with Serum electrolytes after Every dose of Amphotericin B
- Fill Amphotericin monitoring chart

Inj Amphotericin B Deoxycholate(C-AmB)

Test
dose

- 1 mg in 100 mL D5 over 20 minutes

Pre-
hydratio
n

- 500 mL NS over 30 minutes

Therape
utic dose

- 1.0-1.5 mg/kg/day Amphotericin B in 500 mL D5 with 10 Units HIR over 3 hrs (To be covered in black sheet)

Post
Hydratio
n

- 500 mL NS over 30 minutes

Watch
for:

- Urine output , Renal function Test (pH, Bl. Urea, S. Creatinine, Electrolytes)
- Fill Amphotericin monitoring chart

Patients who are intolerant to Amphotericin B

- Posaconazole (300mg twice on day 1, followed by 300mg daily)
- After 3-6 weeks of Amphotericin B therapy, **consolidation therapy** (posaconazole) for 3-6 months

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 antibiotics/antifungals **only and only when indicated.**

PREVENTION

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.

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

Advice to patients and care givers for early detection

Danger signs of mucormycosis

- Abnormal black discharge or crust or blood from nose
- Nasal blockage
- Headache or eye pain
- Swelling around the eyes, double vision, redness of eye, loss of vision, difficulty in closing eye, inability to open the eye, prominence of eye
- Facial numbness or tingling sensation
- Difficulty in chewing or opening mouth
- Regular self-examination–
 - Full face examination in day light, for facial swelling (especially nose, cheek, around the eye) or black discoloration, hardening, and pain on touch
 - Loosening of teeth
 - Black areas and swelling inside the mouth, palate, teeth or nose (oral and nasal examination using torch light, as far as possible you can see)

Summary

- Good glycemic control during management of COVID 19
- Rational and optimum use of corticosteroids
- If systemic steroid is used, closely monitor blood sugar and signs of secondary infections.
- Proper indication, dose and duration of steroid therapy
- No antifungal prophylaxis is recommended
- Discharge advice about the early symptoms or signs of mucormycosis crucial 2- 6 weeks post COVID.

Reference

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THANK YOU