RHINOCEREBRAL MUCORMYCOSIS

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MUCORMYCOSIS

- Caused by fungi of the Rhizopus and Mucor species, which are ubiquitous saprophytic organisms, not uncommonly infecting the immunocompromised host.
- These fungi have a predilection to invade blood vessels, causing infarction and necrosis.
Predisposing factors:

- Diabetes mellitus
- Immunocompromised (aids/organ transplant/iatrogenic)
- Haematological malignancies
- DRUGS like CORTICOSTEROIDS- overuse, misuse, abuse
- Covid 19 severe infection
COURSE OF DISEASE:

- Fungal spores enter via oral & nasal cavity
- invade sinus rapidly
- Causing vasculitis & thrombosis
- Black eschar formation

CLINICAL features:

- Facial and PeriOrbital swelling
- Images of clinical manifestations
MUCOR MYCOSIS REFERS TO......
infection caused by fungi in order of mucorales.

Most common species are...rhizopus (m c),rhizomucor,cunninghamamella,apophysomy ces,saksenaea,absidia,muccor,andsyncephal astrum.
MAJOR ROUTE OF INFECTION

- INHALTION.
- INGESTION.
- TRAUMATIC INOCULTION.
Pathophysiology

- Angioinvasion
- Vessel thrombosis
- Tissue necrosis
MUCORMYCOSIS CLINICAL PRESENTATION

- Five clinical forms of mucormycosis: Rhinocerebral, pulmonary, gastrointestinal, primary cutaneous and disseminated.
- Rhinocerebral type has the highest frequency and mortality.
RHINOCEREBRAL MUCORMYCOSIS

**Clinical features**

- Onset with nasal stuffiness, epistaxis and facial pain.
- Later, proptosis, chemosis and ophthalmoplegia.
- Fever and confusion.
- Black necrotic eschar on the nasal turbinates or palate: *very characteristic*
RHINOCEREBRAL MUCORMYCOSIS

- 50% of cases occur in patients with DM.
- 50% CASES OF TOTAL CASES OF MUCOR MYCOSIS.
- Usually occurs during an episode of DKA, with disruption of host defense mechanisms, thereby permitting growth of Rhizopus oryzae. Such growth is inhibited by correction of acidosis.
RHINOCEREBRAL MUCORMYCOSIS

**Diagnosis**

- Punch biopsy of the lesion followed by fungal stains and culture.
- Histological examination reveals the characteristic broad, branching hyphae of Rhizopus invading the tissue.
- CT or MRI of the head reveal air-fluid level in the sinuses and involvement of deep tissues.
RHINOCEREBRAL MUCORMYCOSIS

Complications

- Cavernous sinus thrombosis.
- Multiple cranial nerve palsies.
- Visual loss.
- Frontal lobe abscess.
- Carotid artery or jugular vein thrombosis causing hemiparesis.
RHINOCEREBRAL MUCORMYCOSIS
KEY POINTS:

- Mucormycosis is not a disease of healthy person
- All Diabetic patient should have good sugar control
- Environmental Hygiene – Proper maintenance of humidifier
  - Daily cleaning of oxygen mask and tube
- Reuse of mask should be avoided.
- Irrational use of steroid should be avoided
- Antibiotic overuse - avoid
What is Mucormycosis?

Mucormycosis is a fungal disease which occurs in patients with the underlying conditions and predisposing factor such as diabetes mellitus, rampant misuse/overuse of steroids, malignancies, organ transplantation etc. Mode of infection is through inhalation of fungal spores from air. It is not contagious.

Time of presentation: variable but usually around 3rd week of onset of symptoms of COVID-19.

Reasons for increase in Mucormycosis in COVID-19 patients

1. Uncontrolled hyperglycemia due to any reason
2. Misuse, overuse and irrational use of steroids.
3. Prolonged ICU stay, unhygienic humidifiers and irrational use of broad spectrum antibiotics may also be associated with mucormycosis
4. Pre-existing co-morbidities such as haematological malignancies, use of immunosuppressants, solid organ transplant etc.

Signs and symptoms:

1. Facial pain, pain over sinuses, pain in teeth and gums
2. Paraesthesia / decreased sensation over half of face.
4. Nasal crusting and nasal discharge which could be blackish or blood tinged.
5. Conjunctival infection or chemosis.
6. Periorbital swelling.
7. Blurring of vision/ diplopia.
8. Loosening of teeth
9. Discolouration (pal) of palate/ turbinate insensitive to touch, eschar over palate
10. Worsening of respiratory symptoms, haemoptysis, and chest pain; headache, alteration of consciousness and seizures etc

Diagnosis:

- KOH mount and microscopy, histopathology of debrided tissue (presence of Ribbon like asperate hyphae 5-15 µ thick that branch at right angles). Culture(don’t wait for results to initiate therapy as mucormycosis is an emergency.
- Relevant radiological investigations such as CT of sinuses, CT chest for suspected pulmonary involvement (presence of more than 10 nodules, reverse halo sign, CT bronchus sign, pleural effusion-highly suggestive of mucor), MRI brain etc to see the extent of systemic involvement

Management:

- One should have a high index of suspicion of invasive fungal infection such as Mucormycosis in the presence of predisposing conditions as mentioned above. Timely initiation of treatment reduces mortality. Multidisciplinary Team approach is required. Treatment of Mucormycosis involves combination of surgical debridement and antifungal therapy.
- Liposomal Amphotericin B in initial dose of 5mg/kg body weight (10 mg/kg body wt in case of CNS involvement) is the treatment of choice. It should be diluted in 5% dextrose, it is incompatible with normal saline/ Ringer Lactate. It should be given over 2–3 hours and should be started with full dose from day 1. Monitoring for kidney function tests and serum electrolytes is recommended. It has to be continued till a favourable response is achieved and disease is stabilized which may take 3-6 weeks following which step down to oral Posaconazole (300 mg delayed release tablets twice a day for 1 day followed by 300 mg daily) or Isavuconazole (200 mg 1 tablet 3 times daily for 2 days followed by 200 mg daily) shall have to be taken for prolonged period as per advice of the physician.
- The therapy has to be continued until clinical resolution of signs and symptoms of infection as well as resolution of radiological signs of active disease and elimination of predisposing risk factors such as hyperglycemia, immunosuppression etc. It may have to be given for quite long periods of time.
- Conventional Amphotericin B (deoxy cholate) in the dose 1-1.5mg/kg may be used if liposomal form is not available.
- Kidney Functions must be monitored during the entire management period.
Rhino-orbital-cerebral Mucormycosis

TREAT (Target Recognizing Early & Aggressively Treat) MUCOR

- Uncontrolled diabetes mellitus
- Treated for COVID-19 with corticosteroids
- Treated for COVID-19 with immunomodulators
- Treated with mechanical ventilation
- Long standing Oxygen therapy

Facial pain
Sinus headache
Stuffy nose
Decreased vision
Bloody nasal discharge
Dental pain

Facial swelling
Facial discoloration
Ptosis
Proptosis
Restricted EOM
CRAO
Ophthalmoplegia
Panophthalmitis
Palatal eschar
Nasal eschar

CBC
FBS, PPBS and HbA1c
RFT
Deep nasal swab for Grams, KOH and CFW + plate blood agar and fungal media (SDA or PDA)
Diagnostic nasal endoscopy
MRI orbit, PNS and brain with contrast
CT PNS

Examination

Broad management guidelines

Medical management

- Induction with Liposomal Amphotericin B (L-AMB) 5 to 10 mg/kg/day for 2 weeks (all patients)
- Dual therapy: L-AMB + Oral Posaconazole dose 300 mg BD for day 1 and then 300 mg OD for 2 weeks (all patients)
- Oral Posaconazole 300 mg BD for a further 2-4 weeks till radiological stabilization (all patients)

Surgical management

- Early surgical debridement of sinuses (all patients)
- Transcutaneous retrobulbar Amphotericin B (TRAMB) 1 ml of 3.5 mg/ml (select cases only)
- Orbital Exenteration (patients with extensive orbital involvement)

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Why the surge in Mucormycosis

- COVID-19 has tendency to worsen diabetes and also precipitate diabetes in previously normal individuals.
- The Covid 19 infection itself is associated with neutropenia and may lead to immune compromise caused by impaired or inappropriate immune responses.
- Immunosuppressive treatments are being widely used for treatment of Covid-19 infection.
- The severity of Mucor infection is largely dependent on the patient's immunity and general health.
- Coexistence of Covid – 19 infection with high blood sugar levels, and immunosuppressive treatments would expectedly increase incidence and severity of Mucormycosis.
- Mucor infection may occur during Covid-19 infection, or after a few weeks of apparent recovery from it.

Covid-19 Infection and Rhino-orbito-cerebral Mucormycosis
Treatment Organization & Guidance

Checklist of sentinel signs/symptoms to be monitored in patients admitted with Covid-19

- Nasal sinuses, Mucor infection (relatively early disease)
- Yes / Orbital Mucor infection (moderately advanced disease)
- Headache and naso-occlusion especially if persistent or severe and not responding to pain medicines.
- Nasal crusting and nasal discharge which could be brownish or blood tinged
- Pain or loss of vision on face
- Discoloration of skin of face / localized facial puffiness
- Loss of sense of smell, taste
- Discoloration/ulceration of palate
- Eye swelling or redness, double vision, loss of vision, Eye pain, drooping eyelid
- Intracranial infection (very advanced disease)
- II-VI cranial nerve palsies (Cavernous sinus involvement) ; signs of MCA thrombosis

Treatment principles

Urgent intervention to minimize progression and mortality / loss of eye

- Treatment of co-morbid illness/ blood sugar control & of Covid illness
- To review Covid treatments to minimize immunocompromise.
- Twice daily evaluations as per Mucor Checklist above for progression to orbital / intracranial involvement.
- Confirmation of Diagnosis by
  - KOH Smear/ Biopsy of involved lesion with appropriate precautions.
    - Radiological signs in the initial phase may often be subtle and minimal and may not demonstrate fluid simulating and bone erosion. Lack of these signs does not exclude the diagnosis.
- Antifungal treatment with Amphotericin B / Posaconazole.

In situations of high clinical suspicion: consider initiation of anti-fungal chemotherapy prior to microbiological confirmation.

- Early surgical debridement after stabilization of systemic illness and ensuring facilities for post surgical care / ventilation as anticipated.

For supplementary notes visit: https://drive.google.com/file/d/1Y3SNa7oH0qW6Z3e6e60XJNdPf54PBqS/view?usp=sharing
EVIDENCE BASED ADVISORY IN THE TIME OF COVID-19
(Screening, Diagnosis & Management of Mucormycosis)

Mucormycosis - if uncared for - may turn fatal
Mucormycosis is a fungal infection that mainly affects people who are on medication for other health problems that reduces their ability to fight environmental pathogens.

- Sinuses or lungs of such individuals get affected after fungal spores are inhaled from the air.

This can lead to serious disease with warning signs and symptoms as follows:
- Pain and redness around eyes and/or nose
- Fever
- Headache
- Coughing
- Shortness of breath
- Bloody vomits
- Altered mental status

What predisposes
- Uncontrolled diabetes mellitus
- Immunosuppression by steroids
- Prolonged ICU stay
- Co-morbidities - post transplant/malignancy
- Vancomycin therapy

How to prevent
- Use masks if you are visiting dusty construction sites
- Wear shoes, long trousers, long sleeve shirts and gloves while handling soil (gardening), moss or manure
- Maintain personal hygiene including thorough scrub bath

When to Suspect (in COVID-19 patients, diabetics or immunocompromised individuals)
- Sinusitis - nasal blockade or congestion, nasal discharge (blood/bloody), facial pain on the cheek bone
- One sided facial pain, numbness or swelling
- Blackish discoloration over bridge of nose/palate
- Toothache, loosening of teeth, jaw involvement
- Blurred or double vision with pain; fever, skin lesion; thrombosis & necrosis (eschar)
- Chest pain, pleural effusion, hemothorax, worsening of respiratory symptoms

Dos
- Control hyperglycemia
- Monitor blood glucose level post COVID-19 discharge and also in diabetics
- Use steroids judiciously - correct timing, correct dose and duration
- Use clean, sterile water for humidifiers during oxygen therapy
- Use antibiotics/antifungals judiciously

Don’ts
- Do not miss warning signs and symptoms
- 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
- Do not hesitate to seek aggressive investigations, as appropriate (KOH staining & microscopy, culture, MALDI-TOF), for detecting fungal etiology
- Do not lose crucial time to initiate treatment for mucormycosis

How to manage
- Control diabetes and diabetic ketoacidosis
- Reduce steroids (if patient is still on) with aim to discontinue rapidly
- Discontinue immune-modulating drugs
- No antimicrobial prophylaxis needed
- Extensive Surgical Debridement - to remove all necrotic materials
- Medical treatment
  - Install peripherally inserted central catheter (PICC line)
  - Maintain adequate systemic hydration
  - Infuse Normal saline IV before Amphotericin B infusion
  - Anti fungal Therapy, for at least 4-6 weeks (see the guidelines below)
- Monitor patients clinically and with radiology imaging for response and to detect disease progression

Team Approach Works Best
- Microbiologist
- Internal Medicine Specialist
- Intensivist
- Neurologist
- ENT Specialist
- Ophthalmologist
- Dentist
- Surgeon (maxillofacial/plastic)
- Biochemist

Detailed management guideline & information available on the following:
- https://www.jmp.org/v3/mypaper/Indian%20Advisory%2072231- 6A98512C019551.png
- https://www.jmp.org/v3/mypaper/Indian%20Advisory%2072231- 6A98512C019551.png

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Solspre Nasal Spray
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4.5 ★ 65 Ratings & 31 Reviews