MUCORMYCOSIS
CLINICAL FEATURES

Dr. Ilad Alavi Darazam
Assistant Professor
Clinical Fellowship in Immunodeficiency and Transplant Infectious Diseases,
Loghman Hakim Hospital, SBMU
- Loghman Hospital, Mucormycosis Trend during 15 years
HOST DEFENSE AGAINST MUCORMYCOSIS

• Individuals who
  – lack phagocytes or
  – have impaired phagocytic function
• are at higher risk.
The most frequent portal of entry:

- **Respiratory tract** →→ ciliated bronchial cells and their mucus → pulmonary alveolar macrophages

- **Gastrointestinal tract**

- **Direct inoculation** through sites of skin breakdown (trauma, burn) or exit sites of central venous catheters
Spores are inhaled, then deposited in the nasal turbinates and alveolar space.

Conidia reach distal alveolar space and begin to germinate.

Macrophages phagocytose conidia.

Neutrophils attack hyphal forms. Acquisition of free iron supports hyphal proliferation.

Angioinvasive growth in tissue with hemorrhage, thrombosis, and necrosis.

Impaired by glucocorticoids.

Impaired by glucocorticoids, hyperglycemia, acidosis, neutropenia.
Among patients with hematologic malignancy, those with acute myelogenous leukemia (AML) have the highest risk for mucormycosis, with incidences ranging from 1% to 8%.
- RF: renal failure, diabetes mellitus, and prior voriconazole and/or caspofungin

- Tacrolimus: ↓ risk
Liver transplant recipients were more likely to have disseminated disease and had earlier development of mucormycosis after transplantation versus other SOT recipients (median, 0.8 vs 5.7 months).
Corticosteroid Use and Rheumatic Diseases

Additional predisposing factors for opportunistic mucormycosis include:
- hypocomplementemia,
- nephrotic syndrome,
- uremia,
- leukopenia, and
- diabetes mellitus.
• Prolonged Use of Voriconazole:

??
CLINICAL MANIFESTATIONS

• The clinical hallmark of invasive mucormycosis is tissue necrosis resulting from angioinvasion and subsequent thrombosis.
6 major clinical forms:

- (1) rhino-orbito-cerebral,
- (2) pulmonary,
- (3) cutaneous,
- (4) gastrointestinal,
- (5) disseminated, and
- (6) uncommon rare forms, such as endocarditis, osteomyelitis, peritonitis, and renal infection
The most common reported sites:

- **sinuses (39%)**, 
- lungs (24%), and 
- skin (19%)

Dissemination developed in 23% of these cases.
The overall **mortality rate** for the disease is

- 44% in diabetics,
- 35% in patients with no underlying conditions, and
- 66% in patients with malignancies.
The **mortality rate** varied with the site of infection and host:

- 96% of patients with disseminated infections,
- 85% with gastrointestinal infections, and
- 76% with pulmonary infections
The major risk factors

- uncontrolled diabetes mellitus in ketoacidosis,
- other forms of metabolic acidosis,
- treatment with corticosteroids,
- organ or bone marrow transplantation,
- neutropenia,
- trauma and burns,
- malignant hematologic disorders, and
- deferoxamine therapy in patients receiving hemodialysis
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<th>PREDISPOSING CONDITION</th>
<th>PREDOMINANT SITES OF INFECTION</th>
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<td>Diabetes mellitus</td>
<td>Rhinocerebral, sino-orbital, cutaneous</td>
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<td>Malignancy (typically hematologic</td>
<td>Pulmonary, sinus, cutaneous, sino-orbital, disseminated</td>
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<td>malignancy)</td>
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<td>Hematopoietic stem cell transplantation</td>
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<td>Intravenous drug use</td>
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<td>Deferoxamine therapy</td>
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<td>gastrointestinal</td>
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<td>Trauma</td>
<td>Cutaneous, ocular</td>
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Pulmonary Mucormycosis

Most often:

- Neutropenic patients with cancer undergoing induction chemotherapy

- HSCT and have graft-versus-host
• Prolonged high-grade fever (38°C) unresponsive to broad-spectrum antibiotics

• Non-productive cough: common

• Hemoptysis, pleuritic chest pain, and dyspnea: less common
• In rare circumstances, an endobronchial or tracheal lesion, especially in diabetics: airway obstruction, resulting in lung collapse/invasion of hilar blood vessels with subsequent massive hemoptysis

• Pulmonary mucormycosis may invade lung-adjacent organs, such as the mediastinum, pericardium, and chest wall.
• on chest images: nonspecific and indistinguishable from those of pulmonary aspergillosis

Infiltration, consolidation, nodules, cavitations, atelectasis, effusion, posterior tracheal band thickening, hilar or mediastinal lymphadenopathy, and even normal findings
Figure 6. Necrosis in a 59-year-old man who underwent renal transplant. (a) Axial CT image demonstrates a necrotic consolidation in the left lower lobe with adjacent pleural effusion. (b) Axial CT image depicts enlargement of the consolidation after 20 days with new pleural thickening. (c) Axial CT image shows central cavitation in the left lower lobe lesion. (d) Gross photograph shows the left lung with the necrotic cavity exposed.
• presence of multiple lung nodules (≥10) and pleural effusion on initial CT scans was an independent predictor of pulmonary mucormycosis.

• Reversed halo sign: more common in patients with mucormycosis than other invasive pulmonary fungal infections
Rhino-Orbito-Cerebral Mucormycosis (ROCM)

- The most common form: in diabetes mellitus

The fungus invades the **cranium** through either:
- the orbital apex,
- the orbit,
- superior orbital fissure and
- cavernous sinus route or
- through the maxillary and mandibular nerves to Meckel’s cave; or
- through the sphenoid sinus via the clivus
- cribriform plate of the ethmoid bone
Orbital involvement in ROCM is common...results from the spread of infection from:

- the ethmoidal sinuses via
  - blood vessels or
  - the lamina papyracea, or
- from the maxillary sinus via the infraorbital foramen.
Orbital involvement presents with

• ophthalmoplegia (with or without pain),
• proptosis and
• partial or complete loss of vision.
The finding of ophthalmoplegia and proptosis with ethmoidal or maxillary sinusitis should strongly arouse suspicion of ROCM.
suggest mucormycosis

- multiple cranial nerve palsies,
- unilateral periorbital facial pain,
- orbital inflammation,
- eyelid edema,
- blepharoptosis,
- proptosis,
- acute ocular motility changes,
- internal or external ophthalmoplegia,
- headache, and
- acute vision loss
Proptosis occurs owing to necrotic eschar at

• the orbital apex and edema of the extraocular muscles.
• Partial loss of vision suggests infiltrative or compressive optic neuropathy,

whereas

• complete loss of vision suggests either posterior ischaemic optic neuropathy or central retinal artery occlusion.
When routed through the **cavernous sinuses**, intracranial infection leads to:

- maxillary and mandibular nerve palsies and
- **internal carotid** artery thrombosis,
- **pseudoaneurysm** or,
- in rare cases, **carotid cavernous fistula**.
From the **sphenoid sinus**, mucor travels across the **clivus** to the **basal meninges** and the **basilar artery**, leading to **thrombosis** or **rupture** with subarachnoid hemorrhage.
A black necrotic eschar is the hallmark of mucormycosis.

- Bone destruction is often seen only late in the infection course after soft-tissue necrosis has occurred.
Cutaneous Mucormycosis

- Gradual, and it may progress slowly, or it may be fulminant:
  leading to gangrene and hematogenous dissemination
Gastrointestinal Mucormycosis

• Premature neonates,
• malnourished children,
• individuals with HMs,
• diabetes mellitus,
• a history of corticosteroid use

✓ Stomach is most commonly affected
Disseminated Mucormycosis

• The organ most commonly associated with dissemination is the lung.

• Although the brain is a common site of spread, metastatic lesions may also be found in the liver, spleen, heart, and other organs.

• Without appropriate treatment, disseminated mucormycosis is always fatal.
• Endocarditis, osteomyelitis, peritonitis, and pyelonephritis

• A rare cause of prosthetic or native valve endocarditis

• Hematogenous osteomyelitis is extremely rare.
DIAGNOSIS

• the identification of organisms in tissue by histopathology with culture confirmation

• polymerase chain reaction (PCR)-based techniques on histologic specimens

• Antigen tests for Aspergillus (galactomannan) and other fungal species (β-d-glucan) are not useful for mucormycosis.
• Almost always requires histopathological evidence of fungal tissue invasion.
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