Mucormycosis of Central Nervous System

Role Of Neurosurgical Treatment

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INTRODUCTION

Definition:
The term mucormycosis refers to invasive disease caused by filamentous fungi belonging to the order Mucorales.

Risk Factors:
- Poorly controlled DM
- Immunosuppressed patients such as
  - Hematological cancer
  - Recipients of solid organ
  - Hematopoietic stem cell transplantation,
- Sustained severe trauma to soft tissues,
PATHOGENESIS

- Patients with diabetes mellitus usually develop *rhino-orbital-cerebral mucormycosis* (ROCM)

- Patients with hematological neoplasms tend to develop *sino-pulmonary disease*,

- **Trauma patients** present with *necrotizing skin and soft tissue infections*
PATHOGENESIS

- In all anatomical locations, relentless tissue invasion and infarction secondary to angioinvasion are the hallmarks of mucormycosis.
# Patterns of Central Nervous System (CNS) Mucormycosis

## Table 1. Patterns of Central Nervous System (CNS) Mucormycosis in Different Patient

<table>
<thead>
<tr>
<th>Underlying Condition</th>
<th>Proportion of CNS Involvement</th>
<th>Form of CNS Involvement</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Rhinocerebral</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>43%</td>
<td>43–52%</td>
</tr>
<tr>
<td>Malignancy</td>
<td>4–19%</td>
<td>4–15%</td>
</tr>
<tr>
<td>Stem cell transplantation</td>
<td>11%</td>
<td></td>
</tr>
<tr>
<td>Trauma</td>
<td>1%&gt;</td>
<td>1%&gt;</td>
</tr>
<tr>
<td>Injection drug use</td>
<td>67%</td>
<td>5%</td>
</tr>
<tr>
<td>Overall</td>
<td>12.8–44.1%</td>
<td>11.3%</td>
</tr>
</tbody>
</table>

Review: Mucormycosis of the Central Nervous System

Amanda Chikley ¹, Ronen Ben-Ami ¹,²,*,† and Dimitrios P Kontoyiannis ³,*,†
Involvement of the CNS occurs:

- 70% due to contiguous spread from the paranasal sinuses and orbits
- 30% are divided equally between isolated CNS infection and hematogenous
ANATOMIC PATTERN OF CNS INVOLVEMENT

- Most common location >>>>> Cavernous Sinus

- Less Common Location >>>> Parenchymal Involvement (frontal and Temporal lobe)

- Very Less Common:
  - Sagittal sinus thrombosis
  - Epidural and subdural abscess
  - Meningitis is rare, but when present, it may manifest as obstructive hydrocephalus due to infiltration of the ventricular lining
Cavernous Sinus Involvement

- Mucormycosis of the **ethmoid sinus** involvement is most risk factor for involvement and thrombosis of cavernous sinus,

- the **valveless emissary veins** draining this sinus traverse the lamina papyracea and facilitate fungal invasion of periorbital tissue, the orbital apex and the cavernous sinus
INTRACRANIAL INVOLVEMENT

- Infection of the sphenoid sinus can extend into the cavernous sinus, or invade the carotid artery, and from there embolize to the frontal and parietal lobes.
PARENCHYMAL INVOLVEMENT

- Fungal hyphae grow along the internal elastic lamina and extend into the arterial lumen
- Intravascular *thrombosis* and intimal hyperplasia
- Cerebral infarction and hemorrhagic necrosis,
- Hyphal invasion of the necrotic brain parenchyma occurs in advanced CNS mucormycosis and is often a preterminal event.
**ENDOTHELIUM INVASION**

- *Glucose-regulated protein 78 (GRP78)* was identified as a putative endothelial cell receptor for Mucorales.

- Iron and glucose induce GRP78 expression.

- *Spore coat protein homologs (CotH)*, present in Mucorales but absent in non-pathogenic fungi, were identified as fungal ligands for GRP78.
CLINICAL FEATURES
Radiologic Finding in CNS

- The three most frequent imaging findings are:
  1. Cavernous sinus thrombosis
  2. Brain infarction
  3. Internal carotid artery occlusion

- the inferior parts of the frontal lobes usually is primarily parenchymal involvement
**Radiologic Finding in CNS**

- Isolated Cerebral Mucormycosis
  - Case: altered mental status, headache, hemiplegia and dysarthria in a person with a history of intravenous drug injection

- Imaging: typically shows *unilateral basal ganglia* involvement
  - Infection may progress rapidly to involve the contralateral basal ganglia

- Lesions may also appear in the cerebellum and fourth ventricle
RECOMMENDATIONS FOR TREATMENT OF CNS MUCORMYCOSIS

- **Surgical treatment**
  - Debridement of extracranial site of infection:
    Sinus debridement using endoscopic approach for early disease and open surgery for extensive disease.

- **Consider indications for neurosurgery:**
  - Increased intracranial pressure (e.g. hemispheric stroke)
  - Obstructive hydrocephalus
  - Lesions compressing the spinal cord
RECOMMENDATIONS FOR TREATMENT OF CNS MUCORMYCOSIS

Antifungal treatment

- **Initial treatment:**
  Liposomal amphotericin B 5-10 mg/kg/day IV for initial 28 days.

- **Alternative:** Isavuconazole 300mg TID for 2 days followed by 300mg QD, IV or PO.

- **Duration of treatment:** at least 6 months. Factors affecting treatment duration are the extent of surgery done and immune status of the patient.
RECOMMENDATIONS FOR TREATMENT OF CNS MUCORMYCOSIS

Ancillary treatment

- Correction of hyperglycemia and ketoacidosis.
- Discontinue or reduce dose of immunosuppressive drugs, when possible.
- Consider hyperbaric oxygen for rhino-orbito-cerebral mucormycosis.
SURGICAL OUTCOME

- Debridement of infected brain tissue is associated with severe morbidity and uncertain benefits.

- Decisions regarding the surgical approach, its goals and extent require careful discussion among neurosurgeons, infectious diseases specialists, radiologists, patients and their families.

- Radical excision of fungal brain abscess or granuloma should be avoided.
**Case 1**

- A 40 y/o male
- Headache
- Mild left ptosis
- DM
- Post COVID
CASE 1
CASE 2

- A 33 y/o male
- Headache and seizure
- DM
- Post COVID
CASE 2
CASE 2

- Clinical sign of ICP rising 2 weeks after endonasal debridement.
CASE 2

After transcranial approach
Case 3

- A 55 y/o male
- NLP on left eye and frozen
- DM
Macroscopic Examination:

Specimens received in 2 separate formalin containers and consist of
A: Multiple irregular tan gray soft tissue fragments totally measuring 2x0.8x0.5 cm. TS in 1 block
B: Two irregular tan soft tissue fragment measuring 1x0.5x0.5 cm. TS in 1 block

Microscopic Examination:

Histologic findings confirm the diagnosis.

Diagnosis:

A, B: Cerebellar and brain abscess, resection:
Gliotic brain tissue with extensive necrosis and broad pauciseptate right-angle branching fungal hyphae consistent with mucormycosis
Thanks For Your Attention

Any Question?