Mucormycosis

CONSULT ID

While benign inhalation of spores (mucormycetes) commonly occurs among non-immunocompromised individuals, disease is usually limited to those with risk factors (see below). For those with disease, mucormycosis is associated with high mortality. Rhino-orbital-cerebral and pulmonary infections are the most common syndromes of mucormycosis. Rhino-orbital-cerebral mucormycosis is associated with acute sinusitis, fever and nasal ulceration/necrosis. Pulmonary mucormycosis presents with fever, cough, dyspnea and sometimes hemoptysis.
Consultation with **infectious diseases is mandatory** for clinical concerns of mucormycosis.

Risk factors for mucormycosis

Recent neutropenia (<0.5x 10^9 neutrophils/ L) for > 10 days
Active hematologic malignancy
Receipt of allogenic hematopoietic cell transplantation
Receipt of solid organ transplantation
Treatment with T-cell immunosuppressants (eg: calcineurin inhibitors, tumor necrosis factor-a blockers, lymphocyte-specific monoclonal antibodies, immunosuppressive nucleoside analogues) during the past 90 days
Prolonged corticosteroids (>0.3 mg/kg prednisone over 3 weeks in the past 60 days)
Treatment with B-cell immunosuppressants (eg: Bruton's tyrosine kinase inhibitors)
Inherited severe immunodeficiencies (eg: chronic granulomatous disease, STAT 3 deficiency,severe combined immunodeficiency)
Acute graft-versus-host disease grade III or IV involving gut, lungs, or liver refractory to steroids
Poorly controlled diabetes with ketoacidosis (rhino-cerebral)

DIAGNOSTIC CONSIDERATIONS

- Chest and sinus CT = initial diagnostic imaging (X-ray insufficient). If CT concerning for sinus involvement --> MRI to R/O ocular, cavernous sinus or intracranial involvement and ENT consultation for direct visualization and biopsy with culture.
- Consultation with respirology is indicated for bronchoscopy or to obtain tissue biopsy in pulmonary cases.
- Definitive diagnosis: **tissue biopsy** and demonstration of Mucorales on histopathology (and ideally culture), or, culture recovery from sterile site (eg. pleural fluid).
- If mucormycosis suspected, call laboratory to ensure safe and adequate sample processing.
- Mucormycosis is **not associated with positive 1,3-beta-D-glucan or galactomannan**. These tests cannot exclude or confirm mucormycosis.

TREATMENT CONSIDERATIONS:

Treatment of mucormycosis involves multiple modalities including **surgical debridement of necrotic tissue, early administration of antifungal therapy and addressing the predisposing factor** (eg: treating hyperglycemia or decreasing immunosuppression). In the right clinical scenario, initiation of liposomal amphotericin B may be indicated while awaiting tissue biopsy or if histopathology is non-diagnostic.

PHARMACOLOGIC TREATMENT

Initial therapy	**Liposomal amphotericin B**[1] 5 mg/kg IV daily[1,2] is the usual starting dose For patients with CNS involvement start at 10mg/kg IV daily Maximum dose of 500-1000 mg daily for patients weighing over 100 kg. Consult pharmacy to adjust in cases of obesity and CKD.	Duration of ampho B therapy depends on extent of clinical disease and adequacy of surgical debridement (duration as per ID consultation).
Step-down therapy	**Posaconazole**[3,4] delayed-release tablets (300 mg q12h on the first day, then 300 mg once daily) PO taken with food OR **Isavuconazole**[5]: Loading dose 200mg q8h x 6 doses then 200mg PO daily	The timing and choice of stepdown should be made with the input of the infectious diseases consultant and ideally guided by microbiology results, drug interactions, and prior antifungal exposures. Duration depends on clinical disease evolution and host immunosuppression. Often many months.

[1] Caution: amphotericin B, including its liposomal formulations, may cause nephrotoxicity. If CrCl under 50mL/min, please involve pharmacist for dosing. Consider pre-dose hydration, limit use of concomitant nephrotoxic agents and monitor creatinine and electrolytes daily until stability achieved.
[2] There is no convincing evidence for combination therapy.
[3] Check serum trough concentration of posaconazole one week after initiation of therapy (goal: trough >1 mcg/mL). Refer to MUHC ASP Azole Therapeutic Drug Monitoring guidelines for details.
[4] Significant drug-drug interactions and prolongs QTc. Consult pharmacy, obtain baseline ECG at the start of therapy and 3 days after treatment initiation.
[5] Significant drug-drug interactions, shortens QTc interval. Obtain baseline ECG and 3d after treatment initiation.

REFERENCES

- Roden MM, et al. Epidemiology and Outcome of Zygomycosis: A Review of 929 Reported Cases. *Clin Infect Dis*. 2005;41(5):634-653. doi:10.1086/432579
- Marty FM, et al. Isavuconazole treatment for mucormycosis: a single-arm open-label trial and case-control analysis. *Lancet Infect Dis*. 2016;16(7):828-837. doi:10.1016/S1473-3099(16)00071-2

Drafted by C. Boodman (ID) Reviewed by M. Semret (ID), D. Vinh (ID), M. Cheng (ID), F. Bourdeau (pharmacy). Approved by ASP committee on May 19, 2021; approved by P&T committee on June 23, 2021.