Candidemia

CONSULT ID

Candidemia is defined as *Candida* fungal species in the blood, identified on blood culture. Untreated candidemia is associated with elevated mortality and thus *Candida* in the blood should always be treated. Candidemia can be associated with hematogenous seeding and complications such as endophthalmitis and endocarditis.

Infectious diseases consultation is encouraged for all patients with Candidemia.

The most common *Candida* species at the MUHC are: *C. albicans* (66%), *C. glabrata* (20%), *C. parapsilosis* (8%), *C. tropicalis* (3%), *C. krusei* (2%).

Risk factors for candidemia

Central venous catheters
Total parenteral nutrition
Broad-spectrum antibiotic use
Candida colonization at multiple sites (e.g. skin, GU tract, respiratory tract)
Gastrointestinal perforations/ abdominal surgery
Injection drug use
Burns
Immunosuppression (eg: neutropenia, ongoing chemotherapy, solid organ or hematopoietic cell transplant)

TREATMENT CONSIDERATIONS:

Treatment of candidemia involves multiple modalities including source control (eg: removing central lines), antifungal therapy and evaluation for metastatic disease. All patients with candidemia should undergo an **ophthalmologic examination by an ophthalmologist**, in the presence or absence of ocular symptoms.

1) Ensure 2 sets of blood cultures drawn **before** antifungal administration.
2) Prompt initiation of antifungal therapy within 12 hours of initial fungemia, when blood gram stain shows yeast[1] (before speciation and susceptibility testing)
3) Remove central venous catheter, if present, within 24 hours of gram stain result.
4) **Repeat blood cultures** daily to document clearance (1st day of negative blood cultures).
5) **Ophthalmological examination within 7-14 days of culture result, unless neutropenic.**[2]
6) Cases involving immunosuppression, prosthetic heart valves or persistent fungemia: echocardiogram to exclude endocarditis.
7) After 5 days of echinocandin therapy, may step down to oral (or IV) fluconazole in patients with fluconazole-susceptible Candidemia, IF patient afebrile x 24h, hemodynamically stable, Candidemia has cleared, and non-neutropenic.

[1] Among immunocompromised patients, yeast in the blood could also indicate other fungi, such as cryptococcus.
[2] Neutropenia may diminish sensitivity of ophthalmologic exam; **timing** should be discussed with ID.

PHARMACOLOGIC TREATMENT

Initial antifungal therapy **Candidemia only**	**Caspofungin**[1] 70 mg IV loading dose, then 50 mg IV die
Known/suspected ocular/CNS involvement	**Liposomal Amphotericin B**[2] 4mg/kg IV q24h
Preferred antifungal step-down for *C. albicans* and other fluconazole susceptible species[5]	**Fluconazole**[3] 400mg PO (or IV if PO not tolerated) die
Total duration	14 days total from first negative blood culture result EXCEPT if metastatic complications (endocarditis, endophthalmitis, septic arthritis, osteomyelitis) Total duration includes both caspofungin and possible fluconazole step-down.

[1] Caspofungin: if Child-Pugh B or C hepatic insufficiency adjust dosing with pharmacist.
[2] L-Ampho B: no renal dose adjustment; max dose 400mg if body weight > 100kg (consult pharmacist).
[3] Fluconazole: adjust dose if CrCl under 50 ml/min. Order initial ECG (monitor for QTc prolongation), monitor liver enzymes, verify potential drug-drug interactions. Fluconazole is highly bioavailable: oral therapy is appropriate for most patients. **If BMI ≥30 kg/m²:** Dosing based on **actual body weight** - 6 mg/kg once daily (maximum daily dose: 1.6 g)
[5] **All *Candida krusei* are intrinsically fluconazole resistant**. Some isolates of *Candida glabrata* and *Candida parapsilosis* are fluconazole resistant.

Additional considerations:

- For non-neutropenic patients with sepsis, empiric antifungal therapy is not indicated.
- For critically-ill patients with ongoing fever or hypotension despite antibiotic therapy, consult infectious diseases prior to starting empiric antifungal therapy.

REFERENCES

- Pappas PG, Kauffman CA, Andes DR, et al. Clinical Practice Guideline for the Management of Candidiasis: 2016 Update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2016;62(4):e1-e50. doi:10.1093/cid/civ933
- Fernández-Cruz A, Cruz Menárguez M, Muñoz P, et al. The search for endocarditis in patients with candidemia: a systematic recommendation for echocardiography? A prospective cohort. *Eur J Clin Microbiol Infect Dis*. 2015;34(8):1543-1549. doi:10.1007/s10096-015-2384-z
- Johnson MD, Lewis RE, Dodds Ashley ES, et al. Core Recommendations for Antifungal Stewardship: A Statement of the Mycoses Study Group Education and Research Consortium. *J Infect Dis*. 2020;222(Supplement_3):S175-S198. doi:10.1093/infdis/jiaa394

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 20, 2021; approved by P&T committee on June 23, 2021.