Candidemia

MICROBIOLOGY

- Small budding yeast abundant in the environment, and common colonizer of the human GI tract
- Generally opportunistic; predominantly causes infection in compromised hosts (immunocompromised, structural compromise)
- Major risk factors include indwelling central venous catheter, recent surgery (in particular intraabdominal), glucocorticoid use, and preceding broad-spectrum antimicrobial use
- Candida can seed to various deep physiologic sites, including but not limited to the liver, eye, heart, and CNS
- Candida isolated on urine cultures is most often colonization or contamination as opposed to true infection.
- Candida isolated from the respiratory tract is almost always a contaminant. True Candida pneumonia is exceedingly rare.
- The most commonly isolated species in human infections is Candida albicans, which is highly susceptible to fluconazole. Candida glabrata may be fluconazole resistant, and when susceptible typically requires higher doses. Candida krusei is intrinsically resistant to fluconazole.

Candida Susceptibility by Species

Candida Species	General Susceptibilities	Resistance
C. albicans, C. tropicalis, C. parapsilosis, C. dubliniensis, C. guillermondi	Fluconazole Micafungin Amphotericin B	*Minimal*
C. lusitaniae	Fluconazole Micafungin	Amphotericin B
C. glabrata	Micafungin Amphotericin B Voriconazole, Posaconazole	Fluconazole (If susceptible to fluconazole, high dose fluconazole is necessary)
C. krusei	Micafungin Amphotericin B Voriconazole, Posaconazole	Fluconazole (intrinsically resistant)
C. auris	Micafungin +/-Amphotericin B	Fluconazole (intrinsically resistant)

INITIAL MANAGEMENT

Empiric Therapy

Classification	Empiric Therapy
Clinically Stable *No sepsis or septic shock*	Micafungin 100 mg IV q24h **OR** Fluconazole 800 mg PO/IV once, then 400 mg PO/IV daily
Critically Ill *Sepsis or septic shock*	Micafungin 100 mg IV q24h
Suspected endocarditis or infected cardiac device	Micafungin 150 mg IV q24h

Doses may require adjustment for renal insufficiency

- Regardless of isolate susceptibility, micafungin is suggested as empiric therapy in critically ill patients. Azoles have shown inferiority in this setting.

✓ Repeat blood cultures x 2 sets immediately when blood cultures return positive, then q48h until clear
  - At least **one set** of blood cultures should be peripheral

✓ Initiate empiric therapy with micafungin until species and/or susceptibility results return
  - Micafungin has limitations with respect to penetration of different physiologic sites (CNS and eye most notably, urinary penetration is controversial)

- ✓ Identify the source of infection and control the source where applicable
- ✓ Remove or exchange any hardware that can feasibly be removed or exchanged (central venous catheters, etc)
    - Removal of central venous catheters in neutropenic patients with candidemia should be individualized as source is often GI. Routine catheter removal in this population may not be necessary.
- ✓ Hardware that is exchanged while the patient is candidemic should be **replaced** when blood cultures are clear to reduce risk of recurrence
- ✓ Duration of therapy is minimum 14 days from negative blood cultures

- ✓ Infectious Diseases consultation STRONGLY RECOMMENDED

Echocardiography

- ✓ TTE is not necessary in all patients with candidemia.
- ✓ Consider TTE if:
    - Clinical stigmata of infective endocarditis
    - Sustained candidemia
    - Persistent fever despite appropriate treatment
    - Prosthetic valve or cardiac implanted electronic device
    - Injection drug use

Ophthalmological Examination

- ✓ Routine ophthalmologic exam is not necessary for all patients with candidemia.
- ✓ Consider ophthalmologic exam for patients:
    - with signs or symptoms concerning for ocular infection (e.g., ocular pain, decreased visual acuity, conjunctival injection, hypopyon)
    - unable to report symptoms (e.g., intubated and sedated)
- ✓ Ophthalmological exam may be falsely negative in neutropenia. Consider deferring/repeating exam after neutrophil recovery to improve sensitivity

METASTATIC COMPLICATIONS

- Candida can seed from the blood to numerous other physiologic sites. However, historic rates of ocular involvement (e.g., endophthalmitis) may be overstated.
- Candida has a particular propensity for biofilm formation and attachment to hardware
- Sustained candidemia in particular should be investigated for source control issues or metastatic foci
- Patients with prolonged/profound neutropenia with candidemia should be evaluated for chronic disseminated (hepatosplenic) candidiasis using abdominal imaging.

DIRECTED THERAPY:

- Timing of transition
    - Transition from micafungin to fluconazole (usually within 5-7 days) in patients who are clinically stable, cleared blood cultures, and have fluconazole-susceptible isolate.
- Dosing
    - Fluconazole 400 mg PO/IV daily
    - If *C. glabrata*, fluconazole 800 mg PO/IV daily
    - Fluconazole has high oral bioavailability. Oral dosing is equivalent to IV dosing in those with a functional GI tract.
- Duration
    - Minimum 2 weeks treatment
    - May be longer if underlying source control issue or endovascular infection

REFERENCES

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