Endoftalmite in corso di Candidemia da Candida albicans

Ercole Concia
**Background**

- Invasive Candidiasis is a condition strictly associated with medical progress, in particular for the increasing complexity of surgical procedures.

- Of all *Candida* species more than 90% of invasive disease is caused by 5 pathogens (*C. albicans*, *C. glabrata*, *C. tropicalis*, *C. parapsilosis* and *C. krusei*).

- Candidemia is one of the most common healthcare-associated bloodstream infections in US and European hospitals, typically ranking as the third or fourth most common cause of healthcare-associated BSI (bloodstream infection).
Background

- Candidemia is associated with up to 47% attributable mortality and several studies have demonstrated that mortality is closely linked to both timing of therapy and source control.

- A worse outcome and selection of resistant strains are caused by inappropriate initial therapy and/or delay in prescription.

- Recently, it has been observed a shift towards non-albicans species, especially in some particular settings (Intensive care units, hematological and transplant units).
Case Report

Donna di 55 anni
In Anamnesi patologica remota si segnala:
• Diabete mellito tipo II

La paziente presentava un difetto di motilità esofagea che le causava un’importante disfagia.

Andava pertanto incontro a progressivo dimagrimento e scadimento delle condizioni generali dovute a malnutrizione.
Ricoverata in Chirurgia veniva sottoposta ad intervento chirurgico correttivo di acalasia esofagea.

Tale intervento non risultava risolutivo per cui veniva sottoposta ad un secondo intervento correttivo.

Dopo alcuni giorni dal secondo intervento la paziente presentava iperpiressia, superiore ai 38,5° C.

Gli esami ematochimici mostravano:
- GB 14000/mmc (N 78%)
- PCR 153 mg/L
- Creatinina nella norma
La paziente presentava Rx torace nella norma, non alterazioni dell’esame urine. Portatrice di CVC e alimentata con NPT (nutrizione parenterale totale). Ferita chirurgica in ordine.

Dopo esecuzione di due set di emocolture iniziava terapia antibiotica ad ampio spettro con:

Piperacillina/tazobactam 4,5 g ogni 8 ore + Vancomicina 1g ogni 12 ore
What are main risk factors for invasive Candida infections?
Domanda 1

What are main risk factors for invasive Candida infections?

✔ Terapia antibiotica prolungata
✔ Chirurgia
✔ Diabete
✔ Terapia cortisonica
### Risk Factors for IC

#### Table 3  Risk factors for IC

<table>
<thead>
<tr>
<th>Hospitalisation in ICU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute/chronic organ dysfunction requiring intensive care/invasive procedures (e.g. mechanical ventilation, vasoactive drugs, renal substitution and extracorporeal circulation systems, high-volume fluid or haemocomponents infusions, tracheostomy and others)</td>
</tr>
<tr>
<td>Solid organ transplantation (and type)(^a)</td>
</tr>
<tr>
<td>Onco-haematological diseases (and type) and stem cell transplantation, especially with graft-versus-host disease (GVHD)(^a)</td>
</tr>
<tr>
<td>Surgery (especially abdominal surgery and surgical revision), trauma and burn patients</td>
</tr>
<tr>
<td>Paediatric and neonatal intensive care units(^a)</td>
</tr>
<tr>
<td>Multiple underlying medical conditions (e.g. elderly patients in medical wards)</td>
</tr>
<tr>
<td>Immunosuppressive therapy</td>
</tr>
<tr>
<td>Renal failure requiring haemodialysis or haemofiltration</td>
</tr>
<tr>
<td>Neutropenia(^a)</td>
</tr>
<tr>
<td>APACHE score</td>
</tr>
<tr>
<td>Multiple site colonisation</td>
</tr>
<tr>
<td>Duration of hospital stay</td>
</tr>
<tr>
<td>Previous history of <em>Candida</em> infection</td>
</tr>
<tr>
<td>Total parenteral nutrition and use of indwelling catheters</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>Previous prolonged antibiotic therapy</td>
</tr>
</tbody>
</table>

\(^a\) Will not be discussed because they are not within the scope of the present consensus
Risk Factors for IC

In all clinical settings the most common risk factors:
  • Surgery
  • Pancreatitis
  • Central vascular catheters
  • Total parenteral nutrition
  • Prolonged broad spectrum antibiotic therapy
    • Diabetes mellitus
  • Multiple sites colonization
    • Renal failure/dialysis
Risk stratification for IC

- Corrected Candida colonization index (cCCI):
  \[(\text{colonized sites} / \text{tested sites}) \times (\text{heavy growth sites/colonized sites})\]
  A value $\geq 0.4$ is an important risk factor for IC.

- Ostrosky-Zeichner rule:
  Systemic antibiotic therapy and CVC plus two or more of these variables (TPN, dialysis, major surgery, pancreatitis and treatment with steroids or other immunosuppressive agents)
  Negative predictive value (NPV) of 97% for developing IC.

- Candida score (CS):
  Presence of TPN, surgery, multi-focal colonization (1 point each), severe sepsis (2 points).
  Subjects with a score $\geq 2.5$ had almost eight times higher risk for have IC. Strong NPV.
La paziente presentava Rx torace nella norma, non alterazioni dell’esame urine. Portatrice di CVC e alimentata con NPT (nutrizione parenterale totale). Ferita chirurgica in ordine.

Dopo esecuzione di due set di emocolture iniziava terapia antibiotica ad ampio spettro con:

Piperacillina/tazobactam 4,5 g ogni 8 ore + Vancomicina 1g ogni 12 ore

Tre giorni dopo le emocolture risultavano positive per Candida albicans.
How to make diagnosis of Invasive candidiasis?
How to make diagnosis of Invasive candidiasis?

- Diagnosi di terapia invasiva
- Coltura da vari campioni biologici
- Emocoltura
- Galattomannano
Diagnosis

Blood cultures

• Are currently considered diagnostic *gold standard* for invasive candidiasis.
• The overall sensitivity of blood cultures for diagnosing IC is roughly 50%.
• It may be negative in case of extremely low-level candidemia, intermittent candidemia, deep-seated candidiasis that persist after sterilization of bloodstream or deep-seated candidemia due to direct inoculation.
• Slow turnaround times (median 2-3 days, range 1-7 days).
• Become positive late in the disease course
Diagnosis

Mannan antigen and antimannan antibodies

- Separate low sensitivity and specificity, which improve substantially when two methods are combined

- Mannan sensitivity/specificity: 58% - 93%
- Antimannan IgG sensitivity/specificity: 59% - 83%

- Combined assay specificity/sensitivity: 83% - 86% with best performance for *C. albicans*, *C. glabrata* and *C. tropicalis*.

- Approved for use in clinical practice in Europe, not in US.
Diagnosis

Beta-D-glucan

• Cell wall constituent of *Candida* species, but also present in several other fungi (*Aspergillus* spp., *Pneumocystis jiroveci*, others).
• Not specific for *Candida*
• **Strong NPV** → Used better to *exclude* an invasive fungal infection
• Potentially identify *Candidemia* days before blood cultures.
• Sensitivity 75-80%, specificity 80%
• False positive results are quite common, especially in ICU patients (*Bacteriemia* due to *G+/G-, Intravenous Pip/tazo* and *Amoxi/clav*, *hemodyalisis*, fungal colonization, intravenous albumin or immunoglobulin, surgical gauze and other material containing glucan).
Diagnosis

PCR test

- Shorten the time to diagnosis
- Sensitivity 95%, specificity 92%
- Potential advantages: identify Candida species and molecular markers for drug resistance
- More expensive
- Lack of standardization methodologies.
Diagnosis

Table 1 ITALIC definition of diagnostic categories of invasive candidiasis (IC)

“Invasive candidiasis (IC)” indicating both deep-seated *Candida* infection and candidaemia.

In terms of certainty of diagnosis and consequent therapeutic strategies, the following diagnostic categories (modified from [166]) were used:

Proven IC: cultural evidence of *Candida* or evidence of yeast cells or hyphae or pseudohyphae at histology or at direct examination, in a normally sterile tissue or organ, i.e. excluding urine, sputum, fluids from bronchoalveolar lavage, mucous membrane swabs and specimens from skin sites.

Probable IC: concomitant presence of an underlying disease predisposing to IC, adequate risk factors (see risk stratification), with/without signs of active infection [26], with at least one positive antigen test (e.g. BDG, mannan/antimannan).

Possible IC: concomitant presence of an underlying disease predisposing to IC, adequate risk factors (see risk stratification), with signs of active infection [26], but without any microbiological confirmation.
Tre giorni dopo le emocolture risultavano positive per *Candida albicans*.

Iniziava terapia con Amfotericina-B desossicolato
What is the treatment of choice for candidemia?
What is the treatment of choice for candidemia?

- Voriconazolo
- Anfotericina lipidica
- Echinocandina
An echinocandin is recommended as initial therapy for candidemia (strong recommendation; high-quality evidence)

- CASPOFUNGIN: loading dose 70mg, then 50mg daily
- MICAFUNGIN: 100mg daily
- ANIDULAFUNGIN: loading dose 200mg, then 100mg daily
Therapy

ECHINOCANDINS

- **Significant fungicidal activity** against most Candida species
- **Success in approximately 70-75%** of patients
- Favorable safety profile
- Limited drug interactions
- *In vitro* reduced activity against some strains of *C. parapsilosis*, but not difference in clinical response at therapy
- Caspofungin, Micafungin and Anidulafungin are considered interchangeable in adult patients with candidemia.
Fluconazole 12mg/kg loading dose, then 6mg/kg daily is an acceptable alternative to an echinocandin as initial therapy in selected patients. (strong recommendation; high-quality evidence)

Transition from an echinocandin to fluconazole is recommended for patients who are clinically stable, have isolates that are susceptible to fluconazole, and have negative repeated blood cultures following initiation of antifungal therapy. (strong recommendation; moderate-quality evidence)
Therapy

FLUCONAZOLE

• Remember Fluconazole-resistant strains (C. glabrata) and species (C. krusei)
• Step-down therapy from an echinocandin or AmB usually occurs within 5-7 days
• Can be taken orally (useful to complete treatment after discharge)
**Therapy**

**VORICONAZOLE**

**Voriconazole** 6 mg/kg twice daily for two doses, then 3mg/kg twice daily is effective for candidemia, but offers little advantage over fluconazole as initial therapy.

(strong recommendation; moderate-quality evidence)

Voriconazole is recommended as step-down oral therapy for selected cases of candidemia due to *C. krusei*.

(strong recommendation; low-quality evidence)
Therapy

VORICONAZOLE

- Activity against most Candida species
- Frequent administration if compared with other treatments
- Less predictable pharmacokinetics
- More drug interactions
- Less tolerance

Less attractive for initial therapy
AMPHOTERICIN B (AmB)

Lipid formulation AmB (3-5 mg/kg daily) is a reasonable alternative if there is intolerance, limited availability or resistance to other antifungal agents. (strong recommendation; low-quality evidence)

- Broad activity against Candida species, with the exception of C.lusitaniae, which is frequently resistant.
- Lipid formulations of AmB are preferred to AmB deoxycolate for less side effects (renal impairment)
Domanda 4

How long do you have to treat candidemia?
Domanda 4

How long do you have to treat candidemia?

- 14 giorni
- 21 giorni
- 14 giorni dopo la prima emocoltura negativa
- Dipende dal malato
Follow-up blood cultures should be performed every day or every other day to establish the time point at which candidemia has been cleared (strong recommendation; low-quality evidence)
TREATMENT DURATION

Recommended duration of therapy for candidemia without obvious metastatic complications is for 2 weeks after documented clearance of Candida species from bloodstream and resolution of symptoms attributable to candidemia (strong recommendation; moderate-quality evidence)
Tre giorni dopo le emocolture risultavano positive per *Candida Albicans*.

Iniziava terapia con Amfotericina-B desossicolato

Dopo 4-5 giorni di terapia la paziente improvvisamente presentava perdita del visus pressoché completo da entrambi gli occhi
What is probably the cause of this symptom?
What is probably the cause of this symptom?

- Endoftalmite endogena
- Endoftalmite esogena
- Effetto collaterale della terapia
All non-neutropenic patients with candidemia should have a ophthalmological examination, preferably performed by an ophthalmologist, within the first week after diagnosis. For neutropenic patients, it is recommended to delay the examination until neutrophils recovery.

(strong recommendation; low-quality evidence)
Endophthalmitis

ENDOGENOUS

Most cases of Candida endophthalmitis are endogenous, occurring as a complication of candidemia.

EXOGENOUS

Exogenous cases are rare and occurring following trauma or a surgical procedure. *Candida parapsilosis* is the most common species involved in exogenous cases, especially in post surgical outbreaks. This species appears to survive well in irrigation fluids and on prosthetic materials.
Endophthalmitis in Candidemia

Pathogenesis

Candida reaches the eye through bloodstream, so the initial manifestation is usually chorioretinitis or choroiditis. If there is not involvement of the macula, this stage is often asymptomatic. The term endophthalmitis refers to those cases with significant vitritis.

Infection and inflammation of the vitreous cause its opacification and patients develop decreased vision.

With inflammation spreading to aqueous humor, eye pain may also be a presenting symptom.
Endophthalmitis in Candidemia

Epidemiology

Incidence varies from 2% to 26%, with most cases being attributable to chorioretinitis and only 0-6% having significant vitritis.

The major multicentre trial, involving 370 patients with candidemia, possible or probable eye involvement occurred in 16%, only 1,6% classified as having endophthalmitis.

The main risk factor of eye involvement is the duration of candidemia

In outpatients the major risk factor is intravenous drug use.

Candida albicans is the most common pathogen involved in endophthalmitis (92%), followed by C. tropicalis
Endophthalmitis in Candidemia

Diagnosis

In patient with documented candidemia typical findings of chorioretinitis at ophthalmological examination is enough to make diagnosis.

In other cases a samples of vitreous (and/or aqueous if involved) may be obtained by an ophthalmologist and submitted for stains and cultures.

Vitreous sample are obtained either by needle aspiration or vitrectomy.
Endophthalmitis
What is treatment options for Candida endophthalmitis?
What is treatment options for Candida endophthalmitis?

- Echinocandine
- Voriconazolo
- Itraconazolo
Endophthalmitis in Candidemia

Treatment

- For fluconazole/voriconazole susceptible isolates, Fluconazole, loading dose 12mg/kg then 6-12 mg/kg daily OR Voriconazole loading dose 6mg/kg intravenous twice daily for two doses, then 4mg/kg intravenous or oral twice daily is recommended (strong recommendation; low-quality evidence)

- For fluconazole/voriconazole resistant isolates, liposomal AmB, 3-5mg/kg intravenous daily, with or without oral flucytosine, 25mg/kg 4 times daily is recommended (strong recommendation; low-quality evidence)
Endophthalmitis in Candidemia

Treatment

- With macular involvement or vitritis, systemic antifungal therapy as noted above PLUS intravitreal injection of either AmB deoxycholate, 5-10μg/0.1mL sterile water, or Voriconazole, 100 μg/0.1mL sterile water or normal saline, to ensure a prompt high level of antifungal activity is recommended (strong recommendation; low-quality evidence)

- Vitrectomy should be considered to decrease the burden of organisms and allow the removal of fungal abscesses that are inaccessible to systemic antifungal agents in patients with important vitritis (strong recommendation; low-quality evidence)
Treatment

- The duration of treatment should be at least 4-6 weeks, with the final duration depending on resolution of the lesions as determined by repeated ophthalmological examinations (strong recommendation; low-quality evidence).

- Most patients infected with a fluconazole-resistant species can be treated with Voriconazole (Es. C. krusei).
Penetration of antifungal agents into eye

<table>
<thead>
<tr>
<th>Compound</th>
<th>Cornea</th>
<th>Vitreous</th>
<th>Aqueous</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluconazole</td>
<td>O</td>
<td>×</td>
<td>×</td>
</tr>
<tr>
<td>Itraconazole</td>
<td>O</td>
<td>×</td>
<td>×</td>
</tr>
<tr>
<td>Voriconazole</td>
<td>×</td>
<td>O</td>
<td>×</td>
</tr>
<tr>
<td>Posaconazole</td>
<td>×</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>AmBd</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>ABLC</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>L-AMB</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>5-FC</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Andisafungin</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Caspofungin</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Micafungin</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
</tbody>
</table>

- Red: <0.5 volte conc. plasma
- Yellow: >0.5-5 volte conc. plasma
- Green: >5 volte conc. plasma
- White: dati mancanti
Penetration of antifungal agents into eye

### Echinocandins

<table>
<thead>
<tr>
<th>Drug</th>
<th>Typical adult dosing</th>
<th>Oral bioavailability</th>
<th>$C_{\text{max}}$ (µg/mL)</th>
<th>AUC (mgxh/L)</th>
<th>Protein (%)</th>
<th>CSF (%)</th>
<th>Vitreus (%)</th>
<th>Urine (%)</th>
<th>Metabolism</th>
<th>Elimination</th>
<th>$T_{\frac{1}{2}}$ (h)</th>
<th>PK:PD (total drug unless indicated)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANI</td>
<td>200 mg x 1 loading dose then 100 mg/d</td>
<td>&lt;5</td>
<td>6-7</td>
<td>99</td>
<td>84.0</td>
<td>&lt;5</td>
<td>0</td>
<td>&lt;2</td>
<td>None</td>
<td>Feces</td>
<td>26</td>
<td>$C_{\text{max}}$:MIC&gt;10 or serum (unbound) AUC:MIC &gt;20</td>
</tr>
<tr>
<td>CAS</td>
<td>70 mg loading dose, then 50 mg/d</td>
<td>&lt;5</td>
<td>8-10</td>
<td>119</td>
<td>97.0</td>
<td>&lt;5</td>
<td>0</td>
<td>&lt;2</td>
<td>Hepatic</td>
<td>Urine</td>
<td>30</td>
<td>$C_{\text{max}}$:MIC&gt;10 or serum (unbound) AUC:MIC &gt;20</td>
</tr>
<tr>
<td>MICA</td>
<td>100 – 150 mg/d; 50 mg/d (prophylaxis)</td>
<td>&lt;5</td>
<td>10-16</td>
<td>158</td>
<td>99.0</td>
<td>&lt;5</td>
<td>&lt;1</td>
<td>&lt;2</td>
<td>Hepatic</td>
<td>Feces</td>
<td>15</td>
<td>$C_{\text{max}}$:MIC&gt;10 or serum (unbound) AUC:MIC &gt;20</td>
</tr>
</tbody>
</table>
Penetration of antifungal agents into eye

Echinocandins

Mycafungin concentrations in vitreous of noninflamed eyes in experimental animals are very low, ranging from undetectable to 0.034 μg/mL.

Anidulafungin levels in the vitreous have ranged from undetectable to 0.184 μg/mL, when very high dosages were used.

In rabbit model, at dosage of 1 mg/kg/die, caspofungin was undetectable in vitreous of inflamed eyes.

In rabbits intravitreal injection of 15 μg micafungin was nontoxic; intravitreal echinocandin use has not been reported in humans.

At this time it is prudent to not use echinocandins for treatment of endophthalmitis

## Penetration of antifungal agents into eye

### Azoles

<table>
<thead>
<tr>
<th>Drug</th>
<th>Typical adult dosing</th>
<th>Oral bioavailability</th>
<th>C&lt;sub&gt;max&lt;/sub&gt; (µg/mL)</th>
<th>AUC (mgxh/L)</th>
<th>Protein (%)</th>
<th>CSF (%)</th>
<th>Vitreus (%)</th>
<th>Urine (%)</th>
<th>Metabolism</th>
<th>Elimination</th>
<th>T&lt;sub&gt;½&lt;/sub&gt; (h)</th>
<th>PK:PD (total drug unless indicated)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FLU</td>
<td>6-12 mg/kg/d</td>
<td>&lt;90</td>
<td>6-20</td>
<td>400-800</td>
<td>10.0</td>
<td>&gt;60</td>
<td>28-75</td>
<td>90</td>
<td>Minor Hepatic</td>
<td>Renal</td>
<td>31</td>
<td>AUC:MIC &gt;25</td>
</tr>
<tr>
<td>ITRA</td>
<td>200 mg twice daily</td>
<td>50</td>
<td>0.5-2.3</td>
<td>29.2</td>
<td>99.8</td>
<td>&lt;10</td>
<td>10</td>
<td>1-10</td>
<td>Hepatic</td>
<td>Hepatic</td>
<td>24</td>
<td>AUC:MIC &gt;25</td>
</tr>
<tr>
<td>VOR</td>
<td>6-12 mg/kg every 12 h for 2 doses, then 4mg/kg every 12 h</td>
<td>&gt;90</td>
<td>3.0-4.6</td>
<td>20.3</td>
<td>28.0</td>
<td>60</td>
<td>38</td>
<td>&lt;2</td>
<td>Hepatic</td>
<td>Renal</td>
<td>6</td>
<td>AUC:MIC &gt;25</td>
</tr>
<tr>
<td>POS</td>
<td>600-800 mg/d in divided doses</td>
<td>ND</td>
<td>1.5-2.2</td>
<td>8.9</td>
<td>99.0</td>
<td>ND</td>
<td>26</td>
<td>&lt;2</td>
<td>Modest Hepatic</td>
<td>Feces</td>
<td>25</td>
<td>AUC:MIC &gt;400 (8-25 free drug)</td>
</tr>
</tbody>
</table>

**Notes:**
- FLU: Fluconazole
- ITRA: Itraconazole
- VOR: Voriconazole
- POS: Posaconazole
- PK:PD: Pharmacokinetics:Pharmacodynamics
Penetration of antifungal agents into eye

Azoles

Experimental data in rabbits show that Fluconazole levels achieved in the vitreous are approximately 50% of peak plasma levels and 150% of through plasma levels. In humans vitreous concentrations are approximately 70% of those in plasma.

In a study with 14 patients with noninflammed eyes Voriconazole levels in vitreous were 38% of plasma concentrations. Concentrations <250 μg/mL in vitreous had no toxic effects, Voriconazole usual dosage for intravitreal injection is 100 μg/0,1 mL of saline solution.
Penetration of antifungal agents into eye

### Amphotericin-B

<table>
<thead>
<tr>
<th>Drug</th>
<th>Typical adult dosing</th>
<th>Oral bioavailability</th>
<th>$C_{\text{max}}$ (µg/mL)</th>
<th>AUC (mgxh/L)</th>
<th>Protein (%)</th>
<th>CSF (%)</th>
<th>Vitreus (%)</th>
<th>Urine (%)</th>
<th>Metabolism</th>
<th>Elimination</th>
<th>$T_{1/2}$ (h)</th>
<th>PK:PD (total drug unless indicated)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMB</td>
<td>0.6-1.0 mg/kg/d</td>
<td>&lt;5</td>
<td>0.5-2.0</td>
<td>17.0</td>
<td>&gt;95.0</td>
<td>0.4</td>
<td>0.38</td>
<td>3-20</td>
<td>Minimal</td>
<td>Feces</td>
<td>50</td>
<td>$C_{\text{max}}$:MIC 4-10 or AUC:MIC &gt;100</td>
</tr>
<tr>
<td>ABLC</td>
<td>5 mg/kg/d</td>
<td>&lt;5</td>
<td>1.7</td>
<td>14.0</td>
<td>&gt;95.0</td>
<td>&lt;5</td>
<td>0.38</td>
<td>&lt;5</td>
<td>Minimal</td>
<td>ND</td>
<td>173</td>
<td>$C_{\text{max}}$:MIC 40 or AUC:MIC &gt;100</td>
</tr>
<tr>
<td>LAMB</td>
<td>3-5 mg/kg/d</td>
<td>&lt;5</td>
<td>83</td>
<td>555</td>
<td>&gt;95.0</td>
<td>&lt;5</td>
<td>0.38</td>
<td>5</td>
<td>Minimal urine; feces</td>
<td>Minor</td>
<td>100-153</td>
<td>$C_{\text{max}}$:MIC 40 or AUC:MIC &gt;100</td>
</tr>
</tbody>
</table>
Penetration of antifungal agents into eye

Amphotericin-B

AmB penetrates poorly into the vitreous. Better in inflamed eyes. Higher levels could be achieved with liposomal AmB (0.47 ± 0.21 μg/mL) then with AmB-d (0.16 ± 0.04 μg/mL). Doses from 20 μg to 100 μg have been administered intravitreal without toxicity. However, the dose typically administered ranges from 5 μg to 10 μg.

Flucytosine is synergistic with AmB in killing Candida and achieves high levels in all intraocular compartments in rabbits and humans, due to the small size of this molecule.
Tre giorni dopo le emocolture risultavano positive per *Candida Albicans*.

Iniziava terapia con *Amfotericina-B desossicolato*

Dopo 4-5 giorni di terapia la paziente improvvisamente presentava perdita del visus pressoché completo da entrambi gli occhi.

La paziente rispondeva alla terapia antifungina impostata, guarendo dalla candidemia e dall'endidoftalmite; tuttavia perdeva quasi completamente l’uso della vista.
Endoftalmite in corso di Candidemia da Candida albicans

Ercole Concia

Thanks for your attention

FAD-FADOI: Infezioni invasive da Candida