Succesful treatment of a *Candida guilliermondii* sepsis

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Case presentation

- 56-year-old man, diabetes mellitus type 2 and hypertensive cardiomyopathy
- ICU admission: acute necrotising pancreatitis of idiopathic origin
- Ventilator-associated pneumonia with P. aeruginosa
- Parenteral nutrition
- Fungemia → **fluconazole (FLU)**

Case presentation

- No focus found
  - Central venous catheter changed
  - Transesophageal echocardiography
  - Fundoscopy
  - Cultures of pancreatic necrosis > fine needle aspiration and necrosectomy
- Identification: *C. guilliermondii*
- Fungigram: intermediate susceptibility for FLU (MIC 32 mg/l) → **switch to voriconazole (VRCZ)**

Case presentation

- 1st Positive blood cultures: second strain of *C. guilliermondii*, resistant to FLU (MIC 64 mg/l)
  → **VRCZ + liposomal amphotericin B (L-AmB)**
- Dose adjustment of VRCZ according to weekly therapeutic drug monitoring (TDM)
- Stop L-AmB as soon as TDM VRCZ within range

Candida guilliermondii

- Rare
- Temporal change in species distribution over the last 20 years[1]
- ↓ Innate virulence compared to C. albicans
- Serious pathology: mostly fungemias and deep-seated infections in cancer patients
- Greater propensity to express multidrug resistance than other organisms of the genus Candida

1. Arendrup MC., Curr Opin Crit Care 2010; 445-452

Epidemiology

- Limited observations[1]
- Widely distributed
  - in nature
  - on human skin
- Mostly recovered in cancer, hematology and dermatology services
- Pseudo-outbreak in pediatric patients in Brasil[2]

1. Arendrup MC., Curr Opin Crit Care 2010; 445-452
2. Servolo Medeiros et al., JCM 2007; 942-947

Question 1 The following are known risk factors for Candida guilliermondii infection:

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1 - Hematological malignancy

2 - Longterm antifungal treatment

3 - Mechanical ventilation

4 - Sedation

Question 1 The following are known risk factors for Candida guilliermondii infection:

1 - Hematological malignancy 0%

2 - Longterm antifungal treatment 0%

3 - Mechanical ventilation 0%

4 - Sedation 0%

Risk factors

- **Hospitalisation in general; admission to intensive care**
- Malignancy (hematological > solid tumours)
- Graft-versus-host disease
- Bacteremia
- Neutropenia
- Colonisation by the same organism
- Dental device

- **Treatments**:
  - **Antibiotics**
  - **Total parenteral nutrition**
  - **Gastric ulcer prophylaxis**
  - Steroids
  - Long-term antifungals
  - Chemotherapy
  - Stem cell transplantation
- **Intravascular catheters** (in-hospital, handling by patient or relatives)

Question 2 The incidence of candidemia has increased over the last decades. Which of the following is true?

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1 - C. albicans is still the major pathogen

2 - Mainly C. glabrata infection incidence has increased

3 - Non-albicans Candida spp. occur more frequently in cancer patients, but are less common among ICU and surgical patients, children or HIV-positive patients

4 - All of the above are true

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1 - C. albicans is still the major pathogen — 0%

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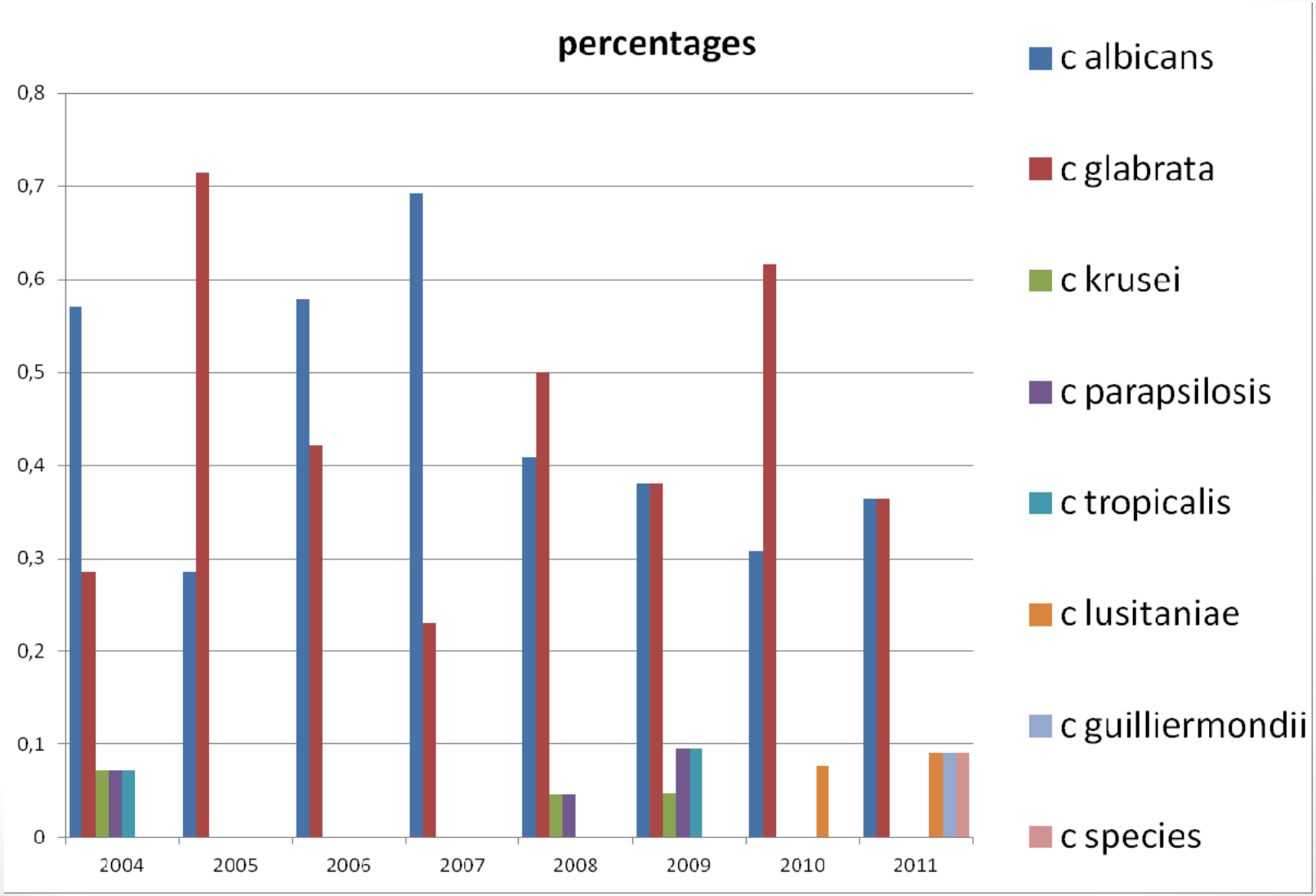
3 - Non-albicans Candida spp. more frequently in cancer patients, but < ICU/surgery/children/HIV-pts — 0%

4 - All of the above are true — 0%

Change in Candida distribution in ICU, Antwerp University Hospital



Diagnosis

- Yeast-like organism
- Easily grows on Sabouraud dextrose agar, but not on the Sabouraud broth surface
- Colonies are typically flat, moist and smooth, with cream or yellow pigmentation
- Extremely difficult to differentiate phenotypically from C. famata → correct characterisation by genome-based assays

Question 3: Candida guilliermondii is

1. As susceptible to FLU as to VRCZ

2. More susceptible to FLU as to VRCZ

3. Less susceptible to FLU as to VRCZ

4. Not susceptible to FLU nor to VRCZ

Question 3: Candida guilliermondii is

As susceptible to FLU as to VRCZ	0%
More susceptible to FLU as to VRCZ	0%
Less susceptible to FLU as to VRCZ	0%
Not susceptible to FLU nor to VRCZ	0%

Susceptibility and treatment

- **AZOLES**
  - *C. guilliermondii*: ↓ susceptibility to FLU (75.2%) compared to C. albicans (97.8%) [1]
  - No widespread azole resistance, most strains show panazole susceptibility
  - Empirical treatment with FLU
  - VRCZ more active than FLU (91%) = similar to C. glabrata [1]
  - Resistance > efflux pumps, alteration of the target enzyme of azoles (14 α-demethylase) [2]

1.Savini et al., Mycoses 2010; 434-441
2.Arendrup MC, Curr Opin Crit Care 2010; 445-452

Susceptibility and treatment

- **ECHINOCANDINS**
  - The least echinocandin-susceptible yeast [1]
  - Inherent and acquired echinocandin resistance: sporadically observed
  - MICs for echinocandins 2- to 100-fold higher for *C. guilliermondii*
  - Imperfect correlation between MICs and clinical outcome [2]
  - Treatment success rate with an echinocandin 89% with an overall mortality of 19%.[1, 3]

1. Colombo et al., AAC 2010; 1864-1871
2. Savini et al., Mycoses 2010; 434-441
3. Chen et al., CMI 2009; 662-669

Susceptibility and treatment

- **POLYENES**
  - Most strains show susceptibility to L-AmB
  - Intrinsically less susceptible to polyenes

- **FLUCYTOSINE**
  - Limited studies
  - Most isolates susceptible[1]

1. Colombo et al., AAC 2010; 1864-1871

Conclusion

- Rates of C. non-albicans fungemias have increased over the past years
- Importance of correct identification at species level
- Multidrug resistance in *C. guilliermondii* is of concern
- Start empirical treatment in C. non-albicans fungemia with an echinocandin, followed by targeted treatment guided by susceptibility testing results