Candida guilliermondii complex is characterized by high antifungal resistance but low attributable mortality: a report of 20 cases of candidemia

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BACKGROUND

Although *Candida albicans* is the most common species causing candidemia, non-*albicans Candida* species have emerged in recent years. The epidemiology of candemia caused by the most common non-*albicans* species has been previously reported. However, the epidemiology of the candidemia caused by uncommon species, such as *Candida guilliermondii* has been poorly assessed.

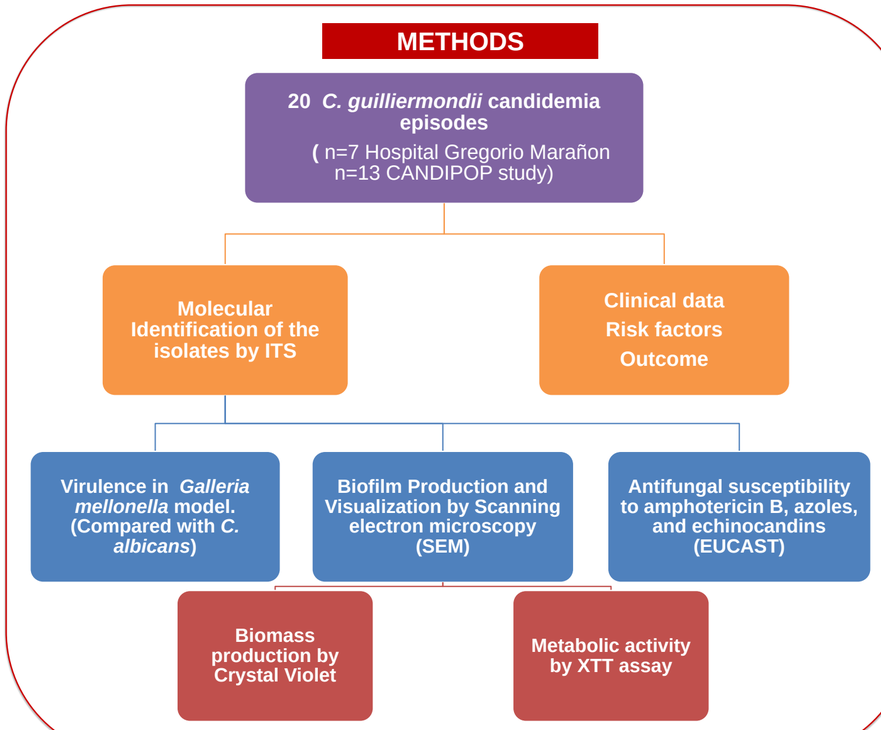
C. guilliermondii complex causes up to 2% of all cases of candidemia and is characterized by decreased susceptibility to azoles and echinocandins. Clinical data from patients with this infection is scarce.

OBJECTIVES

• Describe 20 patients with candidemia caused by *C. guilliermondii* complex collected in a population-based study and from a hospital in Madrid.

• Characterize the microbiological characteristics of the isolates in terms of antifungal susceptibility, biofilm production, and virulence.

METHODS



RESULTS

Clinical Data

The patients description is shown in Table 1.

Table 1. Underlying conditions of patients with *C. guilliermondii* complex candidemia

Patients characteristics and co-morbidities	*C. guilliermondii* complex (n=20)
Days of admission prior the diagnosis, (median days, IQR)	22 (7 – 61)
Median age, years (median years, IQR)	59 (24 - 76)
Age <1 year	3 (15%)
Male sex	10 (50%)
Diabetes mellitus	1 (5%)
Malignancy	13 (65%)
Solid tumor	9 (70%)
Hematological malignancies	4 (30%)
Solid transplant recipient	2 (10%)
Risk factors for candidemia	
Central venous catheter	17 (85%)
Total parenteral nutrition	6 (30%)
Neutropenia (<500 cell/mm^3)	7 (35%)
Abdominal surgery	4 (20%)
Corticosteroid use	6 (30%)
Prior fungal therapy (month prior diagnosis)	8 (40%)
Azole exposure (month prior diagnosis)	7 (35%)
Management	
CVC-removal	15 (88.2%)
Initial antifungal treatment	19 (95%)
Fluconazole	9 (45%)
Amphotericin B	4 (20%)
Echinocandins	5 (25%)
Voriconazole	1 (5%)
Outcome	
Complications	2 (10%)*
7d and 30d crude mortality	1 (5%) and 3 (15%)
Attributable mortality	3 (15%)

*Endocarditis and endophtalmitis

Initial fluconazole treatment was changed in 5 patientes (56%) to amphotericin B (n=2) or echinocandins (n=3).

Microbiological Data

The molecular identification leads to classify the isolates as *C. guilliermondii* senso stricto (n=16), and *C. fermentati* (n=4). Table 2 shows the antifungal susceptibility of the isolates. Up to 25% (5/20) of the isolates were fluconazole-resistant.

Table 2. Antifungal susceptibility of the isolates tested to azoles, echinocandins and amphotericin B.

Antifungal	MIC µg/mL	
	Geometric Mean	Range
Fluconazole	5.27	(0.5 - 64)
Posaconazole	0.08	(0.031 - 1)
Voriconazole	0.09	(≤0.015 - 2)
Caspofungin	0.34	(0.25 - 2)
Micafungin	0.27	(0.25 - 4)
Anidulafungin	1.03	(0.5 - 1)
Amphotericin B	0.31	(0.062 - 0.5)

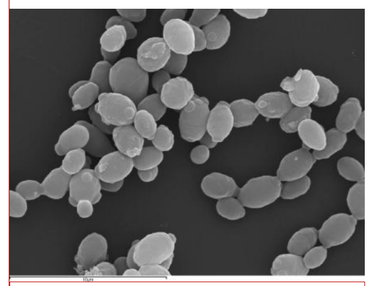


Figure 1. SEM of *C. guilliermondii* senso stricto biofilm. Magnification 2000X.

Biofilm formation showed that the isolates were moderate (55%) or low biofilm-forming (45%) and produced mostly biofilms with low metabolic activity (65%).

The biofilm structure by SEM showed biofilms characterized by a layer of clamped blastospores with the absence of hyphae or pseudo-hyphae (Figure 1)

The *G. mellonella* model showed that *C. guilliermondii* was less virulent than *C. albicans* (6 vs. 1 mean survival days, respectively; *P*<0.001) (Figure 2).

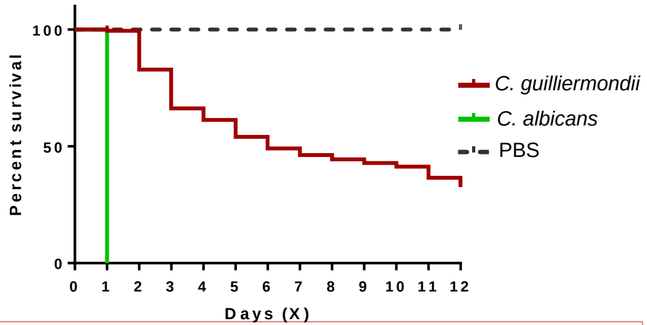


Figure 2. Differences in the median survival of *G. mellonella* larvae infected with *C. guilliermondii* complex species and *C. albicans.*

CONCLUSIONS

• Malignancy, neutropenia, or central venous catheters were found as the most common predisposing factors to candidemia caused by *C. guilliermondii* complex.

• The isolates showed diminished susceptibility to fluconazole and echinocandins.

• The low biofilm formation and the lack of virulence shown in the *G. mellonella* model matched the favorable outcome of the patients infected by *C. guilliermondii*

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