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BRIEF REPORT

First case of *Candida auris* isolated from the bloodstream of a Mexican patient with serious gastrointestinal complications from severe endometriosis

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Abstract

A 58-year-old woman was diagnosed with severe endometriosis and had multiple gastrointestinal tract complications for many years. *Candida auris* and *C. parapsilosis* were isolated from the bloodstream. Identification of *C. auris* was confirmed by amplification and sequencing of the internal transcriber spacer and the D1/D2 domain of the large rRNA gene subunit. Antifungal susceptibility was tested in both isolates using the Clinical Laboratory Standards Institute protocol M27-A3/S4. The patient evolved favorably with systemic antifungal therapy consisting of caspofungin and liposomal amphotericin B.

Keywords *Candida auris* · Endometriosis · Susceptibility · Clinical case · Lytic enzymes · Identification

Introduction

Candida auris was first isolated from the secretion of the external ear canal of a female patient in 2009 [1]. Since then, many communications have suggested the involvement of this yeast in numerous medical conditions, including severe diseases. Bloodstream infections are the most frequent invasive illnesses with in-hospital mortality rates of up to 70% [2]. Infections with *C. auris* generally involve patients with underlying medical comorbidities and noteworthy healthcare exposure, with infections classically taking place weeks after hospital admission [2, 3]. However, isolation of this yeast in clinical specimens is likely underestimated largely because it is not achievable to characterize *C. auris* using manual or commercial biochemical recognition systems, which are mainly used in conventional clinical laboratories [4]. *Candida auris* is recognized as an emerging multidrug-resistant yeast and its correct identification is crucial for appropriate therapy. Herein, we report the first case of *C. auris* infection identified in Mexico, a case in a patient with a long history of complications arising from stage IV endometriosis.

Clinical case

A 58-year-old woman with a 28-year history of severe stage IV endometriosis had multiple hospitalizations due to perforation of the abdominal viscera. She presented with kidney failure from invasion of the ureters, for which she was on a hemodialysis program. Due to abdominal sepsis, she was admitted to the hospital at the beginning of May 2020. Serial blood cultures and culture of the catheter tip grew *Staphylococcus epidermidis*. The central venous catheter was removed and the patient was started on daptomycin with good evolution. Two weeks later, the patient had

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fever again. Blood cultures were taken from both the central venous catheter and the hemodialysis catheter. Serial blood cultures were taken each day, for 3 days, and from different sites: central catheter and Mahurkar catheter. These blood cultures grew yeasts, which were identified as *C. parapsilosis* and *C. auris*. The Mahurkar catheter was changed and *C. auris* was isolated from the tip. Skin (armpits, groin), urine, and stool samples of the patient were taken but we did not find *Candida auris*. Treatment was started with caspofungin (70/50 mg/kg), and 48 h later, liposomal amphotericin B (3 mg/kg) was added as empirical treatment for a total treatment time of 18 days. Susceptibility data were available later. The patient went two weeks without fever before stopping antifungal treatment; blood cultures were taken on different days and *Candida auris* was not isolated. The patient evolved afebrile and stable; all antibiotics and parenteral nutrition were suspended. One week later, the patient presented with a sudden abdominal pain and septic shock. Four days later, the patient died despite all the maneuvers performed. All cultures from the blood and catheter samples taken during this period were negative.

Identification

The blood culture showed two types of colonies (20-1496 and 20-1498). Carbohydrate assimilation tests for both isolates were carried out with API 20C (bioMérieux), Phoenix (Becton Dickinson), and Micro Scan (Beckman Coulter). Isolate 20-1496 was identified as *C. parapsilosis* with a high probability (99, 98, and 90%, respectively). Isolate 20-1498 showed variability in its identification: *Rhodotorula glutinis*, API 20 C/99.7%; *Candida haemulonii*, Phoenix BD/99%; and *Candida famata*, Micro Scan/46.1%.

Later, molecular identification for both isolates was performed using matrix-assisted laser desorption/ionization time of flight (MALDI-TOF, Bruker Daltonics), which reported *C. parapsilosis* (20-1496, score 2.06) and *C. auris* (20-1498, score 2.3). At the time of reporting the presence of *Candida auris*, the hospital began to monitor surfaces and equipment in the hospital areas where the patient had been. *Candida auris* has not been isolated from any sample taken. At present, the infection committee of the hospital is swabbing different body surfaces of patients and the staff that work there. Moreover, the laboratory is on alert identifying all the yeasts detected in clinical specimens examined. Also, the committee is on alert for the detection of new cases of patients with *C. auris*. So far no source of contamination has been found.

Confirmation of *C. auris* was performed by sequence analysis of the ITS1-5.8S-ITS2 and D1/D2 ribosomal regions. Primers ITS4 (5′-GGA AGT AAA AGT CGT AAC AAG g-3′) with ITS5 (5′-TCC TCC GCT TAT TGA TAT GC-3′), and F63 (5′-GCA TAT CAA TAA GCG GAG GAA AAG-3′) with R365 (5′-GGTCCG TGT TTC AAG ACG-3′) were used with the following program: 95 °C for 4 min, followed by 30 cycles at 94 °C for 1 min, 55 °C for 1 min 30 s, 72 °C for 1 min 30 s, and a final elongation step of 72 °C for 5 min. Obtained sequences were compared with previously reported sequences in both GenBank (https://blast.ncbi.nlm.nih.gov) and the ISHAM Barcoding database (https://its.mycologylab.org/). Both sequences were homologous to *C. auris* with 97–99% for ITS (GenBank accession # MT04968) and 99% for D1/D2 (GenBank accession #MT704969). The ribosomal region sequences analyzed suggest that isolate 20-1498 belongs to clade IV (South American), based on a maximum homology with three strains from this clade (AR0385, AR0386, B11245) [5, 6].

Antifungal susceptibility testing was done using the Clinical laboratory Standards Institute protocol M27-A3/S4 broth microdilution method [7]. Amphotericin B, fluconazole, itraconazole, voriconazole, posaconazole, caspofungin, anidulafungin, and 5-flucytosine were evaluated. *Candida parapsilosis* ATCC 22019 and *C. krusei* ATCC 6258 were used as quality control strains. *Candida auris* 20-1498 exhibited high minimum inhibitory concentrations to amphotericin B, fluconazole, and itraconazole (Table 1). On the other hand, *C. parapsilosis* 20-1496 was susceptible to all antifungal agents tested.

Lytic activity evaluated for DNase, hemolysin, phospholipase, aspartyl-protease, and esterase capabilities following previously reported methods [8]. Isolate 20-1496 was positive for both hemolysin and phospholipase activity but showed no lytic capability for the other substrates evaluated. Isolate 20-1498, in contrast, only showed positive lytic activity for aspartyl-protease.

Table 1 Antifungal susceptibility testing of *C. auris* and *C. parapsilosis*

Microorganism	MIC (μg/ml)						
	FLC	ITC	PSC	VRC	AMB	CAS	5-FC
C. auris (20-1498)	> 64	1	0.5	1	2	0.5	0.5
C. parapsilosis (20-1496)	1	0.125	0.06	0.125	0.125	0.25	0.125

FLC fluconazole, *ITC* itraconazole, *PSC* posaconazole, *VRC* voriconazole, *AMB* amphotericin B, *CAS* caspofungin, *5-FC* 5-flucytosine, *MIC* minimal inhibitory concentration

Discussion

This report describes a case of *C. auris* involved in mixed candidemia with *C. parapsilosis* isolated from a woman with many gastrointestinal complications that took place throughout 28 years after her diagnosis of severe endometriosis. This patient had risk factors that have been widely published in the literature when *C. auris* is isolated from clinical specimens, such as hospitalization in the intensive care unit, use of broad-spectrum antibiotics, and placement of different types of catheters, surgeries, and renal insufficiency [2, 3].

Candida auris is recognized as an emerging multidrug-resistant yeast. Some groups have reported resistance to fluconazole, amphotericin B, echinocandins, and triazoles [3]. At this time, there are no clinical MIC breakpoints reported for *C. auris*; however, the CDC has recommended the following interpretation according with the CLSI-M60: fluconazole (≥ 32 µg/ml), amphotericin B (≥ 2 µg/ml), echinocandins (≥ 4 µg/ml for anidulafungin and micafungin, and ≥ 2 µg/ml for caspofungin) [9]. According to those recommendations, our isolate is categorized as resistant to FLC and AMB. Despite having only one isolate of *C. auris*, its antifungal susceptibility profile is very similar to most of the strains studied by Lockhart et al. (2017) who evaluated the antifungal susceptibility of 54 isolates collected over 3 years. They found that 50 isolates were resistant to fluconazole, 29 to voriconazole, and 19 to amphotericin B. The number of strains resistant to echinocandins and 5-flucytosine was very low (4 and 3, respectively) [3].

Regarding lytic activity of DNase, hemolysin, phospholipase, aspartyl-protease, and esterase capabilities, it is difficult to conclude because we tested only one isolate, but other reports have described the production of aspartyl-protease [10].

To our knowledge, this is the first reported case of *C. auris* isolated from the bloodstream in a Mexican patient. Additionally, to our understanding, it is the first report in a patient with a long history of complications in the gastrointestinal tract derived from stage IV endometriosis.

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Compliance with ethical standards

Conflict of interest The authors declare no conflict of interest.

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