Case Report

Candida auris infection in the central catheter of a patient without sepsis symptoms

Infección por *Candida auris* en el catéter central de un paciente sin síntomas de sepsis

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OPEN ACCESS

Citation: Castro LA, Álvarez MI, Rojas F, Giusiano G, Martínez E. Colomb Med (Cali). 2019; 50(4): 293-98. http://doi.org/10.25100/cm.v50i4.4248

Received : 13 Oct 2019
Revised : 01 Nov 2019
Accepted : 15 Dec 2019

Keywords:
Antifungal agents, Candida auris, central venous catheters, Colombia, MALDI-MS, minimum inhibitory concentration, yeast, Fluconazole, Amphotericin B, Itraconazole, Voriconazole, Endocarditis

Palabras clave:
Agentes antimicóticos, Candida auris, Catéter Venoso Central, Colombia, MALDI-MS, Concentración Inhibitoria Mínima, levadura, Fluconazol, Amfotericina B, Voriconazol, Itraconazol, Endocarditis

Abstract

Background:

Candida auris is an emerging yeast frequently reported as resistant to multiple antifungal drugs commonly used to treat *Candida* infections. This specie can colonize the patient's skin and has great ability for producing outbreaks in hospitals. *C. auris* is phylogenetically related to other Candida species, can be misidentified using conventional biochemical or commercial methods and requires specific technology for its identification.

Case report:

We report the first isolate of *C. auris* in Cali, Colombia, from a central venous catheter in a 37-year-old patient with rheumatoid arthritis and endocarditis who did not have symptoms of sepsis. The yeast was initially misidentified as *C. haemulonii* using the Phoenix system and subsequently identified as *C. auris* by matrix-assisted laser desorption/ionization-time-of-flight mass spectrometry (MALDI-TOF MS). The broth microdilution method was used to determine the minimum inhibitory concentration; the isolate was susceptible to fluconazole, itraconazole, voriconazole and amphotericin B.

Conclusions:

This report contributes to knowledge of the epidemiology of *C. auris* infections in individuals with underlying disease and describes an isolate with a behavior different from what is usually reported.

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Conflict of Interest:
All the authors declare that they do not have any conflict of interest.

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RESUMEN

Antecedentes:

Candida auris es una levadura emergente, informada con frecuencia como resistente a diversos antifúngicos usados comúnmente para tratar infecciones por *Candida*. Esta especie puede colonizar la piel y tiene gran capacidad de producir brotes en ambientes hospitalarios. Está filogenéticamente relacionada con otras especies de *Candida*, es mal identificada por los métodos bioquímicos o comerciales, y requiere tecnología específica para su identificación.

Reporte de caso:

Se informa el primer aislamiento de *C. auris* en Cali, Colombia en un paciente de 37 años con artritis reumatoide y endocarditis, sin síntomas de sepsis, a partir de la punta de catéter venoso central. La levadura inicialmente se identificó como *C. haemulonii* por el sistema Phoenix® y posteriormente como *C. auris* por espectrometría de masas desorción/ionización láser asistida por una matriz con detección de masas por tiempo de vuelo (MALDI-TOF MS). Se determinó la concentración inhibitoria mínima por el método de microdilución en caldo que mostró un aislamiento sensible a fluconazol, itraconazol, voriconazol y anfotericina B.

Conclusión:

Este informe contribuye al conocimiento de la epidemiología de las infecciones por *C. auris* en individuos con enfermedad subyacente y describe un aislamiento con un comportamiento diferente a lo indicado en otros estudios.

Introduction

Candida auris is an emerging yeast with reported resistance to multiple antifungal drugs commonly used to treat *Candida* infections [1,2].

This species was isolated from the external ear canal of a Japanese patient [3]. Since then, it has been found in blood and other clinical samples in India, South Africa, Kenya, Kuwait, the United Kingdom, the United States, Israel, Colombia, Venezuela, Panama, Pakistan, Bangladesh, Spain, Germany, Norway, Oman, South Korea, Canada, the United Arab Emirates, Saudi Arabia, Iran, Singapore, Thailand, Malaysia, Switzerland, Netherlands, Russia, China, France, Austria, and Belgium [1,4,5].

This fungus is the agent of nosocomial infections causing candidemia and other invasive diseases, such as pericarditis and respiratory and urinary tract infections, especially in immunocompromised patients undergoing long-term hospitalization [1,2].

Candida auris can colonize patients' skin and other anatomical sites, and has been isolated from healthcare environmental surfaces and equipment. This can lead to spread of *C. auris* among patients in healthcare facilities causing epidemic outbreaks [1,6].

Conventional biochemical or commercial methods used in microbiology laboratories cannot differentiate *C. auris* from other species of the genus *Candida* or even from other yeast genera. Currently, *C. auris* is not found in the database of available commercial systems; Phoenix (BD, Diagnostics, USA) misidentified isolates as *C. haemulonii* or *C. catenulata*; Vitek 2 (bioMérieux, Marcy l'Etoile, France) as *C. haemulonii* or *C. catenulata*; MicroScan (Beckman Coulter) as *C. famata, C. lusitaniae, C. guilliermondii* or *C. parapsilosis;* also, API 20 C AUX (bioMérieux, Marcy l'Etoile, France) as *Rhodotorula glutinis* or *C. sake* [1]. Most likely, the close phylogenetic relationship of these species with *C. auris* contributes to this problem [1].Currently, disease control organizations such as the *Centers for Disease Control and Prevention* (CDC), the *European Centers for Disease Control* (ECDC) and *Public Health England* (PHE) recommend that any of the above-mentioned yeasts be considered as probable *C. auris* [7]. Definitive identification must be performed by matrix-assisted laser desorption/ionization-time-of-flight MALDI-TOF mass spectrometry or by molecular methods based on the sequencing of genetic loci such as the DI/D2 region of the ribosomal DNA or the internal transcribed spacer (ITS) region [8].

Case report

This a 37 year-old male patient, with a past medical history of epilepsy, rheumatoid arthritis for the last two years, and left eye uveitis, and lost of follow-up for several months and not taking any medication including the prescribed prednisone, admitted to the hospital for an acute severe pain in the left lower extremity with limited movement and function. Positive findings at physical exame included monoparesis in his left lower extremity and an abscess in the left axillary region. With initial diagnosis of relapsing rheumatoid arthritis, left lower mononeuropathy to be ruled out, and an axillaty abscess, treatment with prednisone, vancomycin and cefepime was started, and antibiotics were later switched to cefazolin, until clinical resolution of the lesion. Blood cultures were performed on days 1 and 2 of hospitalization, with negative results.

On day 4, with a modified diagnosis of Rhupus syndrome by the rheumatology service, methotrexate, chloroquine, and leflunomide were added to the treatment, and these medications were continued until his hospital discharge. The patient remained under observation in hospital for his rheumatologic disease. Uveitis in the left eye was confirmed in hospital and he received one drop of prednisolone every 6 hours until he improved.

At 13 days of hospitalization, the patient reported precordial pain and an initial transthoracic echocardiography suggested mitral valve vegetation, therefore, on next day, a transesophageal echocardiographic study is performed confirming the diagnosis of endocarditis with the findings of a 50 x 14 mm mitral valve vegetation, along with mild mitral and moderate to severe aortic valve insufficiency. Initial empirical treatment with meropenem and vancomycin was initiated and after surgical replacement of both valves on day 25 daptomycin and cefepime were continued for 28 days more. Blood cultures drawn before initiation of antibiotics and cultures of the removed valve were negatives.

At day 52, 2 days before the end of antibiotic treatment, an external filtration was observed at the insertion site of the subclavian central catheter, without local signs of infection nor fever or other signs of a systemic inflammatory response. The catheter was removed 3 days later and the tip sent for microbiological culture, but simultaneous peripheral blood culture samples were not taken. A yeast was isolated and identified as *C. haemulonii* by the Phoenix® system (BD, Diagnostics, USA).

At day 62, 7 days after the culture request, the patient was discharged considering his stable condition, without signs or symptoms of systemic infection. The microbiological finding was considered not relevant by the treating physicians. The patient continued with outpatient monitoring as well as cardiac rehabilitation by other health care providers assigned by his health insurance plan. No further clinical data was available for this patient.

According to recommendations of disease control organizations for yeast identified as *C. haemulonii*, the isolate was further processed using a MALDI-TOF mass spectrometry system (Bruker Daltonik, Bremen, Germany) at another research hospital, where it was identified as *C. auris* (score >2).

The yeast was sent to the Instituto de Medicina Regional, Universidad Nacional del Nordeste, Argentina, for *in vitro* antifungal susceptibility testing. The minimum inhibitory concentrations (MICs) of fluconazole, itraconazole, voriconazole, and amphotericin B were determined by the broth microdilution method standardized by the Clinical and Laboratory Standards Institute (CLSI) [9] resulting on 8 µg/mL, 0.06 µg/mL, 0.06 µg/mL and 1 µg/mL, respectively. No MIC data were provided for echinocandins. As there are currently no established *C. auris*-specific susceptibility cut-off points by CLSI, the CDC recommends to cautiously interpret *C. auris* MICs based on those established for closely related *Candida* species. With this in mind, this *C. auris* isolate would be considered as susceptible to fluconazole (MIC <32 µg/mL), and amphotericin B (<2 µg/mL).

Of note, the patient was discharged before final C. *auris* identification was obtained, the institutional infection control committee was informed of the finding, and close epidemiological surveillance followed this notification with no new cases found in the next several months.

Discussion

The correct and quick identification of *C. auris* as well as timely communication of its existence in a hospitalized patient are important in order to implement strategies to prevent outbreaks caused by this species and lead to appropriate antifungal treatmen [4]. Similarly to our case, many publications describing *C. auris* highlight that this species is frequently misidentified [1,10,11]. The time required to derive the isolate to another institution for its definitive identification can lead to decisions such as considering the isolate irrelevant, even discharging the patient without instituting control measures. Although the strategies recommended by the CDC [12] were not implemented at the hospital, additional isolates of *C. auris* have not been obtained. Reports from different countries, including Colombia, inform multidrug-resistant isolates of this species producing outbreaks [2,10-12]. The only isolate from our patient had a different behavior and has not been redetected.

Candida auris es frequently misidentify with other closely related *Candida* species as *C. haemulonii* by commercial identification systems, as presented with the isolated strain in this patient and similar to what was reported in other cases [5,10]. At present the accurate identificación of *C. auris* should be confirmed using accepted methods sucha as MALDI-TOF MS or molecular identification techniques like sequencing, polymerase chain reaction (PCR), real-time PCR and amplified fragment length polymorphism fingerprinting (AFLP) [4,13]. In accordance with other publications, the isolation strain was identified correctly by MALTI-TOF MS for being an adequate method for identifying *C. auris* [5,6,11,13].

Currently, there are no specific susceptibility breakpoints for *C. auris*; however, the CDC has proposed tentative MIC values for certain antifungals. Strains with MIC of ≥32 µg/mL for fluconazole and MIC of ≥2 µg/mL for amphotericin B can be considered strains with microbiological resistance to these drugs, for voriconazole and other second-generation trizoles, fluconazole resistance can be contemplated surrogate marker [8]. The strain isolated in this study had a MIC of 8 µg/mL to fluconazole, lower than the cut-off point proposed by the CDC, but within the ranges reported in other publications (4 to 256 µg/mL) [7,8,10,14]. Our isolate showed lower MIC than values found in a multicenter study conducted in northern Colombia, where 58.8% of the isolates had higher MIC for fluconazole and all were resistant to amphotericin B [10]. In the central area of Colombia, multidrug-resistance in one of the three *C. auris* isolates studied has also been reported [11]. In addition, *C. auris* has been reported to be resistant to polyenes (approximately 50%), echinocandins (5-10%) and nearly 50% exhibited simultaneous resistance to two classes of antifungals (azoles and polyenes) [4].

Antifungal susceptibility testing of *C. auris* isolates from different Colombia regions showed variable results, from low to high MIC with different antifungal agents [10,11]. Considering these observations, it could be assumed that strains of different clades of *C. auris* might be circulating in Colombia.

Our patient was immunocompromised, with a long term ICU and hospital stay, treated with a long course of wide-spectrum antibiotics and several immunosuppressor agents, complicated by mitral valve endocarditis, who underwent major cardiac surgery with double valve replacement and required central venous catheter placement for several weeks. All these conditions have been considered classic risk factors for deep-seated *Candida* infections and candidemia, and some of them for *C. auris* infections [15-17]. In this case, however, there was no evidence of *C. auris*-associated infection, only colonization, with potential further risk of clinical impact and epidemiological alert for hospital dissemination and outbreak.

Conclusions

This report contributes to knowledge of the epidemiology of *C. auris* infections in individuals with underlying disease and describes an isolate with a behavior different from what is usually reported. This case is an example of the importance of timely confirming the identification, since conventional laboratory techniques can lead to misidentification and consequently inappropriate management.

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