Candida auris osteomielitis: Case report

Claudia Marcela Fernández-Chagüendo1, Ingrid Johana Girón-Mera1, Darío Fernando Muñoz-Mora1, Fabiola Eugenia González-Cuellar1

1 Universidad del Cauca - Faculty of Health Sciences - Department of Internal Medicine - Research Group of the Center for Studies in Microbiology and Parasitology - Popayán - Colombia.


Abstract

Introduction. Candida auris is an opportunistic yeast associated with multiple infections, which was first reported in 2009 in Tokyo, Japan. Provided that it has great antifungal resistance to azoles and amphotericin B, its treatment options are limited, and therefore an empiric therapy using echinocandins such as micafungin should be considered.

Case presentation: A rare case of a 48-year-old male patient with osteomyelitis caused by C. auris was reported in the city of Popayán, Colombia. The patient had a history of femoral head fracture, paraplegia due to firearm-related injury and neurogenic bladder, and reported having experienced abundant purulent foul-smelling secretions through trochanteric right ulcer for 15 days. MRI images revealed myositis and bone intensity alterations, which allowed diagnosing him with osteomyelitis.

Due to repeated isolations of C. haemulonii in several bone samples, antifungal management was initiated. However, since no improvement in the patient’s condition was observed, a culture was sent to the Colombian National Institute of Health to identify the pathogen considering the repeated isolations of C. haemulonii and its apparent resistance to antifungals. C. auris was finally confirmed as the pathogen.

Conclusion. Osteomyelitis by C. auris is a rare entity, which must be considered when treating patients with predisposing risk factors such as long hospital stays, bearing in mind that this is an inpatient-associated opportunistic infection.

Keywords: Osteomyelitis; Candida auris; Drug Resistance, Fungal (MeSH).

Resumen

Introducción. Candida auris es una levadura oportunista asociada a múltiples infecciones que, en 2009, fue descrita por primera vez en Tokio, Japón. Dado que tiene una gran resistencia antifúngica a los azoles y a la anfotericina B, su manejo es limitado, por lo que se debe considerar iniciar un tratamiento empírico con equinocandinas como la micafungina.

Presentación de caso. Caso inusual de osteomielitis por C. auris en un hombre de 48 años de Popayán, Colombia, con antecedentes de fractura de cabeza de fémur, paraplejia por herida con arma de fuego y vejiga neurogénica. El paciente tenía cuadro clínico de 15 días de evolución consistente en salida abundante de líquido purulento fétido en úlcera derecha por presión trocanterácea. Mediante resonancia magnética se identificaron miositis y alteraciones de intensidad ósea, por lo que fue diagnosticado con osteomielitis.

Debido a la identificación de aislamientos repetidos de Candida haemulonii en varias muestras óseas, se inició manejo antifúngico; sin embargo, ya que no se observó ninguna mejora en la condición del paciente, el cultivo fue enviado al Instituto Nacional de Salud para confirmar la identificación del patógeno debido a aislamientos repetidos de C. haemulonii y su aparente resistencia a los antifúngicos. Finalmente, el patógeno identificado fue C. auris.

Conclusión. La osteomielitis por C. auris es una entidad inusual cuyo diagnóstico debe ser considerado en pacientes con factores de riesgo predisponente, como aquellos con larga estancia hospitalaria, ya que esta es una infección oportunista asociada a pacientes hospitalizados.

Palabras clave: Osteomielitis; Candida auris; Farmacorresistencia fúngica (DeCS).
Introduction

*Candida auris* is an opportunistic yeast associated with multiple infections. It was first described in Tokyo, Japan, in 2009, after being isolated from external ear discharge of a 70-year-old patient. Two years later, 3 cases of *C. auris* associated with fungemia were described in South Korea; their isolates were erroneously reported as *C. haemulonii* and *Rhodotorula glutinis*, making evident how difficult it can be to identify this fungus. After its discovery, *C. auris* has been reported around the world and more cases are reported every day. In America, the first case was reported in March 2012 in the intensive care unit (ICU) of a tertiary care hospital in Maracaibo, Venezuela. In Colombia, the first reports were made in Santa Marta, Bogotá D.C., and Valledupar in 2013; then, between 2015 and 2016, isolations were reported in Barranquilla, and in 2016, an outbreak occurred in a pediatric ICU in Cartagena. In 2017, 77 cases of *C. auris* were reported in the U.S., and the pathogen was found in mattresses, beds, windows, chairs, infusion pumps, and countertops, indicating environmental contamination.

*C. auris* osteomyelitis is a highly drug-resistant and difficult-to-treat pathology, and available literature on this subject is scarce. For this reason, to provide adequate treatment, it is necessary to use correct identification methods that allow making a precise and timely diagnosis.

The following is a rare case of *C. auris* osteomyelitis in a man in whom it was possible to isolate this microorganism in a tissue sample by means of matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS), which was analyzed at the Instituto Nacional de Salud (National Institute of Health - INS) of Colombia.

Case presentation

The following is the case of a 48-year-old man, truck laborer, who attended a secondary healthcare center on March 27, 2017, after experiencing abundant purulent foul-smelling secretions through trochanteric right ulcer for 15 days. The patient had a history of right femoral head fracture and gunshot wound in 2012, which caused him paraplegia due to T12 spinal cord injury and neurogenic bladder that had been treated with intermittent catheterization.

Upon physical examination, the patient was found in acceptable general conditions, alert and oriented to person, place, time, and situation; his vital signs were: blood pressure: 100/60 mmHg, heart rate: 100 bpm, respiratory rate: 22 bpm, temperature: 35.9°C, and oxygen saturation: 99%. The subject had a stage 2 ulcer of 8 cm in diameter superinfected with purulent secretion in the right trochanteric region and a stage 1 ulcer of 3 cm in diameter superinfected with seropurulent secretion inside and devitalized patches. The right femoral trochanter was exposed, finding a soft and porous bone, as well as exposure of osteosynthesis material suggestive of osteomyelitis. Blood and ulcer secretion cultures were performed, yielding negative results for pathogenic microorganisms.

A week after the trochanteric ulcer evolved to stage 4, a nuclear magnetic resonance (NMR) of the right thigh was performed, showing alterations in bone density and post-surgical changes in both the neck and the diaphysis of the femur. Similarly, severe myositis was observed in the gluteus and hamstring muscles, which later extended through the anterior and lateral thigh to the greater trochanter, findings that suggested a diagnosis of osteomyelitis.

Four days after the NMR, the patient’s clinical condition worsened due to bleeding in the surgical wound of the right femur; a blood culture was then performed, isolating multidrug-resistant *Pseudomonas aeruginosa*, for which trochanteric ulcer lavage and curettage surgery was performed. In the inguinal region, lesions compatible with cutaneous candidiasis were found; they were managed with topical treatment.

One month after the patient’s condition deteriorated, another culture was taken from a new sample of right femur bone, isolating *C. haemulonii* sensitive to amphotericin B, itraconazole, fluocytosine, voriconazole, and fluconazole; in the case of the latter, the sensitivity of the fungus depended on the dose used and the minimum inhibitory concentration (MIC) was 16. The identification of this pathogen allowed diagnosing chronic osteomyelitis, for which treatment with itraconazole was initiated (200 mg every 12 hours for 2 days and then 200 mg every 24 hours until completing 4 to 6 weeks). A week after starting this treatment, the patient had an allergic drug reaction, so itraconazole was switched to fluconazole (400 mg every 12 hours). A plastic surgery was performed to cover the skin with flaps to repair the defect caused by the ulcer because there were no signs of local infection or systemic inflammatory response. The patient continued with antifungal treatment with fluconazole and received intravenous steroid due to persistent rash.

Since the patient’s condition did not improve, the culture was sent to the INS to confirm the pathogen due to repeated isolations of *C. haemulonii* and its apparent resistance to antifungal agents. Finally, it was possible to establish the presence of *C. auris* by means of the MALDI-TOF MS technique, which analyzes the proteomic profile through the creation of a specific mass spectrum of each genus and species, allowing the precise identification of the yeast and, thus, determining antifungal susceptibility.

Discussion

*C. auris* is an emerging and opportunistic yeast with worldwide presence and responsible for a large number of clinical manifestations, ranging from simple fungal colonization to deep infections and candidemia. Moreover, it has great potential for transmission of infections and is often multi-resistant to antifungal drugs. When treatment fails, fungemia can occur, which is accompanied by high mortality rates. Since it was first described, *C. auris* has spread around the world and health authorities have been on the alert.
In this regard, Chowdhary et al.\textsuperscript{12} reported that isolates of this pathogen had already been reported in South Korea, India, Pakistan, Israel, Kenya, South Africa, Spain, UK, Germany, Norway, USA, Venezuela, and Colombia by 2017. Then, by 2018, several studies reported cases in China, Saudi Arabia, Canada, Switzerland, United Arab Emirates, Malaysia, Oman, and Brazil.\textsuperscript{13-16} In Colombia, the INS issued a global emergency alert in 2016 for invasive infections caused by C. auris and established guidelines for its timely and proper identification.\textsuperscript{17}

Multiple C. auris outbreaks and related studies suggest that transmission occurs in hospital settings, as it has been isolated in patient rooms and ICUs, and indicate that colonization can occur in different parts of the body such as the nares, groin, armpits, and rectum.\textsuperscript{12,13} In addition, according to Sears & Schwartz,\textsuperscript{7} clinically speaking, it is an agent that causes fungemia, ventriculitis, otomastoiditis, complicated intra-abdominal infections, pericarditis, complicated pleural effusions, and vulvovaginitis.

The risk factors associated to infection by this pathogen are similar to those of other types of Candida spp: immunosuppression, significant medical comorbidities (diabetes mellitus or chronic kidney disease), malignancies with or without chemotherapy, central venous or urinary catheter, recent invasive surgery, parenteral nutrition, continuous exposure to broad-spectrum antibiotics, prolonged hospital stay, ICU stay, stays in a nursing home, low birth weight, and early neonatal sepsis.\textsuperscript{9,10,12,18-20}

On the other hand, some studies have shown that factors such as history of prolonged hospitalizations, underlying respiratory conditions, vascular surgeries, previous exposure to antifungal drugs and low APACHE II scores increase the probability of developing C. auris fungemia with respect to other types of Candida spp.\textsuperscript{9,20} Furthermore, according to Chowdhary et al.,\textsuperscript{12} this yeast has virulence factors such as proteinases and phospholipases and forms biofilms that facilitate its adherence in the environment and to hospital equipment such as catheters.

The group of fungi that causes the greatest number of osteoarticular infections is Candida, comprising at least 15 different species, of which C. albicans is the most common. Also, as immunosuppression and antifungal exposure increases, the incidence of infections caused by Candida non albicans also increases.

C. auris is phylogenetically related to C. haemulonii and C. ruelliae\textsuperscript{19} and is usually mistaken for various species, as in the present case.\textsuperscript{19} This is also reported in the study by Kathuria et al.,\textsuperscript{22} where the fungus remained unnoticed in microbiology laboratories because 90% of isolates characterized by commercial identification systems mistakenly labeled it as C. haemulonii.

Fluconazole to treat C. auris has shown high minimum inhibitory concentration (MIC), which in many cases reaches >64 mg/L, and, therefore, has a high rate of treatment failure.\textsuperscript{13,14} Other drugs to which C. auris is resistant are azoles such as itraconazole, voriconazole and isavuconazole, and there is also variability in the susceptibility of isolates to amphoterocin B.\textsuperscript{14} Given this great resistance, initiating empirical treatment with echinocandins, such as micafungin, should be considered since they have yielded the best results, even though cases with reduced susceptibility have been reported.\textsuperscript{12}

A genetic study in India found genes related to anti-fungal resistance (ERG3, ERG11, FKS1, FKS2 and FKS3) and important ABC and MFS carrier genes in multidrug resistance (MDR) pumps. This could explain why C. auris\textsuperscript{23} is multi-resistant and the possible reasons why groups of antibiotics such as azoles, including fluconazole, fail, as happened in the case presented here.

Although the literature reports high resistance to anti-fungal drugs,\textsuperscript{14,16,21} in the reported case, treatment with azole was effective: itraconazole had low MIC (<0.125), while fluconazole had dose-dependent susceptibility.

### Conclusion

C. auris osteomyelitis is a rare entity whose diagnosis should be considered in patients with predisposing risk factors, such as long hospital stays, since this is a resistant and opportunistic infection associated with hospitalized patients.

### Ethical considerations

The present work is a retrospective case report in which no interventions on the subject were performed by the researchers. Therefore, this is a minimal risk research, approved by the Research Ethics Committee of the Clínica La Estancia by means of Minutes No. GCI-42 of March 12, 2018.

### Conflicts of interest

None stated by the authors.

### Funding

None stated by the authors.

### Acknowledgements

None stated by the authors.

### References


