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Esther Ríos[a,*], Iciar Rodríguez-Avial[b], Esther Culebras[b], Carmen Rodríguez-Avial[a]

[a] *Departamento de Medicina (Microbiología), Facultad de Medicina, Universidad Complutense de Madrid, Madrid, Spain*
[b] *Servicio de Microbiología, Hospital Clínico San Carlos, Madrid, Spain*

* Corresponding author.
E-mail address: erios02@ucm.es (E. Ríos).

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Intermittent bladder irrigation with liposomal amphotericin B for the treatment of fluconazole-resistant *Meyerozyma guilliermondii* cystitis in an immunosuppressed adolescent

Instilaciones vesicales intermitentes con anfotericina B liposomal para el tratamiento de una cistitis por Meyerozyma guilliermondii *resistente a fluconazol en un adolescente inmunodeprimido*

Urinary tract infection (UTI) is the third leading cause of nosocomial infection in paediatrics.[1] Although most infections are of bacterial origin, fungal aetiology is increasing due to *Candida* species with less sensitivity to azoles.[2] The treatment of these infections is complex due to a lack of therapeutic options.

We present the case of a 16-year-old patient with a left pelvic metastatic osteosarcoma undergoing chemotherapy who required permanent bladder catheterisation because of tumour compression. He had a history of urinary infections in the previous two months caused by *Candida parapsilosis* and *Meyerozyma guilliermondii* (*Candida guilliermondii*), which had been resolved by replacing the catheter and treatment with fluconazole. After receiving a cycle of chemotherapy and being in a state of neutropenia, the patient developed sepsis of abdominal origin, requiring broad-spectrum antibiotic therapy with meropenem, amikacin and vancomycin. In this context, *M. guilliermondii* was isolated in his urine, persisting in successive urine cultures despite the catheter being replaced once again and treatment with intravenous fluconazole for two weeks. Blood cultures were negative and renal ultrasound showed no significant findings apart from bilateral pyelocalyceal dilation secondary to obstruction caused by the tumour mass. The antifungal susceptibility tests showed resistance to fluconazole (MIC 16 μg/mL), with sensitivity to the other antifungals tested. With these findings, it was decided to start combined treatment with intravenous micafungin, which was continued for 14 days, and daily bladder irrigation with liposomal amphotericin B (30 mg/100 ml); 100 ml was introduced through the catheter, clamped for 10 min only. The treatment was well tolerated, with no adverse effects detected, and it was continued for five days, achieving microbiological eradication.

Treating asymptomatic candiduria is not indicated in paediatrics unless the patient develops symptoms or belongs to a group at risk of spread (neutropenia, need for urological manipulation, newborn or a kidney transplant). The treatment of choice is oral fluconazole,[3,4] with amphotericin B deoxycholate, flucytosine, or bladder irrigation with amphotericin B deoxycholate recommended for resistant species.[3] In our case, amphotericin B deoxycholate is not available for use in Spain, and flucytosine was ruled out because it is associated with myelotoxicity in up to 22% of patients.[5] Liposomal amphotericin B, triazole derivatives and echinocandins have limited excretion in the urine. We opted for intermittent bladder irrigation with liposomal amphotericin B, in combination with micafungin as systemic treatment in view of the patient's neutropenia. The concentration of echinocandins in urine is very low (0.7% of the plasma concentration in the case of mucafungin). Still, there are reported cases of successful use in the treatment of candiduria due to *Candida* species resistant to fluconazole,[6,7] although there have also been therapeutic failures.[8] We cannot, therefore, rule out that micafungin may have contributed to our patient being cured.

Most of the literature consulted for bladder irrigation with amphotericin B refers to using the deoxycholate form. We only found one case of intravesical administration of the liposomal form. This was a 65-year-old female patient who developed septic shock of abdominal origin, with isolation of *C. parapsilosis* in blood culture, urine culture and surgical wound. As part of the treatment of candiduria, bladder irrigation with liposomal amphotericin B was used continuously for three days at a concentration of 50 mg/l with a good outcome.[9] Our case is the first to be described in a paediatric patient.

Intravesical administration of amphotericin B deoxycholate is more effective using continuous rather than intermittent irrigation. The most commonly used concentration is 50 mg/l, although a higher concentration is used in intermittent administrations.[10] In our case, intermittent instillations of liposomal amphotericin B were administered as the urinary catheter had only one lumen, and catheter replacement was difficult. The concentration we used was effective in intermittent irrigation with amphotericin B deoxycholate[10] and was used for five consecutive days with good results.

We would conclude that intravesical instillation of liposomal amphotericin B may be a safe alternative in treating azole-resistant *Candida* species cystitis. However, more extensive studies are needed to support this assertion.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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Ana Capilla-Miranda[a,*], Diego Plaza-López[b], Paloma Garcia-Clemente[c], Fernando Baquero-Artigao[d,e]

[a] *Servicio de Inmunología, Reumatología e Infectología Pediátrica, Hospital Universitario Virgen del Rocío, Sevilla, Spain*
[b] *Servicio de Hemato-Oncología Pediátrica, Hospital Universitario La Paz, Madrid, Spain*
[c] *Servicio de Microbiología, Hospital Universitario La Paz, Madrid, Spain*
[d] *Servicio de Pediatría, Enfermedades Infecciosas y Patología Tropical, Hospital Universitario La Paz, Madrid, Spain*
[e] *CIBERINFEC, Instituto de Salud Carlos III, Madrid, Spain*

* Corresponding author.
E-mail address: anacapillam@gmail.com (A. Capilla-Miranda).

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Unusual microscopic finding in a hepatic abscess content

Hallazgo microscópico inusual en muestra de absceso hepático

Among all parasitic diseases, amoebiasis is the third most frequent cause of mortality in the developing world, with more than 100,000 deaths reported annually.[1] In developed countries, mostly immigrants, travelers from endemic areas and men who have sex with men (MSM) are affected.[1,2]

Entamoeba histolytica is the only invasive among *Entamoeba* group and has two parasitic forms: cyst and trophozoite stages. Transmission occurs after ingestion of cysts from contaminated food or water or after person-to-person contact (oral-anal sex).[1–3] Once cysts reach the small intestine, they become trophozoites, the invasive form.[1,4]

Extraintestinal disease (10%) is represented by the amoebic liver abscess (ALA). A delay in the correct diagnosis may evolve into rupture of the abscess, with high mortality associated.[5] Diagnosis of ALA is mainly serologic, with more than 90% of cases testing positive. Image techniques and direct microscopic visualization, help to make the definitive diagnosis.[1,2,6] Visualization of cysts in the abscesses content may occur but is an extraordinary unlikely finding, as the invasive form that reaches the liver is the trophozoite.[1,2,7]

We here report a case of a 31-year-old transgender woman who was admitted to the ICU presenting with abdominal sepsis secondary to a liver abscess. She referred a frequent habit of alcohol consumption and to be a sex worker, as well as no travels to tropical areas since she arrived in Spain in 2016 from Colombia, her country of origin.

Scan findings showed a 14 cm diameter cyst occupying a great part of the right liver lobe. Hematological and biochemical profiles were: Hb 10.0 g/dL, Ht 29.2%, CRP 32.77 mg/dL, leukocytosis (25,000/μL), GOT 210 U/L, GPT 182 U/L.

The following day, an echo-guided drainage was performed, obtaining 450 cc. Samples were sent to the Microbiology department including serum samples. Empirical antimicrobial therapy was initiated with ceftriaxone 2 g/12 h and metronidazole 750 mg/8 h.

Direct observation of the abscess content showed cysts of *E. histolytica/dispar* (Fig. 1), followed by confirmation of the species by immunochromatography (TECHLAB® E. HISTOLYTICA QUIK CHEK™). Antimicrobial therapy was then readjusted to metronidazole at same dosage plus paromomycin for 10 days.

We have available two different serological tests for the detection of *E. histolytica* IgG antibodies: one Latex-agglutination technique (BICHRO-LATEX AMIBE FUMOUZE®) and an ELISA assay (SCIMEDX®). The ELISA usually follows a positive agglutination test. In our patient, the latex-agglutination test was positive, but the ELISA assay tested negative. Therefore, a second serum sample was sent 7 days later which tested positive for both tests, indicating seroconversion. Stool samples resulted negative for microscopy examination. Screening for HIV and Hepatitis virus was performed on serum samples, resulting negative for both tests.

At day 5 the patient was discharged from the ICU. Paromomycin was administered for 5 more days once metronidazole was finished. At day 21, discharge from hospital was decided.

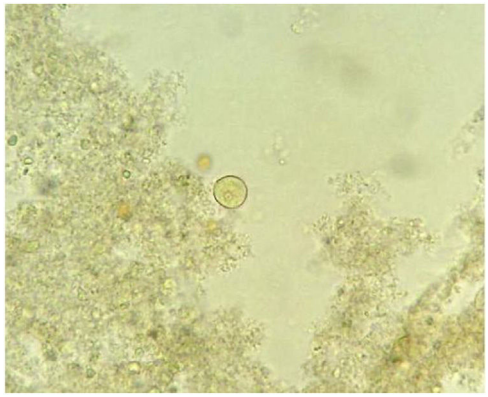

Fig. 1. Cyst of *Entamoeba histolytica*.