days. One week after the end of treatment and due to the persistence of the agitation, the doctor ordered a new urine culture. Again, the same microorganism was isolated (>100,000 CFU/mL), and a new treatment was prescribed, with ciprofloxacin 250 mg bid for two weeks.

In a third urine culture taken 3 weeks later, *A. creatinolyticus* was isolated once again in a lower count (less than 10,000 CFU/mL) and the antimicrobial susceptibility profile remained unchanged. At this point, the clinical status of the patient had improved but she had developed a cystocele, and we considered that the organism was colonizing the urinary tract.

As we have previously mentioned, there is only one reported case of bacteremia due to this microorganism in an elderly person with diabetes and acute cholangitis.[3] On the other hand, another case reported describes the isolation of *A. creatinolyticus* strains found in the urine of patients with neuroblastoma[4] and low levels of creatinine in serum and urine. The authors emphasized that this bacterium possesses creatinase, an enzyme able to hydrolyze creatinine, but they did not find any clinical evidence of urinary infection caused by this organism.

In our patient, the existence of urinary tract infection based on the recent change on her clinical or functional status (acute confusional disorder, discomfort or agitation)[5] was confirmed twice by the presence of significant bacteriuria due to *A. creatinolyticus*. The patient clinical status improved but finally developed a cystocele due to the weakening of the pelvic muscles indicating that the organism was colonizing the bladder of the patient.

Another species of this bacterium have also been described[6,7] as the etiologic agents of urinary tract infection (*A. albus*, *A. aurescens*, *A. cumminsii*, *A. protophormiae)*, and according to our case, we must include *G. creatinolyticus* (bfn. *Arthrobacter*) as an emerging pathogen causing urinary infection in the elderly.

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Sandra Nabal Díaz, Juan M. García-Lechuz Moya *, Saray Mormeneo Bayo, María Isabel Millán Lou

Servicio de Microbiología, Hospital Universitario Miguel Servet, Zaragoza, Spain

* Corresponding author.
E-mail address: jmgarcialechuz@salud.aragon.es (J.M. García-Lechuz Moya).

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Candida albicans skull base osteomyelitis due to malignant otitis externa: The role of echinocandin therapy associated with surgical debridement☆

Osteomielitis de la base del cráneo secundaria a otitis externa maligna por Candida albicans: *papel del tratamiento con equinocandina asociado a desbridamiento quirúrgico*

Malignant otitis externa (MOE), also called necrotising otitis externa, is a rare condition in Spain, with the annual incidence recently being estimated at 1.30 cases per million population.[1] It generally affects older patients with poorly controlled diabetes or immunosuppression.[1] After originating in the squamous epithelium of the external auditory canal (EAC), MOE can invade adjacent bone structures and lead to life-threatening skull base osteomyelitis. Although over 90% of episodes are caused by *Pseudomonas aeruginosa*, MOE caused by *Aspergillus* spp. is well reported in patients with human immunodeficiency virus (HIV) infection or neutropenia, with other fungal aetiologies being rarer.[2–4] We present a case of MOE due to *Candida albicans* complicated by skull base osteomyelitis in a patient without predisposing factors and we discuss the role of echinocandins in the treatment of this unusual scenario.

This was a 63-year-old male patient, originally from Ecuador but resident in Spain for over 20 years, whose previous medical history included hypertension, dyslipidaemia, subclinical hypothyroidism and gout. His usual treatment consisted of bisoprolol, simvastatin and acetylsalicylic acid. The symptoms had begun at least two months before the initial consultation and consisted of earache, hearing loss and otorrhoea from the right ear (RE). Otoscope examination at that time showed an EAC with oedematous and erythematous walls, with the eardrum intact. After a cycle of topical treatment with dexamethasone and gentamicin, repeat otoscope examination revealed a laceration in the floor of the EAC exposing bone tissue, with an inflammatory reaction and abundant otorrhoea. The patient reported progressive worsening of the earache and preauricular pain despite analgesic treatment. Once the clinical diagnosis of MOE was established, treatment was started with oral and topical ciprofloxacin and a computed tomography (CT) scan of the ears and mastoids was requested. The CT scan showed areas of osteolytic rarefaction affecting the walls of the right EAC, with bone sequestration and small gas bubbles, findings consistent with skull

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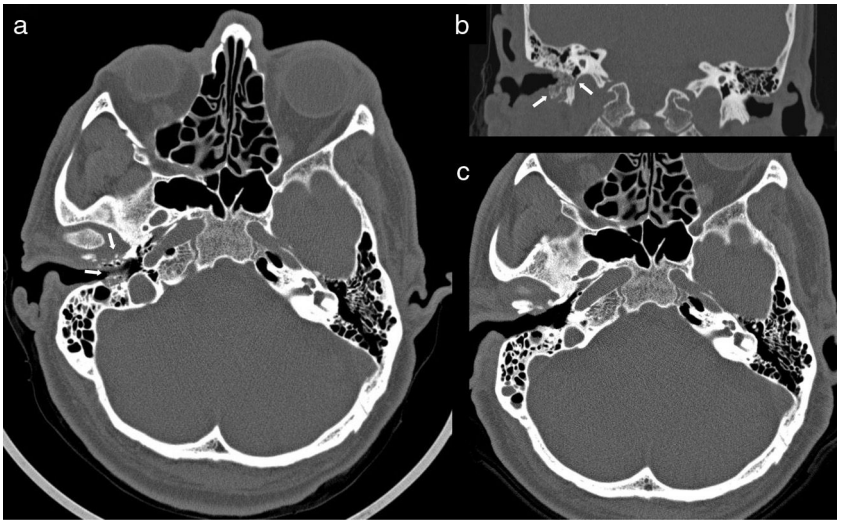

Fig. 1. Computed tomography (CT) of ears and mastoids with axial (a) and coronal images (b) performed at the time of diagnosis of skull base osteomyelitis associated with right malignant otitis externa (MOE), which shows areas of osteolysis affecting the anterior and posterior walls and the floor of the external auditory canal, with sequestrations and small gas bubbles inside the compact bone and increased soft tissue inflammation (white arrows); (c) follow-up CT performed five months after surgical debridement and after a 3-month cycle of antifungal treatment confirming the resolution of MOE and of the osteomyelitis component.

base osteomyelitis secondary to MOE (Fig. 1a and b). The patient was operated on using a retro-auricular approach, confirming the bone destruction of the posterior, inferior and anterior walls of the EAC, and was completed with meatoplasty and canaloplasty by milling (until a flat area of healthy bone tissue was obtained) and subsequent coverage with a temporal fascia graft. Culture of all three samples obtained during the procedure (including bone tissue and soft tissue) was positive for *C. albicans*, with a large number of colonies and no other microbiological isolates. The EAC skin biopsy showed fibrous connective tissue and necrobiotic material, with no evidence of malignancy or demonstration of fungal structures. Under direct questioning, the patient denied any history of ear trauma or gardening activities. Basic immunodeficiency screening was negative, and repeat basal blood glucose levels and glycated haemoglobin (5.7%) were both normal. The patient was given a three-week cycle of anidulafungin (200 mg loading dose followed by 100 mg every 24 h), and treatment was subsequently completed with fluconazole (400 mg every 24 h) orally for three months and topical cleaning of the RE with boric acid alcohol solution. The patient's earache and otorrhoea gradually improved and finally disappeared, and he remains asymptomatic at the time of writing. A follow-up CT scan five months later showed the complete normalisation of the anatomy of the EAC and the mastoid cells (Fig. 1c).

As a rare condition, the few examples of fungal MOE in the literature are mainly caused by *Aspergillus fumigatus* and are limited to patients with diabetes or with various forms of immunosuppression (advanced HIV infection, acute myeloid leukaemia with profound neutropenia, steroid treatment or primary phagocytic disorders).[2–4] Although in our case there was no histological study of the bone tissue from the walls of the EAC to demonstrate tissue invasion by fungal structures, the isolation of *C. albicans* in all the intraoperative samples, the absence of alternative agents and the response to the antifungal treatment gave us a high degree of certainty about the diagnosis. In the largest series of fungal MOE published to date (nine cases diagnosed in a single centre over 18 years), 89% of patients had a history of diabetes.[5] Compared to the cases produced by *P. aeruginosa*, patients with fungal MOE were more likely to have paralysis of the seventh cranial nerve and skull base involvement throughout the radiological follow-up.[5] A recent systematic review of the literature from the year 2000 onwards identified 25 cases of fungal MOE, out of which *Candida* spp. was the causative microorganism in seven (all patients had diabetes).[3] That makes the absence of apparent risk factors in our case quite striking. The Netea group investigated innate and adaptive immunity at a functional level in a series of six patients without underlying immunosuppression who had developed skull base osteomyelitis caused by *Aspergillus*. Compared to healthy controls, a lower production of interleukin (IL)-17 and IL-22 was observed in peripheral blood mononuclear cells subjected to a specific antigen stimulus for *A. fumigatus* and *C. albicans*, suggesting a deficient Th17 response against fungal pathogens, which could act as a predisposing factor.[6]

While there is no established optimal approach to fungal MOE, the reversal of the underlying factors (particularly adequate metabolic control of diabetes) combined with extensive surgical debridement and prolonged antifungal treatment seems to be key. In the aforementioned series, surgical debridement was necessary in 78% of fungal MOE cases, compared to only 18% of patients with bacterial aetiology infection (mostly *P. aeruginosa*) who required such a procedure.[5] In terms of the antifungal regimen, most of the published cases were given a triazole (fluconazole, voriconazole or itraconazole), sometimes associated with amphotericin B for the first few weeks.[2,3,5] The average duration of treatment in the systematic review of the literature was 178 days[3], although it is not possible to establish a firm recommendation in this regard. An echinocandin (caspofungin) was only used in one case of MOE by *A. flavus* as part of the treatment (which also included hyperbaric therapy and a prolonged course of voriconazole), obtaining a favourable outcome.[7] In our patient, fluconazole treatment was continued for a total of 110 days, in line with the average duration of 100 days reported in the Hamzany et al. series.[5] It is possible that the absence of immunosuppression, the administration of an induction cycle with echinocandin and the lower virulence of *Candida* compared to filamentous fungi contributed to the marked clinical improvement, negating the need for longer courses of treatment. Although the treatment of MOE with skull base involvement is not specifically addressed, the most recent clinical practice guidelines recommend the use of fluconazole (6 mg/kg every 24 h) for 6–12 months, either alone or preceded by at least two weeks of an echinocandin, for *Candida* osteomyelitis.[8] An experimental model of *A. fumigatus* otitis media showed that the use of caspofungin for seven days produced a clinical, microbiological and histological response comparable to that obtained with amphotericin B.[9] As our experience shows, the

fact that echinocandins are able to penetrate bone tissue[10], combined with their good safety profile, makes this group of antifungals an attractive option for the treatment of *Candida* MOE extending to the skull base.

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Mario Fernández-Ruiz [a,*], María Ruiz-Ruigómez [a], José Montojo [b]

[a] *Unidad de Enfermedades Infecciosas, Hospital Universitario 12 de Octubre, Instituto de Investigación Hospital 12 de Octubre (imas12), Madrid, Spain*
[b] *Servicio de Otorrinolaringología, Hospital Universitario 12 de Octubre, Madrid, Spain*

* Corresponding author.
E-mail address: mario_fdezruiz@yahoo.es (M. Fernández-Ruiz).

Mycoplasma genitalium: Using a commercial molecular technique that facilitates rapid detection of mutations associated with resistance to macrolides☆

Mycoplasma genitalium: *utilización de una técnica molecular comercial que facilita el análisis rápido de mutaciones asociadas con resistencia a macrólidos*

The bacterium *Mycoplasma genitalium* (MG) is a species recently described as a cause of sexually transmitted infections, with particular importance due to its resistance to some antibiotics.[1] The accepted empirical treatment in episodes of non-gonococcal urethritis is doxycycline (IUSTI and ECDC guidelines) and azithromycin (CDC guidelines). The indicated dosage of azithromycin is 500 mg/first day and 250 mg/four further days. The reports in the literature of variable and increasing rates of MG macrolide resistance make it necessary to analyse its susceptibility to these antibiotics. The IUSTI European guidelines recommend the use of molecular tests for the detection of MG and associated resistance, as they provide a clinical advantage and propose the most appropriate treatment. As little is known in Spain about the susceptibility of MG to macrolides,[2,3] we decided to carry out a study of the mutations associated with macrolide resistance on strains isolated at our hospital.

We studied 20 clinical samples frozen at 80 °C from 17 patients, corresponding to 17 episodes of infection. In these samples, MG had been previously detected by commercial PCR (BD Max Mycoplasma/Ureaplasma®, Madrid, Spain). There were 15 samples from 12 males (eight urethral exudate, four rectal exudate, two balanopreputial exudate and one semen sample) and five samples from five females (four endocervical exudate and one vaginal exudate). These patients were studied in the Urology, Gynaecology, Infectious Diseases and Accident and Emergency Department of Hospital Virgen de las Nieves in Granada, from April 2017 to September 2018. The mean age of the patients was 26.2 years (18–36 years). All samples were analysed simultaneously using the ResistancePlus® MG kit (SpeeDx), a multiplex qPCR which, in a single well, detects MG and five mutations in 23S rRNA associated with azithromycin resistance (A2058G, A2059G, A2058T, A2058C and A2059C).

Of the 20 samples studied, three were negative for the detection of MG. In the identification by BD MAX, these samples had shown some amplification cycle (Ct) values greater than 30. Of the 17 positive samples, corresponding to 15 infection episodes, mutations were found in six samples corresponding to four episodes (26.7%). These six samples belonged to four patients (three males and one female). After reviewing their medical records as far as it was documented, it seemed that given the absence of any subsequent specific treatment, the positive result for MG had not been assessed by the treating physician.

This study needs to be extended with more positive MG samples to assess the level of resistance in the different study populations. The ResistancePlus® MG test was simple to perform and adapted to the routine practice of our laboratory. The PlexPCR® technique failed to detect MG in three samples. However, considering its relatively high Ct values, we assume a low positivity which, added to the freeze/thaw process, may explain the negative result. The results of the test used are in accordance with the latest recommendations for the management of patients infected with MG with the aim of

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