negative control urine cultures. Unfortunately, semen culture was not requested at any time.

We present the first case of chronic prostatitis due to ESBL-*K. pneumoniae* treated with once-daily tigecycline. This approach resolved the adverse events caused by ertapenem and allowed the patient to be early discharged.

Carbapenems are associated with diarrhea, neutropenia or asthenia.[1] In our case, ertapenem caused numerous adverse events, with a probable causal relationship according to the Naranjo Scale. Due to the absence of therapeutic alternatives, need for prolonged antibiotic duration, penetration issues, risk of adverse effects and possibility of discharge, tigecycline was chosen as a potential alternative.[2]

Tigecycline is a third generation tetracycline whose use in UTI is controversial due to its limited urinary excretion (5–35%).[3,4] However, it may be an alternative in the treatment of prostatitis.[2]

In terms of pharmacokinetics, tigecycline presents an excellent tissue penetration, showing a high volume of distribution (7–9 L/kg).[5–7] Prostate penetration depends on the lipophilicity and degree of ionization of the drug. Tetracyclines, due to their high lipophilicity, penetrate up to 90–100% in the prostatic tissue, although specific data for tigecycline are lacking.[5–7] Other interesting characteristics include its long elimination half-life (42 h), allowing the once-daily administration.[7,8] This dosing has shown optimal therapeutic levels (maximum concentration 1.5 mg/L), considering that, for *Enterobacterales*, its pharmacokinetic/pharmacodynamic index is the area under the curve/MIC ≥ 15–20. These concentrations guarantee sufficient levels based on the established cut-off of 0.5 mg/L.[5–8] However, this approach is experimental with very limited clinical evidence.[7,8]

Tigecycline has demonstrated clinical and microbiological cure in complicated UTIs (77.4–78.6% and 85.7%, respectively).[3,9] Concerning prostatitis, some cases have demonstrated its clinical effectiveness without safety issues.[3,6,9,10]

In our case, the use of tigecycline for the treatment of ESBL-*K. pneumoniae* prostatitis optimized tolerability, avoiding ertapenem-associated adverse effects while maintaining clinical effectiveness. Once-daily administration regimen allowed early hospital discharge to home hospitalization, reducing the risk of nosocomial complications, and improving patient's quality of life.

Conflict of interest

There is no conflict of interest or source of funding for the present study.

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Streptococcus oralis, an opportunistic pathogen in crystalline keratopathy

Streptococcus oralis, *un patógeno oportunista en la queratopatía cristalina*

Case

This is the case of a 55-year-old patient with type 2 diabetes mellitus and microangiopathy treated with metformin (850 mg twice daily). He also had open-angle glaucoma, a diabetic retinopathy associated with macular oedema for which he had received 14 intravitreal injections in his right eye (RE) and eight injections in his left eye (LE) with aflibercept (40 mg/ml), as well as retinal detachment in his LE that required pars plana vitrectomy (23 g and endolaser for small paravascular tears). In addition, he reported frequent use of daily contact lenses. The patient suffered from progressive worsening of visual acuity in his RE with conjunctival hyperaemia and photophobia. Examination of his RE revealed a cloudy cornea, as well as two lateral corneal ulcers (3 × 2 mm) and another in the medial region in a crescent shape. Corneal scraping samples were taken for microbiological study.

The corneal scraping sample was inoculated on trypticase soy agar with 5% sheep blood (Becton Dickinson, Franklin Lakes, NJ, USA), Sabouraud agar with chloramphenicol (BD™) and chocolate agar, in addition to specific culture for the detection of *Acanthamoeba* spp. For the culture of *Acanthamoeba* spp., one to two colonies of *Escherichia coli* or *Enterobacter aerogenes* were emulsified in Page's solution until a homogeneous turbidity was achieved,

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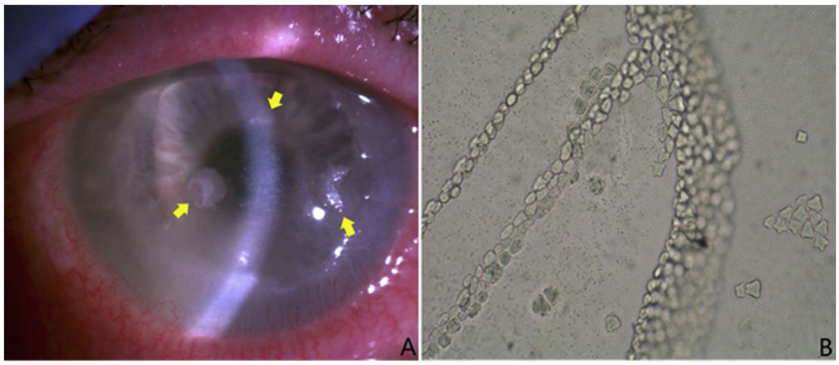

Fig. 1. (A) Three thinned lesions with sublesional endothelial halo and with a crystalline appearance (yellow arrows). Samples were taken from them and were sent to the microbiology laboratory for culture and anatomical pathology for study. These lesions were colonised by *S. oralis*. (B) Typical growth of *Acanthamoeba* spp. cysts in Page's medium covered with *Escherichia coli*. Presence of laminae contiguous with cysts. Without staining and with magnification ×100.

and 0.2 ml of this solution was then inoculated in a Petri dish. Subsequently, the sample was inoculated in this medium and visualised every 24–48 h, with growth observed after four days Fig. 1b, example of growth in Page's medium). A positive PCR for *Acanthamoeba* spp. confirmed the result. Treatment was started alternately with propamidine (0.1%/10 ml every two hours) and chlorhexidine (0.02%/10 ml every two hours) eye drops.

The clinical evolution was initially good, but the patient subsequently started to experience progressive worsening, with persistent corneal ulcer and annular infiltrate. In addition, three thinned lesions with a sublesional endothelial halo and with a crystalline appearance (Fig. 1a) appeared and the decision was taken to perform another corneal scraping for culture. The scrape sample was re-cultured in the same culture media as above. In this case, growth of *Streptococcus oralis* was observed, susceptible to penicillin, vancomycin and tetracyclines, whereupon treatment with eye drops with moxifloxacin was initiated (5 mg/ml every six hours), which was later replaced by eye drops reinforced with vancomycin and penicillin eye drops (50 mg/ml and 330,000 U/ml, respectively, every two hours alternately). In the anatomical pathology, colonies of compacted bacterial-like microorganisms were observed in the most superficial third, as well as cysts consistent with infestation by *Acanthamoeba* spp.

In the view of the lack of improvement, a penetrating keratoplasty was performed after a month and a half of treatment, with a corneal suture required one week later due to positive Seidel (communication between the anterior and exterior chamber). The surgically obtained corneal sample was processed by microbiological cultures, as well as PCR for *Acanthamoeba* spp. and 16S rDNA sequencing, being negative for all tests. Following the penetrating keratoplasty, the patient presented a progressive clinical improvement and close follow-up by the Ophthalmology department showed clearing of the cornea.

Discussion

Infectious crystalline keratopathy is a form of indolent infectious keratitis characterised by characteristic needle-shaped opacities associated with minimal or no inflammatory reaction. Some authors call it "non-inflammatory intrastromal bacterial colonisation" and avoid the term "infection" due to the absence of inflammation. It was first described by Gorovoy et al.[1] when gram-positive cocci were discovered colonising the cornea of a patient after penetrating keratoplasty. Apparently, the microorganisms enter the corneal stroma through an epithelial defect that can be exploited by virulent or opportunistic pathogens which proliferate. When the usual immune response is attenuated by localised immunosuppression, it allows microorganisms to be eventually surrounded, sometimes by a biofilm[2].

Characteristically, the most common causal agents of this syndrome are *Streptococcus* alpha-haemolytic cells of the viridans group, especially, *Streptococcus mitis*[2–4]. This association between *Streptococcus* spp. and crystalline keratopathy could be related to the possible abundant production of a mucopolysaccharide biofilm, although more studies are needed to confirm this association[4]. Other pathogens that can be the cause of this pathology are other gram-positive cocci (coagulase-negative *Staphylococcus*, *Enterococcus faecalis*...), and to a lesser extent, gram-negative bacilli and fungi such as *Candida albicans*, among others[2,3,5,6].

In most cases, the necessary epithelial defect appears after surgery associated with the use of topical corticosteroids (frequent after corneal surgeries)[1]. The use of a sterile field or the correct cleaning and sterilisation of the instruments, the detection of risk factors (such as blepharitis or tear duct obstruction) and the use of povidone-iodine could reduce the colonisation and participation of opportunistic pathogens such as *S. oralis.* The use of local anaesthetics, as well as previous keratitis due to *Achantamoeba* spp. (usually after contact lens wear), is also associated with crystalline keratopathy[2–4]. Another hypothesis indicates that microorganisms could establish an endosymbiotic relationship with *Acanthamoeba* spp. and when the amoebas begin to die after the use of antiseptics they are released from their interior and attach to the cornea[7].

A corneal scraping should be carried out to identify the causative microorganism, although sometimes the depth of the lesions will not be reached and a corneal biopsy may be necessary to confirm the diagnosis[8]. Another diagnostic option is to perform a fine needle aspiration and PCR, which would also avoid the use of invasive techniques.

The first therapeutic option is topical broad-spectrum antibiotics, which must be reinforced to try to cross the biofilms formed by some microorganisms[2,9]. When there is no improvement, the intrastromal route should be chosen[10]. The use of laser (excimer laser or Nd:YAG) as an adjuvant therapy to topical treatment can be useful to prevent the formation of biofilm[6]. In the event of disease case progression, surgical excision of the infiltrated tissue appears to be necessary. Anterior lamellar dissection is performed for more superficial lesions, while penetrating keratoplasty is reserved for deeper lesions (the entire cornea is replaced as opposed to lamellar or selective keratoplasty, if only the affected layers are replaced)[9].

Crystalline keratopathy requires rapid diagnostic and therapeutic action, and will sometimes require other complementary actions such as the use of laser or surgery to eliminate the settled bacteria completely. Limiting the use of corticosteroids and/or local anaesthetics, together with close clinical follow-up after this type of surgery, is deemed essential.

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Authors

Domingo Fernández Vecilla: drafted the scientific text, reviewed the literature.

Silvia López-Plandolit Antolin: helped draft the case report, reviewed the literature, and provided the images.

Miren Josebe Unzaga Barañano: helped with the conception of the case, reviewed it and helped to modify it.

José Luis Díaz de Tuesta del Arco: reviewed the case, helped to modify it, and reviewed the literature.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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Azithromycin and moxifloxacin resistance-associated mutations in *Mycoplasma genitalium*, in the Region of Murcia, by a commercial PCR assay

Detección mediante PCR de mutaciones asociadas a resistencia a azitromicina y moxifloxacino en Mycoplasma genitalium *en la Región de Murcia*

Dear Editor:

Mycoplasma genitalium (MG) is an extremely slow-growing and fastidious organism to culture, and it was not until the first polymerase chain reaction (PCR) was developed that its role as a pathogen in human disease was established. This sexually transmitted infection (STI) is a well-recognized cause of non-gonococcal urethritis (NGU).[1,2]

European treatment guidelines recommend azithromycin for the treatment of uncomplicated MG infection and moxifloxacin for uncomplicated macrolide-resistant MG infection.[2]

The rapid emergence and spread of antimicrobial resistance in MG is a growing concern. Antimicrobial resistance rapidly spread to Europe, where the reported azithromycin resistance rate ranges from 20.1% to 35.6%, and mutations associated with fluoroquinolone resistance were found in 1.9–3.7% of MG infections.[3,4]

The established gold standard method for detection of mutations associated with antimicrobial resistance is Sanger sequencing of resistance-determining regions in the 23S rRNA and the *parC* genes. However, few commercial assays are available for this pur-

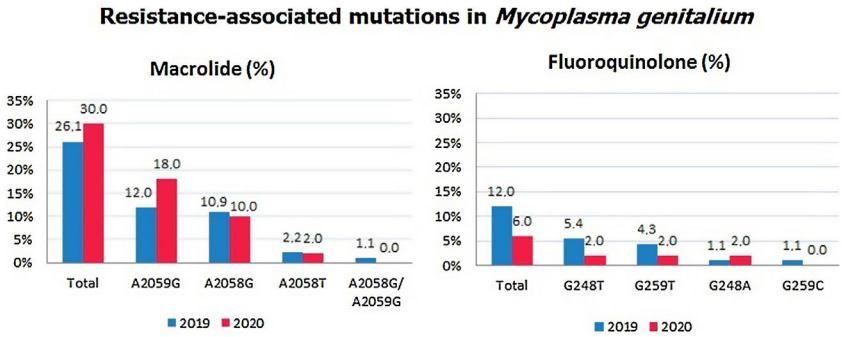

Fig. 1. Prevalence of single-nucleotide mutations detected in *Mycoplasma genitalium* by year.