Journal français d'ophtalmologie xxx (xxxx) xxx.e1—xxx.e4

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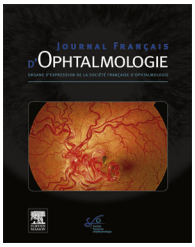

LETTER TO THE EDITOR

Citrobacter koseri as emergent microorganism in infectious keratitis

Citrobacter koseri comme micro-organisme émergent dans les kératites infectieuses

Introduction

Citrobacter koseri (formerly known as *C. diversus*) is a facultative anaerobic gram-negative bacillus of the family Enterobacteriacae. *Citrobacter* species are isolated from water, soil, food, and the intestinal tracts of humans and animals. The organism usually infects immunosuppressed hosts [1]. To the best of our knowledge, the available literature regarding ophthalmology consists of either a few case reports or limited case series.

We present two cases of infectious keratitis secondary to *Citrobacter koseri* which interestingly were diagnosed in the same month.

Case description

Patient 1

A 77-year-old diabetic man came to our emergency room with complaints of severe ocular pain and blurred vision in his right eye (OD) with a best-corrected visual acuity (BCVA) of hand movement. His ocular history included refractory glaucoma in both eyes (OU). OD had previously undergone a phacoemulsification and an Ahmed valvule surgery with subsequent endothelial failure. Due to the severe corneal decompensation, patient was wearing a bandage contact lens while he was waiting for a corneal transplant. BCVA OU was hand movement. Slit-lamp biomicroscopy revealed a severe conjunctival injection and a 4 mm paracentral epithelial defect surrounded by ring-shaped stromal infiltration with feathery borders and a 2 mm inferior endothelial plaque (Fig. 1). A 0.5 mm satellite epithelial defect was also detected. Intraocular pressure (IOP) was normal. The anterior chamber (AC) was quiet. Corneal scraping was performed, and the patient was started on empiric antibiotic therapy with fortified topical ceftazidime 10 mg/0.5 ml and vancomycin 5 mg/0.5 ml hourly, and cycloplegic agent twice. Microbiological studies revealed *C. koseri* sensitive to cefuroxime, gentamicin, ciprofloxacin and trimethoprim-sulfamethoxazole. The patient kept on ceftazidime, and ciprofloxacin eye drops qid was added. After one week, the symptoms of pain and blurred vision decreased and, albeit the cornea was still edematous, a decrease in the size of the endothelial plaque and infiltration of the stroma was observed. Three weeks after treatment, a remission of the infection was observed with clinical improvement of pain and quality of vision (Fig. 1).

Patient 2

A 74-year-old woman presented to the emergency eye service with a 2-day history of left eye (OS) discomfort. She complained of pain, epiphora, and steadily decreasing vision. She was not a contact lens wearer, and there was no history of ocular trauma. Significant ocular history of OS included pseudoexfoliation glaucoma, pseudophakic bullous keratopathy and band keratopathy. BCVA was 0 OD and 2.30 OS LogMar (20/20 and hand movement, respectively). Slit-lamp biomicroscopy of the OS revealed conjunctival injection, a paracentral corneal ulcer with surrounding stromal edema and a dense endothelial plaque, Tyndall ++++, flare ++++ and a hypopion of 3 mm (Fig. 2). The patient's IOP was 20 mmHg in OD and 28 mmHg in OS. Fundus examination was not possible in OS due to severe corneal and AC inflammation and the OD evaluation was within normal limits. Specimen samples of corneal scraping were inoculated onto blood, chocolate and Sabouraud agar plate surfaces for culture. Because of these clinical features we suspected mixed keratitis, so fortified topical ceftazidime, tobramycin and fluconazole were administered hourly and a cycloplegic agent twice. Microbiological studies revealed *C. koseri* sensitive to cefuroxime, gentamicin, ciprofloxacin and trimethoprim-sulfamethoxazole. Although the corneal edema and infiltrate showed progressive improvement, the endothelial plaque remained stable and there was an increasingly dense collection of fibrine in the AC. The BCVA dropped to light perception. The patient underwent AC washout with sample collection and intracamerular injection of 0.1 ml of ceftazidime (10 mg/0.5 ml) and 0.1 ml of voriconazole (500 μg/0.5 ml). Samples of AC did not detect any pathogen. Therefore, we hypothesize that *C. koseri* causes dense, sterile endothelial plaques caused by the severe inflammatory reaction. Next follow-ups revealed BCVA was 20/100 and steady clinical improvement with decreased pain and an improvement in the size and depth of ulceration with resolution of the AC reaction and beginning of central leukoma (Fig. 2). Currently, the patient is waiting for a corneal transplantation.

Discussion

Infectious keratitis is one of the most important causes of corneal blindness in various parts of the world [2]. Atypical and emerging microorganisms remain a major challenge for clinicians. Therefore, a high degree of clinical suspicion is

Please cite this article as: F. Urbinati, C. Rocha-de-Lossada, J. García-Montesinos et al., *Citrobacter koseri* as emergent microorganism in infectious keratitis, J Fr Ophtalmol, https://doi.org/10.1016/j.jfo.2022.06.011

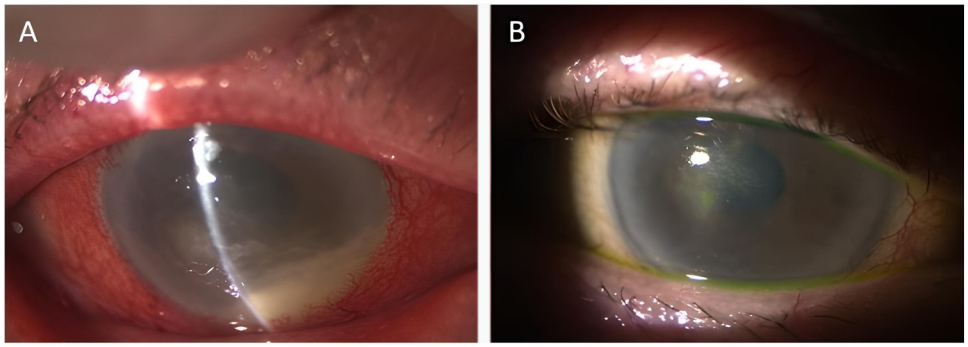

Figure 1. Slit-lamp image. A. Paracentral epithelial defect surrounded by ring-shaped stromal infiltration with feathery borders and an inferior endothelial plaque. B. Resolution of inferior endothelial plaque and stromal infiltration with the formation of a corneal leukoma.

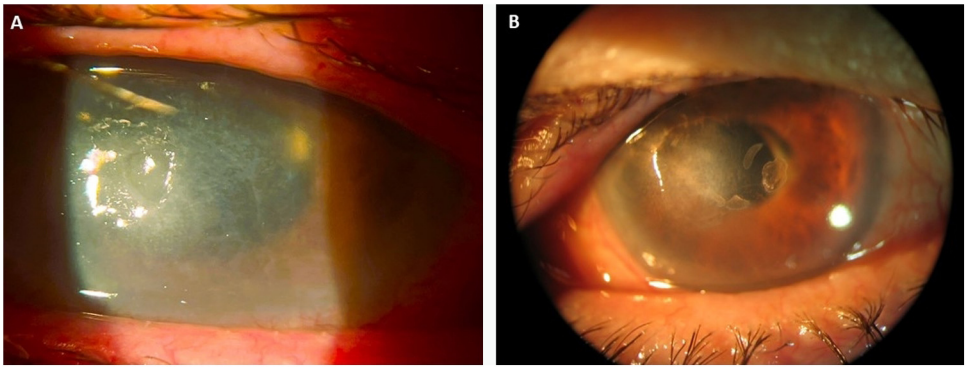

Figure 2. A. One week after diagnosis. Slit-lamp image: paracentral corneal ulcer with surrounding stromal edema and a dense endothelial plaque. B. After anterior chamber washout. Slit-lamp image: improvement in the size and depth of infiltration and resolution of the anterior chamber reaction with the formation of a central corneal leukoma. The band keratopathy was a previous feature of the patient.

essential to ensure timely recognition of infective keratitis caused by these rare and emerging microorganisms [2].

Regarding the specific clinical features, an interesting study [3] revealed that endothelial plaque was strongly associated with fungal infection with the highest odds ratio of 8.00. However, even for corneal specialists diagnosing infectious keratitis in a clinical setting, the probability to get a precise infective type of etiology is less than 70%. Consequently, microbiology cultures remain the gold standard to identify the etiology in infectious keratitis [4]. Unfortunately, the overall yield from stain and culture remains unsatisfactory due to time consuming and often, poor sensitivity [5]. Moreover, in our center, the use of routine fresh exam, special stainings such as Gomori, PAS, acridine orange, calcofluor white, KOH or polymerase chain reaction are not routinely performed for infectious keratitis. We also lack a confocal microscope, so the diagnosis of fungal keratitis is delayed until the fungi grow in the Sabouraud agar plate, which can take a variable amount of time (up to three weeks) [6].

Ocular infections secondary to *C. koseri* have been described as a single case of panophthalmitis and phthisis in a vitrectomized eye, and it has been isolated in two cases of infectious crystalline keratopathy [1,7,8]. However, there is only one reported case of *C. koseri* presenting as a corneal ulcer [9]. Similar to our cases, it occurred in elder diabetic patients or with previous corneal involvement, presenting as a corneal ulcer with infiltrate, surrounding stromal edema and endothelial plaque with severe flare. It has been reported that ocular surface disease is a risk factor for mixed keratitis (bacterial and fungal). Given that both patients had severely compromised ocular surface (both had bullous keratopathy and glaucoma, one previous Ahmed valve surgery and the other pseudoexfoliation syndrome and band keratopathy), and slit-lamp examination revealed a massive endothelial plaque, we suspected a mixed keratitis [10]. Nevertheless, microbiology of corneal scraping only revealed *C. koseri*. MALDI-TOF Microflex mass spectrometry (Bruker Daltonics, Bremen, Germany) identified *C. koseri*. Protein profile obtained from corneal samples matched to *C. koseri* with a score of 2.52 (excellent identification: 100% credibility with a score greater than 2.00) (Fig. 3). The first patient improved with topical fortified antibiotics. The second case showed a progressive worsening of the AC inflammation, so an AC washout was performed in order to rule out a fungal coinfection.

Interestingly, these two patients were diagnosed with infectious keratitis caused by *C. koseri* in the same month. Moreover, a third patient with the same clinical features but with negative results in corneal scrapings and cultures was successfully treated in our ophthalmology service in the same period. However, we could not assure that this final keratitis case was caused by *C. koseri* despite the similarity of the clinical appearance and being diagnosed in the same month as the other two patients.

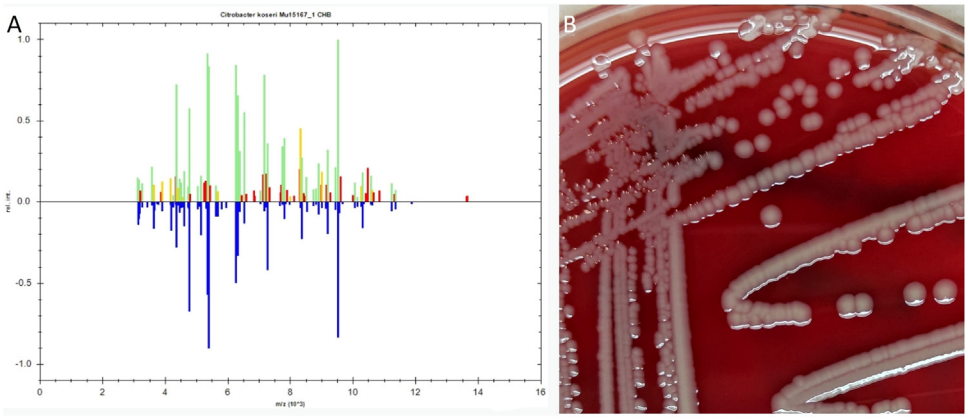

Figure 3. A. Identification of *Citrobacter koseri* by MALDI-TOF Microflex mass spectrometry (Bruker Daltonics, Bremen, Germany). B. Isolation of *C. koseri* on a blood-agar plate.

Conclusion

We present two confirmed cases of C. *koseri* infectious keratitis, an extremely rare microorganism in ocular tissues as an etiological agent, with advanced ocular surface involvement and the presence of an endothelial plaque simulating a fungal infection. This new clinical scenario supports an atypical bacterial keratitis presentation. This case report confirms the importance of corneal scraping with standard stainings and antibiogram for accurate diagnosis and treatment of infectious keratitis. Nevertheless, clinical suspicion remains an important diagnostic tool. Secondarily, we would like to highlight that *C. koseri* might be an emerging pathogen that could be related to corneal infections. We would like to raise an alert to our colleagues in the scientific community that this atypical infection may appear in their daily practice clinic as in ours. We believe that the report of more cases of *C. koseri* infectious keratitis in the future will let us describe better the clinical manifestations of this infection and find the risk factors associated. We hypothesize that clinical findings on these patients could be partially related to the previous damage of ocular surface for different factors and a poor general hygiene behavior in immunocompromised, elder patients. The intensive (and frequently improper) wearing of facial masks [11] (in Spain at the moment of the diagnosis it was compulsory to wear them both outdoors and in public indoors) may also have played a contributing role [12].

Disclosure of interest

The authors declare that they have no competing interest.

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https://doi.org/10.1016/j.jfo.2022.06.011