Letter to the Editor

Extended spectrum beta-lactamase producing *Klebsiella pneumoniae*-related keratitis

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Dear Editor,

Extended-spectrum beta-lactamase (ESBL) producing Gram-negative bacteria are global problems both in the hospital and the community.[1,2] Keratitis is a rare but potentially eye threatening infection.[3,4] Fortunately, ESBL-producing *Enterobacteriaceae* are very rare in the etiology of ocular infections. Recently Jyahar-Bharathi *et al.*[4] conducted microbiological analysis of 135 Gram-negative clinical ophtalmological isolates and reported a 7% ESBL-producer rate. However, it is not mentioned if any of the keratitis associated *Klebsiella pneumoniae* strains were ESBL-producing or not. The aim of this paper is to present the first detailed clinical report of a keratitis case due to an ESBL-producer *K. pneumoniae* strain, who was successfully treated with imipenem/cilastatin (I/C).

A healthy 15-year-old boy underwent uneventful deep anterior lamellar keratoplasty for keratoconus (DALK) in the right eye. Prophylactic tobramycin eyedrops were started following surgery. However, on postoperative day 1, the patient reported severe pain in the operated eye, which started during the night. His visual acuity was limited to counting fingers. Ocular findings included the following: severe, diffuse conjunctival infection; numerous white infectious foci at the interface of graft-recipient bed and the points of suture bites (Fig. 1A). Despite vancomycin (50 mg/ml) and ceftazidime (100 mg/ml) empirical eye drop therapy application hourly for six hours, pain increased, the infectious white foci became a confluent white plaque and purulent secretion was observed overflowing from graft recipient at the cornea junction (Fig. 1B). Thirty hours after DALK, urgent regrafting was performed with the diagnosis of graft related acute bacterial infection. Intensive topical ceftazidime and vancomycin were continued and amphotericin B was added, while topical steroid was stopped. The infected graft was removed and a tissue sample was sent for microbiological culture. Gram stain of the material did not yield any specific organism. Infection progressed despite intensive topical combination antimicrobial antibiotherapy (Fig. 1C). Culture yielded Gram-negative bacilli identified as *K. pneumoniae* with conventional methods. The strain was found to be resistant to amikacin, ampicillin, aztreonam, gentamicin, ceftriaxone, cefuroxime, cefepime, cephazoline, piperacillin/tazobactam, ampicillin/sulbactam, and cotrimaxasole, but sensitive to meropenem and imipenem, by disk-diffusion susceptibility test on Mueller Hinton agar (Oxoid, Basingstoke, UK) performed and interpreted according to Clinical Laboratory Standards Institute criteria.[5] The strain was found as ESBL-producing by double disk approximation test.[1,4,5] Topical steroid was stopped and topical imipenem/cilastatin (5 mg/ml) was initiated using one drop per hour. Purulent secretion and white focuses at the corneagraft interface disappeared in 3 days (Fig. 1D); graft epithelization was completed in 5 days (Fig. 1E). After 7 days, imipenem was stopped. Therapy was switched to routine keratoplasty prophylaxis with tobramycin and dexamethasone eye drops. Final visual acuity was 20/24 at the postoperative first year with a totally clear graft (Fig. 1F).

The main etiological agents in keratitis developing after lamellar keratoplasty are *Staphylococcus spp.*, *Pseudomonas spp* and fungi. *Enterobacteriaceae* including *Klebsiella spp.* are relatively rare.[3,6] Recently, Zarei-Ghavanati *et al.*[6] reported the first case of *K. pneumoniae* keratitis after DALK treated with ceftazidime.

The major empirical treatment options of bacterial keratitis are cephazolin + aminoglycoside or ceftazidime + vancomycin.[3] In the presented case vancomycin + ceftazidime were used as initial therapy since multidrug-resistant bacteria are common in our hospital's flora. However, the patient did not respond to empirical therapy. It was learnt that culture yielded *K. pneumoniae* and antibiogram revealed ESBL-production. Hence, the treatment was switched to

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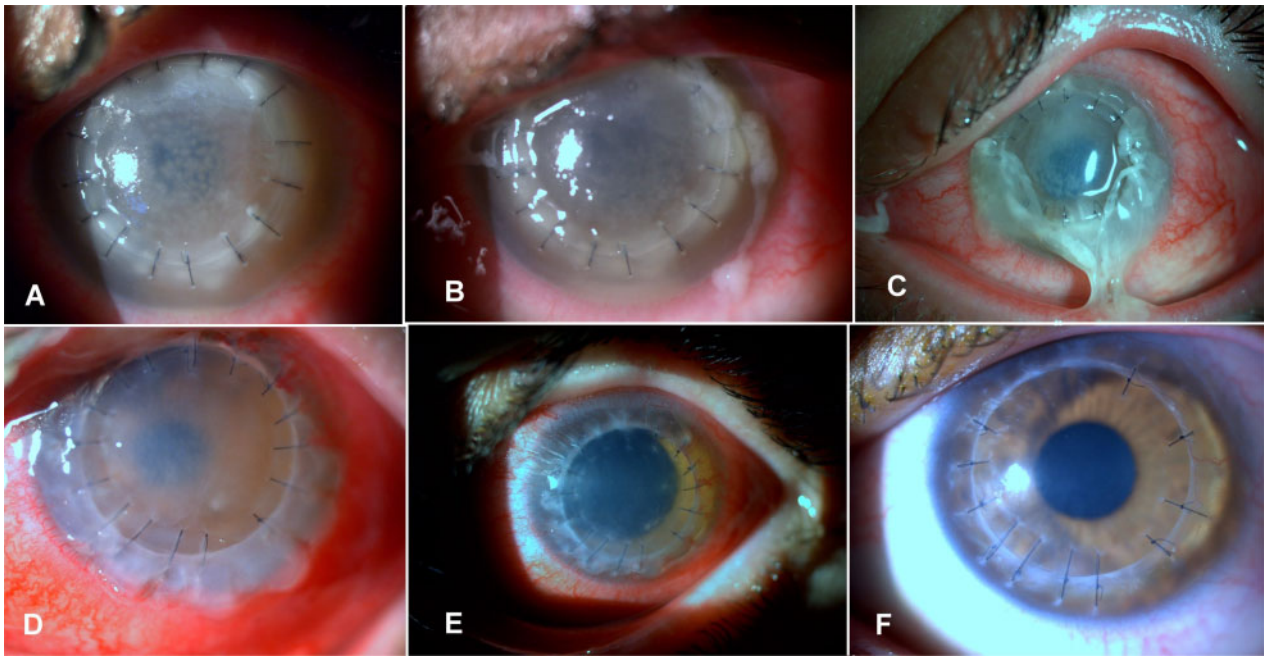

Figure 1 ***a*** **Ocular findings at the beginning of the ceftazidime+vancomycin;** ***b*** **Ocular findings after 30 hours after the ceftazidime+vancomycin;** ***c*** **Ocular findings before the start of imipenem/cilastatin;** ***d*** **Ocular findings on the 3. day of imipenem cilastatin;** ***e*** **Ocular findings on the 5. day of imipenem/cilastatin;** ***f*** **Ocular findings one year after infection.**

I/C. The reasons for choosing I/C were that ESBL-producing *K. pneumoniae* was resistant to other available beta-lactams. In the literature there is a published animal study and several clinical cases of keratitis reporting successful outcome with I/C.[7–9] We did not use meropenem due to the fact that we could not find any published experience. In addition I/C was more economical than meropenem. Ertapenem was not in the market, when the presented case was treated.

The cornea transplanted to the presented case was received from a patient in the intensive care unit of our setting. Staying in the intensive care unit is an important factor that increases the risk of colonization and infection by ESBL-producing Gram-negative bacteria.[2] ESBL-producing *K. pneumoniae* rates are quite high in our setting including ICUs. In 2005 ESBL-producer rate was 35% in the nosocomial bacteremia related *K. pneumonia* strains throughout the hospital.[8] Nevertheless, cultures of the cornea performed before the transplantation did not yield any pathogen. The surveillance cultures (rectal and oropharingeal swabs) taken from the patient and the operation room did not yield any similar pathogen, either. We can speculate that probable post-operative contamination probably caused the infection. However, we did not encounter any additional ESBL-producing *K. pneumoniae* related nosocomial infection in the ophthalmology clinic after this case. Hence, this case is considered to be a sporadic infection.

Another important issue should be discussed in this paper is the superiority of lamellar keratoplasty technique to penetrating keratoplasty on behalf of limiting graft infection to the cornea. Graft infection remained as external corneal infection due to the barrier role of the intact Descemet's membrane of the recipient cornea. Purulent discharge did not enter to the anterior chamber and hypopyon was not seen. On the other hand, endothelial rejection was not considered as an issue, even in the steroid cessation period between second to seventh days of surgery.

To our knowledge this is the first detailed clinical case report related to management of ESBL-producing *K. pneumoniae* related keratitis. It emphasizes the importance of microbiological sampling in the management of post-operative keratitis. The excellent outcome with good final visual accuity suggests that I/C may be a salvage therapy option in the treatment of keratitis related to ESBL-producing *K. pneumoniae* and raises the question whether I/C may be used as empirical therapy in settings with high ESBL rates.

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