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A case of suture-related bacterial keratitis and its treatment with topical imipenem

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Introduction

Risk factors for the development of corneal infection include loose or broken sutures, corticosteroid use, persistent epithelial defects, contact lens use, keratoconjunctivitis sicca, and a history of herpes simplex virus keratitis. Most of the data regarding suture-related keratitis come from literature on penetrating keratoplasty [1]. However, suture-related keratitis following cataract surgery appears to be a rare event [2].

The treatment of bacterial keratitis in patients with or without sutures is similar. In the treatment of serious suture-related corneal infections, topical fortified antibiotic combinations like vancomycin (50 mg/mL) and gentamicin (14 mg/mL) [3] or ceftazidime (50 mg/mL) and vancomycin (50 mg/mL) [3] have been used successfully. However, despite intensive topical, subconjunctival, and systemic antibiotics, corneal perforation can develop [2]. Therefore, selection of the appropriate agent and treatment planning are important for treatment of corneal infections. A beta-lactam antibiotic, imipenem, has often been used systemically and as an intravitreal therapy. However, no study has reported the topical use of imipenem as a monotherapy in the treatment of bacterial keratitis in patients with or without corneal sutures. This report presents the treatment of corneal infection with topical imipenem (50 mg/mL) as monotherapy in a patient who developed an infectious corneal complication due to a broken corneal suture after extracapsular cataract extraction with posterior chamber intraocular lens implantation.

This is to certify that this article has not been presented in a meeting and that the authors did not receive any financial support from any public or private sources and have no financial or proprietary interest in a product, method, or material described herein.

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Case report

A 76-year-old man was admitted to our hospital (Rize University, Faculty of Medicine, Education and Research Hospital, Department of Ophthalmology, Rize, Turkey) with complaints of pain, redness, and blurred vision in the right eye since 1 week before admission. Hourly treatments with topical moxifloxacin 0.5 % ophthalmic solution (Vigamox, Alcon Laboratories, Inc., Fort Worth, TX) had been started at an outside clinic 5 days prior to admission at our institution. His medical history was significant for extracapsular cataract surgery with corneal incision in his right eye, performed in another clinic approximately 1 year prior to presentation. On eye examination, right eye visual acuity was limited to the detection of hand movement. Severe conjunctival hyperemia and ciliary injection were evident. On slit-lamp examination, an approximately 8-mm-long

corneal incision in the upper paracentral region and a broken corneal suture over the incision, covered with infiltration, were identified. In addition, a 3×5-mm corneal opacity was identified around the suture. Severe anterior chamber reaction, hypopyon, and fibrin within the anterior chamber were also identified on slit-lamp examination (Fig. 1). A posterior chamber lens implant was evident in the capsular bag. Media haze prevented detailed examination of the vitreous and fundus. B-scan ultrasonography imaging showed no evidence of vitreous opacities.

Initially, the broken suture was removed, and then, corneal scraping was performed for culture under direct slit-lamp visualization. Samples (corneal scraping material and suture) were sent for gram staining and both bacterial and fungal culture determination. Topical moxifloxacin 0.5 % ophthalmic solution was discontinued, and topical fortified antibiotics, vancomycin (50 mg/mL), and ceftazidime (50 mg/mL) were started hourly. Over the next 2 days, hypopyon and stromal thickening increased (Fig. 2). Microscopic examination of samples with Gram staining showed predominance of gram-positive (GP) cocci along with fewer gram-negative (GN) bacilli. Culture studies using conventional methods grew methicillin-resistant *Staphylococcus epidermidis* (MRSE). Antibiotic sensitivity of the agent was determined in accordance with the recommendations of the Clinical and Laboratory Standards Institute disk diffusion method using Mueller-Hinton agar. The MRSE identified in the culture was resistant to penicillin, gentamicin, erythromycin, and clindamycin but was susceptible to vancomycin and linezolid. Oxacillin (1 μg) and cefoxitin (30 μg) disks were used to verify methicillin resistance, and the infectious agent was resistant to both. Cultures showed no GN bacterial growth. Topical vancomycin (50 mg/mL) and ceftazidime (50 mg/mL) were discontinued, and hourly monotherapy with topical imipenem (50 mg/mL) was started. One day later, hypopyon partially resolved; anterior chamber reaction decreased owing to

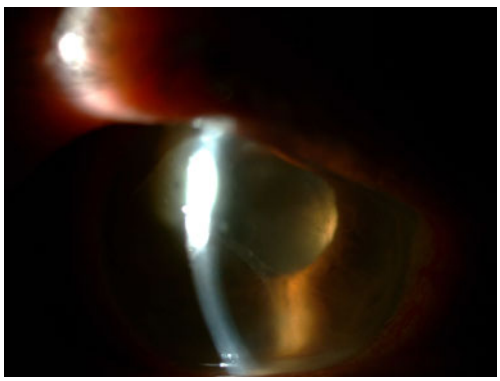

Fig. 1 Suture-related bacterial keratitis. Stromal infiltration is observed at the superotemporal incision. Severe anterior chamber reaction, hypopyon, and fibrin within the anterior chamber are evident

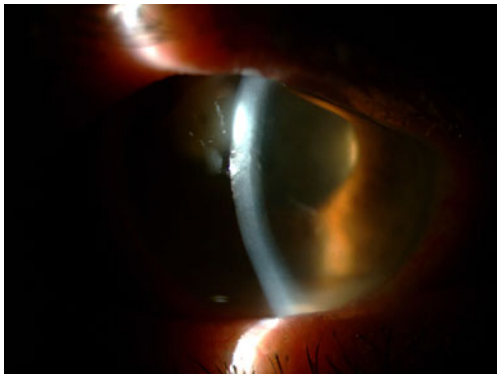

Fig. 2 Anterior chamber reaction, hypopyon, and stromal thickening increased over 2 days under antimicrobial treatment

which topical imipenem treatment was continued. Hypopyon and anterior chamber reaction improved, and stromal infiltration decreased within 1 week after topical imipenem was started (Fig. 3). Other corneal sutures were removed. The application range of topical imipenem was reduced, according to corneal lesion healing. Three weeks after initial presentation, corneal lesion recovery was achieved with residual scarring with vascularization (Fig. 4).

Discussion

Corneal grafts with loose sutures are particularly predisposed to the development of an infection. A loose suture thread is a risk factor for microbial keratitis after keratoplasty, because organisms easily attach to the suture thread and migrate into the cornea [4]. Previous studies have evaluated the presence of microorganisms on broken or loose sutures and concluded that eroded sutures harbor bacteria and should therefore be removed as early as possible following surgery [5]. The most common causative pathogens involved in bacterial keratitis are *Staphylococcus aureus* (30.56 %) and *S. epidermidis* (30.56 %) [6]. *S. epidermidis* was identified by culture in the present case.

Topical vancomycin (50 mg/mL) and ceftazidime (50 mg/mL) were used empirically as the initial infection did not respond to topical moxifloxocin. After 2 days of empiric therapy, hypopyon and stromal thickening increased compared to initial presentation. This case of microbial keratitis did not respond to topical vancomycin, ceftazidime, or moxifloxocin. Although both GN and GP bacteria were identified from samples, further treatment decisions were necessary prior to culture growth. Taking into consideration the corneal toxicity, a single topical antibiotic, effective against both GN and GP microorganisms, was chosen instead of adding an additional antibiotic to the treatment regimen. Topical imipenem (50 mg/mL), a beta-lactam antibiotic, was selected.

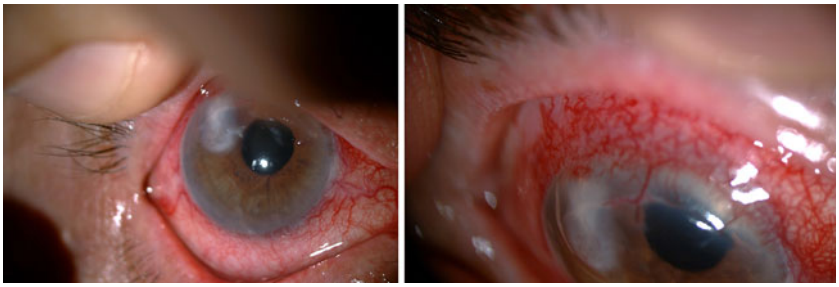

Fig. 3 One week after receiving topical imipenem treatment. Stromal infiltration decreased and hypopyon resolved

Of all antibiotics, beta-lactam antibiotics are currently some of the most commonly used. Imipenem is a wide-spectrum beta-lactam that exerts bactericidal effects via inhibition of cell wall synthesis. The most well-known broad-spectrum antibiotic—imipenem—has activity against both GN and GP, and aerobic and anaerobic microorganisms. Compared with other antibiotics and combinations thereof, imipenem is an extremely effective monotherapeutic agent in the treatment of a variety of serious infections. In vitro, imipenem is effective against most clinically significant bacteria. Therefore, imipenem is a good choice for empiric therapy prior to obtaining culture results and antibiotic susceptibilities, especially when resistant or polymicrobial infections are considered [7]. Previous studies have investigated antibiotic susceptibility patterns in conjunctival flora [8]. Conjunctival cultures were obtained, from the injection site, on the day of intravitreal triamcinolone injection prior to application of povidone–iodine or antibiotics. This previous study found 100 % sensitivity to imipenem in *S. aureus*, *Streptococcus* spp, and GN rods, as well as 85 % sensitivity in coagulase-negative staphylococci [8].

In the current case, the susceptibility of *S. epidermidis* to imipenem was not investigated. Although the primary pathogenic bacteria in this case of keratitis were likely to be *S. epidermidis*, it is possible that the infection was polymicrobial because methicillin-resistant, vancomycin-susceptible *S. epidermidis* was grown in culture, but clinically, the keratitis worsened despite topical vancomycin therapy.

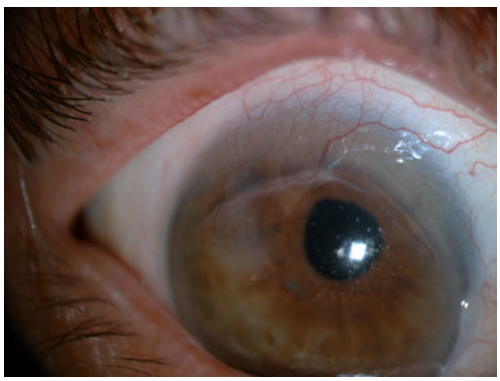

Fig. 4 At discharge, the lesion is cicatrized and angioinvasion is observed throughout the corneal incision

Topical vancomycin is effective in the treatment of MRSE keratitis [9], but studies have demonstrated highly diverse antibiotic resistance profiles and capacity for biofilm formation in *S. epidermidis* strains collected from conjunctivitis, corneal ulcers, and endophthalmitis (28 % demonstrated intermediate vancomycin resistance) [10].

One mechanism of pathogenicity in infectious keratitis is biofilm formation on suture [7]. Glycopeptide antibiotics, like vancomycin, may fail to treat these infections due to a diminished antimicrobial effect on bacteria in the biofilm environment [11]. Therefore, the minimum biofilm eradication concentration is more important than the minimal inhibitory concentration in this setting [12]. Topical vancomycin may have been ineffective in this suture-related case due to the production of a biofilm by *S. epidermidis*. In addition, few GN bacilli were identified in the samples, but GN bacilli did not grow in culture. Vancomycin does not have activity against GN bacteria. Ceftazidime, a third-generation cephalosporin, has strong activity against GN bacteria, and moxifloxocin, a fourth-generation fluoroquinolone, has a wide spectrum of activity that includes GP, GN, and atypical bacteria. Both ceftazidime and moxifloxacin were ineffective in the current case.

Previous studies have investigated the cytotoxicity of vancomycin, teicoplanin, mupirocin, and imipenem in rabbit corneal epithelial cell cultures. Imipenem was determined to be less toxic than other antibiotics to corneal epithelial cells [13]. To the best of our knowledge, topical imipenem was first used in the treatment of experimental *Pseudomonas* keratitis in rabbits. Sawusch et al. [14] injected an aminoglycoside-resistant *Pseudomonas aeruginosa* strain intrastromally, and topical imipenem (5 mg/mL) therapy was initiated 5 h after inoculation using one drop every 30 min for 12 h followed by corneal tissue excision and culture for colony-forming unit counts. According to this previous study, imipenem was highly effective in eliminating colony-forming units compared to untreated controls [14]. A second regimen of one drop per hour for 24 h, beginning 24 h post-inoculation, was also successful in significantly reducing colony-forming units compared to controls [14]. Galvis et al. first used topical imipenem to treat human bacterial keratitis [15]. They used topical imipenem in intracorneal ring segments placed in a patient that

developed late bacterial keratitis due to coagulase-positive *S. aureus*. Topical imipenem (25 mg/mL) was used along with moxifloxacin and vancomycin every 6 h for 14 days, and microbiological culture demonstrated vancomycin/oxacillin-sensitive coagulase-positive *S. aureus*. While coagulase-positive *S. aureus* should be sensitive to imipenem, in that case, the therapeutic effect was likely a result of vancomycin. Therefore, that previous case does not present the use of topical imipenem as a monotherapy. In the current case, topical imipenem was used as a monotherapy, but at twice the dose used in the previous case.

Corneal sutures must be routinely removed in the early postoperative period. If suture-related keratitis occurs, it can be treated with fortified antibiotics after the suture is removed. In the treatment of serious bacterial keratitis, whether or not it is suture-related, topical fortified antibiotics such as vancomycin (50 mg/mL) and gentamicin (14 mg/mL) [3] or ceftazidime (50 mg/mL) and vancomycin (50 mg/mL) [3] can be used as empiric therapy, or antibiotic treatment can be tailored according to antibiotic susceptibility patterns. Imipenem is a broad-spectrum antibiotic that can also be used as a topical treatment either empirically or according to antibiotic susceptibilities, in the treatment of serious bacterial keratitis regardless of the source. The present case describes a suture-related bacterial keratitis successfully treated with topical imipenem (50 mg/mL). Further studies are needed to investigate the efficacy and safety of topical imipenem in the treatment of corneal infections.

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