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Bilateral multifocal *pseudomonas aeruginosa* keratitis in a contact lens-wearing diabetic patient treated with a custom compounded 5% imipenem-cilastatin topical solution

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Abstract

Pseudomonas aeruginosa is a devastating agent of fulminant keratitis in contact lens-wearers, immunosuppressive patients, and refractive surgery patients which may lead to substantial loss of vision, and in severe cases, blindness. In this case report, a 30-year-old diabetic contact lens wearer who had history of sleeping with lenses and prolonged use of the same contact lens presented with multiple foci of keratitis in each eye. No pathogen was detected from corneal scrapings, but the contact lenses and the contact lens case were culture positive for *Pseudomonas aeruginosa*. The keratitis was only partially responsive to topical fortified ceftazidime, topical fortified vancomycin, and topical fluconazole. A decision was made to switch to topical imipenem-cilastatin due to the multiple risk factors, including diabetes, contact lens overuse, and bilateral multifocal corneal involvement, after which the keratitis resolved. Topical imipenem-cilastatin may be a successful alternative treatment in patients with *Pseudomonas* keratitis who do not respond to conventional antibiotic therapy.

Introduction

Pseudomonas Aeruginosa is a devastating agent of fulminant keratitis in contact lens-wearers, immunosuppressive patients, and refractive surgery patients which may lead to substantial loss of vision, and in severe cases, blindness.[1–6]

Contact lens-related *Pseudomonas* keratitis is more frequent in patients who betray hygienic rules for lens solutions and lens storage cases and who sleep with lenses. Corneal scarring may occur due to keratitis and in fulminant cases. Furthermore, corneal perforation may lead to endophthalmitis. Isolation of the pathogen and its antibiotic susceptibility should be performed in order to prescribe the appropriate antibacterial treatment.

In this case report, a 30-year-old type 1 diabetic, contact lens wearer presented with bilateral simultaneous multifocal *Pseudomonas* keratitis who was successfully treated with topical imipenem-cilastatin drops.

Case Report

A 30-year old female patient presented complaining of blurred vision in both eyes for one week, with no improvement after 10 days of taking

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topical moxifloxacin drops she had received elsewhere. The patient has had well-controlled type 1 diabetes for 11 years treated with insulin with HbA1c and blood sugar in normal ranges. The patient had a history of wearing the same contact lens for prolonged periods of time, including the 9 consecutive months preceding her presentation and with sleeping with the lens for several nights in a row.

On clinical examination, her visual acuity was 20/40 in the right eye and hand-motions in the left eye. Slit-lamp biomicroscopy disclosed multiple foci of keratitis, particularly in the superior half of each cornea, with each satellite-like lesion staining with fluorescein. Peripheral corneal thinning and ciliary injection in both eyes were also observed (Figure 1).

The patient was hospitalized and treated with topical fortified ceftazidime, topical fortified vancomycin, and topical fluconazole, along with cyclopentolate and non-preserved artificial tears. Corneal scrapings were sent to microbiology for gram staining, direct microscopic examination, and culture for bacteria and fungi. No pathogen was detected from the corneal scrapings, but the contact lenses and contact lens case were culture positive for *Pseudomonas aeruginosa*. The antibiotic susceptibility of the pathogen was reported as: resistant to gentamycin, levofloxacin, intermediate-resistant to ciprofloxacin, amikacin, tobramycin, aztreonam, and susceptible to piperacillin, colistin, imipenem, meropenem and cefepime.

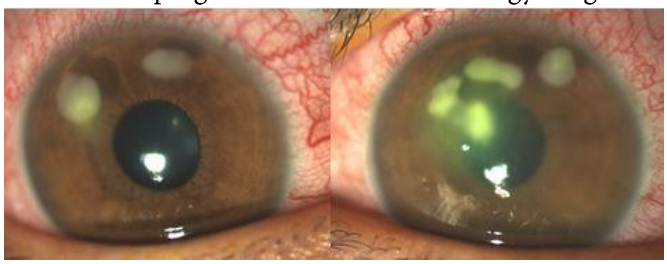

Figure 1
Upon presentation, slit-lamp biomicroscopy demonstrated bilateral multiple foci of keratitis (right eye on left, left eye on right).

On the 7th day of the treatment, only partial and limited response to the fortified ceftazidime and vancomycin treatment was observed. A decision was made to switch to topical imipenem-cilastatin due to the multiple risk factors, including diabetes, contact lens overuse, and bilateral multifocal corneal involvement. Fifty mg of imipenem-cilastatin (Tienam, MSD, Turkey) was compounded with 10 ml of distilled water and pH balanced to obtain a 5% concentration imipenem-cilastatin topical solution.

One drop of the imipenem-cilastatin solution was instilled hourly in each eye for the first 48 hours and then instilled in each eye every 2 hours; thereafter, the frequency was reduced according to the clinical response. The ulcer was considered to be healed once there was corneal epithelialization and resolution of the infiltrate and inflammation. On 6th day of the imipenem-cilastatin therapy, the keratitis foci were found to be smaller and clearer (Figure 2). On the 25th day of the treatment, the corneal epithelium of both eyes was intact, and the final best-corrected visual acuity was 20/30 in the right and 20/60 in the left eye. Small, superficial, lightly opacified corneal scars persisted in the superior half of the both corneas.

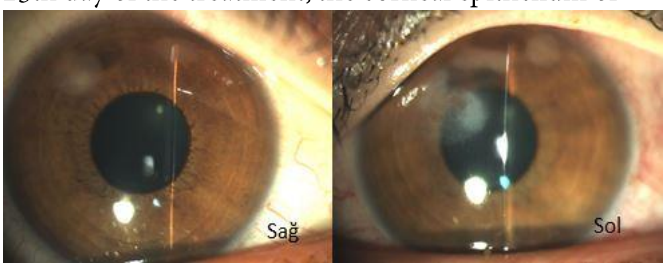

Figure 2
On the 6th day after initiation of topical imipenem-cilastin therapy, slit-lamp biomicroscopy demonstrated that the bilateral multiple foci of keratitis had become smaller and clearer (right eye on left, left eye on right).

Discussion

Pseudomonas Aeruginosa is a frequent pathogen in contact lens related keratitis.[1,5] Although it is reported that a corneal epithelial defect is needed for

this pathogen to enter the cornea to cause an infection, in a study performed in rats, it was shown that pseudomonas forms a biofilm layer in the posterior surface of the contact lens, which may lead to keratitis in the absence of corneal injury.[6-8] It is also known that contact lenses, lens storage boxes, and lens solutions may also act as reservoirs for microorganisms.[9]

Bad hygiene and sleeping with contact lenses increases the risk of corneal infection between 9- and 15-fold, especially with contact lenses that are worn over a prolonged period of time.[5-11] Punit, et al. reported that the risk of infection in patients sleeping with contact lenses is 20 times more than in patients wearing daily contact lenses.[12] Diabetic patients are more prone to bacterial infections due to the pre-existing immunodeficiency associated with the diabetes; also, diabetic infections are more resistant to conventional therapies requiring more complex therapies.[13]

Antibiotic resistance is an important global problem because of widespread usage of antibiotics, often unnecessarily.[14] The unnecessary use of antibiotics results in antibiotic resistance, including the particular development of multidrug-resistant strains of *Pseudomonas aeruginosa* which may result in in fulminant infections.[15] For these reasons, it is reasonable to switch to new treatment modalities in diabetic patients with keratitis resistant to conventional therapies.[16]

Although *Pseudomonas aeruginosa* is generally sensitive to fluoroquinolones, Ku, et al. reported *Pseudomonas aeruginosa* strains are resistant to ciprofloxacin, gentamicin, tobramycin, and amikacin but sensitive to ceftazidime, imipenem, meropenem.[17]

In this case, the antibiotic susceptibility of the pathogen demonstrated sensitivity to imipenem. Because of limited response to ceftazidime and vancomycin, we switched to imipenem. Very recently, studies reported treating multidrug resistant *Pseudomonas* keratitis with topical piperacillin, colistin, and meropenem, antibiotics which are not ordinarily used in ophthalmology.[18-21] Imipenem is available in a combined injectable form with cilastatin. Topical imipenem (0.5%) therapy was found to be successful in *Pseudomonas* keratitis in a rat model.[22] A recent study by Castro, et al. points out the necessity of developing stable forms of fortified imipenem drops with high drug concentrations because commercial eye drops are no longer effective in most cases.[23] Furthermore, Cutarelli, et al. reported that topically used imipenem was less toxic in rabbit corneal epithelial cell cultures than vancomycin, teicoplanin, and mupirocin.[24] Although the use of imipenem in eye infections is rare, it should always be an option for fulminant infections unresponsive to conventional therapies and in general should not be started as primary therapy. In the current case with multiple risk factors, such as diabetes, young age, simultaneous bilateral and multifocal involvement, we switched to topical imipenem-cilastatin therapy with successful result.

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