A case of contact-lens-related keratitis caused by fluoroquinolone- and tobramycin-resistant *Capnocytophaga sputigena*

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Introduction: *Capnocytophaga* species are rare keratitis-causing pathogens. We herein report a case of keratitis caused by a drug-resistant *Capnocytophaga* species in association with contact lenses.

Case presentation: A 64-year-old female who wore a contact lens in her right eye to facilitate repair of the corneal epithelium complained of infection and discharge. Slit-lamp biomicroscopy showed corneal abscessation and hypopyon. Thus, infectious keratitis was diagnosed. Direct microscopy and bacterial culture of a corneal scraping were performed. Because direct microscopy demonstrated the presence of Gram-negative rods, we began treatment with topical 1.5 % levofloxacin and 0.3 % tobramycin every hour. The corneal infiltration increased 4 days after initiating the therapy. The culture report confirmed the presence of a *Capnocytophaga* species with fluoroquinolone and aminoglycoside resistance and susceptibility to cephalosporins and minocycline. We switched to topical 0.5 % cefmenoxime every hour and oral minocycline at 200 mg day^-1^. The corneal inflammation subsided within 2 weeks. The bacterial isolate was identified as *Capnocytophaga sputigena* using 16S rRNA sequencing.

Conclusions: We encountered a case of keratitis caused by *C. sputigena* with reduced fluoroquinolone and aminoglycoside susceptibility.

Keywords: *Capnocytophaga*, fluoroquinolone, keratitis, tobramycin, resistance.

Introduction

Keratitis is a corneal infection that occurs following injury or in association with contact lenses (CLs). Infectious keratitis can progress rapidly and lead to corneal scarring and loss of vision. The severity and prognosis of infectious keratitis depend on the causative agent. *Pseudomonas aeruginosa*, which is a leading cause of keratitis related to CLs, can progress rapidly and exhibit suppurative infiltration (Burns, 1969). An antibiotic ophthalmic solution should be used for the treatment of keratitis. Fluoroquinolones and cephalosporins are often used for empirical treatment or prevention of keratitis (Kowalski et al., 2013; Loh et al., 2009; Ly et al., 2006; Suzuki & Ohashi, 2013). Tobramycin is also a common topical antibiotic used for *P. aeruginosa* keratitis (Kowalski et al., 2013; Suzuki & Ohashi, 2013). A previous study in rabbits showed that 0.3 % (w/v) tobramycin was subtherapeutic in this context because of low drug bioavailability in the dense corneal stroma (Gilbert et al., 1987). However, a combination of tobramycin and fluoroquinolone may exhibit a synergistic effect and is effective for treating *P. aeruginosa* keratitis (Suzuki & Ohashi, 2013). Microbiological examinations such as direct smear and culture are necessary to detect the causative agents of keratitis and select the most appropriate antibiotics. Direct smears of corneal scrapings are especially useful to rapidly distinguish bacteria or fungi as well as Gram-negative or -positive bacteria. When Gram-negative rods are detected in keratitis in association with CLs, *P. aeruginosa* or *Serratia marcescens* should be considered; in such cases, treatment with fluoroquinolone and tobramycin could be used empirically (Kowalski et al., 2013; Suzuki & Ohashi, 2013).

*Capnocytophaga* species are facultative anaerobic Gram-negative bacilli that compose part of the human and animal oral flora. These species rarely cause keratitis...
Capnocytophaga isolates are susceptible to most groups of antibiotics (Jolivet-Gougeon et al., 2007).

We herein report a case of keratitis in association with a CL. The causative microorganism was a Capnocytophaga species with fluoroquinolone and tobramycin resistance.

**Case report**

A 64-year-old female with bilateral visual disturbance visited a private clinic. Severe superficial punctate keratitis (SPK) was found, and she was referred to our hospital. Slit-lamp biomicroscopy revealed SPK in both eyes in the absence of corneal infiltration, and severe conjunctival injection, and dry eye was diagnosed. Although she was treated with ocular lubricants and underwent punctal plug treatment, the SPK persisted. A silicone hydrogel CL (Air Optix) was used to repair the corneal epithelium in the right eye. She complained of infection and discharge in the right eye after having worn the CL for 3 days. Slit-lamp biomicroscopy revealed a dense central corneal infiltration associated with a corneal epithelial defect, and a hypopyon (Fig. 1). Direct microscopy and bacterial culture of corneal scrapings were performed. Direct microscopy demonstrated the presence of Gram-negative rods. We considered a diagnosis of keratitis caused by Gram-negative rods. We speculated that *P. aeruginosa* was the causative agent because of the CL-wearing and clinical findings, and thus began treatment with topical 1.5% levofloxacin and 0.3% tobramycin every hour. The corneal infiltration increased 4 days after initiating the therapy (Fig. 2). The culture report confirmed the presence of a Capnocytophaga species, and antimicrobial susceptibility testing was performed using the microdilution method. The MIC values of the drugs tested are listed in Table 1. The isolate showed decreased susceptibility to fluoroquinolones, tobramycin and macrolides. Because the drug susceptibility results showed that the isolate had good susceptibility to cephalosporins and minocycline, we switched to topical 0.5% cefmenoxime every hour and oral minocycline at 200 mg day$^{-1}$ for 2 weeks. The corneal infiltration and inflammation in the anterior chamber subsided within 2 weeks (Fig. 3). PCR amplification and sequencing of the 16S rRNA region of the isolate were performed to definitively identify the genus and species; the isolate was subsequently identified as *C. sputigena*.

**Discussion**

Infectious keratitis is a severe complication of CL-wearing, and *P. aeruginosa* is the main causative agent of keratitis in association with CLs. In our case, a Capnocytophaga species was isolated and identified as the causative agent of keratitis in association with CLs. Capnocytophaga keratitis

Table 1. *Capnocytophaga sputigena* antibiotic susceptibility profile

<table>
<thead>
<tr>
<th></th>
<th>CMX</th>
<th>TOB</th>
<th>EM</th>
<th>CP</th>
<th>LVFX</th>
<th>GFLX</th>
<th>MFLX</th>
<th>MINO</th>
<th>IPM</th>
</tr>
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<tbody>
<tr>
<td>MIC (µg ml$^{-1}$)</td>
<td>0.5</td>
<td>32</td>
<td>32</td>
<td>8</td>
<td>16</td>
<td>4</td>
<td>4</td>
<td>&lt;0.25</td>
<td>0.25</td>
</tr>
</tbody>
</table>

CMX, Cefmenoxime; TOB, tobramycin; EM, erythromycin; CP, chloramphenicol; LVFX, levofloxacin; GFLX, gatifloxacin; MFLX, moxifloxacin; MINO, minocycline; IPM, imipenem.
has been reported in several studies (Alexandrakis et al., 2000; Chodosh, 2001; Font et al., 1994; Heidemann et al., 1988; Pamel et al., 1989; Roussel et al., 1985; Ticho et al., 1990). Alexandrakis et al. reported 10 cases of Capnocytophaga keratitis and reviewed 14 cases from the literature. In their reports, predisposing factors for Capnocytophaga keratitis were eye trauma and persistent corneal epithelial defects, but not CL-wearing. Because our patient used a CL to treat a corneal epithelial disorder, both the corneal epithelial disorder and the CL-wearing were risk factors for keratitis. Little is known about how Capnocytophaga species (which are common members of the oral flora) cause keratitis, but we speculate that sputum may sometimes contaminate the eye, translocating micro-organisms from the oral cavity. Slit-lamp biomicroscopy showed dense corneal infiltration with hypopyon. Because direct microscopy demonstrated the presence of Gram-negative rods, we considered the presence of CL-related keratitis caused by P. aeruginosa. The patient was treated with levofloxacin and tobramycin, which is empirical therapy for P. aeruginosa keratitis. However, the corneal infiltration increased after this treatment; treatment with levofloxacin and tobramycin failed because of the low susceptibility of the Capnocytophaga isolate to these agents. Antimicrobial susceptibility testing of Capnocytophaga species has shown that these organisms are typically susceptible to clindamycin, linezolid, tetracycline, chloramphenicol, imipenem and cefepime, including β-lactamase inhibitors (Jolivet-Gougeon et al., 2007). Their susceptibility to fluoroquinolones and aminoglycosides varies greatly. Although clinical isolates of Capnocytophaga species have been shown to be susceptible to quinolone antimicrobial agents (Hawkey et al., 1987; Rummens et al., 1986), Gomez-Garcés et al. (1994) reported a strain of C. sputigena with a ciprofloxacin MIC of 16 μg ml⁻¹. Furthermore, aminoglycoside MICs ranged from 0.05 to 64.00 μg ml⁻¹ (Bremmelgaard et al., 1989; Roscoe et al., 1992). Thus, fluoroquinolones or tobramycin for empirical therapy of keratitis caused by Gram-negative rods could fail in patients with drug-resistant Capnocytophaga keratitis. In previous reports, Capnocytophaga keratitis was treated with vancomycin, cephalosporin, tobramycin, clindamycin or fluoroquinolones, but the visual prognosis in these cases was poor and several eyes required keratoplasty or enucleation (Alexandrakis et al., 2000; Heidemann et al., 1988; Ticho et al., 1990). Some patients responded to topical and subconjunctival clindamycin (Roussel et al., 1985). Our patient responded to cefmenoxime ophthalmic solution and oral minocycline. Minocycline is known to penetrate the ocular tissue effectively and has anti-inflammatory, antimitelroproteinase, and anti-apoptotic properties (Lee et al., 2012; Tabbara & Cooper, 1989). Thus, minocycline in combination with cefepime may be useful for treatment of Capnocytophaga keratitis. For effective treatment of keratitis caused by drug-resistant Capnocytophaga, antibiotics should be chosen carefully according to the results of confirmatory susceptibility testing.

In conclusion, we encountered a case of CL-related keratitis caused by C. sputigena with reduced fluoroquinolone and tobramycin susceptibility. Ophthalmologists should diagnose Capnocytophaga keratitis as early as possible and refer patients for antimicrobial susceptibility testing.

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References


