Acute exacerbation of staphylococcal catarrhal infiltration associated with treatment for *Pseudomonas aeruginosa* keratitis

A case report

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**Abstract**

**Rationale:** Simultaneous presentation of peripheral infiltrates, which can be easily misidentified as satellite lesions, is rarely observed in patients with acute infectious keratitis.

**Patient concerns:** A 70-year-old woman was referred to our clinic due to acute mucopurulent keratitis following application of a therapeutic soft contact lens for the treatment of epithelial defects caused by entrance of soil foreign bodies into the eye. The patient was diagnosed with *Pseudomonas* keratitis, following which she was treated with alternating administration of fourth-generation fluoroquinolone (Vigamox) and 5% fortified cefazidime eyedrops every 2 hours. Although infectious keratitis rapidly improved, discrete catarrhal infiltrates at the corneolimbal junction (10- to 2-o'clock and 7- to 8-o'clock positions) were rapidly aggravated, forming bead-like stromal pustules inversely proportional to the extent of *Pseudomonas* keratitis.

**Diagnosis:** Acute exacerbation of staphylococcal catarrhal infiltration associated with treatment for *Pseudomonas aeruginosa* keratitis.

**Interventions:** Addition of 1% prednisone acetate eyedrops (Pred Forte) four times per day.

**Outcomes:** Dramatic improvement was observed at the sites of catarrhal infiltration without recurrence of infectious keratitis.

**Lessons:** Clinicians should thus remain aware of the risk for co-occurring non-infectious, immune-related keratitis, as treatment for infectious keratitis may induce significant aggravation of non-infectious keratitis.

**Abbreviation:** PASP = *Pseudomonas aeruginosa* small protease.

**Keywords:** catarrhal infiltration, keratitis, marginal, *Pseudomonas aeruginosa*, *Staphylococcus*...
before referral. She had no history of eye surgery or keratitis in either eye. During the initial examination, we evaluated unaided visual acuity in the patient’s left eye, which was capable of distinguishing hand-motion only and did not respond to attempts at correction. Slit-lamp examination revealed a central, well-demarcated, mucopurulent epithelial defect (4.0 x 4.5 mm) with thick stromal infiltrations. Creamy white subepithelial infiltrates were observed at the corneolimbal junction (10- to 2-o’clock and 7- to 8-o’clock positions), although no epithelial defects were observed over either lesion. In addition, the patient exhibited 1+ blepharitis on both upper and lower eyelids. The anterior chamber exhibited 3+ cellular reaction with mild cyclitic membrane formation (Fig. 1A and B). Corneal scrapings and cultures were obtained using a No. 15 Bard-Parker blade (Aspen Surgical, Caledonia, MI) with cotton-tipped swabs. Initial corneal scrapings were positive for gram-negative bacilli. The patient was hospitalized and treated with 0.5% moxifloxacin (Vigamox, Alcon Laboratories, Fort Worth, TX), 5% (50 mg/mL) fortified ceftazidime (Tazime injection, Hanmi Pharma, Seoul, Korea), and 5% (50 mg/mL) vancomycin (Hanomyacin injection, Samjin Pharm, Seoul, Korea) eyedrops. For the loading dose, eyedrops were instilled every 10 minutes for 1 hour, every 30 minutes for 2 hours, and hourly for 6 hours. Subsequently, antibiotic eyedrops were alternatively instilled bihourly.

On the fifth day after hospitalization, the central epithelial defect had shrunk to 2.5 x 1.8 mm in size, and mucopurulent discharge had markedly decreased. Although the anterior chamber exhibited 2+ cells without visible cyclitic membranes,
coincidence, corneolimbal infiltrates were refractory to antimicrobial treatments. Marked aggravation of the infiltrates, which had formed a bead-like pattern elevated from the corneal surface, was observed (Fig. 1C and D).

On the sixth day after admission, aggravation of corneolimbal lesions had again increased, and band-like infiltration was observed along the limbus. Corneal scrapings and cultures were again obtained to evaluate infiltrates affecting the conjunctiva near the corneal limbus, following which corneal biopsy of infiltrates at the 11-o’clock position was performed for histological analysis. The surface of the eyelid and upper lid cilia were also swabbed to obtain cultures for the identification of staphylococcal colonization. Eight days after admission, corneal scrapings were negative for microbial organisms, although *S. epidermidis* was identified in cultures. Corneal biopsy of the limbal lesions revealed numerous neutrophilic infiltrates around the peripheral lesion. We suspected that the patient’s peripheral lesions were marginal staphylococcal infiltrates, following which she was treated with 1% prednisone acetate eyedrops (Pred Forte, Allergan, Irvine, CA) 4 times per day while maintaining the previous antibiotic eyedrop regimen (Vigamox, 5% fortified vancomycin and ceftazidime 4 times per day). One day after the treatment with steroid eyedrops, considerable improvements in pain and redness were observed. Complete healing of the epithelial defect was observed on day 11 (Fig. 1F). Two weeks after the initiation of steroid eyedrop treatment, corneolimbal lesions had completely resolved, without recurrence of bacterial keratitis. However, thinning of the central cornea was apparent.

### 3. Discussion and conclusion

In the present case, multiple corneolimbal infiltrates and severe mucopurulent keratitis due to non-staphylococcal, *P. aeruginosa* infection were observed at the time of presentation. Fortunately, the patient stated that the acute exacerbation of ocular pain and redness occurred following application of the therapeutic contact lens, and—given the history of soil foreign body entrance in the eye—*Pseudomonas* infection was suspected. Therefore, both fortified third-generation cephalosporin (5% ceftazidime) and fourth-generation synthetic fluoroquinolone (moxifloxacin 0.5%) eyedrops were alternatively loaded prior to obtaining scraping report or culture findings. Signs and symptoms of *Pseudomonas* keratitis dramatically improved following initiation of these treatments.

Although multiple peripheral infiltrates were observed during the initial examination, these lesions were overlooked as satellite lesions of central keratitis or reactive changes induced by severe keratitis. Therefore, paradoxical rapid aggravation of corneolimbal catarhral infiltrations despite dramatic improvement in central *Pseudomonas* keratitis appeared unusual. In addition, although improvements were observed in the central epithelial defects and surrounding areas of infiltration, rapid aggravation of conjunctival edema, hyperemia, and peripheral corneal infiltrates was observed for several days. Based on these findings, I suspected that the patient’s symptoms may have been associated with other conditions such as scleritis or autoimmune-related peripheral ulcerative keratitis. However, thorough re-evaluation of initial slit-lamp images revealed that the initial peripheral lesions were separated from the limbus (lucid interval), while no epithelial defects were observed over any of the lesions. Furthermore, *S. epidermidis* was isolated from the second corneconjunctival culture, despite negative cultures for the eyelid and cilia swabs. As *Staphylococcus aureus* has also been previously identified in the conjunctiva and eyelid,[19] I strongly suspected the co-occurrence of marginal catarhral infiltrates due to noninfectious, immune-related keratitis.

Moreover, although staphylococcal catarhral infiltrates were strongly suspected, the decision to administer corticosteroids during culture-proven bacterial keratitis was complex due to the risk of acute exacerbation of keratitis and reactivation of remnant *Pseudomonas*. In addition, the use of steroid eyedrops during hospitalization and the treatment for bacterial keratitis remains controversial, as this may lead to progression of corneal thinning or damage.[19] Two weeks after the initiation of treatment with 1% prednisone acetate eyedrops in the present case, marked thinning of the area in which *Pseudomonas* keratitis had developed was confirmed using anterior segment optical coherence tomography, although the infiltrates at the corneolimbal junction had not yet completely resolved.

The mechanism underlying the findings observed in the present case remains to be determined, as no similar cases can be found in the literature. However, a previous study indicated that treatment with the LasA protease of *P. aeruginosa* (a staphylolytic endopeptidase) significantly improved clinical scores in a rabbit model of *Staphylococcus* keratitis.[10] Although *Staphylococcus* colonization was not observed on the eyelid in the present study (culture-negative result at eyelid swab and cilia), secreted protease from *Pseudomonas* organisms in the corneal stroma may have suppressed *Staphylococcus* colonization on the eyelid or conjunctiva. While successful treatment eliminated *Pseudomonas aeruginosa*, the titers of staphylolytic protease may have abruptly decreased. In addition, broad-spectrum coverage of antimicrobial agents may have disturbed the normal flora of the ocular surface or eyelid, enabling the selective and explosive growth of a resistant strain of *Staphylococcus* and potentiating exposure of the cornea to *Staphylococcus* antigens.

In conclusion, simultaneous presentation of peripheral infiltrates, which can be easily misidentified as satellite lesions, is rarely observed in patients with acute infectious keratitis. Clinicians should thus remain aware of the risk for co-occurring noninfectious, immune-related keratitis, as treatment for infectious keratitis may induce significant aggravation of noninfectious keratitis.

### Author contributions

**Conceptualization:** Jong Hwa Jun.

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**Validation:** Jong Hwa Jun.

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