Infectious Keratitis Caused by *Stenotrophomonas maltophilia* and Yeast Simultaneously

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Purpose: To report a case of coinfection of the human cornea by *Stenotrophomonas maltophilia* and yeast.

Methods: A 59-year-old woman presented with a corneal ulcer. The corneal lesion worsened suddenly after initial improvement with empirical antibiotic treatment. A culture revealed *S. maltophilia*. The keratitis rapidly progressed despite treatment with sensitivity-proven antibiotic agents. Eventually, the patient underwent therapeutic penetrating keratoplasty.

Results: Pathology of the cornea showed yeast forms and pseudohyphae scattered over the cornea. After surgery, the inflammation was controlled without any signs of recurrent infection.

Conclusion: Coinfection of the cornea by *S. maltophilia* and yeast may occur in a susceptible cornea and may not be controlled by standard medical treatment.

Key Words: coinfection, infectious keratitis, *Stenotrophomonas maltophilia*, yeast

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Stenotrophomonas maltophilia, which was previously designated as *Pseudomonas maltophilia* and *Xanthomonas maltophilia*, is emerging as a multiresistant nosocomial strain.[1] Patients infected with *S. maltophilia* usually have underlying immunodeficiency, a history of long-term or multiple hospitalizations, or exposure to invasive devices and/or broad-spectrum antimicrobials.[2]

This organism has been reported as an opportunistic ocular infection that occurs mostly in patients with ocular compromise, and it is characteristically resistant to broad-spectrum antibiotics.[3] Several cases of infectious keratitis caused by *S. maltophilia* and 1 case of coinfection with *S. maltophilia* and filamentous fungus have been reported.[3–6] We report here a corneal ulcer caused by coinfection with *S. maltophilia* and yeast, proven by culture and histopathology.

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CASE REPORT

A 59-year-old woman with a peripheral corneal ulcer in her right eye was referred to our clinic. She had undergone pterygium excision in the same eye 2 years previously. Two months before, conjunctival flap advancement surgery was performed to treat progressive scleral thinning at the previous excision site. Two days before her visit, she developed sudden pain in her right eye. She was referred for treatment under suspicion of an infectious corneal ulcer.

On initial ophthalmologic examination, uncorrected visual acuity was hand motion in her right eye. She had a small stromal infiltration with an overlying epithelial defect in the nasal perilimbal cornea, accompanied by severe uveitis. No organism was identified by smear and culture of the corneal scrapings. Because 3-day empirical treatment with topical 5% cefazolin and 1.3% tobramycin yielded no improvement, the treatment was changed to topical 5% vancomycin and 2% amikacin. After that, the corneal epithelium healed completely, and the infiltrates decreased during the next 7 days. To control the severe inflammation, we started oral prednisolone, 40 mg/d, with tapering, and topical 1% prednisolone acetate 4 times a day. Several days later, the inflammation was well controlled, and her visual acuity had improved to 20/100. However, a toxic keratopathy was newly developed, and we changed topical antibiotics to 0.3% ofloxacin to control the corneal toxicity. One week after changing eye drops, the patient complained of ocular pain and a rapid decrement of vision. On examination, she had dense stromal suppuration with an overlying epithelial defect on more than one half of the cornea and accompanied by hypopyon (Fig. 1A). We began topical vancomycin, amikacin, 0.3% amphotericin B, and oral fluconazole 200 mg/d empirically after obtaining a smear and culture of the scrapes from the lesion. Gram stain of the smear revealed gram-negative rods. After 48-hour cultures on blood plate agar, *S. maltophilia* was identified by a conventional method using the API 20 E system. Ceftazidime (Becton, Dickinson and Company, Sparks, MD), ciprofloxacin (Oxoid Limited, Basingstoke, Hampshire, England), cefepime (Oxoid Limited, Basingstoke, Hampshire, England), gentamicin (Oxoid Limited, Basingstoke, Hampshire, England), levofloxacin (Oxoid Limited, Basingstoke, Hampshire, England), trimethoprim/sulfamethoxazole (Oxoid Limited, Basingstoke, Hampshire, England), tetracycline (Oxoid Limited, Basingstoke, Hampshire, England), and piperacillin (BioMérieux Inc., Durham, NC) were susceptible. However, determination of the minimal inhibitory concentrations was not available because of the absence of reference values for this rare strain in our laboratory. We changed the treatment to topical 5% ceftazidime and 0.3% ciprofloxacin on the basis of the sensitivity tests. Despite treatment with the above medications, corneal melting and hypopyon progressed, and the patient complained of persistent severe ocular pain. We changed the topical antibiotics to fortified piperacillin and started oral trimethoprim-sulfamethoxazole, which was also proven by sensitivity test. We added again topical amphotericin B and oral fluconazole without further scrapings or excision of the active melting cornea. However,

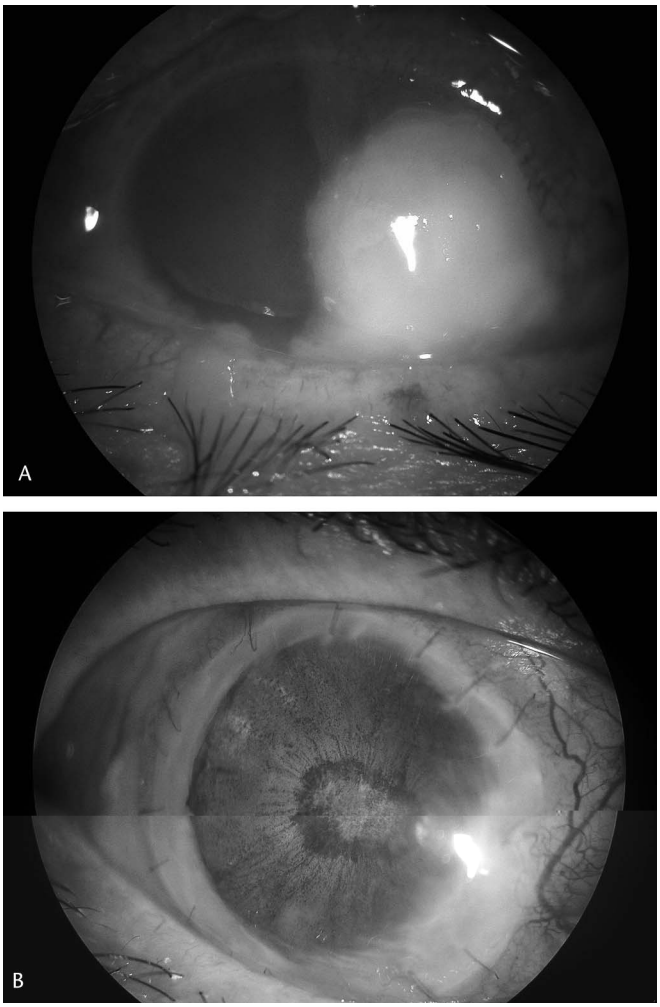

FIGURE 1. Slit-lamp photographs. A, Dense stromal suppuration of more than one half of the cornea is noted. B, Two months after therapeutic penetrating keratoplasty, the inflammation was well controlled without any sign of the recurrent infection.

the lesion continued to progress. Shortly thereafter, the patient underwent therapeutic penetrating keratoplasty.

Because the active corneal suppuration reached the limbal area, the entire cornea including the lesion was excised, and an equal-sized donor graft was cut round using a corneoscleral scissors. The diameter of the graft was approximately 10.5 to 11.0 mm. After excision of the host cornea, all inflammatory debris in the anterior chamber was carefully removed, and the exposed intraocular tissue was irrigated vigorously with 160 μg/mL of gentamicin in balanced salt solution. She was started on treatment with oral prednisolone 40 mg/d, oral fluconazole 200 mg/d, topical 0.3% ciprofloxacin, and topical 1% prednisolone acetate 4 times a day. Periodic acid-Schiff and Gomori methenamine silver staining of the excised cornea showed many yeast forms and pseudohyphae scattered over the cornea, consistent with *Candida* species (Fig. 2). However, identification of the strain was not attainable because the yeast did not grow on 2-week tissue cultures. The patient continued with topical medication, and her oral prednisolone was tapered during the next 2 months. After surgery, postoperative inflammation was well controlled without any signs of recurrent infection (Fig. 1B).

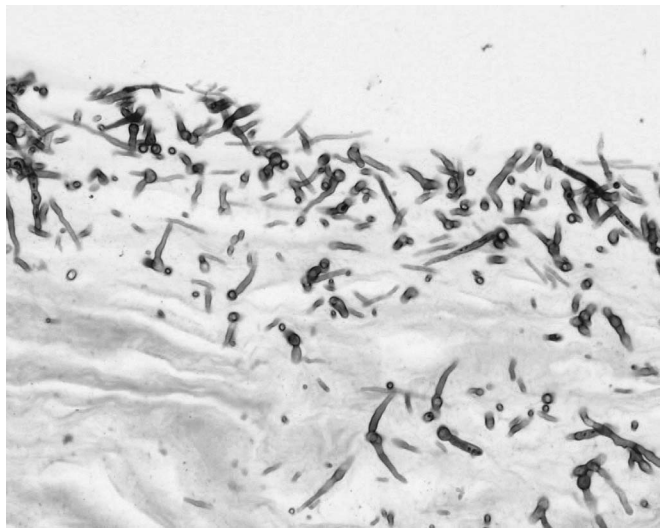

FIGURE 2. Gomori methenamine silver stain of the host cornea. Pseudohyphae and yeast forms were noted (×1000).

DISCUSSION

S. maltophilia is an aerobic, nonfermenting, gram-negative bacillus that is readily isolated from water, soil, various plants, and animals. It has also emerged as an important nosocomial opportunistic pathogen in immunocompromised hosts, associated with debilitating illness, surgical procedures, indwelling catheters, long-term antibiotic therapy, and malignant neoplasms.[7] This organism was considered previously to have limited pathogenicity. However, in severely compromised patients, it may be associated with significant morbidity and mortality.[8] Ocular infections by *S. maltophilia* are thought to be community acquired. Underlying ocular surface abnormalities, such as trauma, a history of penetrating keratoplasty, or the use of soft contact lenses, play an important role in pathogenesis.[3] Coinfection with *S. maltophilia* and *Aspergillus fumigatus* has been reported.[6] However, infectious keratitis in which *S. maltophilia* and yeast were identified simultaneously by culture and pathology have not been previously reported.

The exact pathogenesis of this case is unclear. The initial corneal ulcer had a good response to fortified vancomycin and amikacin. *S. maltophilia* or fungi were not thought to be causes of the initial ulcer because these organisms were not susceptible to those antibiotics. Prior exposure to broad-spectrum topical antimicrobial agents or topical steroids have been consistently associated with keratitis caused by *S. maltophilia* or *Candida* species.[9,10] We propose that one or both of *S. maltophilia* and yeast might have been inoculated during the course of initial treatment. This may have occurred through contaminated topical eye drops, during the process of corneal scraping, or some other route of opportunistic transmission.

After improvement of the initial ulcer, we changed the topical antibiotics to ofloxacin to control the corneal toxicity. However, several days later, the ulcer rapidly deteriorated. We thought that the early change of topical antibiotics, or a

coinfection by antimicrobial-resistant organisms such as fungi, might have caused this aggravation. Because the lesion rapidly progressed, threatening the integrity of the eye, we added topical and systemic antifungal agents empirically without waiting for laboratory confirmation of fungi.

Therapeutic penetrating keratoplasty is often considered as a means to manage infectious keratitis that is refractory to conventional medical treatment. To prevent recurrent infection, the size of the trephination must be large enough to include the entire corneal lesion. Because the perilimbal cornea was involved in this patient, a large-diameter graft was needed to eliminate the entire suppurative lesion. The risk of rejection, complicated by the large-diameter graft and the possibility of continued microbial proliferation, placed us in a dilemma over whether to use steroids postoperatively.[11] For that reason, before we started topical and systemic steroids, a complete debridement of the inflammatory material and a vigorous irrigation with the antibiotic solution were carried out intraoperatively.[12]

Infectious keratitis caused by *S. maltophilia* and yeast has common risk factors such as a compromised cornea, exposure to broad-spectrum antibiotic agents, and topical immunosuppressants. Thus, coinfection of the cornea by *S. maltophilia* and yeast may occur in the susceptible cornea as in this case. If the progression of keratitis by *S. maltophilia* is not controlled using an appropriate antibiotic agent, and/or any findings of fungal infection such as severe anterior chamber inflammation are observed, the possibility of coinfection by these 2 organisms must be considered.

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