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Simultaneous Triple Microbial Keratitis

Dear Editor,

Polymicrobial keratitis could constitute a more sight-threatening condition than monomicrobial keratitis because microbial pathogenicity is augmented and therefore resistant to antimicrobial agents [1]. Triple infection keratitis indicates simultaneous infection by three different pathogens; however, few related cases of corneal cross-linking and severe ocular surface disease have been reported [2,3]. Here, we describe a catastrophic clinical course of simultaneous triple microbial keratitis, and the missed opportunity for ocular preservation because the possibility of simultaneous infection was neglected.

A 71-year-old male patient was referred to our hospital complaining of aggravated keratitis despite vigorous antimicrobial treatment. He had a history of diabetes and had experienced a foreign body sensation in his right eye for 1 week. He was initially treated in a local eye clinic: 0.5% moxifloxacin eye drops (Vigamox, Norvatis AG, Basel, Switzerland) were administered every 2 hours but were ineffective. He was referred to a local general hospital, and the smear and culture of a corneal scrape performed at that hospital were negative. A combination of fortified ceftazidime and fortified voriconazole eye drops was administered hourly because the causative microbe was unknown. Finally, he was referred to our hospital because a hypopyon was present with aggravated infiltration and pain. Upon presentation, right-eye visual acuity was only hand motion, and a 6.5 × 6.0-mm-sized central infiltration of a feathery margin with 1.0-mm hypopyon was observed. Tiny scattered satellite infiltrates were also identified (Fig. 1A). Corneal scraping was performed at two sites. Empirical fortified 5% vancomycin (Hanomycin injection; Sam-Jin Pharma, Seoul, Korea), 5% ceftazidime (Tazime injection; Hanmi, Seoul, Korea), and 0.15% amphotericin B (f-AMB) were administered every 10 minutes initially and then tapered to every 2 hours over a period of 6 hours. At 2 days postadmission, initial culture revealed *Streptococcus salivarius*. At 4 days postadmission, the hypopyon had nearly disappeared, and ocular pain had improved (Fig. 1B); therefore, we tapered f-AMB because we suspected that fungal coverage was not needed. Beginning at 6 days postadmission, the hypopyon and corneal infiltration were slightly aggravated (Fig. 1C). We suspected superinfection or coinfection by another microbe; therefore, we performed another corneal scraping and administered f-AMB. The second culture revealed *Staphylococcus cohnii* subspecies *Urealyticum* at 8 days postadmission; concurrently, loading doses of fortified vancomycin and intravitreal voriconazole injection (100 μg/0.1 mL; Vfend, Pfizer, New York, NY, USA) were administered (Fig. 1D). These therapies were unsuccessful, and therapeutic penetrating keratoplasty with a corneal biopsy was performed at 11 days postadmission. Periodic acid-Schiff and Gomori methenamine-silver nitrate staining revealed numerous hyphae with branching on corneal biopsy, indicating *Fusarium*

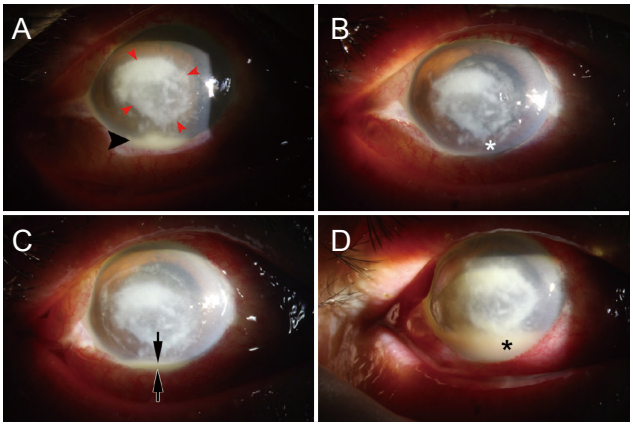

Fig. 1. Serial slit lamp findings of this case study. (A) At initial presentation, a 6.5 × 6.0-mm-sized central thick infiltration with a 1.0-mm hypopyon was observed (black arrowhead). The lesion showed a partially feathery margin at the inferior and scattered satellite lesions (red arrowheads). (B) At 4 days postadmission, the hypopyon was nearly absorbed (asterisk). (C) At 2 days after cessation of fortified amphotericin B, the hypopyon appeared (arrows), and corneal infiltration was slightly aggravated. (D) Markedly advanced corneal infiltration with a 3.0-mm hypopyon (asterisk) was observed compared with the presentation at 4 days postadmission.

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spp. Natamycin (Natacyn, Vigamox, Norvatis AG) was administered hourly, but the keratitis became aggravated at the recipient site. The patient agreed to enucleation of his right eye, and there was no subsequent recurrence of fungal infection at the surgical site.

In this case, we neglected consideration of the possibility of simultaneous microbial infection, particularly involving fungus. Because fungal keratitis generally shows a relatively slow progression, we diagnosed monomicrobial keratitis by *Streptococcus* species upon initial microbial isolation. Moreover, we made the critical mistake of tapering f-AMB at 4 days postadmission. We did not suspect simultaneous fungal infection at the time of the 2nd smear and culture because a *Staphylococcus* species was isolated in the 2nd corneal scrape. Subsequently, intravitreal voriconazole with f-AMB was administered due to strong suspicion of fungal infection; however, the keratitis did not respond to the f-AMB, although it had previously responded. Thus, the patient may have retained his right eye if f-AMB had been continued. This case report provides two important lessons regarding antimicrobial treatment. Polymicrobial keratitis is rare but possible, and the causative microbe may not be determined during initial corneal smear and culture. If there is no response to antimicrobial treatment consistent with the isolated microbe, physicians should consider simultaneous microbial infection; smear and culture must be immediately repeated at multiple corneal sites. Polymicrobial keratitis could mask or modify the clinical characteristics of microbes, and simultaneous triple microbial keratitis typically includes fungal infection [3,4]. If keratitis exhibits extraordinary clinical presentation, antifungal coverage must be included. In addition, clinicians should be cautious in modifying initial empirical antimicrobial treatment after isolation of the causative microbe. In our case, the patient had poorly controlled diabetes; thus, the impaired corneal epithelial barrier function may have enabled invasion of multiple microbes due to localized or systemic immunosuppression.

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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