CASE REPORT

Microcyclosporella mali: a novel fungal keratitis in a post-penetrating keratoplasty patientNeil Vyas,¹ Saba Al-Hashimi,² Wuqaas Munir³¹Department of Ophthalmology, UCLA, Los Angeles, California, USA²Department of Ophthalmology, Boston University Medical Center, Boston, Massachusetts, USA³Department of Ophthalmology, University of Maryland, College Park, Maryland, USA**Correspondence to**
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SUMMARY

An 86-year-old woman underwent penetrating keratoplasty for pseudophakic bullous keratopathy and presented with an acute corneal ulcer thereafter. Examination demonstrated a fluffy white infiltrate and epithelial defect with subsequent endothelial plaque formation and anterior chamber inflammation. The ulcer was cultured, and fortified topical vancomycin and tobramycin were initiated but failed to significantly improve the clinical course. Cultures were ultimately positive for fungus *Microcyclosporella mali* that responded well to topical natamycin with stabilisation of the ulcer after 6 weeks of topical therapy. This is the first reported case of fungal keratitis due to *M. mali*.

BACKGROUND

Fungal keratitis (keratomycosis) remains a diagnostic and therapeutic challenge to many ophthalmologists. Delay in treatment can result in significant ocular morbidity. Treatment typically consists of topical antifungal agents either solely or in conjunction with oral antifungal agents. More severe cases non-responsive to medical management may require therapeutic penetrating keratoplasty.¹ There are many associated risk factors including history of penetrating keratoplasty, soft contact lens wear, chronic topical steroid use, penetrating trauma and ocular surface disease.²

This is the first described case of fungal genus *Microcyclosporella* causing a corneal infection. It behaved similarly to other fungi that cause keratitis and responded well to standard topical treatment.

CASE PRESENTATION

An 86-year-old Vietnamese woman was seen urgently for the evaluation of an acute corneal ulcer of the right eye. She had a history of bilateral cataract extraction with intraocular lens insertion approximately 10 years earlier, resulting in pseudophakic bullous keratopathy of both eyes. She underwent penetrating keratoplasty to alleviate symptoms of pain and improve vision in the right eye 3 years prior. The postoperative course was complicated by elevated intraocular pressure (IOP), which eventually normalised with the use of topical aqueous suppressants, timolol 0.5% twice daily and brimonidine 0.2% twice daily to the right eye. Prednisolone acetate 1% was slowly tapered to once daily in the right eye. One year from surgery, she continued to show no evidence of infection or corneal graft rejection. She was subsequently lost to follow-up in our clinic and presented to the emergency room 11 months later with a 1-week history

of pain, tearing, photophobia and discomfort in her right eye. She reported that she had not used any eye medication for over 2 months and had experienced no recent trauma to her right eye.

Her vision on initial examination was hand motions right eye and 20/400 left eye. There was no relative afferent pupillary defect. IOP by applanation tonometry was 40 mm Hg in the right eye and 14 mm Hg in the left eye. Motility was full in both eyes. Slit lamp examination of the right eye was notable for moderate conjunctival injection and full thickness corneal graft with a large (5.0×5.2 mm) central epithelial defect with corneal oedema and infiltrate (figure 1). Examination of the left eye showed mild conjunctival injection and diffuse microcystic oedema of the cornea with Descemet's membrane folds and a posterior chamber intraocular lens in good position.

INVESTIGATIONS

Given the poor view to the posterior segment in the right eye, a B-scan ultrasound was performed, which was unremarkable. Corneal scrapings were obtained for Gram stain and cultured on blood, chocolate and Sabouraud Agar plates along with thioglycolate broth. Initial cultures were positive for coagulase-negative *Staphylococcus* spp (from broth only) sensitive to vancomycin. Confocal microscopy was attempted and while it was of poor quality, it did not show any fungal or acanthamoebal elements.

Cultures became positive for *Scytalidium* fungal spp at day 18. However, after further review by the fungus testing laboratory at The University of Texas HSC in San Antonio, the speciation was confirmed to actually be *Microcyclosporella mali*. The laboratory confirmed this by combined phenotypic characterisation and DNA sequencing of the following

Figure 1 Large central ulcer with fluffy infiltrate and epithelial defect stained with fluorescein.

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targets: ITS, D1/D2. This speciation was finalised 80 days after initial culture.

TREATMENT

Initially the patient was started on fortified vancomycin and tobramycin drops every hour in the right eye along with dorzolamide-timolol and brimonidine twice daily for IOP lowering. After the report of a positive fungal culture, the patient was switched to natamycin 5% six times daily and the fortified antibiotic drops were discontinued. Her topical therapy was successfully discontinued after 6 weeks of antifungal coverage.

OUTCOME AND FOLLOW-UP

Over the course of the first week on fortified ophthalmic antibiotics, the patient's corneal epithelial defect minimally improved and the fluffy white opacity in the cornea surrounding the defect persisted. She was noted to subsequently develop an endothelial plaque with anterior chamber debris and early peripheral corneal neovascularisation. After being switched to antifungal therapy, the patient's cornea improved over the next 2 months, at which time it had fully epithelialised and no active infiltrate was noted. As a result of her infection, she was left with a vascularised stromal scar (figure 2). She remains stable without evidence of recurrence 7 months following initial resolution.

DISCUSSION

Fungal infections of the cornea can consist of either yeast or filamentous fungi (moulds). Over 105 species of fungi have been implicated in causing corneal infection and the incidence is rising worldwide.³

To the best of our knowledge, this report represents the first case of a human corneal or ocular infection caused by the *Microcyclosporella* genus of fungus. This case is consistent with other more common ocular fungal pathogens such as *Candida*, *Fusarium* and *Aspergillus*, in that it is slow growing and mildly virulent. There was no significant suppuration, despite the delay in treatment. The stromal infiltrate responded well to topical natamycin therapy. Like other fungal species, *Microcyclosporella* grew slowly in culture, and therefore clinicians should maintain a high degree of suspicion as cases may persist for some time before a final diagnosis is confirmed. Given the lack of other reports and prevalence of this genus of fungus, initial culture results most closely matched that of *Scytalidium*. It was not

until detailed phenotypic analysis could be performed at a specialty laboratory that the final species was determined.

To the best of our knowledge, there are no other reported cases of any type of human infection caused by this organism. The lack of published cases may be due to the fact that this fungus was only recently discovered and distinguished taxonomically in 2010.⁴ It is possible that, as more cases are reported and awareness of this species increases, microbiology laboratories may become better at identifying this fungus allowing for more accurate and quicker diagnosis.

It is unknown how this patient may have encountered this organism as that she lives in an urban environment. However, given its proclivity for pomaceous fruits such as apples, it is not a species that is ubiquitously present and therefore unlikely to be a contaminant. The patient's associated risk factors for developing fungal keratitis include her history of penetrating keratoplasty and chronic topical steroid use.²

Although this is the first reported case, *Microcyclosporella* presented and behaved similarly to other types of fungal keratitis. It also responded well to traditional antifungal therapy. This case again highlights the importance of having a high clinical suspicion for fungal causes of infectious keratitis for cases that do not respond well to traditional antibiotic therapy.

Learning points

- ▶ Fungal keratitis remains a diagnostic and therapeutic challenge to many ophthalmologists.
- ▶ Associated risk factors for fungal keratitis include history of penetrating keratoplasty, soft contact lens wear, chronic topical steroid use, penetrating trauma and ocular surface disease.
- ▶ A high index of suspicion for fungal keratitis should be maintained in a patient who fails to respond appropriately to standard therapeutic agents for bacterial ulcers.
- ▶ Although a rare cause of fungal keratitis, *Microcyclosporella* did present and behave similarly to more common causes of fungal keratitis and responded well to standard antifungal topical therapy.

Figure 2 Resultant central stromal scar with vascularisation and resolution of infiltrate and epithelial defect.

Contributors NV was the primary author of this article. SA-H was responsible for providing background information, revising the article and submitting it for publication. WM was the attending physician responsible for the patient, and is the guarantor and final editor.

Competing interests None.

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