Contact lens associated keratitis due to *Tintelnotia destructans*

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**ABSTRACT**

We report the first case of *Tintelnotia destructans* associated keratitis in a contact lens wearer in Australia. Corneal scrape showed fungal elements on direct microscopy leading to a prompt diagnosis of fungal keratitis and early topical and systemic antifungal therapy. The isolate was eventually identified by ITS gene sequencing. This case highlights the importance of accurate identification and antifungal susceptibility testing for the management of fungal keratitis.

1. Introduction

Fungal keratitis is a rare but severe sight-threatening condition. The estimated annual incidence of fungal keratitis is 0.32 and 0.6 cases per million individuals in the United Kingdom and Denmark, respectively [1,2]. A systematic review found that the highest proportion of fungal keratitis was in studies from India and Nepal [3]. Although fungal keratitis occurs worldwide, the aetiology is strongly related to geographical region, socioeconomic status and climatic condition [4]. Corneal ulcers caused by filamentous fungi are more common in the tropical or subtropical areas while *Candida* species more commonly cause corneal ulcers in temperate regions [5]. These trends are also observed in the Australian context where studies in the tropical Far North Queensland show that *Fusarium* is the commonest causative fungus, whereas *Candida* species predominate in the temperate Victorian region [6,7]. There are more than 100 different fungal species that have been documented to cause fungal keratitis [5]. *Tintelnotia destructans* associated keratitis was described for the first time in 2016, with two previous cases published in the literature [8–10]. We describe here the first case of *Tintelnotia destructans* associated keratitis in Australia.

2. Case

A 60-year-old immunocompetent contact lens wearer presented in April 2019 (day 0) with two weeks of left eye irritation, reduced visual acuity and photophobia, referred to a tertiary ophthalmology service after no response to topical chloramphenicol, ofloxacin and dexamethasone. There was no history of eye trauma or surgery, nor occupational exposure to dust. The only significant past medical history was a left eye corneal ulcer 15 years prior. On examination, visual acuity in the affected left eye was 6/15. There was a deep white corneal infiltrate with corresponding epithelial defect but no satellite lesions (Fig. 1). Corneal scrape showed narrow septate fungal elements by Gram stain, hence, oral voriconazole was started in addition to hourly day-and-night natamycin 5% and voriconazole 1% eye drops, in combination with empiric topical antibacterial therapy.

Small fungal colonies were observed on blood agar and Sabouraud agar with chloramphenicol by 48 hours. Lactophenol cotton blue (LPCB) stain was used to perform microscopic preparation of the fungal colonies, which showed flask-shaped, initially hyaline, later becoming dark brown to black pycnidia. The pycnidia contained single-celled hyaline conidia without conidiophores suggesting a provisional identification of *Phoma*-like species (Fig. 2). Subsequently, sequencing of the internal transcribed spacer region of the ribosomal DNA had 100% match with a CBS isolate 127737 of *Tintelnotia destructans* (NR-147684.1) [11]. The isolate was tested by Matrix-Assisted Laser Desorption/Ionization-Time Of Flight (MALDI-TOF) mass spectrometry (MS) Bruker by the broth extraction method however no acceptable identification was obtained. This is however not unexpected as the Bruker MALDI-TOF database does not include reference spectra for *Tintelnotia* species. The isolate was sub-cultured onto oatmeal agar and malt extract agar (MEA). The colonies were red-brown and granular with central white aerial tufts (Fig. 3) on both agar plates, with colony...
diameter of 2.7 cm on MEA after 7 days at 24 °C. Growth was restricted at 40 °C which is consistent with T. destructans.

Susceptibility testing was performed by the Sensititre YeastOne YO10 microbroth dilution method with minimum inhibitory concentrations (MIC) for posaconazole 0.25mg/L, voriconazole 0.5mg/L, itraconazole 0.12mg/L, fluconazole 16mg/L, amphotericin 1mg/L and flucytosine > 64mg/L. Echinocandin minimum effective concentrations were very high, > 8mg/L.

At D +9, a once-off intrastromal injection of voriconazole 1% was administered. At D +14, the patient was discharged from hospital with oral voriconazole and 2-hourly natamycin 5% and voriconazole 1% eye drops. With gradual improvement in the vision, the frequency of antifungal eye drops was reduced to 4-hourly at D +28.

The anterior segment optical coherence tomography done on D +37 showed disruption of the corneal architecture in the area of the infiltrate, with increased intensity in the anterior two thirds of the stroma and focal corneal thinning (Fig. 4).

With improvement in the appearance of the corneal infiltrate and epithelial defect at D +65, natamycin 5% and voriconazole 1% eye drops were reduced to 6-hourly administration, while she continued oral voriconazole with levels in the therapeutic range. At the last review at D +191, there was a stable scar and thinning of the cornea but her visual acuity had returned to baseline at 6/7.5. Antifungal therapy was discontinued during this review.

3. Discussion

Fungi of the novel genus, Tintelnotia, have recently been recognised to cause ocular and nail infections in humans [8–10]. Tintelnotia destructans is named for its ability to destroy human nails [9]. Tintelnotia belong to the class Coelomycetes, order Pleosporales and family Phaeosphaeriaceae [9]. The genus was named after Dr Kathrin Tintelnot, former head of the Mycology Division of the Robert Koch Institute, Berlin, Germany [9]. Coelomycetous fungi are a large and phylogenetically heterogeneous group of filamentous fungi characterized by the production of conidia within conidiomata [12]. Our isolate showed the classic morphological features of a coelomycete but it was only with the assistance of molecular methods that we were able to identify it conclusively.

Human infections by coelomycete fungi are usually acquired by traumatic implantation of contaminated fomites [13]. They have been reported to cause systemic and localised infections such as cutaneous and subcutaneous mycosis, deep tissue infection, onychomycosis, endophthalmitis, pneumonia and osteomyelitis [13]. Ocular injury is the major mechanism of developing fungal keratitis, though other recognised risk factors include ocular disease, ocular surgery, contact lens usage and systemic diseases [4,14,15]. In this case, the only risk factor was contact lens usage. The first reported case of T. destructans keratitis also involved a contact lens wearer [8,9] who had progressive infection on standard antifungal therapy and eventually improved after seven weeks of oral terbinafine, daily intracameral voriconazole and...
amphotericin B. Treatment was continued with polyhexamethylene biguanide and topical terbinafine 2-hourly for another 2 months as well as a weaning regimen of topical prednisolone [8,9]. The second case of T. destructans keratitis occurred after ocular trauma and the patient was treated successfully with oral and topical voriconazole for at least five months following penetrating keratoplasty [10].

Standard therapy is yet to be established. Our isolate had a similar in vitro susceptibility profile to the first isolate of T. destructans [8,9], with high MEC against echinocandins; and high MICs to fluconazole and fluconazole but low MICs against amphotericin and triazoles. On the other hand, the isolate from Habbe et al. had low MICs against amphotericin, echinocandin, terbinafine and triazoles except isavuconazole [10]. The reported MICs for natamycin was 2mg/L and isavuconazole was 4mg/L [10]. Although there are no standardised breakpoints, antifungal susceptibility testing helped guide antifungal therapy in our case. With the combination of oral and topical antifungal therapy, the patient’s visual acuity has returned to baseline.

In achieving a good outcome for fungal keratitis, this case highlights the importance of early aggressive therapy, accurate identification, and the assistance of antifungal susceptibility testing for rare fungi which have few cases reported in the literature.

Declaration of competing interest

There are none.

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