A rare case of fungal keratitis caused by Tintelnotia destructans

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Case Report

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Abstract

Background

Fungal keratitis is a rare, potentially sight-threatening fungal infection of the cornea, and a major global cause of visual impairment and blindness. *Tintelnotia destructans*, a filamentous fungus, is an unusual virulent ocular pathogen. Little is known about this fungi's association with ophthalmological conditions and there is no standardized treatment protocol in guidelines.

Case presentation:

We report a rare case of *T. destructans*-associated keratitis in a 45-year-old woman, without history of corneal trauma and a regular contact lenses user, presenting with eye discomfort and redness. Conjunctival hyperemia and a corneal abscess located inferiorly parapupilarly with an epithelial lesion was detected and topical ciprofloxacin eye drops was initiated. *In vivo* confocal microscopy (IVCM) revealed fungal hyphae growing perpendicularly through the corneal collagen lamellae, suggesting keratomycosis. Culture from corneal scrapings identified the hyphomycete as *T. destructans.* The diagnosed corneal abscess was treated successfully with natamycin and terbinafine, resulting in symptom regression.

Conclusions

T. destructans is an opportunistic pathogen causing severe keratomycosis with no standardized treatment. Early diagnosis using IVCM and fungal culture, guided by *in vitro* susceptibility testing, can allow prompt intervention.

Background

Fungal infections of the cornea (mycotic or fungal keratitis, keratomycosis) present as suppurative, usually ulcerative, lesions. Fungal keratitis is a rare, potentially sight-threatening fungal infection of the cornea, and a major global cause of visual impairment and blindness [1]. Early and proper diagnosis of the causative organism is critical for effective treatment to prevent long-term complications. *Tintelnotia destructans* is a genus of filamentous fungus that belongs to the *Phaeosphaeriaceae* family within the order *Pleosporales* characterized by coelomycetous anamorph (hollow fungi) class [2, 3]. Little is known about this fungi's association with ophthalmological conditions. *T. destructans* associated keratitis was first described in 2016 and named after its ability to destroy toenails by forming delicate fruiting bodies within the hard nail substance [4]. Although fungal keratitis occurs worldwide, its etiology is strongly related to the geographical region, climatic condition, and socioeconomic status of an individual. Coelomycetes colonize dead organic matter and water bodies in warm and tropical regions [4, 5]. In Europe, the incidence of filamentous fungal keratitis is increasing, varying between 0.6 and 1.5 cases per

million per year [1], with predisposing factors being contact lens wear, trauma, ocular surgery and topical steroids; half to two-thirds of these patients are contact lens-wearers. Herein, we report a rare case of *T. destructans* associated fungal keratitis, which followed a severe course that dramatically improved within a few days after initiating targeted antifungal treatment.

Case Presentation

A 45-year-old immunocompetent female patient presented with eye discomfort and redness at our ophthalmology in Hospital Universitario Virgen Macarena, Seville, Spain. She was a regular user of contact lenses and had no previous corneal trauma. Examination revealed conjunctival hyperemia and a corneal abscess located inferiorly parapupilarly with an epithelial lesion measuring 3 × 4 mm (Fig. 1a). After corneal sampling for microscopy and culture, topical ciprofloxacin eye drops were initiated as an empirical treatment for corneal abscesses. With no improvement with antibiotic treatment after three days, and awaiting the culture results, an *in vivo* confocal microscopy (IVCM) was performed with a laser-scanning confocal microscope (Heidelberg Retina Tomograph III with the Rostock Cornea Module (HRT3/RCM), Heidelberg Engineering, Germany). IVCM revealed straight and mainly unbranched hyphae growing perpendicularly through the corneal collagen lamellae (Fig. 1b), which suggested a diagnosis of keratomycosis. Accordingly, treatment with voriconazole 2% eye drops (hourly) was initiated with a dose of 200 mg/12 h, and doxycycline 50 mg/day, with iodine povidone 0.6% eye drops as a coadjuvant. Doxycycline was used as corneal matrix metalloproteinase inhibitor to boost ocular surface repair mechanisms. Three weeks later, the corneal sampling culture confirmed the presence of a filamentous fungus, subsequently identified as *T. destructans*. The corneal scraping culture performed on Sabouraud agar revealed an orange-colored filamentous fungus with white aerial mycelium, which turned brown after 5 days of incubation. The observed growth of a hyphomycete with globose fruiting bodies (pycnidia) was observed microscopically. It was identified as *Tintelnotia destructans* based on its macroscopic and microscopic characteristics. It is a genus in the family Phaeosphaeriaceae that contains two species, *T. opuntiae* and *T. destructans*. Based on this report, the patient was enquired about any symptoms in her toenails, which revealed an onychomycosis in her left big toe for months. A dermatologist's evaluation was requested but had an inconclusive result. Notably, the patient had been taking antifungal medications for several weeks before the nail scraping. *In vitro* susceptibility testing was performed at the #Centro Nacional de Microbiología in Madrid, Spain# using the methodology of the European Committee on Antimicrobial Susceptibility Testing (EUCAST). The lowest minimum inhibitory concentration were amphotericin 0.25 mg/L, itraconazole 0.5 mg/L, voriconazole 1 mg/L, posaconazole 0.25 mg/L, isavuconazol 8 mg/L, terbinafine 0.25 mg/L, caspofungin 0.25 mg/L, micafungin 0.008 mg/L, and anidulafungin 0.015 mg/L. The drug of choice in *Tintelnotia* infection is natamycin; however, we had to administer voriconazole eye drops because of an ongoing national shortage of natamycin. After EUCAST, the voriconazole eye drops was replaced with micafungin 0.1% (hourly) because the patient did not respond to voriconazole. However, after a few days the inflammation worsened, and a hypopyon, typical of a fungal infection, developed. Fortunately, by this time natamycin 5% eye drops was available and was thus administered every 2 h with terbinafine (500 mg every 12 h, orally) replacing

micafungin. Cyclosporine 2% eye drops was added as an anti-inflammatory coadjuvant. The drugs were well-tolerated, and the severity of the corneal infection was sufficiently resolved 4 weeks after starting this combined therapy. The severity of the infection and its progression, together with its subsequent resolution, showed that a combined therapy with natamycin 5% eye drops and terbinafine 200 mg orally played a key role in the elimination of the fungus.

Discussion and Conclusions

The symptoms of keratitis caused by *T. destructans* are similar to other keratomycosis cases, which include eye irritation, reduced visual acuity, and photophobia. With slit-lamp bi-microscope evaluation, corneal ulcer with stromal infiltrates could be observed, which probably caused hypopyon [2]. For an accurate diagnosis, culture of corneal scraping is essential for identification of *T. destructans*.

Using IVCM, filamentary structures and hyphal growth patterns consistent with fungal elements can be recognized, as noted this case (Fig. 1b; Video 1) [3]. As the corneal sampling culture evaluation is time-consuming, IVCM can provide an early diagnosis of keratomycosis as it allows non-invasive real-time direct visualization of potential fungal pathogens and manifesting infection directly in the patient's cornea [6, 7]. Patients with probable fungal keratitis are asked if they have other symptoms such as onychomycosis, which can be a clue to suspect *T. destructans*, and the nail scrapings could be sampled before any antifungal treatment is initiated. Our patient's nail scraping was taken after starting voriconazole eye drops and this could have affected the culture findings. Although a standard therapeutic strategy for *T. destructans* infections is not yet established, a prolonged treatment is fundamental. In some reported cases, the treatment lasted for at least 5 months [4]; however, our patient improved drastically just in a week and the signs were solved in a month. Some reported cases have highlighted the importance of treatment with terbinafine [3, 5].

Until the culture results are obtained, broad-spectrum antimycotics and antibiotics are prescribed. Antifungal susceptibility tests are helpful in choosing the most effective treatment [3, 4]. In some reported cases, keratoplastia was required despite medical treatment [2]. In the present case, intensive therapy with topical natamycin 5% every 2 h, povidone-iodine 0.6% eye drops, terbinafine 500 mg mg/day (every 12 h), and doxycycline 50 mg/day could resolve the infection.

In conclusion, *T. destructans*-associated keratomycosis is a rare corneal infection with no standardized treatment. In our case, the use of natamycin combined with oral terbinafine rapidly facilitated resolution of this condition. Further investigations are needed to determine the individual contributions of each drug and to assess whether oral terbinafine monotherapy or natamycin eye drops alone are sufficient for management. Additionally, IVCM could play an important role in earlier detection of keratomycosis.

List Of Abbreviations

EUCAST, European Committee on Antimicrobial Susceptibility Testing; IVCM, *in vivo* confocal microscopy

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Informed consent to publish was obtained from the patient.

Availability of data and materials

If requested by the editors, We will provide the data/information or will cooperate fully in obtaining and providing the data/information on which the manuscript is based, for examination by the editors or their assignees.

Competing interests

The authors report there are no competing interests to declare.

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Authors' contributions

MC, BM, ERDR and IR contributed to the definition of intellectual content and design of the manuscript.

MC and IR made de manuscript preparation and editing.

JL performed the microbiological examination of the cornea scraping.

JC contributed to the approach to antifungal treatment.

All authors looked for literature search and participated in the manuscript review.

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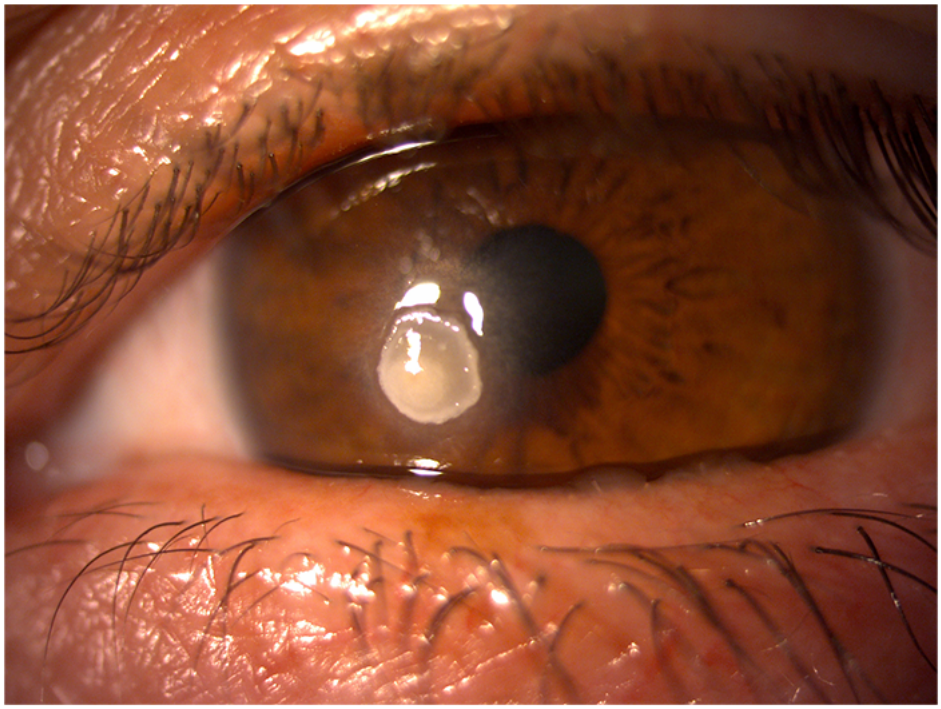
Figures

A



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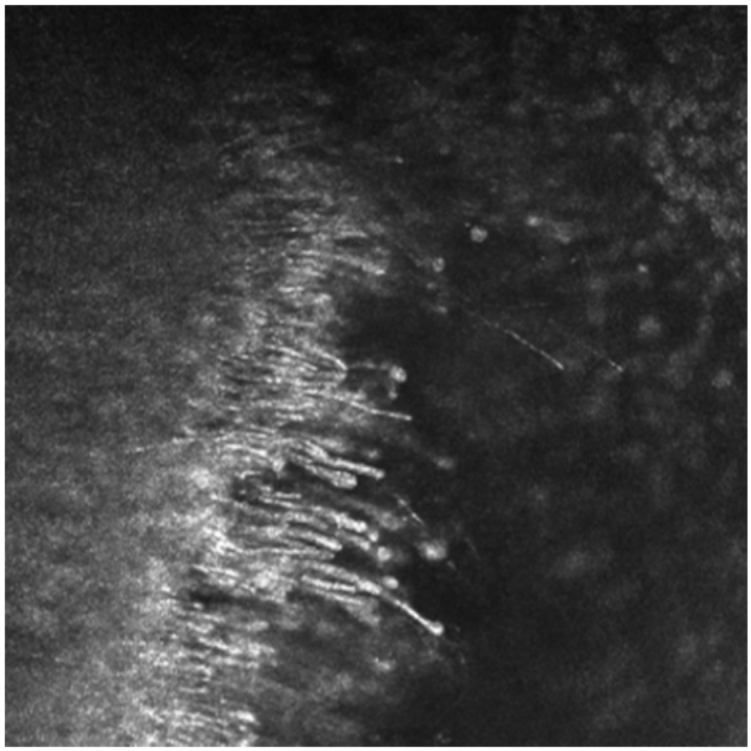

Figure 1

Ophthalmological examinations

a. Slit-lamp examination reveals conjunctival hyperemia and a corneal abscess located inferiorly parapupilarly with an epithelial lesion of 3 × 4 mm.

b. *In vivo*confocal microscopy reveals straight and mainly unbranched hyphae growing perpendicularly through the corneal collagen lamellae.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Video1.m4v