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# *Pyrenocheata unguis-hominis*: A new cause of fungal keratitis in a contact lens wearer

Sima Nissan [a,*], Jerina Boelens [b], Katrien Lagrou [c,d], Dimitri Roels [a]

[a] Department of Ophthalmology, Ghent University Hospital, Corneel Heymanslaan 10, 9000, Ghent, Belgium
[b] Department of Clinical Biology, Ghent University Hospital, Corneel Heymanslaan 10, 9000, Ghent, Belgium
[c] Department of Microbiology, Immunology and Transplantation, KU Leuven, Herestraat 49, 3000, Leuven, Belgium
[d] National Reference Centre for Mycosis, Department of Laboratory Medicine, University Hospitals Leuven, Leuven, Belgium

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ABSTRACT

*Purpose: Pyrenochaeta unguis-hominis* (syn. *Neocucurbitaria unguis-hominis*) is a rare fungal species belonging to the Coelomycetes group, mostly isolated from infected nails and skin.
We present a case of contact lens-related fungal keratitis caused by *Pyrenochaeta unguis-hominis*.
*Observations:* We present a case of a 69-year-old woman with multiple risk factors for a fungal keratitis including ophthalmological history of herpetic keratitis, contact lens wear and chronic steroid use. At presentation, the corneal ulcer resembled a recurrent herpetic keratitis but evolved into a more dense stromal infiltrate despite antiviral therapy. Microscopic examination, culture and staining of corneal tissue obtained by scraping showed mycelia. PCR and matrix-assisted laser desorption/ionization time-of-flight mass spectrometry confirmed the presence of *Pyrenochaeta unguis-hominis*. Topical antifungal treatment was able to dim the inflammation. Because of a persistent epithelial defect, an amniotic membrane transplantation was performed. Although corneal epithelium was restored, stromal scarring in the visual axis resulted in substantial vision loss.
*Conclusions:* To our knowledge no other cases of fungal keratitis caused by *Pyrenochaeta unguis-hominis* have been described. Early diagnosis can allow prompt initiation of antifungal treatment, which should be guided by *in vitro* susceptibility testing.

## 1. Introduction

The genus Pyrenochaeta belongs to the group Coelomycetes and its species are widely found in the environment but are rarely involved in human infections.[1,2] The human pathogenic species include *Pyrenochaeta unguis-hominis* (syn. *Neocucurbitaria unguis-hominis*) isolated from infected nails and skin and *Pyrenochaeta keratinophila* isolated from corneal scrapings in fungal keratitis.[1–5]

To our knowledge this is the first case of keratitis caused by *Pyrenochaeta unguis-hominis* in a patient with history of herpetic keratitis and contact lens wear.

## 2. Case Report

We present a case of a 69-year-old woman known in our ophthalmology department with a history of herpetic keratitis 10 years prior. Scleral contact lenses were used to optimize visual acuity, which was reduced to 20/50 because of corneal scarring and thinning. Manipulation of the scleral lenses was sometimes done by hand instead of a contact lens plunger. Sudden foreign body sensation and excessive tearing were mentioned as reasons for an urgent consultation.

At presentation the best-corrected visual acuity (BCVA) was down to 20/200. Biomicroscopy showed a hazy cornea with a central epithelial defect overlying a region of stromal melting (Fig. 1A). Our patients' chronic treatment with dexamethasone eyedrops once daily and oral acyclovir 400mg/day was adjusted to dexamethasone drops 2 times per day, oral acyclovir 2.4g/day, oral doxycycline 200mg/day and topical ofloxacin eyedrops 4 times per day. Seven days later, ganciclovir ointment 3 times per day and topical dorzolamide/timolol twice daily were added because of suspicion of hypertensive herpetic keratouveitis.

Due to lack of improvement 12 days after presentation, with the appearance of a white and slightly elevated corneal infiltrate (Fig. 1B), a scraping was performed. Hourly voriconazole 1% eyedrops were added to the treatment, dexamethasone was stopped and ganciclovir ointment

* Corresponding author.
*E-mail address:* sima.nissan@ugent.be (S. Nissan).

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was tapered. Atropine 1% was added to prevent posterior synechiae formation. Viral PCR was negative for herpes simplex virus (HSV) and varicella zoster virus (VZV). Preventive treatment with oral acyclovir 1.6g/day was maintained to avoid viral reactivation. At this stage, BCVA was down to counting fingers.

Microscopic examination of corneal material after Gram and calcofluor-white staining identified mycelia (Fig. 1C & D). Culture confirmed the presence of a fungus, suspected by its typical white fluffy aspect, which was later identified as *Pyrenochaeta unguis-hominis* by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS).[6] Identification was confirmed with sequence analysis in the Belgian National Reference Centre for Mycosis. Since *Pyrenochaeta unguis-hominis* is mostly isolated from nails (onychomycosis), samples of the nails were taken but the fungus could not be visualized microscopically nor cultured.

Empirical treatment with hourly alternating topical voriconazole 1%, amphotericin B 0.15% and oral itraconazole 100mg/day was started, awaiting the result of *in vitro* susceptibility testing. The European Committee on Antimicrobial Susceptibility Testing (EUCAST) methodology showed a minimal inhibitory concentration (MIC) value of 0.50μg/ml for amphotericin B and a MIC value of >16.0μg/ml for both voriconazole and itraconazole.

Antifungal therapy diminished inflammation and stopped further deterioration but did not result in complete epithelial closure (Fig. 2A). Therefore, five weeks after starting antifungal therapy an amniotic membrane transplantation (AMT) was performed to optimize corneal healing combined with a synechiolysis of the existing posterior synechiae.[7]

Postoperatively, topical treatment consisted of alternating topical voriconazole 1% and amphotericin B 0.15%, ofloxacin eyedrops and ointment. Oral itraconazole 100mg/day and acivlovir 1,6g/day were continued. One week after AMT, itraconazole and voriconazole were stopped, amphotericin B was slowly tapered.

Three months after AMT BCVA was still limited to counting fingers. The amniotic membrane was integrated in the anterior corneal stroma and the corneal defect was almost completely closed with residual irregularity. The anterior chamber was calm, however despite the use of atropine and a partial synechiolysis a subtotal seclusio pupillae was present. Intraocular pressure was normal. Antibiotic ointment was stopped after epithelial closure.

Seven months after AMT a calm anterior segment was observed. Central corneal scarring limited visual acuity to counting fingers (Fig. 2B). A penetrating keratoplasty combined with an extracapsular cataract extraction and intraocular lens implantation was performed to restore visual function. One month after surgery, the corneal graft was clear without recurrence of herpetic or fungal keratitis.

## 3. Discussion

Infectious keratitis remains one of the leading causes of monocular blindness worldwide.[8,9] Fungal keratitis accounts for 1–45% and up to 56% of infectious keratitis depending upon geographic distribution.[10,11] It is more common in tropical and subtropical countries and is the principal cause of blindness in Asia but is relatively rare in temperate regions and developed countries.[5,11,12] Diagnosis and treatment of fungal keratitis remains an important and difficult task.[5]

Corneal trauma has been considered the predominant predisposing factor accounting for 40–60% of patients with fungal keratitis.[12] Other predisposing factors are contact lens wear, longtime topical or systemic antibiotic or steroid use, diabetes, underlying immunodeficiencies, history of ocular surgery, ocular surface problems and pre-existing HSV keratitis.[5,12]

The history of previous herpetic keratitis, steroid use and contact lens wear made our patient highly susceptible to fungal keratitis. When our patient presented with a corneal epithelial defect overlying a previous herpetic scar, an initial diagnosis of recurrent herpetic keratitis was made. Due to lack of improvement after starting antiviral therapy and the appearance of a new stromal infiltrate, an additional scraping and culture was performed. The presence of mycelia confirmed the diagnosis of fungal keratitis, for which antifungal therapy was initiated. The *Pyrenochaeta unguis-hominis keratitis* might have been a superinfection of an underlying herpetic keratitis given the previous history, although viral PCR was negative.

Human infections by coelomycetous fungi are relatively rare in

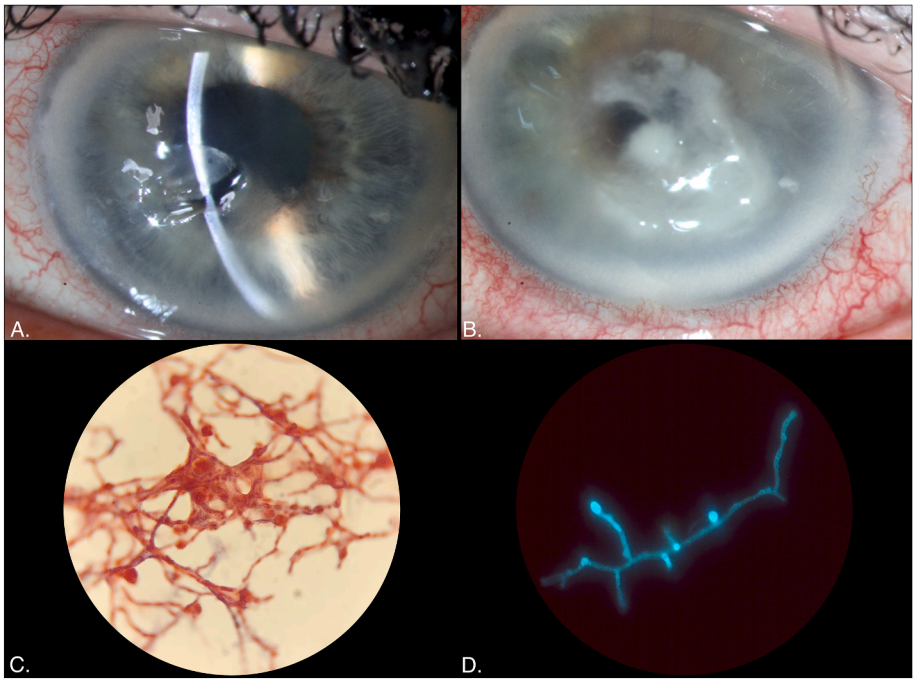


**Fig. 1.** A. Corneal thinning at presentation B. Notice appearance of a new white corneal infiltrate 12 days after presentation C. Gram-staining of corneal scrapings showing mycelia D. Calcofluor-white staining showing immunofluorescent mycelia.

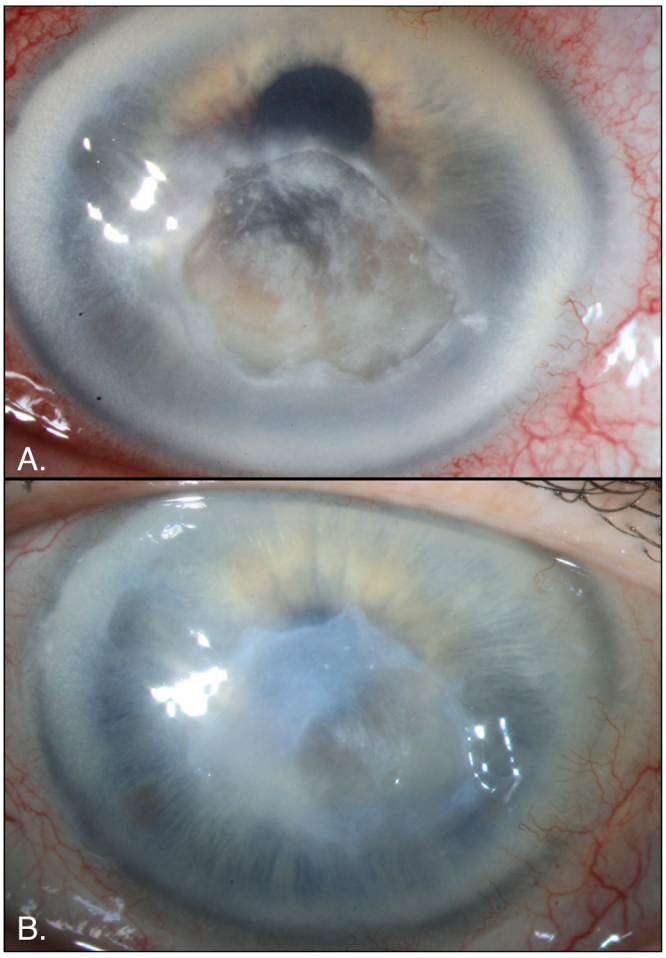


**Fig. 2.** A. Notice persistent corneal epithelial defect and thinning 3 weeks after presentation B. 7 months after AMT a corneal scar remains with an intact overlying epithelium. Notice subepithelial amniotic remnants.

comparison with other fungi.[5] To our knowledge no other eye-related infection with *Pyrenochaeta unguis-hominis* has been described. Until now, *Pyrenochaeta unguis-hominis* has only been isolated from skin and nails.[1,2] In an effort to prove a causal relationship between onychomycosis and fungal keratitis following fingernail trauma, samples of our patients' nails were sent for laboratory analysis, but the fungus could not be identified nor cultured.

Microscopic examination using Gram and calcofluor white staining allowed fast identification of mycelia and initiation of antifungal therapy.[12,13] Direct microscopic examination and culture remain the reference standard for etiological diagnosis of fungal keratitis.[12] Direct microscopic examination has a broad sensitivity range but is negatively affected by insufficient amount of material, small ulcer size and depends on the experience of the observer. Also, it is less adequate to identify pathogens up to the species level.[12–14]

Culture has the most important role in diagnosis and treatment of fungal keratitis because of the highly specific results. However, it requires an experienced microbiologist, enough sample, more time and has a low sensitivity.[12,13]

MALDI-TOF mass spectrometry was used for further identification. It consists of ionization of molecules followed by separation and plotting to a spectrum, which is then compared to known spectra.[6,15] It has the potential to provide accurate identification at species level if enough reference spectra are available.[15] Additional PCR was performed for confirmation of the pathogen given the rarity of *Pyrenochaeta unguis-hominis*. PCR is fast compared to culture and is accurate as a diagnostic tool for mycotic keratitis but not every laboratory can offer this technique.[12,13,16,17]

Treatment remains difficult because of the limited choice of antifungal agents and the poor outcome of fungal keratitis.[9,18] A synergetic effect between antifungal drugs against fungi isolated from patients with keratomycosis has been described, but the efficacy of those different combinations might differ for every fungus.[12]

Antifungal susceptibility testing helps in choosing or adapting the treatment, and more so if confronted with a resistant keratomycosis or in case of an uncommon pathogen.[4,12] Unfortunately, the antifungal susceptibility of coelomycetous fungi is poorly known.[19] According to Garcia-Hermoso et al.[19] the treatment of this group of fungus remains empirical. Although amphotericin B, triazoles and terbinafine have shown some efficacy, the data are insufficient for them to be appointed as the recommended treatment for coelomycetous fungi.[4,19]

In our patient, an empiric treatment with topical voriconazole 1% and oral itraconazole was started due to the unavailability of natamycin. Amphotericin B 0.15% was added based on *in vitro* susceptibility testing. *In vitro* susceptibility for our isolate showed the lowest MIC for amphotericin B (0.50μg/ml) and a MIC value of >16μg/ml for voriconazole. The scraping performed for diagnostic purposes enhanced the penetration of amphotericin B by debriding and removing the overlying epithelium. Improvement was noted after optimized treatment, but an additional amniotic membrane transplantation was necessary to achieve closure of the corneal epithelial defect. Although corneal perforation was prevented in our patient, corneal scarring resulted in profound vision loss. A penetrating keratoplasty combined with an extracapsular cataract extraction was necessary to restore visual function.

## 4. Conclusion

We describe a case of *Pyrenochaeta unguis-hominis* keratomycosis, a fungus known to cause skin and nail infections. To our knowledge no other cases of keratomycosis caused by this pathogen have been described. Even when treated with combined topical and oral antifungals, *Pyrenochaeta unguis-hominis* keratitis can result in severe corneal scarring and profound visual impairment. Early diagnosis can allow prompt initiation of antifungal treatment, which should be guided by *in vitro* susceptibility testing. Further research is needed to develop standardized treatment protocols specifically for keratitis caused by coelomycetous fungi.

## Patient consent

For this Case Report and accompanying images, a written informed consent was obtained from the patient.

## Acknowledgments and Disclosures

None.

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