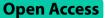
CASE REPORT



Phaeoacremonium iranianum - a new corneal pathogen



Xiaona Liu¹, Xiuhai Lu², Juanjuan Zheng¹, Shujuan Liu¹ and Man Li^{1*}

Abstract

Background *Phaeoacremonium* is typically found in the environment and can cause diseases in woody plants. It is rarely responsible for infections in humans.

Case presentation In this report, we present a case of corneal infection caused by *Phaeoacremonium iranianum*. Caused a fan-shaped grayish-white ulcer measuring approximately 4 mm×3 mm inferior nasal cornea. The ulcer appeared relatively dry, with noticeable swelling and cloudiness in the surrounding cornea. The visual acuity after infection was 0.25. We started an aggressive antifungal therapy. Our antifungal susceptibility testing revealed the Minimum Inhibitory Concentration of anifengin was 4 µg/ml, Micafengin and carpofungin exceeding 8 µg/ml, fluorocytosine was 32 µg/ml, posaconazole was 1 µg/ml, voriconazole was 0.5 µg/ml, itraconazole was 2 µg/ml, fluconazole was 64 µg/ml, and amphotericin was 0.05 µg/ml. The patient underwent keratectomy combined with antifungal therapy. A month later, the conjunctiva of the right eye was congested, and a 4*4 mm corneal opacity was visible inferior nasal cornea, with local obvious thinning and a little keratic precipitates on the inner skin, and the infection has been controlled.

Conclusions We detail the progression and treatment of this infection to contribute to the clinical understanding and management of such cases.

Keywords Phaeoacremonium Iranianum, Keratitis, Fungus

Introduction

Corneal ulceration is a major cause of monocular blindness second to cataracts in developing countries [1]. Currently, fungal keratitis is emerging as a common etiology for severe sightthreatening ocular diseases [2]. Moreover, fungal keratitis has a longer healing time and leads to five times more corneal perforations, which makes it a much more severe condition [3]. The most common

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species causing fungal keratitis have been identified to be

Fusarium, Aspergillus, and Curvularia among filamen-

tous fungi and Candida among the yeast groups [4]. The

occurrence of Phaeoacremonium infections in humans

has increased over the past two decades, and although

most cases have been ascribed to known species, several

unknown species have also been recorded [5]. Phaeoac-

remonium fungi are widely distributed in the environment, particularly in soil, wood, and other plant matter. At present, 29 species of *Phaeoacremonium* have been

reported [6]. Phaeoacremonium parasiticum was the first

species of Phaeoacremonium reported to cause phaeo-

hyphomycosis in humans [7]. Subsequently, P. rubrige-

num, P. parasiticum, and P. inflatipes have been reported

from phaeohyphomycosis cases [8-10]. Most reported

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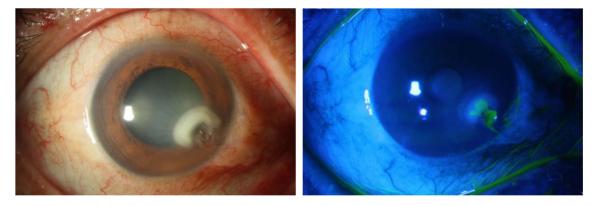


Fig. 1 A round yellowish-white infiltrate with well defined margins at 4 o'clock midperipheral cornea. An 4 mm×3 mm ulcer in the center of the invasion, limbal neovascularization, with an impending perforation and radiating Descemet's membrane folds



Fig. 3 Corneal scraping displayed numerous branching hyphae. (Fluorescence staining, magnification ×400)

Fig. 2 Microscopy revealed a significant presence of mycelium-like structures and inflammatory cells extending from the focal area of the right cornea to the middle layer (mesocortex)

Phaeoacremonium cases have involved subcutaneous abscesses, cysts, or chronic or acute osteoarthritis in immunocompetent or immunocompromised patients; these cases were often initiated by traumatic inoculation [9]. An overview of the various cases documented as being caused by the species newly described (*P. alvesii, P. amstelodamense, P. griseorubrum, P. krajdenii,* and *P. tardicrescens*) shows an infection pattern consistent with that of *P. parasiticum* [5]. But *Phaeoacremonium irania-num* reports are lacking.

Case report

A 66-year-old man patient attended our hospital on July 4, 2019 with complaints of blurred vision and pain in the right eye. History revealed that his right eye was scratched with a leaf. He had been using tobramycin and dexamethasone eye ointment, but his symptoms had not improved. Upon examination, his right eye had a visual acuity of 0.25, and intraocular pressure measured 8mmHg. There was no redness or swelling in the right eyelid, but the nasal conjunctiva appeared congested. A round yellowish-white infiltrate with well defined margins at 4 o'clock midperipheral cornea. An 4 mm×3 mm ulcer in the center of the invasion, limbal neovascularization, with an impending perforation and radiating Descemet's membrane folds.(see Fig. 1). The anterior chamber was moderate depth with no hypopyon. Confocal microscopy revealed a significant presence of mycelium-like structures and inflammatory cells extending from the focal area of the right cornea into the middle layer (see Fig. 2). Corneal scraping demonstrated numerous branched hyphae (see Fig. 3). The clinical diagnosis was fungal keratitis (right eye). Treatment was initiated with natamycin eye drops (hourly), fluconazole eye drops (every half hour), levofloxacin eye drops (six times a

day), sodium bromfenac eye drops (twice a day), atropine eye gel (once a day), and oral terbinafine tablets (0.25 g daily). The patient returned two days later, reporting relief from right eye discomfort. However, a followup ophthalmic examination revealed worsening corneal infiltration(see Fig. 4), and the patient declined hospitalization but continued the prescribed medication. Four days later, fungal colonies were detected in laboratory culture, suspected to be Fusarium based on lactophenol cotton blue staining and fluorescence staining (see Fig. 5). Ten days later, a re-examination using confocal microscopy showed a significant presence of myceliumlike structures in the deep stromal layer and the corneal endothelium(see Fig. 6). Due to ineffective drug treatment and deep lesion infiltration see Fig. 7, the patient was advised to undergo corneal transplantation, which he refused. Nineteen days later, the fungus strain isolated from a corneal scrape was identified as Phaeoacremonium iranianum(see Fig. 8). Antifungal susceptibility testing revealed the Minimum Inhibitory Concentration (MIC) of anifengin was 4 µg/ml, Micafengin and carpofungin exceeding 8 µg/ml, fluorocytosine was 32 µg/ml, posaconazole was 1 μ g/ml, voriconazole was 0.5 μ g/ml, itraconazole was 2 μ g/ml, fluconazole was 64 μ g/ml, and amphotericin was 0.05 µg/ml. Keratectomy of the right eye was performed 21 days later. After surface anesthesia, a 45° knife was used to make a corneal incision 1 mm along the edge of the ulcer, and a small amount of necrotic corneal tissue was removed along the incision. The corneal stroma layer was slightly cloudy and the descemet membrane was observed, and the lesion infiltrated deeply, so the resection was stopped, and keratoplasty was recommended for the patient within a limited time. After surgery, apply ofloxacin eye ointment to cover eyes. However, the patient declined keratoplasty and was discharged with a medication regimen, including natamycin eye drops (hourly), gatifloxacin eye drops (four times a day), diclofenac sodium eye drops (four times a day), ofloxacin eye ointment (once before bedtime), and voriconazole eye drops (10 mg/ml, hourly). One month later, The conjunctiva of the right eye was congested, and a 4*4 mm corneal opacity was visible inferior nasal cornea, with local obvious thinning and mild keratic precipitates see Fig. 9. Continue using voriconazole eye drops(Q2h), the infection was contained.

We conducted both macroscopic and microscopic examinations of the pathogenic strain isolated from the excised cornea. The front side of the colony displayed a brownish color with a fluffy or wooly texture, while the back side appeared dark brown on the PDA plate (refer to Fig. 5a). The hyphae were initially hyaline but later turned brown, with some developing rough walls. Phialides were brown, possessed thick walls, and were slender, tapering slightly toward the tip, measuring $15-50 \mu m$ in length. They often proliferated and featured small, funnelshaped collarettes(refer to Fig. 5b). Conidia, frequently forming clusters, were hyaline, thin-walled, cylindrical to sausage-shaped, measuring $3-6 \times 1-2 \mu m$, and expanded over time(refer to Fig. 5c). Notably, numerous circling structures were commonly observed in small cultures on slides (see Fig. 5d).

Discussion

Phaeoacremonium fungi are widely distributed in the environment, particularly in soil, wood, and other plant matter [11]. At present, 29 species of Phaeoacremonium have been reported [6]. Phaeoacremonium parasiticum was the first species of Phaeoacremonium reported to cause phaeohyphomycosis in humans [7]. Subsequently, P. rubrigenum, P. parasiticum, and P. inflatipes have been reported from phaeohyphomycosis cases [8-10]. Most reported Phaeoacremonium cases have involved subcutaneous abscesses, cysts, or chronic or acute osteoarthritis in immunocompetent or immunocompromised patients; these cases were often initiated by traumatic inoculation [9]. An overview of the various cases documented as being caused by the species newly described (P. alvesii, P. amstelodamense, P. griseorubrum, P. krajdenii, and P. tardicrescens) shows an infection pattern consistent with that of *P. parasiticum* [5].

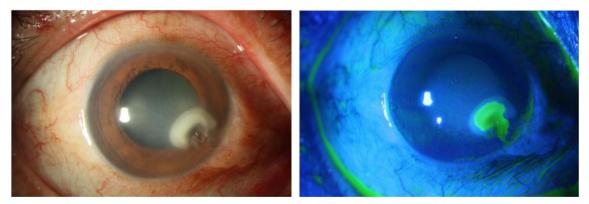


Fig. 4 Two days later, a follow-up ophthalmic examination revealed worsening corneal infiltration

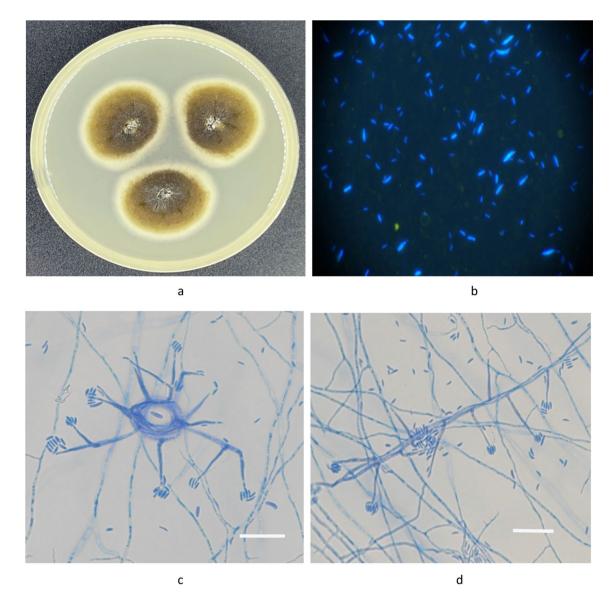


Fig. 5 (a) *P. iranianum* colony on Potato Dextrose Agar (PDA) medium plates after 9 days of incubation at 28 °C, (**b**) along with conidia from the original plate, stained with fluorescence (magnification ×400). (**c,d**) Microscopic morphology of *P. iranianum* on slide culture stained with cotton blue (magnification ×400, scale bar = 20 µm)

The morphology of *Phaeoacremonium* genus is intermediate between *Acremonium* and *Phialophora* genus and all are pathogens implicated in opportunistic infections [7]. Cultures of *Phaeoacremonium* grow slowly, lanose with radially folded. Culture on Sabouraud's dextrose agar (SDA) at 37°C produced growth of colonies that were initially glabrous, off-white and then went on to become velvety grayish-brown on aging [12]. The conidiogenous cells were subhyaline to pale brown. *Phaeoacremonium* show medium brown hyphae, which become pale brown to hyaline and verruculose. The phialides have a funnel-shaped collarette and show a wide variety of diverse forms, including ellipsoidal, obovate, cylindrical, or allantoid (sausage-like) [5]. Morphologically, *Phaeoacremonium* is morphologically similar to *Acremonium*, and the two can easily be confused by inexperienced clinical microbiologists. *Phaeoacremonium* is different mainly because of its darkly pigmented colonies and the conspicuous collarettes of its conidiogenous cells [10]. Elena Petrovi'c was the first to report *Phaeoacremonium iranianum*. The developed fungal colonies were brownish on PDA, reverse darker brown; circular shaped with an entire edge; and with aerial, opaque, and cottony mycelium and branched septate hyphae. The isolate produced hyaline, unseptate, and ovoid conidia. An average conidia body length was (oblong-ellipsoidal) $4.5 \times 1.5 \,\mu\text{m}$ [13].

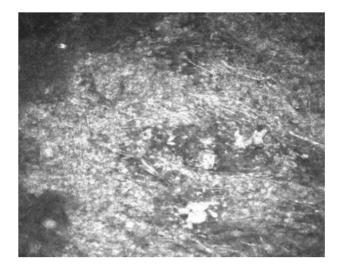


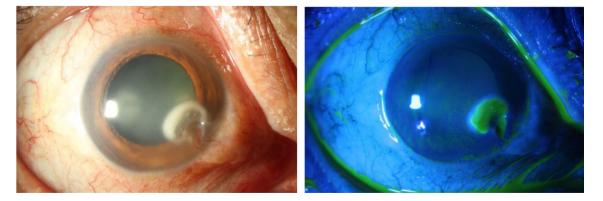
Fig. 6 A significant presence of mycelium-like structures in the deep stromal layer and the corneal endothelium

There is no standardized treatment for these rare fungal infections. Massa H's research indicated that amphotericin B, voriconazole, and posaconazole exhibited low MIC values and proved to be effective in treatment [14]. Tummidi S suggested that surgical wound excision can be combined with systemic Itraconazole therapy for several months. Antifungals such as amphotericin, fluconazole, posaconazole, ketoconazole, terbinafine, and 5-fluorocytosine (5FC) may be for patients with severe disease, poor response or hepatic toxicity to itraconazole [15–17]. According to Badali H, voriconazole, posaconazole, and isavuconazole are active against Phaeoacremonium. In contrast, all isolates were resistant to itraconazole and fluconazole. The geometric mean MIC of amphotericin B in the present study was 0.4 g/ml, suggesting that this drug may have a significant role in the management of Phaeoacremonium infections [16]. There is a documented case of Phaeoacremonium parasiticum endophthalmitis where enucleation was avoided through a treatment regimen involving intravitreal antibiotics, amphotericin, and oral voriconazole, resulting in the patient's vision stabilizing at 6/18 [18].

To the best of our knowledge, there have been no prior reports of eye infections caused by *Phaeoacremonium Iranianum*. Our cultures exhibited the typical characteristics of *Phaeoacremonium*, with curly growth in a waterbased medium. Antifungal susceptibility testing revealed anifengin at 4 μ g/ml, Micafengin and carpofungin exceeding 8 μ g/ml, fluorocytosine at 32 μ g/ml, posaconazole at 1 μ g/ml, voriconazole at 0.5 μ g/ml, itraconazole at 2 μ g/ml. In this case, keratectomy combined with natamycin and voriconazole yielded positive results.

Conclusions

Clinicians should be alert to this newly identified corneal pathogen that can cause keratitis. It can cause relatively dry, off-white corneal ulcers. It is sensitive to natamycin and voriconazole in our case. Identify the strain and administer according to the drug sensitivity result is crucial for achieving the best prognosis. In severe cases, a combination of surgical procedures may be necessary, including potential corneal transplantation.



CTGBCATCGATGAAGAACBCAGCGAAATGCGATAAGTAATGTGAAATTGCAGAATTCAGTGAATCATCGAATCTTGAACG CACATTGCGCCOCCTAGCTATTCTGCGGGGATGCCTGTCCGAGGATCACGTGATGCATCGATCG

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lo.	Reference description	Score	Probability 👔	Similarity 👔 🌡	Fragments ?	Overlap 👔	Direction ?	Rating ?	Alignment
71	SH1581100.08FU EU128028 Fungi, Ascomycota, Sordariomycetes, Togniniales, Togniniaceae, Phaeoacremonium, Phaeoacremonium iranianum	884.41	0	100.00 %	1	92.99 %	+/+	****	Show alignments
72	SH1581100.08FU EU128029 Fungi, Ascomycota, Sordariomycetes, Togniniales, Togniniaceae, Phaeoacremonium, Phaeoacremonium iranianum	884.41	0	100.00 %	1	92.99 %	+/+	*****	Show alignments
73	SH1581100.08FU EU128030 Fungi, Ascomycota, Sordariomycetes, Togniniales, Togniniaceae, Phaeoacremonium, Phaeoacremonium iranianum	884.41	0	100.00 %	1	92.99 %	+/+	*****	Show alignments
74	SH1581100.08FU KF179096 Fungi, Ascomycota, Sordariomycetes, Togniniales, Togniniaceae, Phaeoacremonium, Phaeoacremonium iranianum	874.90	0	100.00 %	1	91.99 %	+/+	****	Show alignments
75	SH1581100.08FU AF197992 Fungi, Ascomycota, Sordariomycetes, Togniniales, Togniniaceae, Phaeoacremonium, Phaeoacremonium iranianum	863.81	0	100.00 %	1	90.82 %	+/+	*****	Show alignments
76	SH1581100.08FU JF275863 Fungi, Ascomycota, Sordariomycetes, Togniniales, Togniniaceae, Phaeoacremonium, Phaeoacremonium iranianum	855.88	0	100.00 %	1	89.98 %	+/+	****	Show alignments
77	SH1581100.08FU AY179941 Fungi, Ascomycota, Sordariomycetes, Togniniales, Togniniaceae, Phaeoacremonium, Phaeoacremonium iranianum	844.79	0	100.00 %	1	88.82 %	+/+	*****	Show alignments
78	SH1581100.08FU KF764531 Fungi, Ascomycota, Sordariomycetes, Togniniales, Togniniaceae, Phaeoacremonium, Phaeoacremonium iranianum	860.64	0	99.82 %	1	90.82 %	+/+	****	Show alignments
2	CBS 101357 CBS 101357_ex30353_20717_JTS Phaeoacremonium Iranianum, Phaeoacremonium iranianum, Filamentous fungi, Holotype of Phaeoacremonium iranianum L Moster, Grafenhan, W. Gams & Grous, Italy, Actinidia chinensis, stained wood, publicly available rDNA ITS sequences (mirk4056)	835.28	0	99.81 %	1	88.15%	*/-	****	Show alignments
42	MIRRI0066932 CBS 101357_ex30353_20717_ITS CBS 101357, Actinidia chinensis, stained wood, Italy, Phaeoacremonium iranianum, its: Sequences ITS	835.28	0	99.81 %	1	88.15 %	*/-	****	Show alignments
79	SH1581100.08FU KR909219 Fungi, Ascomycota, Sordariomycetes, Togniniales, Togniniaceae, Phaeoacremonium, Phaeoacremonium minimum	881.24	0	99.66 %	1	97.66 %	+/+	****	Show alignments

Fig. 8 The sequencing result was Phaeoacremonium iranianum



Fig. 9 A 4*4 mm corneal opacity was visible inferior nasal cornea

Supplementary Information

The online version contains supplementary material available at https://doi.or g/10.1186/s12886-025-04064-1.

Supplementary Material 1

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"Not applicable" in this section.

Author contributions

Xiaona Liu and Man Li were major contributor in writing the manuscript. Xiuhai Lu, Juanjuan Zheng and Shujuan Liu analyzed and interpreted the result regarding the disease. All authors read and approved the final manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

"Not applicable" in this section.

Ethical statement

The authors confirm that this material is original and has not been published in whole or in part elsewhere; that the manuscript is not currently being considered for publication in another journal; and that all authors have been personally and actively involved in substantive work leading to the manuscript, and will hold themselves jointly and individually responsible for its content.

Consent for publication

The patient has given written informed consent for their personal or clinical details along with any identifying images to be published in this study.

Competing interests

The authors declare no competing interests.

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