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Corneal Chromoblastomycosis Caused by *Fonsecaea pedrosoi*

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Key Words
Fonsecaea pedrosoi · Dematiaceous fungus · Keratitis · Chromoblastomycosis

Abstract
Purpose: To report 2 unusual cases of fungal keratitis due to *Fonsecaea pedrosoi*. ***Methods:*** Two patients were diagnosed with *Fonsecaea pedrosoi* keratitis. Their files were reviewed for predisposing factors, clinical characteristics, microbiological study, treatment, and outcome. ***Results:*** Two consecutive patients presented with brownish pigmented corneal ulcers in their eyes after sustaining eye trauma from vegetative matter. In both cases, corneal scrapings were collected for microscopic examination and culture. Dematiaceous hyphae were seen on the smears, and dark pigmented colonies grew on the culture media, identified as *F. pedrosoi*. Both patients were treated and cured with combined topical antifungal agents and oral itraconazole. The first patient required an amniotic membrane patch, while the second received an intracameral amphotericin B injection. ***Conclusions:*** Pigmented infiltrates can be an important diagnostic clue, but a microscopic evaluation and culture are required to obtain an accurate diagnosis of *Fonsecaea* keratitis. The prompt diagnosis and combined antifungal treatment can prevent morbidity associated with this fungal infection.

Introduction

Fungal keratitis is commonly caused by filamentous fungi, which are divided into two groups: pigmented (dematiaceous) fungi, which produce a characteristic dark or brown pigment (clinically and/or on culture media), and nonpigmented (hyaline or moniliaceous) fungi, which do not produce a pigment. Most previous studies have focused on nonpigmented filamentous fungi as the dominant fungal pathogens responsible for corneal infection.

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Dematiaceous fungi have increasingly gained recognition as agents that cause corneal ulcers, second only to the *Fusarium* and *Aspergillus* species of hyaline fungi [1, 2].

Fonsecaea pedrosoi is a dematiaceous fungus that may cause a cutaneous and subcutaneous infection known as chromoblastomycosis. This fungus is saprophytic and is normally found in soil and plants [3]. Cutaneous chromoblastomycosis is usually difficult to treat and requires prolonged systemic treatment with itraconazole [4, 5]. However, corneal infections caused by this dematiaceous fungus have only been observed in a few cases. In the ophthalmic literature, a few reports including one case series have focused on *F. pedrosoi* keratitis [6–10]. In this report, we describe 2 cases of *F. pedrosoi* keratitis, both presenting after eye trauma, including clinical features, case management, and treatment outcome.

Case 1

A 79-year-old woman suffered from pain, redness, and decreased vision in her right eye, 2 weeks after an eye injury sustained while cutting wood. Visual acuity (VA) at presentation was hand movement in her right eye. An eye examination revealed a flat anterior chamber and subluxated cataract with posterior synechiae. Vitreous opacity obscured a view of the retina. On B-scan ultrasonography, a vitreous haze and attached retina were noted. A diagnosis of traumatic lens subluxation with vitreous hemorrhage was made. Three weeks later, the patient underwent phacoemulsification with posterior chamber intraocular lens implantation and received topical combined antibiotic and steroid treatment as postoperative medication. One week after the surgery, the VA in the affected eye was 1/60. There was a 2.5 × 5 mm brownish stromal infiltration involving the paracentral cornea with satellite lesions in the superior cornea, and no hypopyon was detected (fig. 1a). Corneal scraping was performed for Gram staining and smeared on wet mount slides with 10% potassium hydroxide. Dark-brown septate hyphae were found. The patient was treated with topical ketoconazole 2% hourly and oral itraconazole 200 mg daily.

After 7 days of incubation, dark-pigmented colonies of fungi grew on Sabouraud's medium identified as *F. pedrosoi* (fig. 2d). The patient was kept on topical ketoconazole. The corneal infiltrate decreased in size; however, epithelialization was delayed and the corneal stroma became progressively thin. Then, an amniotic membrane (AM) patch graft was applied to facilitate epithelial healing. The antifungal treatment was continued for another 2 months before being tapered off. On her last follow-up visit at 18 months, her VA in the right eye was 1/60. The cornea was scarred and developed posterior synechiae and foci of iridocorneal adhesion (fig. 1b). Optical penetrating keratoplasty was recommended; however, the patient declined any further surgical intervention.

Case 2

A 50-year-old woman presented with pain, redness, and decreased vision in her right eye, after an injury during cutting tree branches 2 months before. The patient had been treated with combined topical fortified cefazolin 33% and gentamycin 14% as well as amphotericin B 0.3%, as prescribed by a community ophthalmologist. She showed no improvement before being referred.

Her VA at presentation was light perception in the right eye and 6/9 in the left eye, respectively. The right eye revealed a 3 × 6 mm corneal infiltration with a brownish pigment overlaying the lesion (fig. 1c). The anterior chamber cell reaction was 4+, and a vitreous haze

obscured the fundus examination. A B-scan ultrasonography showed vitreous opacity and an attached retina. Corneal scraping was performed and subjected to smear and culture. Fungal elements were detected on 10% potassium hydroxide wet mount and calcofluor white stain (fig. 2a, b). The patient was treated with topical amphotericin B 0.15% hourly. Three days after starting the treatment, the corneal infiltration still continued to worsen. She received an intracameral amphotericin B (5 μg) injection. Then, her treatment was changed to topical ketoconazole 2% hourly and oral itraconazole 100 mg b.i.d.

After 7 days of incubation, the culture from the corneal scraping revealed dark-pigmented colonies identified as *F. pedrosoi* (fig. 2c). Since the patient's condition had not improved, the topical treatment was changed to natamycin 5% hourly, together with corneal debridement. A specimen from the corneal debridement was sent for smear and culture, both of which still showed dark septate hyphae. The infiltrate continuously decreased with slow epithelialization. Serial ultrasonography showed a gradual clearing of the vitreous haze. Natamycin was tapered to 4 times daily, while oral itraconazole 100 mg b.i.d. was continued for another month. At 1 month after treatment, her VA in the affected eye was hand movement, and the corneal infiltration developed into scarring and vascularization with some remaining small epithelial defects (fig. 1d). However, the patient did not return for any further follow-up.

Both patients provided their written inform consent for the treatment. The study adheres to the tenets of the Declaration of Helsinki.

Discussion

Dematiaceous fungus is an organism that has gained recognition as an emerging cause of corneal ulcer, second only to hyaline fungi [1, 2]. To date, no other organism is known to produce a clinically pigmented corneal ulcer. However, macroscopic pigmentation has been reported in 6–27% of corneal ulcers caused by dematiaceous fungi [1, 2]. Among this group of fungal keratitis, *Curvularia* has been reported to be the most common organism [1, 2].

F. pedrosoi is a dematiaceous fungus that can cause skin and subcutaneous infections, but it is a rare pathogen for corneal infection. Skin infections are commonly due to trauma sustained by vegetative matter. Previous case reports of corneal infections include 1 patient who did not have any history of eye injury [7], 2 patients who developed corneal ulcers after plant-related trauma [8, 10] and another case who developed an infection after having injured the eye with a glass [9]. Both of our patients sustained vegetative matter-related eye injuries before their infections gradually developed. The first case also received topical steroids after cataract surgery. Both patients had pigmented infiltrates, which suggested the diagnosis of fungal infection, while only 1 of the previous case reports had this finding [8].

The treatment of skin infections caused by *F. pedrosoi* is difficult [4, 5]. Although long-term oral itraconazole has been found to be an effective treatment, an ideal treatment protocol has not been clearly defined yet. The results from the largest series on fungal keratitis so far indicate no difference between visual outcome for corneal infection by dematiaceous fungi and infection caused by nondematiaceous fungi [2]. Grag et al. [1] suggested that therapeutic debridement, followed by antifungal agents, would be the best treatment for dematiaceous fungal keratitis. Among the previous case reports on *Fonsecaea* keratitis, the first case had chronic fungal keratitis and underwent two penetrating keratoplasty procedures, due to a reoccurring infection with intraocular extension. This case required prolonged systemic itraconazole treatment for 6 months before being fully cured [7]. The second case required a combined treatment of topical natamycin and amphotericin B and oral fluconazole

as well as lamellar keratoplasty and AM transplantation [8]. The last 2 cases have been successfully treated with combined topical amphotericin B 0.5% and oral ketoconazole for up to 3 months [9, 10].

In this study, the treatment with topical antifungal agents (i.e., ketoconazole and natamycin) and oral itraconazole resulted in the slow eradication of the infections. An AM patch was applied to support healing in the first case, while the second case required intracameral amphotericin B injections.

Conclusion

F. pedrosoi is a rare cause of corneal infection. Although the characteristic visible pigmented infiltrate can be an important diagnostic clue, this classical finding may not be apparent in all cases. Therefore, it is important to establish an accurate diagnosis through microscopic evaluation and culture. Although the cases described in this report were treated and cured with a combined therapy, further studies are needed to evaluate the efficacy of new antifungal medications with a broader spectrum in the treatment of this pigmented fungal keratitis.

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Disclosure Statement

None of the authors has any conflicts of interest concerning the case report.

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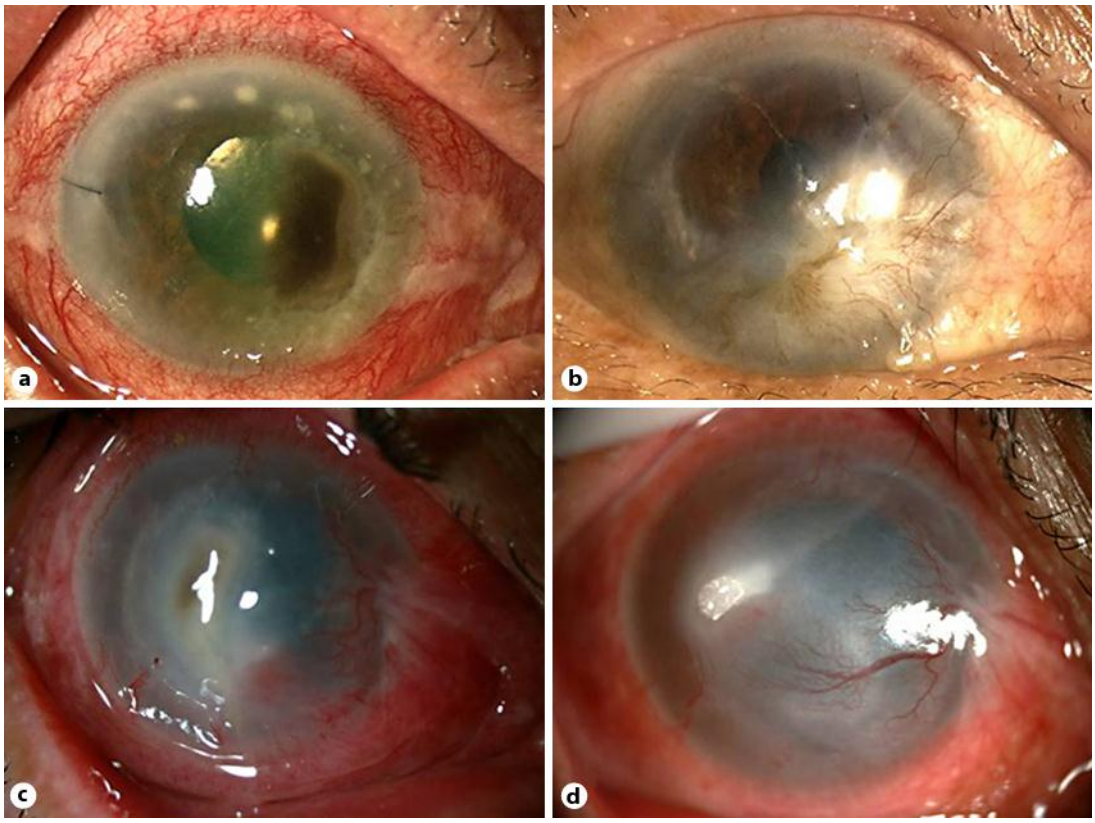

Fig. 1. Photographs of the anterior eye of the patients before and after treatment. **a**, **b** Case 1. **a** A brown pigmented infiltrate in the paracentral cornea with few satellite lesions in the superior peripheral cornea 1 week after cataract surgery. **b** The corneal ulcers developed into scars after the treatment. **c**, **d** Case 2. **c** A corneal infiltrate with central brownish pigments on top of the lesion at presentation. **d** Scar tissue and vascularization replaced the corneal ulcer, with small foci of epithelial defects remaining after 1 month of treatment.

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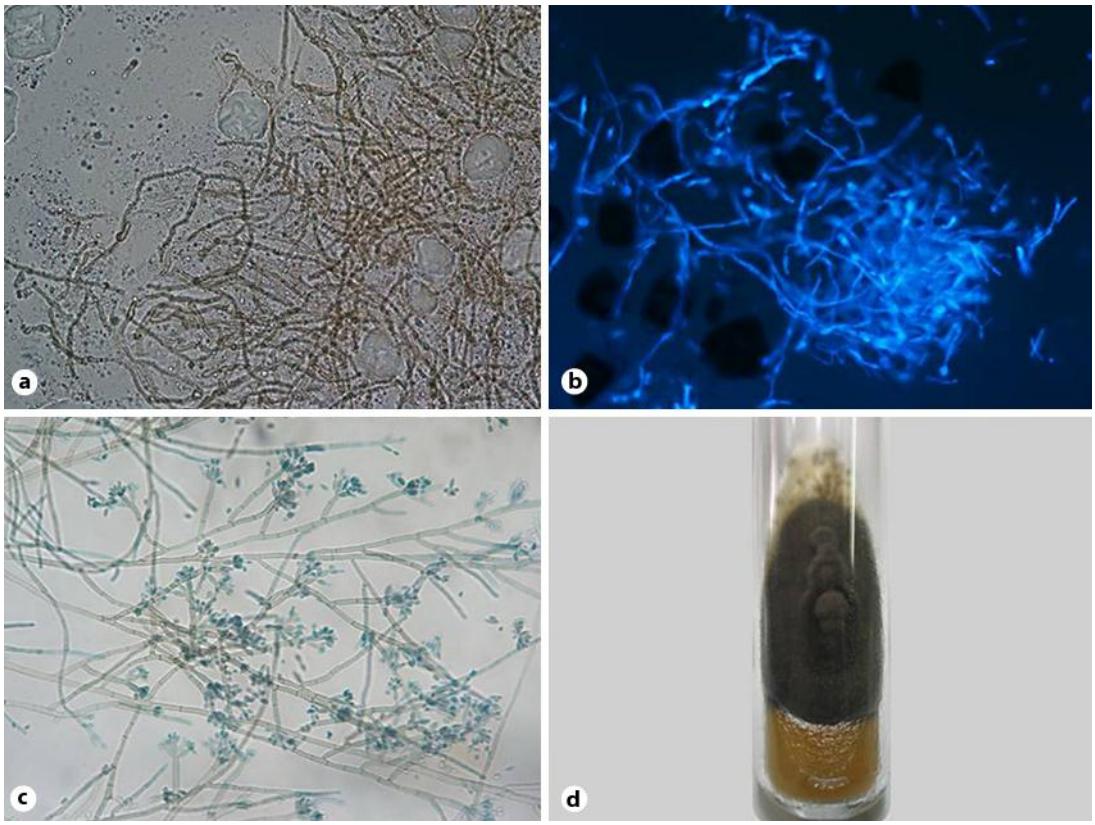

Fig. 2. **a** Potassium hydroxide preparation showing numerous dark septate fungal hyphae. **b** Numerous fungal elements detected on calcofluor white staining. **c** Microscopic analysis of **b** showing fungal hyphae and conidia. **d** Dark pigmented colonies of *F. pedrosoi* growing on Sabouraud's dextrose agar. Magnifications: ×400 (**a**, **b**) ×100 (**c**).