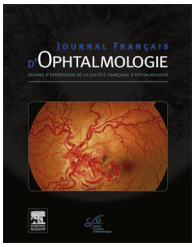
Journal français d'ophtalmologie xxx (xxxx) xxx.e1—xxx.e4

Disponible en ligne sur
ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com



LETTER TO THE EDITOR

Phaeoacremonium parasiticum keratitis: An atypical fungal organism and review of the literature

La kératite à Phaeoacremonium parasiticum : un organisme fongique atypique, revue de la littérature

Introduction

Infective keratitis is one of the most important causes of corneal blindness in various parts of the world [1]. The treatment protocol for infective keratitis caused by the commonly encountered microorganisms is mostly well defined but sometimes conventional therapy fails, or the infection runs an unusual course [1]. Infection by rare and emerging organisms should be suspected under such circumstances. The infrequent occurrence and variable clinical appearance of keratitis by these organisms pose a challenge for the treating clinicians [1]. Added to this difficulty, the development of antibiotic and antifungal resistance has been an increasing clinical concern and has been shown to be associated with an increase in the risk of treatment failure [2].

We present an atypical case of filamentous fungal keratitis due to *Phaeoacremonium parasiticum*, an unusual microorganism resistant to voriconazol.

Case description

A 32-year-old female came to our hospital with complaints of severe ocular pain and blurred vision in her left eye (OS). She had no history of immunosuppression or contact lens use. However, two weeks prior to her presentation, she felt a blow on her eye and a particular ophthalmologist prescribed tobramycin-dexamethasone drops.

Biomicroscopy revealed a severe conjunctival injection and a 1.5 mm central endothelial plaque with feathery borders and satellite lesions surrounded by ring-shaped stromal infiltration (Fig. 1A). Intraocular pressure (IOP) was normal. The anterior chamber (AC) was quiet. Corneal sensitivity was preserved. Best-corrected visual acuity (BCVA) was hand movement. Corneal scraping was performed, and the patient was started with hourly alternating empiric antibiotics (netilmicin 3% and moxifloxacin 5%), antifungic therapy (topical voriconazole 1%, natamycin 5% and oral itraconazole) and atropine 1%. The patient lost follow-up for a week and pain and blurred vision worsened accompanied of stromal destruction and hypopyon. Microbiological studies revealed *P. parasiticum* sensitive to amphotericin B, resistant to voriconazole. Then, the patient replaced voriconazole with hourly amphotericin B 0.15% eye drops and intrastromal injection. Next day, an AC lavage with amphotericin B and conjunctival flap was performed (Fig. 1B). Postoperatively, the pain decreased and she continued with close monitoring. Despite this, seven days later, a completely lysed conjunctival flap and melting were observed (Fig. 1C). Consequently, prior to a B-mode ultrasound (Fig. 1D), a therapeutic penetrating keratoplasty was performed. One day postoperative, there was no pain and BCVA improved to counting fingers. Immediate postoperative treatment included the same antibiotic and antifungal drugs, without steroids eye drops. Subsequently, the patient was stable until some retrokeratic precipitates and graft edema were observed at fourteen days post-keratoplasty (Fig. 1E) She did not refer any symptoms and there were no other signs of fungal recurrence. Therefore, a clinical diagnosis of postoperative inflammation versus acute graft rejection was suspected and topical prednisolone was started. Following, we slowly tapered steroids, having a favorable evolution. At last visit, three months after therapeutic keratoplasty, semitransparent graft, anterior segment quiet and no staining was observed. She developed cataract and VA continued in counting fingers but there were no signs of fungal recurrence (Fig. 1F).

Discussion

P. parasiticum is a known pathogen in the agricultural domain, especially in grapevine culture, and it has been isolated as a human pathogen. It has been implicated as the causative organism in various skin, subcutaneous, joint and heart infections [3,4]. To date, *P. parasiticum* has been incriminated as an uncommon ocular pathogen only in two cases in the literature: in a posttraumatic endophthalmitis [3] and in an infectious keratitis [4]. Keratomycosis uncommonly occurs in the absence of predisposing factors. Corneal trauma (primarily with vegetative matter) has been considered as the predominant predisposing factor accounting for 40% to 60% of patients with fungal keratitis [5]. Other prevailing factors include contact lens wear (as the previous keratitis by *P. parasiticum* reported [4]), long-time topical or systemic antibiotic or steroid use, previous ocular surgery or ocular surface disorders [5]. The history of previous trauma and steroid use made our patient highly susceptible to fungal keratitis.

Certain clinical signs are thought to be more common with specific organisms. In the previous case reported [4], the authors described an ulcer with subepithelial spread as on grapevine leaf with only little destruction of the stroma and circumscribed inflammatory reaction. However,

Please cite this article as: M. García-Lorente, I. Aguilar-Valdez, A.M. García-Albisua et al., *Phaeoacremonium parasiticum* keratitis: An atypical fungal organism and review of the literature, J Fr Ophtalmol, https://doi.org/10.1016/j.jfo.2023.03.029

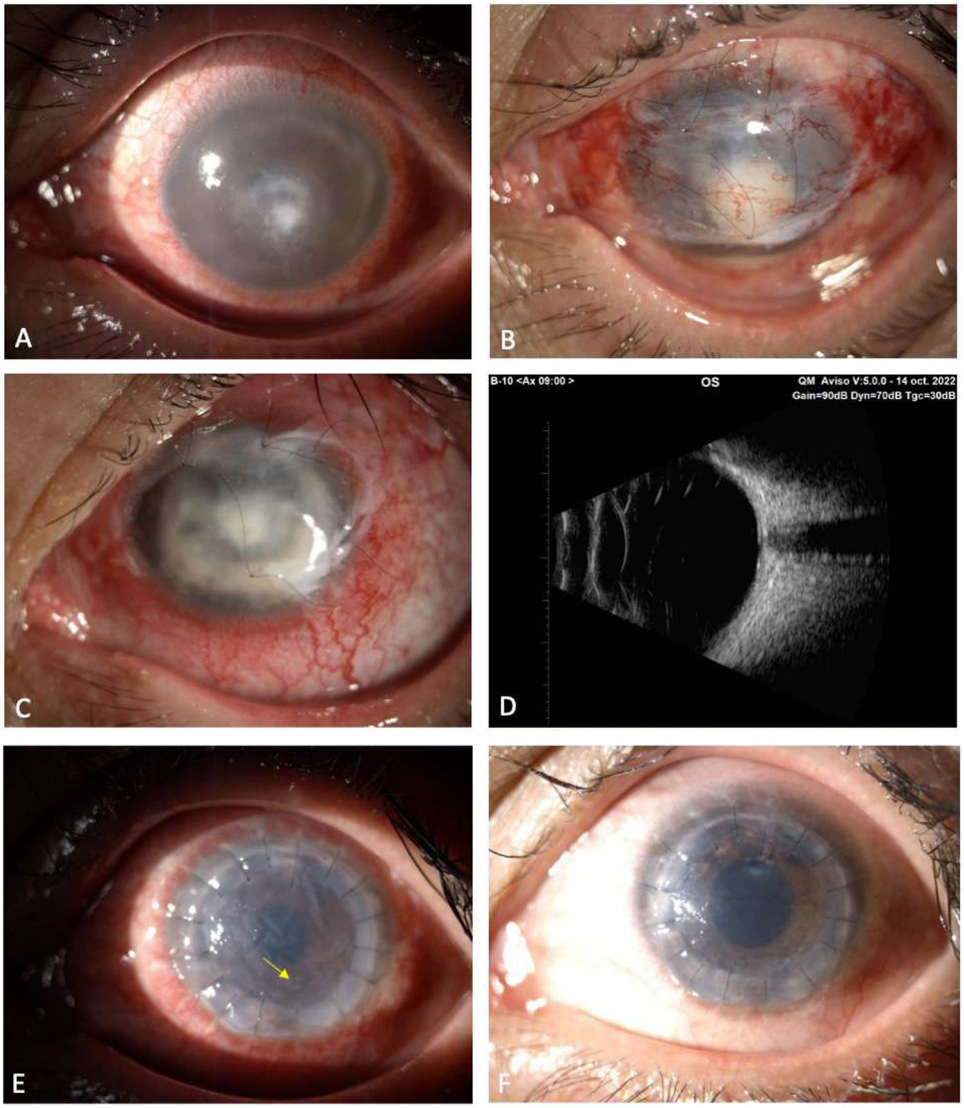


Figure 1. a: slit-lamp image of OS showing loss in corneal transparency with a central endothelial plaque with feathery borders and satellite lesions surrounded by ring-shaped stromal infiltration; b: slit-lamp image of OS showing bipediculated conjunctival flap. Note hypopion and large central infiltrate; c: slit-lamp photograph of OS showing corneal melting and worsening of the infiltrate with conjunctival flap tissue remnants; d: B-mode ultrasound showing axial section of the OS, echolucent lens, applied retina, without evidence of inflammation in the vitreous body that was corroborated at 90—110 decibels; e: slit-lamp photograph of OS showing retrokeratic precipitates (yellow arrow) and graft edema with endothelial folds; f: slit-lamp image of OS showing OS keratoplasty at last follow-up with a semitransparent graft without signs of fungal recurrence.

our patient presented satellite lesions, endothelial plaque, a ring infiltrate and ulcer with irregular borders. In contrast to the low inflammatory reaction reported by Massa [4], our patient developed higher inflammation with hypopion and melting. That fact supports the fact that clinical appearance does not always indicate the origin of the infection [6].

Diagnosis and treatment of fungal keratitis remain a difficult task. Although the mainstay is staining and corneal scrape culture, the latter is slow to grow and can often be negative [7]. In our case, the identification took a week and was made by microculture and PAS staining (Fig. 2). Morphologically, hyphae of *P. parasiticum* had been described as thinner than the classical *Aspergillus* hyphae [4]. The genus *Phaeoacremonium* consists of septate and branching hyphae that can be solitary or in bundles. Characteristically, *P. parasiticum* presents long conidiophores in contrast to other species as *P. inflatipes* or *P. sphinctrophorum* [8].

Regarding the therapeutic management, topical natamycin eye drops 5% remains the most evidence-based treatment for filamentous fungal keratitis [9]. However, currently we do not have direct access to natamycin 5% in Mexico and for this reason it is not used routinely in susceptibility testing. Although these tests are not routinely performed and region-specific antifungal susceptibility data are scarce, testing may prove vital in guiding therapy given the recent emergence of drug resistance [10]. In fact, after analyzing the antifungigram of this atypical microorganism, it showed resistance to voriconazol, being only sensible to amphotericin B. This differs from reported by Massa

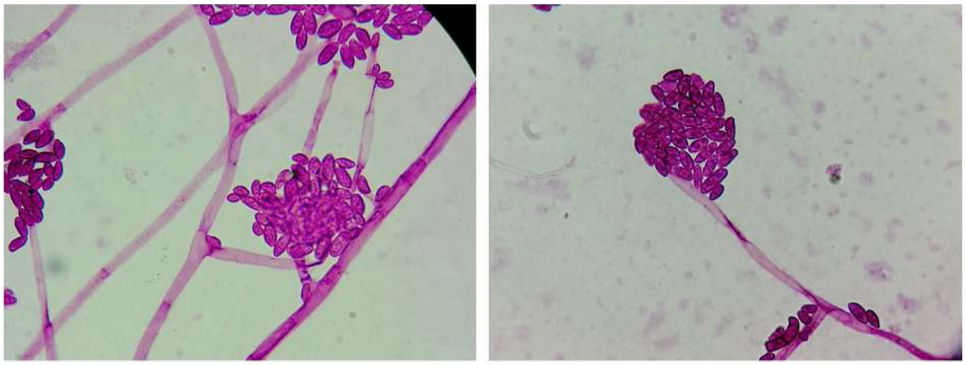


Figure 2. Microphotograph and PAS staining showing *Phaeoacremonium parasiticum* grown from this case. Note the thin, septate and long conidiophores.

et al. [4], which described *P. parasiticum* was sensible to voriconazol and amphotericin B.

Albeit voriconazol 1% is easier to obtain in our country, it was not sensible. Certainly, Prajna et al. [2] suggested that susceptibility to both natamycin and voriconazole may be decreasing over the last decade in South India.

In our case, amphotericin was the unique antifungal option. This drug has been described as an alternative whereas still its use requires access to a compounding pharmacy and is limited by toxicity [9].

To the complex diagnosis of these pathogens, we must add the lack of real availability of topical antifungal. Rocha-de-Lossada et al. [7] highlighted that it is imperative to facilitate access to antifungal and antiamœba eye drugs. These medicaments usually have to be requested through foreign medicine for a specific patient, purchased over the Internet or ordered to prepare a master formula, making it difficult to obtain in a quick way [7].

If that was not enough, filamentous fungal ulcers are already known to have worse outcomes than bacterial ulcers. Unfortunately, as in our case, nearly 50% of severe ulcers perforate or require therapeutic penetrating keratoplasty despite the use of topical and oral antifungal medication [2].

Conclusion

To summarize, this is the second fungal keratitis by *P. parasiticum* reported in the literature. The main difference from the previous report is based on different risk factors, clinical presentation, a torpid evolution and the resistance to a common antifungal. Clinicians should be aware of this new corneal pathogen causing keratitis. Good coordination between the microbiologist and ophthalmologist is required for establishing the accurate diagnosis and appropriate treatment to achieve optimal outcomes.

Disclosure of interest

The authors declare that they have no competing interest.

References

[1] Sahay P, et al. Infectious keratitis caused by rare and emerging micro-organisms. Curr Eye Res 2020;45:761—73, http://dx.doi.org/10.1080/02713683.2019.1708407.

[2] Prajna NV, et al. Patterns of anti-fungal resistance in adult patients with fungal keratitis in south india: a post hoc analysis of 3 randomized clinical trials. JAMA Ophthalmol 2022;140:179—84, http://dx.doi.org/10.1001/jamaophthalmol.2021.5765.

[3] Huynh TK, Lee LR, Ellis D. Late-onset post-traumatic *Phaeoacremonium parasiticum endophthalmitis*. Clin Exp Ophthalmol 2007;35:366—8, http://dx.doi.org/10.1111/j.1442-9071.2007.01486.x.

[4] Massa H, Riat A, Panos GD. First report of a new corneal pathogen: *Phaeoacremonium parasiticum*. Eur J Clin Microbiol Infect Dis 2020;39:2477—80, http://dx.doi.org/10.1007/s10096-020-03980-y.

[5] Mahmoudi S, et al. Fungal keratitis: an overview of clinical and laboratory aspects. Mycoses 2018;61:916—30, http://dx.doi.org/10.1111/myc.12822.

[6] Dalmon C, et al. The clinical differentiation of bacterial and fungal keratitis: a photographic survey. Invest Ophthalmol Vis Sci 2012;53:1787—91, http://dx.doi.org/10.1167/iovs.11-8478.

[7] Rocha-de-Lossada C, et al. Need for real availability of topical antifungal and anti-amoeba eye drugs in the Spanish Health System. Arch la Soc Española Oftalmol 2020;95:e81—2, http://dx.doi.org/10.1016/j.oftale.2020.05.030.

[8] Mostert L, Crous P, Fourie P, Halleen F. A review of *Phaeoacremonium* species involved in Petri disease and Esca of grapevines. Phytopathol Mediterr 2006;45:12—29.

[9] Agarwal S, Khan TA, Vanathi M, Srinivasan B, Iyer G, Tandon R. Review Article Update on diagnosis and management of refractory corneal infections. Indian J Ophthalmol 2022;70:1475—90, http://dx.doi.org/10.4103/ijo.IJO.

[10] Menard M, et al. Microbial profile and clinical outcomes of fungal keratitis at a single-center tertiary care hospital. Clin Ophthalmol 2022;16:389—99, http://dx.doi.org/10.2147/OPTH.S346227.

M. García-Lorente[a,*], I. Aguilar-Valdez[a], A.M. García-Albisua[a], C.E. de la Torre-González[a], J.A. Cruz-Cervantes[b], C. Rocha-de-Lossada[c,d,e,f], G. de Wit-Carter[a]

[a] *Cornea and Refractive Surgery Department, Asociación Para Evitar la Ceguera en México, Hospital Luis Sánchez Bulnes, Street Vicente García Torres 46, San Lucas, Coyoacán, 04030 Ciudad de México, CDMX, Spain*

[b] *Microbiology Department, Asociación Para Evitar la Ceguera en México, Hospital Luis Sánchez*

Bulnes, Street Vicente García Torres 46, San Lucas, Coyoacán, 04030 Ciudad de México, CDMX, Spain
[c] *Ophthalmology Department, Qvision, VITHAS Almería Hospital, Almería, Spain*
[d] *Ophthalmology Department, VITHAS Málaga, Málaga, Spain*
[e] *Ophthalmology Department, Regional University Hospital of Málaga, Málaga, Spain*
[f] *Ophthalmology area Doctor Fedriani, Surgery Department, University of Sevilla, Sevilla, Spain*

[*] Corresponding author.
E-mail address: glorentemaria@gmail.com
(M. García-Lorente)

https://doi.org/10.1016/j.jfo.2023.03.029
0181-5512/© 2023 Elsevier Masson SAS. All rights reserved.