



Fungal Keratitis due to *Rhodotorula glutinis*: A Case Report

Úlcera Corneana por *Rhodotorula glutinis*: Relato de Caso

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ABSTRACT

We describe a case of mycotic keratitis involving a rare fungus and review the literature on *Rhodotorula* keratitis. A 40-year-old man was struck in the right eye with a tree branch and developed a corneal ulcer involving the anterior portion of the cornea. Cultures grew *Rhodotorula glutinis*. The patient was initially treated with topical amphotericin, but only improved with topical and intracameral voriconazole administration. The corneal infiltrate resolved, leaving an anterior stromal scar, and the patient's best-corrected visual acuity was 20/60 in the involved eye.

Cases of *Rhodotorula* keratitis can pose a challenge to the ophthalmologist, with the diagnosis and the treatment regimen, as this yeast may not respond well to commercially available drugs. We report a case of *Rhodotorula* keratitis that was only resolved with voriconazole. Our case reinforces the importance of the early diagnosis and correct management of fungal keratitis involving this rare, but potentially damaging yeast.

KEYWORDS: Antifungal Agents; Corneal Ulcer; Eye Infections, Fungal; Keratitis; *Rhodotorula*.

RESUMO

Descrever um caso de um paciente de 40 anos que, após um trauma no olho direito por material vegetal, evoluiu com úlcera infecciosa de córnea. As culturas da lesão identificaram *Rhodotorula glutinis*. Inicialmente tratado com anfotericina tópica o paciente só obteve melhorar com o uso de voriconazol por via tópica e intracamerar. O infiltrado corneano evoluiu bem, deixando uma cicatriz na porção anterior da córnea e a melhor acuidade visual corrigida foi de 20/60 no olho envolvido.

Casos de úlcera corneana por *Rhodotorula* podem ser um desafio ao oftalmologista, tanto no diagnóstico quanto no tratamento, visto que essa levedura pode não responder bem aos antifúngicos disponíveis. Nosso relato de caso evidência a importância de se fazer o diagnóstico precoce e o manejo correto de úlcera infecciosa por esse fungo raro mas potencialmente grave.

PALAVRAS-CHAVES: Antifúngicos; Infecções Oculares Fúngicas; Queratite; *Rhodotorula*; Úlcera da Córnea

INTRODUCTION

Among severe infectious corneal ulcers, fungal keratitis is most common in developing countries, especially those with a tropical climate.^{1,2} In recent years, however, it has become more frequent in temperate countries as well, possibly as a consequence of the growing number of trauma cases, the widespread use of broad-spectrum antibiotics and steroids, and the increasing use of contact lenses.³

The majority of the cases of mycotic keratitis are caused by the *Fusarium* genus, *Candida* spp., and *Aspergillus* spp.; however, new and rare fungal species have appeared in recent years.¹⁻³

Furthermore, the therapeutic failure rates in fungal keratitis are very high despite appropriate treatment; thus, it is important to identify the species involved and their susceptibility to the available antifungal drugs.^{1,2}

Rhodotorula spp. is a yeast characterized by the production of a coral-red pigment, commensal in the natural environment and in humans. Although previously considered non-pathogenic, it has emerged as an opportunistic etiologic agent both to systemic and to ocular infections. It is usually resistant to common antifungal drugs.^{4,5}

Herein, we describe a case of keratomycosis caused by *Rhodotorula glutinis* after trauma with vegetable matter and discuss the treatment challenges it poses.

CASE REPORT

A 40-year-old man presented with a history of pain, redness, and vision decrease in the right eye following trauma with a twig 7 days prior to the onset of symptoms. He was treated with topical moxifloxacin and prednisolone before referral, with no improvement in his symptoms.

A slit-lamp examination revealed a whitish central corneal infiltration approximately 3×3 mm in size, with irregular margins and a rounded thinning area in the central portion of the infiltrate (Fig. 1). There was no vascularization or hypopyon at the time.

The uncorrected visual acuity was 20/200 in the right eye and 20/20 in the left eye. Ultrasound examination did not show vitreous opacification, and the retina was flat.

Cultures of the cornea were performed for bacterial,

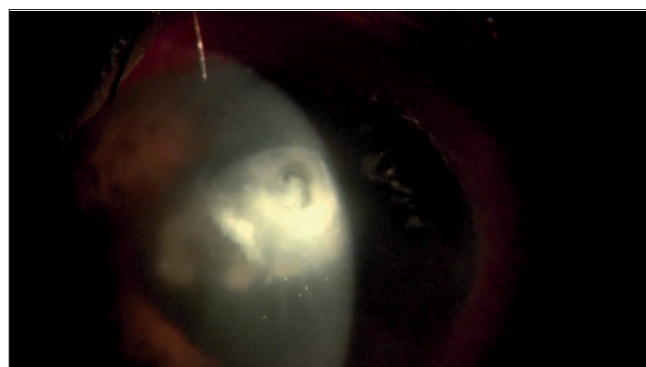


Figure 1. Slit lamp photomicrograph. Appearance of the right eye at the time of presentation.

acanthamoeba, and fungal organisms. The topical corticosteroid therapy was discontinued, and we also reduced the antibiotic regimen. The patient also initiated topical natamycin 5% applied hourly and atropine 1% twice a day.

On direct smears, budding yeast cells without hyphae were observed by Gram staining. After a few days of incubation, distinctive, coral, orange-pigmented, glistening yeast-like mucoid colonies started to grow on Sabouraud Dextrose agar (Fig. 2). The fungal isolate was identified as *Rhodotorula glutinis*.



Figure 2. Orange-red colonies of *Rhodotorula glutinis* on Sabouraud agar culture.

Subsequently, we discontinued moxifloxacin and changed the antifungal to amphotericin B 0.15%, along with systemic therapy consisting of oral ketoconazole 200 mg twice daily. After a brief period of pain relief and partial healing of the epithelial defect, the symptoms worsened, and a congested, non-ulcerated, scleral nodule measuring 1 mm in diameter on the nasal aspect of the limbus was identified. Visual acuity decreased to counting fingers, and hypopyon was noted (Fig. 3).

As the infection worsened despite topical therapy, we performed intracameral amphotericin B injection (10 µg in 0.1 mL), which was repeated 5 days later. With no significant improvement, we applied topical voriconazole

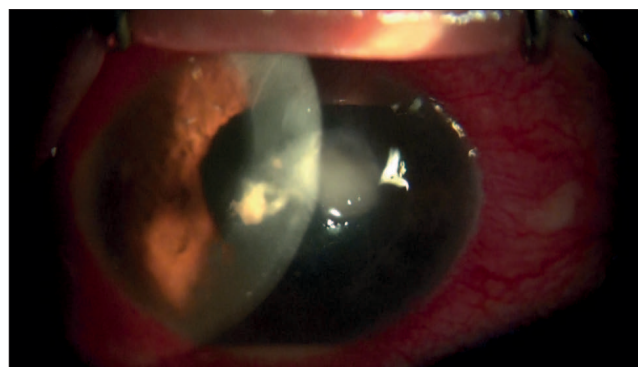


Figure 3. Deep stromal infiltrate and hypopyon are observed after the worsening of the patient's condition.

1% and performed intracameral voriconazole injections (50 µg/0.1mL) every 5 days.

After the third injection, the infection started to resolve, with no further pain, conjunctival redness, or hypopyon. New blood vessels coming from the superior limbus toward the lesion and a dilated pupil (although atropine was discontinued several weeks before) were the other noteworthy features.

The patient was continued on amphotericin and voriconazole for a total course of three months, at which time the medications were discontinued with apparent full resolution of the infectious process. After 6 months with no antifungal medication, the patient was asymptomatic, and his visual acuity improved to 20/60, with a residual scar in the paracentral cornea and a dilated pupil (Fig. 4).

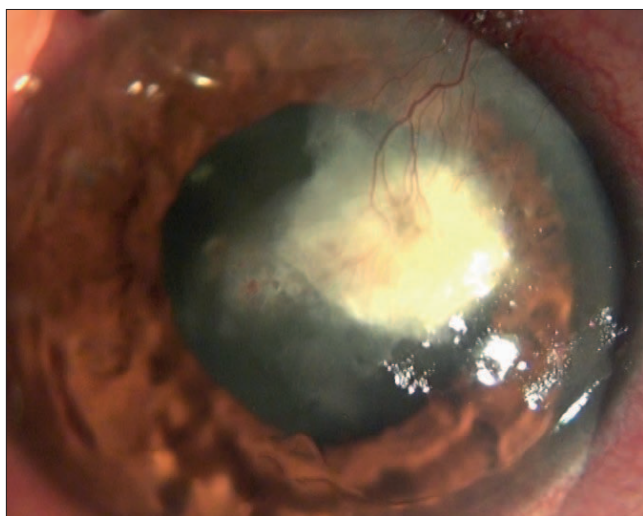


Figure 4. Final aspect of the lesion showing a residual scar, new blood vessels, and a dilated pupil.

DISCUSSION

Rhodotorula spp. are saprophyte yeasts that commonly occur in the environment. Although uncommon in the normal ocular flora, they have been isolated from the skin, conjunctiva, and the respiratory and gastrointestinal tracts, especially in immunocompromised and hospitalized patients.⁶ The genus *Rhodotorula* includes eight species; however, only *R. mucilaginosa*, *R. glutinis*, and *R. minuta* are known to cause human disease.⁴ It produces distinctive orange red colonies when grown on Sabouraud's Dextrose agar.

The first case of *Rhodotorula* infection in a patient with endocarditis was reported in the literature in 1960; however, it was only in 1979 that J. François and M. Rijsselaere reported a case of eye infection due to *Rhodotorula*.⁷ Nevertheless, these authors concluded that this yeast may not be the cause of the keratitis, since *Staphylococcus aureus* was also isolated. Indeed, they performed a simple experiment and concluded that *Rhodotorula* is not pathogenic to the cornea. If accidentally introduced in an eye, this fungus behaves as a foreign body without an invading capacity. Their theory proved erroneous in the following years, when some cases were reported worldwide.

Rhodotorula has reportedly been responsible for cases of keratitis,⁸ dacryocystitis,⁹ corneal lamellar graft infection,¹⁰ scleritis,¹¹ and endophthalmitis.¹² Most of these reports come from Southeast Asia, especially India. Despite the increasing number of reports, *Rhodotorula* is still an extremely rare pathogen. In the largest review of *Rhodotorula* infection we found, published in 2008, 128 cases were included and 7% (nine cases) were of eye infections only after fungemia.⁶ Among the patients in these cases, six were diagnosed with keratitis and were cured, and three were diagnosed with endophthalmitis and eventually became blind.

A study conducted in São Paulo, Brazil, with data from 2005 to 2009 and 1,468 cases of infectious keratitis, reported that among the 149 cases of fungal keratitis found, only two were caused by *Rhodotorula* spp.¹³ The same group had published a previous study with 61 cases of fungal keratitis between 1995 and 1998; however, none of them was caused by *Rhodotorula*.¹⁴

Another study performed in China for 5 years, from 2004 to 2009, with 139 fungal keratitis did not identify any case of *Rhodotorula*.¹⁵ A similar absence of this rare yeast was reported by studies conducted in New Delhi, India (191 cases),¹⁶ in London, UK (79 cases),³ and in Shandong Province, China (596 cases).¹⁷

In a very large compilation of epidemiological and microbiological features of fungal keratitis from a tertiary ophthalmic care center in North India, with 4069 cases of mycotic keratitis, only 21 cases were caused by *Rhodotorula* (0.5%), which makes this yeast the least common cause of fungal keratitis among all the fungi.¹⁸

Currently, amphotericin B appears to be the drug of choice for *Rhodotorula* infection and was the drug used by most cases of fungemia and eye infections reported in the literature.⁶ It was endorsed by the European Society of Clinical Microbiology and Infectious Diseases, which recommends that amphotericin B must be the treatment of choice in *Rhodotorula* infections.¹⁹ In our case, amphotericin alone was not sufficient to control the infection, and the combination of this drug with voriconazole showed better results. The same failure of medical therapy with amphotericin and the need to use voriconazole to achieve cure was reported by Saha *et al* in another case of keratitis caused by *Rhodotorula*.²⁰

The *in vitro* antifungal susceptibility testing of *Rhodotorula* species showed that amphotericin B and flucytosine had the highest *in vitro* activity and fluconazole had the lowest activity, with voriconazole and itraconazole showing intermediate activity.⁵

All patients in cases of *Rhodotorula* keratitis reported in the literature had associated trauma or underwent prior corneal surgery. Topical treatment was not sufficient, and to achieve resolution, most patients required some form of surgical intervention. Although we avoided keratoplasty in our patient, we had to perform repeated intracameral injections of amphotericin and voriconazole.

In summary, although rare, *Rhodotorula* keratitis reports are emerging in the literature, and both ophthalmologists and microbiologists should consider this etiology, especially in persistent corneal infections, and promptly start specific therapy as this yeast may be resistant to some antifungal agents.

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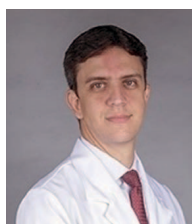
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