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CASE REPORT

Successful salvage treatment of *Lecythophora mutabilis* keratitis with topical voriconazole

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ABSTRACT

Fungal keratitis is an important ophthalmic problem in the developing world. Filamentous fungi are the most frequently reported pathogens in fungal keratitis. This report aimed to present a case with *Lecythophora mutabilis* keratitis that treatment failure was seen with topical and systemic amphotericin B lipid complex. Then she was treated successfully topical voriconazole. *J Microbiol Infect Dis 2011;1 (2): 75-77*

Key words: *Lecythophora mutabilis*, endophtalmitis, amphotericin B lipid complex, voriconazole

Lecythophora mutabilis keratitinde topical vorikonazol ile başarılı kurtarma tedavisi

ÖZET

Fungal keratit gelişmekte olan ülkelerde önemli bir göz sorunudur. Mantar keratitleri içinde filamentöz funguslar en sık bildirilen patojenlerdir. *Lecythophora mutabilis* keratiti olan, topikal ve sistemik amfoterisin-B lipid kompleks ile başarısız tedavi sonrasında topikal vorikonazol ile tedavi edilen bir hasta sunuldu.

Anahtar kelimeler: *Lecythophora mutabilis*, endoftalmit, amfoterisin B lipid komplex, vorikonazol

INTRODUCTION

Fungal keratitis is a common, potentially sight-threatening ocular infection. Filamentous fungi are long considered as a major cause of fungal keratitis. Ophthalmic infections from these fungi are most commonly associated with agricultural and outdoor activities. Of the filamentous fungi, infections from Fusarium and Aspergillus species are the most common.[1,2] *Lecthophora mutabilis* is rarely recognized as cause of keratitis. Treatment of *Lecthophora keratitis* is difficult due to various antifungal drug resistance.[1-5] The most common antifungal treatments are intravenous and/or topical amphotericin B. Voriconazole is a new triazole antifungal agent with the broad spectrum of antifungal activity.[6] The purpose of this case is to report that voriconazole has worked effectively in a patient with *Lecythophora mutabilis* keratitis, who did not respond to standard amphotericin B therapy.

CASE

A 48-year-old farmer woman, presented to hospital with a history of pain, redness and watering in the left eye of 10-day duration. There was no trauma history. She had initially been seen by a local practitioner, who treated her with ciprofloxacin eye drops. Her symptoms did not improve, so she was referred to hospital for further management. On presentation, the best-corrected visual acuity in her left eye was finger counting positive at a distance of one meter. On examination, she was found to have a corneal infiltrations and a hypopyon (2.3 mm) (Figure 1).

In patient with clinical diagnosis of keratitis fortified antibiotics drops (cefazolin 5% half hourly and amikacin 5% half hourly), chloramphenicol %1.5 ophthalmic pomade three times daily and ciprofloxacin 750 mg per oral twice daily were started and ancillary treatment (dexamethasone 21-phosphate disodium 0.1% eye drops) was also added. Corneal scrapings were inoculated

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into blood agar and Mc Conkey agar but bacterial growth could not detect. Because of no improvement was noted on day 10, fluconazole 0.3% eye drops hourly was added to the treatment. On the day 20 the infiltration was progressed. The patient was started to put on fortified amphotericin B lipid complex (0.15%) eye drops due to conventional amphotericin B flacon was not available in the hospital pharmacy. In spite of intensive therapy, the hypopyon was not regressed.

The patient underwent the corneal biopsy procedure in operation theater and the biopsy material was cultured on potato dextrose agar (PDA) and Sabouraud dextrose agar (SDA) media, which were incubated at two temperatures (37^0C and 22^0C). Giant colony formed on both media. The colony on PDA medium was cream-colored with toroidal pale-brown pigmentation. The colony on SDA medium was salmon-colored with central Brown pigmentation. For identification slide culture was made. This revealed that this fungus had bottle-shaped or urceolate conidia-producing cells, phialides, and produced elliptical conidia and brown chlamydospores with smoothly shaped walls. The basal septum of phialides was absent. These results demonstrated that the fungus was *Lecythophora mutabilis*. The epsilometer test (agar diffusion method) for molds was used to determine the minimum inhibitory concentration (MIC) of the isolate to amphotericin B, fluconazole, itraconazole and voriconazole. The MIC (expressed as microgram per milliliter) for amphotericin, fluconazole, itraconazole and ketaconazole was found to be 0.5, 256, 32 and 0.19 respectively. After the final identification of the fungus, Amphotericin B lipid complex 200 mg intravenously was given daily for two weeks but the infiltration continued to progress with descemetocele formation. Although the filamentous fungi were susceptible to amphotericin B, treatment was considered unsuccessful. The patient was put on voriconazole (1%) eye drops at hourly interval to start with for two weeks and thereafter at two-hourly interval.

The patient was treated topically for 8 weeks with voriconazole, after which the keratitis had improved. The corneal desmatocele remained as a complication of the lesion. The patient subsequently underwent amniotic membran transplantation (Figure 2). Throughout the follow-up period, her compliance did not continue.

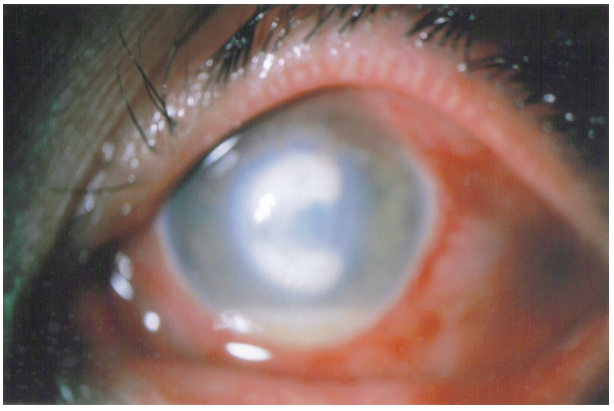

Figure 1. Appearance of eye before treatment

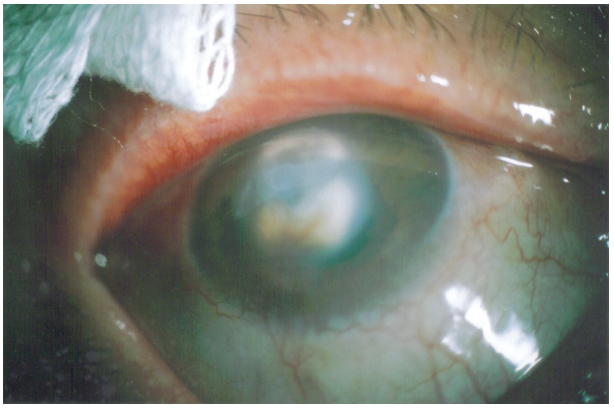

Figure 1. Appearance of eye before treatment

DISCUSSION

Fungal keratitis is a sight-threatening infection that is often difficult to treat. The ultimate goal in the treatment is to conserve vision. Currently, the available antifungal therapies remain inadequate. The greatest clinical experience has been occurred with topical and systemic amphotericin B.[1,6] Amphotericin B has poor ocular penetration after intravenous (IV) administration and, hence, the administration of higher doses may be required to ensure adequate concentration of amphotericin B in the eye; however, IV administration of high-dose amphotericin B is known to cause severe renal toxicity, which can occur in up to 80% of patients. The lipid formulation of amphotericin B now available for clinical use may offer therapeutic advantages. Due to their reduced nephrotoxicity and different pharmacodynamic properties, higher doses of the parent compound may be delivered to infected tissues. Only two clinical case reports on the use of systemic am-

photericin B lipid complex in the treatment of fungal endophthalmitis have been published.[7, 8]

Amphotericin B eye drops are manufactured extemporaneously by hospital pharmacy departments. The most commonly prescribed concentration of the eye drops for fungal keratitis is 0.15%.[1] This patient was treated with topical and systemic amphotericin B lipid complex but that did not prove to be effective in eradicating the mycosis. This result may be due to penetration of amphotericin B lipid complex through the cornea is poor.[1,6] The reported clinical experience of intravitreal injection of AmB-d in humans is limited to case reports and small case series.[6]

Recently, there has been increasing interest in the use of voriconazole for keratitis. Voriconazole has an excellent broad spectrum of antifungal activity and is active against species that are known to be resistant to the other antifungal agents commonly used in fungal keratitis.[12,6,9,10] Voriconazole is increasingly being used, orally in particular, against fungal keratitis. Oral voriconazole is highly bioavailable (96%) and has demonstrated good penetration into the different parts of the eye with sufficient concentrations achieved. However, oral voriconazole can be associated with side effects such as enhanced light perception, color vision changes, visual blurring, skin rash, and hepatotoxicity, which are all transient in nature.[1,2,6]

Voriconazole eye drops, manufactured extemporaneously and used in an off-label manner, have also been prescribed for the treatment of keratitis, with promising results.[1,2,6,9-11] A recent study reported the penetration of voriconazole 1% eye drops administered hourly into the noninfected eye. The eye drops demonstrated a favorable penetration profile, with a trough aqueous humor concentration of 1.90 ± 1.12 μg/mL.[11]

Significantly, this case demonstrates the effectiveness of topical voriconazole, as it resulted in the patient's good and rapid recovery when amphotericin B lipid complex treatment was switched to voriconazole. We suggest that voriconazole 1% eye drops may be a good alternative treatment for patients with fungal keratitis in which progress has halted or regressed despite a regimen of amphotericin B.

Topical voriconazole may have a larger role to play than just as adjunctive therapy to systemic voriconazole. It is a promising, cost-effective option for the management of fungal keratitis, even when caused by *Lecythophora mutabilis*. Our report provides encouraging data regarding the potential of topical voriconazole 1% in the treatment of fungal keratitis.

Conflict of interest

There is no financial or proprietary interest in any materials used in this article

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