Voriconazole Curative Treatment for Acremonium Species Keratitis Developed in a Patient with Concomitant Staphylococcus aureus Corneal Infection: A Case Report

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Abstract. The case of a 49-year-old male Caucasian, with more than a 3-year history of recurrent keratoconjunctivitis treated with steroids, antibiotics and miidriatics, is reported. A combined Acremonium spp. and S. aureus infection was detected. After unsuccessful therapy with fluconazole, the Acremonium spp. infection was eradicated by voriconazole treatment. To our knowledge, this is the first case report of complete regression of this kind of infection by the use of voriconazole. Therefore, we strongly recommend, in the event of a compatible clinical picture, laboratory testing for mycetes even in the absence of traumatic events, and the use of the new generation azoles, in order avoid a keratoplasty intervention and disease progression to severe endophthalmitis.

Acremonium species is a genus of fungi found worldwide and isolated mostly from soil and dead plants. It is classified as deuteromycetes by some authors, while it is included in the ascomycetes group by others. The genus Acremonium contains 100 species. Few of them are pathogens in humans (A. falciforme, A. kiliense, A. recifei, A. potronii). The clinical features of Acremonium spp. infection may vary including onychomycosis, keratitis, endophtalmitis, endocarditis, meningitis and peritonitis, mostly in immunocompromised patients, such as different organ transplant recipients and HIV-infected patients (1).

Fungal keratitis is a rather unusual disease, occurring either after traumatic ocular events, or developing in the presence of other predisposing factors, such as systemic or topical steroids administration, the use of contact lens, diabetes mellitus, any systemic or local immunosuppressive condition or any ocular surface disease (2). The etiology of keratomycosis varies according to different geographical areas, Fusarium being the most common cause in the USA, Candida and Aspergillus in northern climates and Aspergillus the most frequent pathogen detected in India (3).

Case Report

The case of a 49-year-old male Caucasian, seen in our outpatient clinic, who had more than a 3-year history of recurrent keratoconjunctivitis treated with steroids, antibiotics and miidriatics, is reported. His medical history was unremarkable, except for the diagnosis of uncomplicated psoriasis. However, he reported bilateral ocular pain, reddening of the face, weeping and photophobia, without any reduction of visual acuity.

Bilateral conjunctival hyperemia and ring-shaped corneal injection were found on slit lamp examination. One ulcer and two other small epithelial defects were detected in the right eye. Multiple small perilimbal ulcers, with neovascularization and a yellowish stromal perilimbal infiltrate (about 2 mm diameter), were seen in the inferior sectors of the left eye (Figure 1).

In order to identify any pathogen involved, corneal scraping and conjunctival tampons were performed and plated on agar-chocololate, incubated in a 5% CO2 atmosphere, in B.H.I. broth and agar Sabouraud at 37°C, and under conditions for growth of aerobic micro-organisms. These assays showed the development of Acremonium spp. fungi (after 7 days) and Staphylococcus aureus.

Therapy was administered including itraconazole (100 mg twice a day p.o.), ciprofloxacin eye drops, levofloxacin (500 mg once a day p.o.) and miidriatics. After a 10-day therapy,
no pathological evidence was found in the right eye, even with the fluorescein test. In the left eye, an ulcer was detected in the site of the previous stromal infiltrate with a positive fluorescein test (Figure 2).

After 25 days of therapy, the condition of the left eye worsened with the appearance of two new stromal infiltrates, respectively measuring about 0.5 mm and 2 mm, with positive fluorescein test and the persistence of two previous ulcers, even through clear features of epithelial regeneration were observed. The corneal scrape was repeated and once again Acremonium spp. fungi were isolated.

Thus, 40 days from the first isolation, the patient was sent to a department of infectious diseases where a therapy based on liposomal amphotericin B (3 mg/Kg daily) was started. In the first 24 hours, the patient developed a hypersensitivity reaction (fever, rash). So the treatment was changed to a voriconazole-based therapy (400 mg twice a day as an induction in the first day and then 200 mg twice a day administered i.v. for one week and then p.o.).

An ophthalmologic check-up was performed one month after the beginning of this new therapy. The clinical picture was significantly improved with the persistence only of neovascularization in the sites of the two previous stromal infiltrates with negative fluorescein test. Systemic steroid therapy was then added (prednisone 25 mg a day p.o.) for 10 days.

After 2 months of follow-up, no pathological evidence was detectable (Figure 3). The therapy was discontinued after a further 2 months of follow-up. No relapses developed in the subsequent 6 months following therapy interruption.

Discussion

Fungal keratitis is a rather rare ocular disease, though the incidence is probably underestimated because of the difficulty of laboratory isolation (4). An early diagnosis is extremely important because of the risk of progression to exogenous endophthalmitis, which usually has a poor prognosis (4). However, fungi require a previous alteration of the cornea to develop a keratitis. Usually Acremonium spp.-related keratitis follows traumatic events with the inoculation of contaminated material. Surgical procedures are also reported to be associated with fungal keratitis, as well as systemic and/or loco-
regional immunosuppression, that can also promote this kind of ocular opportunistic infection (5).

In our case, no traumatic event had been reported but a bacterial infection (S. aureus) was identified at the same time as the isolation of the Acremonium spp. Among potential pathogenetic hypotheses, psoriasis may also play a significant role, as it is frequently associated with different ocular inflammations including keratoconjunctivitis (6). However, psoriatic ocular manifestations are reported to respond to a single steroid therapy.

The therapy of Acremonium spp. keratitis has been reported to be unsatisfactory, with frequent relapses and progression to the posterior segment, when fluconazole, amphotericin B, griseofulvin and itraconazole therapy was adopted (7). Keratoplasty combined with pharmacological therapy was reported to be the only curative treatment (8).

We are unaware of any previous case report of complete regression of this kind of infection by using voriconazole, a new triazole-derived drug, that has already been used to treat other mycotic systemic infections caused by "difficult" mycetes (9). Further the infection that we describe developed in the absence of any traumatic events, highlighting the possibility of an opportunistic ocular infection by Acremonium spp. under conditions that infrequently allow the growth and virulence of these mycetes.

We confirm the ineffectiveness of traditional antimycotic therapy to overcome the severe persistent ocular infection caused by Acremonium spp. and report the successful treatment by voriconazole. Voriconazole is a fluoropyrimidine derivative of fluconazole with an extended spectrum of activity, available intravenously and orally with an excellent bioavailability, with a good penetration into tissues including the brain (10) and achieving therapeutic aqueous and vitreous levels in the human eye (11). Therefore, we strongly recommend, in the event of a compatible clinical picture, laboratory testing for mycetes, even in the absence of traumatic events and the use of the new generation azoles in order avoid a keratoplasty intervention and disease progression to a severe endophthalmitis.

References


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