Severe mycotic keratoconjunctivitis caused by *Fusarium* sp. in an immunocompetent child successfully treated with intravenous voriconazole and keratoplasty: case report and short review of the literature

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**Abstract**

**Background:** Pediatric mycotic infections in the eye are uncommon. However, ophthalmic infections by several fungal species have been described in immunocompetent subjects. Mycotic keratitis with or without conjunctivitis (MK) may account for more than 50% of all cases, particularly in tropical and sub-tropical areas. The leading mechanism is trauma. Treatment of MK is managed by medical (antifungal agents) and/or surgical means. This is the first case report of a patient with MK by *Fusarium* spp. successfully treated with keratoplasty and intravenous voriconazole, along with topical natamycin.

**Methods:** Keratoplasty was performed and cultures obtained. Both Blood and Sabouraud Agars were used for cultures, and Lactophenol Cotton Blue Staining for microscopic observation.

**Results:** A healthy, 10 year-old female, from the sub-tropical area of Sinaloa, Mexico, was admitted at both the CODET Vision Institute and the General Hospital of Tijuana, Mexico. Seven days after a direct trauma of the right cornea, the patient complained of progressive blurred vision, burning sensation, and itchiness. Clinical examination showed severe keratoconjunctivitis, and a necrotic slough on the cornea. Fungal colonies grew, and microscopic visualization showed typical ovoid, sickle-cell shaped macroconidia characteristics of *Fusarium* spp. The patient received intravenous voriconazole (200 mg every 12 h) and topical natamycin for 7 days prior and 6 days after keratoplasty. Topical natamycin was continued for 3 weeks. At 1-month follow-up, the patient’s outcome was significantly improved, with 90% vision recovery.

**Conclusion:** This is the first pediatric case report of severe MK by *Fusarium* spp. successfully treated with combined intravenous voriconazole, keratoplasty and topical natamycin.

**Keywords:** Mycotic keratitis, Ophthalmic Fusariosis, Intravenous voriconazole

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by medical (mainly topical antifungal agents) and/or surgical means (keratoplasty). This is the first case report of an immunocompetent patient with keratoconjunctivitis caused by *Fusarium* spp. successfully treated with keratoplasty, intravenous voriconazole, and topical natamycin.

**Methods**

Keratoplasty was performed and cultures were obtained, in addition to intraocular hyaluronic acid administration. Both Blood and Sabouraud Agars were used for cultures. Lactophenol Cotton Blue Staining was used for microscopic observation. A consent form was signed by the patient’s mother permitting publication of pictures of the patient’s eye before and after treatment, as well as fungal microscopic colonies.

**Results**

A previously healthy, HIV-negative, 10-year-old female, from the sub-tropical area of Sinaloa, Mexico, was admitted at both the CODET Vision Institute, and the General Hospital of Tijuana, Mexico. Seven days after a direct, accidental trauma of the right cornea from the branch of a plant, the patient complained of progressive blurred vision, along with burning sensation and itchiness on the right eye. Clinical examination showed severe, deep keratoconjunctivitis, and a necrotic slough above the surface of the cornea (see Figure 1).

Ophtalmologic procedure: A 3 mm corneal incision was made, an immediate corneal swab was taken for culture, then placed viscoelastic (hyaluronic acid) to form the anterior segment, extracted with 0.12 forceps, accumulated discharge in the anterior segment, washed with balanced saline solution. At the end of the procedure, suture with nylon 10-0 was placed, and the nut of the suture was inverted so it will not generate friction on the surface of the eye with the eyelid.

Fungal colonies grew on both Blood and Sabouraud Agars, and microscopic visualization showed typical ovoid, sickle-cell shaped macroconidia characteristics of *Fusarium* spp. (see Figure 2). The patient received intravenous voriconazole (200 mg every 12 h) and topical natamycin (every 6 h) for seven days prior to surgery and an additional 6 days after keratoplasty. Topical natamycin was continued for 3 weeks. The patient’s outcome was significantly improved, with 90% vision recovery at the 1-month follow-up appointment (see Figure 3).
Discussion

Ophthalmic mycoses in non-immunosuppressed children, although uncommon, have been associated with high morbidity and even blindness.\(^1,2,4\) Keratoconjunctivitis is the most frequent presentation, but the orbit, lids, lacrimal apparatus, sclera and intraocular structures may also be involved.\(^1,2\) Any review of the literature on ophthalmic mycosis is hampered by several factors. First, there are very few controlled or comparative studies, and much of the information comes from single case reports.\(^1,2,4\) Second, many fungal genera and species have been implicated in ocular infections and it is difficult to give appropriate weight to the significance of these organisms.\(^1,2\) An important publication from 1998 listed 105 species in 35 genera of fungi causing mostly keratitis. However, the criteria to define whether these fungi were pathogenic or contamination were not clearly delineated.\(^3\) A review from 1980 of more than 300 reports pertaining to human fungal infections of the eye published from the late 1940s to 1979 encountered similar difficulties.\(^6\)

Nevertheless, there are consistently six genera associated with fungal keratoconjunctivitis (as well as infecting other ocular structures). Of those infections, most are associated with accidental trauma and soil contamination:\(^4–7\):

- *Fusarium* spp.
- *Aspergillus* spp.
- *Scedosporium* spp.
- *Paecilomyces* spp.
- *Acremonium* spp.
- *Candida* spp.

As mentioned, the genera *Fusarium* spp. is considered to be the most frequent, with most reports coming from India, Bangladesh, Nepal, Paraguay, Ghana, Singapore, and Sri Lanka.\(^7–13\) Trauma and further contamination-infection has been the most common risk factor reported in these studies.

Mycotic keratitis is treated by medical and surgical means. Topical natamycin 5% or Amphotericin-B 0.15% are usually selected as first line antifungal drugs for keratitis caused by filamentous fungi, including *Fusarium* sp.

An analysis was made of 85 patients reported in the literature with keratitis caused by *Fusarium* species. A total of 29 patients had superficial keratitis, of which 22 (76%) received topical antifungals alone and seven required keratoplasty. Interestingly, none of these patients received natamycin. A total of 49 patients had keratitis with deep lesions. Of which six received topical natamycin. Adequate response to topical natamycin was seen in four. The remaining 43 patients did not receive natamycin at any time. Ten (23%) responded to medical therapy alone, and all other patients required keratoplasty.\(^14\) Intravenous antifungal agents were rarely used in either of these studies.

In the case series by Rosa and colleagues in Miami, Florida, 79 patients were reported to have keratitis to *Fusarium* spp. In this publication, all patients with profound keratitis required keratoplasty in addition to both topical natamycin and systemic antifungals. The average duration of treatment was 38 days. None of these patients received intravenous voriconazole.\(^15\)

Voriconazole, either as 1% eye drops or intrastromal, has been reported as a potentially effective for mycotic keratitis.\(^16\) Early human and animal data have reported concentrations of voriconazole in both aqueous and vitreous humors of 40–100% of those observed in serum, while natamycin has shown high concentration in both cornea and conjunctiva but only when used topical.\(^16\) Reports of intravenous use of voriconazole for keratitis caused by *Fusarium* spp. are scarce. There is only one such report from Chile; however, corneal opacity persisted after treatment in that case.\(^17\) Sequence of both successful and failure treatments with several antifungal approaches, as well with excellent photographs, has also been published, but without using intravenous voriconazole.\(^18\)

Our patient received both intravenous voriconazole and topical natamycin pre and post keratoplasty, followed by 3 weeks of topical natamycin. The outcome was 90% visual recovery, making our case the first successful report of combined therapy (surgery, topical natamycin, and intravenous voriconazole) for treatment of keratoconjunctivitis caused by *Fusarium* spp.

Conclusion

This is the first pediatric case report of severe keratoconjunctivitis by *Fusarium* spp. successfully treated with keratoplasty, intravenous voriconazole, topical natamycin. This combined therapy may be considered for future cases and/or evaluated for a clinical trial.
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