An intracameral approach for recalcitrant fungal keratitis

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ABSTRACT

Purpose: To describe 2 cases of recalcitrant fungal keratitis successfully treated with intracameral Amphotericin B.

Methods: Interventional case series.

Results: A 59-year-old female and a 41-year-old male each presented with fungal keratitis, caused by Bipolaris spp. and Fusarium spp. respectively. Both cases were unresponsive to topical antifungals, causing persistent discomfort and decreased vision. The two patients subsequently received a single dose of intracameral amphotericin B (ICAMB) 10mcg/0.1 mL, in addition to continued topical natamycin. Both patients had remarkable results following ICAMB, with best corrected visual acuity of 20/20 and full corneal reepithelization following treatment.

Conclusions: We report 2 cases of intractable fungal keratitis that benefited from intracameral injections of amphotericin B. This route of delivery appears to be very effective because the medication is delivered directly to the deeper layers of the cornea, where fungal infections tend to reside, and where topical and systemic routes have difficulty accessing.

1. Introduction

Fungal Keratitis is a serious and potentially sight threatening infection that accounts for up to 45% of all corneal infections worldwide. The rate of infection varies by geographical location and socio-economic class, with increased occurrences in marginalized populations and warmer/tropical climates. A unique and problematic aspect of mycotic (vs. bacterial) keratitis is the ability of fungi to penetrate through deeper layers of the stroma and Descemet’s membrane, resulting in a higher incidence of corneal perforation and endophthalmitis. While topical antifungal drops are the current standard of care, their limited stromal penetration have resulted in limited success in treating fungal keratitis.

In this paper, we present two cases of intractable fungal keratitis successfully treated with intracameral injections of amphotericin B (ICAMB).

2. Findings

2.1. Case 1

A 59-year-old female with a history of soft contact lens wear was referred to us with complaints of pain, foreign body sensation, and decreased vision in her right eye. She had initially seen an optometrist two days prior and was placed on topical gatifloxacin (0.5%) and prednisolone acetate (1%) four times a day. The patient had no history of ocular trauma, past ocular or systemic disease, but frequently slept with her contact lenses. Examination revealed best corrected visual acuity (BCVA) of 20/400 in the right eye. Slit lamp examination showed a large corneal stromal infiltrate extending 60–70% in depth in the inferotemporal quadrant, with a 2.5mm × 3mm overlying epithelial defect, mild stromal thinning, and mild surrounding stromal edema. The anterior chamber had moderate cell and flare, as well as a 10% hypopyon. An endothelial plaque was not visualized. Fundus exam was unremarkable. Corneal scrapings were sent to be grown on blood agar, chocolate agar, and Sabouraud agar, and resulted in growth of Bipolaris species. The patient was placed on topical natamycin 5% hourly, topical voriconazole 1% hourly, and oral voriconazole 100mg twice daily. Over the course of the next five weeks, despite resolution of the hypopyon, no improvement was noted in the infiltrate (Fig. 1) and the patient developed severe, intractable pain.

Before performing a therapeutic penetrating keratoplasty, we decided to administer an injection of intracameral amphotericin B in the office. The concentration of amphotericin B used was 10mcg/0.1 mL.
same as that used in Yoon et al. After administering topical tetracaine (0.5%), ofloxacin (0.3%), and betadine (5%), a 0.8mm self-sealing limbal paracentesis was made with a sterile superblade, and 0.1mL of amphotericin B (10mcg/0.1mL) was injected into the anterior chamber. Treatment with topical natamycin, topical and oral voriconazole was continued.

One day following the injection, the patient developed a small (3–5%) hypopyon. Three days later, the hypopyon resolved and the corneal infiltrate decreased in size. One week after injection, her vision improved to 20/60 and her pain had resolved. Three weeks after injection, the epithelium was intact and a mild stromal scar remained. Four weeks after injection, her vision improved to 20/20.

2.2. Case 2

A 41-year-old male with history of soft contact wear presented to us with a one-week complaint of pain, redness, and photophobia in his right eye. He had no past medical or ocular history but recalled an incident a few days prior in which he fell off his dirt bike into some swampy, muddy water. He also frequently slept in his contact lenses and used well water at home. He had been treated by his optometrist with well water at home. He had been treated by his optometrist with 

Fungal keratitis remains a significant cause of corneal morbidity due to the ability of fungi to penetrate deep into the posterior cornea and anterior chamber, and limited penetration of topical antifungal agents. Systemic routes have poor bioavailability into the anterior chamber and may have serious systemic side effects. Additionally, as seen in the MUTT II study, oral voriconazole is not helpful in cases of severe fungal keratitis. Subconjunctival injections have limited penetration into the anterior chamber, and have adverse effects such as persistent periorcular inflammation, epithelial ulcerations, and even tissue necrosis. Intra-stromal injections of antifungals have not been shown to be more effective than topical treatments. Lastly, penetrating keratoplasties are invasive, risky, and performed as a last resort.

In each of our cases, the patients had a deep stromal infiltrate that did not respond to prolonged aggressive topical antifungal therapy but resolved promptly after a single intracameral injection of amphotericin B.

Previous reports have demonstrated effectiveness of intracameral administration of antifungals for fungal keratitis. Yoon et al demonstrated that intracameral amphotericin B (ICAMB) is effective in reducing the time of hypopyon resolution and improving final outcomes. Shao et al showed that ICAMB injection leads to faster healing time and resolution of hypopyon compared with topical amphotericin B. Sharma et al demonstrated that ICAMB can be safely administered to improve healing of the cornea and prevent the progression of ulcers, with no complications in more than 80% of patients. Observational adverse effects of ICAMB were mostly limited to post injection pain and discomfort, typically resolved within hours. Other potential complications may include anterior chamber reaction, transient hypopyon formation, secondary infection through the keratolimbal paracentesis, bleeding from mechanical trauma to the iris, and formation of anterior subcapsular cataract in the unlikely event that the needle comes in contact with the anterior lens capsule. Although intracameral anti-fungal injections have been reported for fungal keratitis, this treatment may not be well known amongst many ophthalmologists and cornea specialists.

In conclusion, we believe that intracameral amphotericin B should be considered for deep corneal fungal infections which are recalcitrant to aggressive topical antifungal therapy.

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