

Alternaria keratitis and hypopyon after clear-cornea phacoemulsification

Evangelina Espósito, MD, J. Pablo Maccio, MD, Rodolfo Monti, MD, Laura Cervi, PhD, Horacio M. Serra, PhD, Julio A. Urrets-Zavalía, MD, PhD

We report a case of *Alternaria* keratitis and hypopyon following clear-corneal cataract surgery. A 66-year-old woman presented with a painful red left eye several months after uneventful self-sealing clear-corneal phacoemulsification that was unresponsive to prolonged treatment with topical/oral quinolones and topical corticosteroids. A full-thickness stromal white dense infiltrate in the area of the intrastromal tunnel incision and a 2.0 mm hypopyon were observed. Culture from corneal scrapings revealed *Alternaria* species. Treatment included topical and subconjunctival injections of amphotericin-B (5 mg/mL) and 200 mg of oral ketoconazole. Complete resolution of the corneal infiltration and hypopyon was observed after 30 days of treatment, with no recurrence during 6 years of follow-up. To our knowledge, this is the first report of *Alternaria* species keratitis complicating self-sealing clear-corneal cataract surgery. Topical and subconjunctival injections of amphotericin-B and oral ketoconazole were effective in resolving the corneal abscess and anterior chamber inflammatory reaction.

Financial Disclosure: No author has a financial or proprietary interest in any material or method mentioned.

J Cataract Refract Surg 2014; 40:331–334 © 2014 ASCRS and ESCRS

The variety of fungi isolated from patients with severe keratitis is extensive, and a consensus on appropriate treatment is not well defined.¹ The isolates are essentially saprophytic soil and plant fungi, not usually involved in human infections.² In a large series from India,³ *Fusarium* and *Aspergillus* species were the most common etiologic agents found in fungal keratitis (36.6% and 30.4%, respectively), followed by dematiaceous fungi (15.7%).

Alternaria species is a filamentous dematiaceous ubiquitous mold that is isolated frequently from air, soil, and decomposing vegetation^{4,5} and from human skin.² It is infrequently involved in corneal infections

and generally may infect spontaneously or following trauma, more frequently in tropical regions.³

Alternaria alternata is most commonly isolated from human infections, especially as opportunistic pathogens,³ particularly in immunosuppressed patients and contact lens wearers.^{3–5} Nontraumatic *Alternaria* keratitis was first reported in 1975 in an eye that had been treated for herpetic stromal keratitis with topical idoxuridine and corticosteroids⁶ and has been observed in leprosy⁷ and in diabetic patients.^{3,8–11}

Postsurgical *Alternaria* corneal infection has been reported following cataract surgery,¹⁰ corneal transplantation,^{12,13} and laser in situ keratomileusis.^{14,15} Although ocular fungal infections following ocular surgery are rare, they frequently have a poor prognosis, generally as the consequence of misdiagnosis and inadequate treatment, especially in cases previously treated with topical corticosteroids that may contribute to the fungus spread before clinical signs are evident.^{1,3,9} In some cases, serial smears may be necessary to obtain a positive diagnosis.⁵

CASE REPORT

A 66-year-old woman with a recent diagnosis of diabetes was referred to our department because of a painful, tearing, inflamed left eye. Uneventful self-sealing clear-corneal

Submitted: July 20, 2013.

Final revision submitted: July 25, 2013.

Accepted: July 26, 2013.

From the Department of Ophthalmology (Espósito, Maccio, Monti, Urrets-Zavalía), University Clinic Reina Fabiola, Catholic University of Córdoba and CIBICI-CONICET (Cervi, Serra), Faculty of Chemical Sciences, National University of Córdoba, Córdoba, Argentina.

Corresponding author: Julio A. Urrets-Zavalía, MD, PhD, Department of Ophthalmology, University Clinic Reina Fabiola, Catholic University of Córdoba, Oncativo 1248, 5000 Córdoba, Argentina. E-mail: julioaurrets@gmail.com.

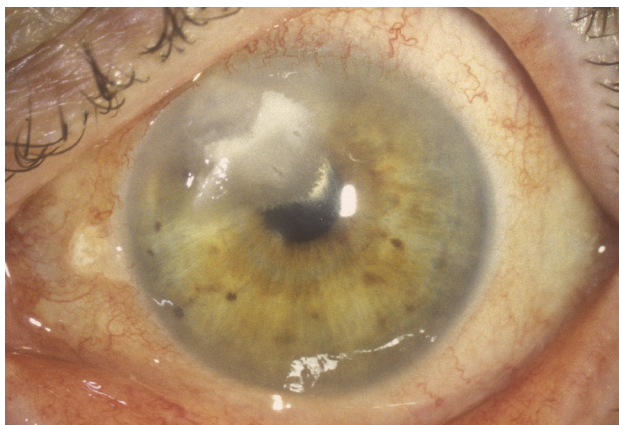


Figure 1. Left eye showing superonasal, juxtalimbal, deep stromal, dense white snowflake-like infiltrate with fernlike margins in the area of the cataract surgery incision. Note the V-shaped mark of the distal end of the intrastromal tunnel, delineated by the deep white stromal infiltration. Hypopyon is not visible because the picture was obtained 1 week after initiation of antifungal treatment.

phacoemulsification with in-the-bag implantation of a foldable hydrophobic acrylic posterior chamber intraocular lens (IOL) had been performed in the left eye 24 weeks earlier. The corrected distance visual acuity (CDVA) at the end of the first postoperative week was 20/25. Blurred vision, red eye, and pain developed in the eye 15 days after surgery. Streptococcal infection was suspected, but 5 months of treatment with topical ciprofloxacin-dexamethasone and oral ciprofloxacin had been ineffective and the inflammation had progressed.

At the time of referral, the CDVA was 20/32 in the right eye and 20/200 in the left eye and the intraocular pressure was 16 mm Hg and 14 mm Hg, respectively. Besides a nuclear cataract, the biomicroscopy and the fundus findings in her right eye were unremarkable. In the left eye, a superior nasal juxtalimbal full-thickness stromal, dense, cotton wool-like infiltrate in the area of the intrastromal corneal tunnel incision and extending deeply to the central cornea (Figure 1) with diffuse fernlike margins (Figure 2) was observed. Translucent filaments extended from the underlying endothelium through the anterior chamber without reaching the iris, and a heaped-up central 2.0 mm hypopyon was present (not shown). The overlying epithelium appeared intact and did not stain with topical 0.25% fluorescein. Conjunctival and episcleral congestion was observed principally in the adjacent area.

After 2 consecutive failed corneal scrapings, a third deeper scraping revealed significant amounts of septate hyphae. After seeding in chocolate agar and Sabouraud agar, culture grew *Alternaria* species. Treatment was started with topical amphotericin-B (5 mg/mL) every 2 hours and 0.3 mL (5 mg/mL) injected under the juxtalimbal superotemporal bulbar conjunctiva. Oral ketoconazole 200 mg every 12 hours was concomitantly initiated. During the first week of treatment, rapid improvement was observed, especially clearing of the hypopyon and anterior chamber filaments. The 0.3 mL amphotericin-B subconjunctival injection was repeated 7 days later. Topical drops of amphotericin-B 6 times a day and oral ketoconazole were continued for a total of 30 days and discontinued when the left eye was calm and without

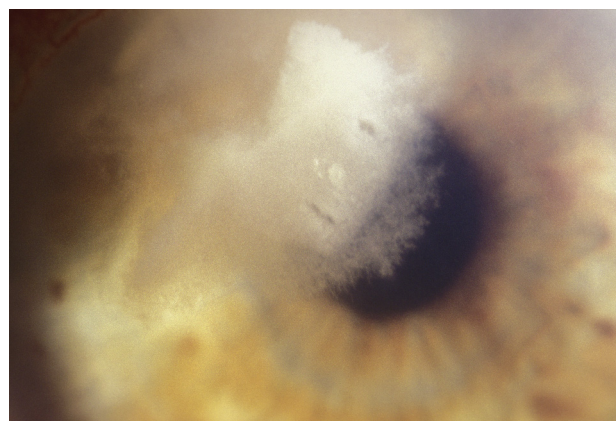


Figure 2. Higher magnification of the left eye showing the fernlike or feathery inferior margin of the lesion.

corneal stromal infiltration. A diffuse and irregular opacity of moderate density of the upper nasal quadrant extending through the central cornea with mild midstroma neovascularization resulted in the area of the previous abscess (Figure 3). The anterior chamber was clean, and the rest of the examination was unremarkable.

The final CDVA in the left eye was 20/63 after a follow-up of 6 years. The patient refused further surgical treatment in the eye.

DISCUSSION

Infectious complications after cataract surgery are generally a serious threat to vision and the eye's integrity. Fungal infection of a self-sealing scleral or corneal incision in cataract surgery is rare; *Aspergillus* and *Candida* have been most frequently found in 1 series in India.⁹ In 2009, Tu¹⁰ reported 3 cases of *Alternaria* keratitis, 1 of which was the case of a 70-year-old man with glaucoma, long-standing diabetes, heart disease, prostate cancer, and concurrent chemotherapy for rectal cancer who developed a "3 mm × 3 mm paracentral corneal ulcer with feathery edges temporal to the pupillary margin" in his right eye 3 months after uneventful phacoemulsification and in whom corneal smear culture from the ulcer revealed *Alternaria* species. However, in that case no relationship between the corneal ulcer and the surgical procedure was inferred and no anterior chamber compromise was mentioned; the *Alternaria* corneal ulcer in that case may not have been directly related to the cataract surgical procedure.

In our patient, symptoms started relatively soon after the surgical intervention. Long-term treatment with topical/systemic quinolones and topical corticosteroids may have facilitated the proliferation of and infection by an intraoperative inoculated *Alternaria* species. The corneal abscess compromised the entire thickness of the corneal stroma with no apparent overlying epithelial defect, spreading from the surgical

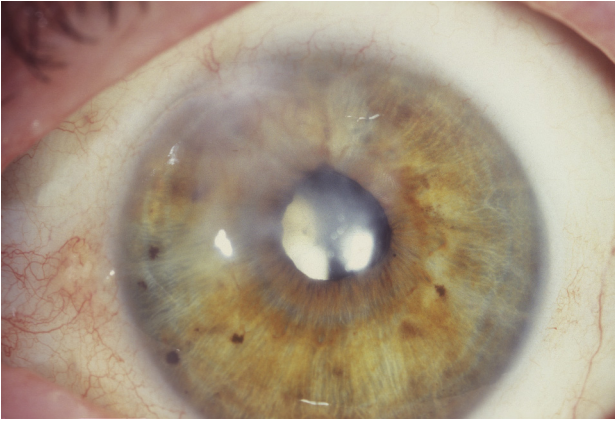


Figure 3. Calm left eye with complete resolution of corneal abscess that left a moderately dense stromal opacity (9 months later).

incision area to the central cornea, delineating the intrastromal surgical tunnel. This was more evident after a few days of treatment because of the decreasing density of the intrastromal abscess (Figure 1).

Various sources of contamination may explain a fungal postsurgical corneal infection.^{9,16} Possible sources from the host include eyelid borders and conjunctiva, especially in associated general conditions such as immunosuppression, diabetes, or leprosy, and after prolonged use of topical corticosteroids and lagophthalmos.^{3,9}

Contaminated surgical instruments, IOLs, or irrigating solutions, and breaches in the sterile technique during the surgical procedure are possible sources of a postsurgical fungi infection.⁹ A poorly constructed wound, loose or broken sutures, and dacryocystitis have also been identified as important predisposing factors.⁹

Airborne propagation from ventilator systems and unattended air conditioning filter systems in the operating room have been related to postsurgical fungal infections.¹⁶ As initial symptoms of corneal infection in our patient started relatively soon after surgery and the patient denied having been exposed directly to an air conditioning source after surgery or suffering an ocular trauma, contamination of the surgical wound may have happened in the surgical room from a contaminant air ventilating system or by a contaminated surgical blade.

Development of *Alternaria* keratitis is insidious, sometimes leading the patient to consult several weeks after the possible time of inoculation, and presenting symptoms may be decreased visual acuity, tearing, photophobia, or a painful red eye.^{1,3,9,10} Clinical presentation may vary, ranging from a corneal ulcer with diffuse borders and some infiltrate in the anterior stroma to a dense cotton wool abscess with feathery edges and eventually hypopyon.^{3,5,17}

Due to rapid fungal corneal penetration, fungal keratitis is the most likely external ocular infection complicated by infective hypopyon.¹⁷ Whether aseptic or infectious, hypopyon is commonly observed in fungal keratitis,^{3,7,18} especially in cases produced by *Fusarium* (59.6%) and *Aspergillus* (61%).¹⁸ Other risk factors for hypopyon include longer duration of symptoms and larger size of lesion.¹⁸ In *Alternaria* keratitis, hypopyon has been observed in 29.4% of cases, particularly in patients with longer duration of symptoms; half the cases have been septic.¹⁸ Our patient presented hypopyon and filaments in the anterior chamber despite having been treated with topical corticosteroids for several months. Although no aqueous humor material was obtained and consequently the nature of the hypopyon was ignored, the hypopyon resolved rapidly after initiation of the antifungal treatment.

Several treatments have been proposed for fungal keratitis depending on its severity and causative agent.¹ Every broad-spectrum antifungal medication may not be effective in all cases.¹⁰ In *Alternaria* keratitis, good results have been obtained with topical drops of fluconazole 0.02%,¹⁰ voriconazole 1%,⁵ ketoconazole,⁷ and amphotericin B.⁸ Topical caspofungin 0.5% associated with intrastromal voriconazole was used in a case with multiple failed treatments.¹⁰ Combined topical with systemic antifungal treatment for *Alternaria* keratitis is generally used in severe or resistant cases and in relapses.^{4,5,13,19} Although natamycin 5% is currently proposed for filamentous fungal keratitis,¹ it has generally been ineffective in *Alternaria* keratitis.^{4,5,10,19} A combination of topical amphotericin B associated with subconjunctival injection of fluconazole may have the advantage of offering a broader spectrum of antifungal coverage, lowering the risk for complications observed with systemic use of amphotericin B.^{1,8,10,11} In our patient, treatment with eyedrops and subconjunctival injections of amphotericin B associated with ketoconazole was very effective in resolving the keratitis and its probable extension to the anterior chamber. The average duration of medical treatment in *Alternaria* keratitis is 3 to 4 weeks.^{1,4,7,8,11}

In conclusion, *Alternaria* species may produce a severe postsurgical corneal infection that may diffuse intraocularly or produce a severe inflammatory response in the anterior chamber and should be suspected in case of a torpid postsurgical corneal infiltration unresponsive to wide-spectrum antibiotics or natamycin. In our case, despite previous prolonged treatment with topical corticosteroids and quinolones, topical and adjacent subconjunctival injection of amphotericin and oral ketoconazole proved to be effective for the complete resolution of both the corneal abscess and anterior chamber signs of

endophthalmitis. To our knowledge, this is the first report of an *Alternaria* species keratitis complicating a self-sealing clear-corneal cataract surgery.

REFERENCES

1. Tuli SS. Fungal keratitis. *Clin Ophthalmol* 2011; 5:275–279. Available at: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3065567/pdf/opth-5-275.pdf>. Accessed September 23, 2013
2. Robertshaw H, Higgins E. Cutaneous infection with *Alternaria tenuissima* in an immunocompromised patient. *Br J Dermatol* 2005; 153:1047–1049
3. Garg P, Gopinathan U, Choudhary K, Rao GN. Keratomycosis: clinical and microbiologic experience with dematiaceous fungi. *Ophthalmology* 2000; 107:574–580
4. Ozbek Z, Kang S, Sivalingam J, Rapuano CJ, Cohen EJ, Hammersmith KM. Voriconazole in the management of *Alternaria* keratitis. *Cornea* 2006; 25:242–244
5. Yildiz EH, Ailani H, Hammersmith KM, Eagle RC Jr, Rapuano CJ, Cohen EJ. *Alternaria* and *Paecilomyces* keratitis associated with soft contact lens wear. *Cornea* 2010; 29:564–568
6. Azar P, Aquavella JV, Smith RS. Keratomycosis due to an *Alternaria* species. *Am J Ophthalmol* 1975; 79:881–883
7. Daniel E, Mathews MS, Chacko S. *Alternaria* keratomycosis in a lepromatous leprosy patient. *Int J Lepr Other Mycobact Dis* 1997; 65:492–494. Available at: <http://ila.ilsl.br/pdfs/v65n4a09.pdf>. Accessed September 23, 2013
8. Zahra LV, Mallia D, Hardie JG, Bezzina A, Fenech T. Keratomycosis due to *Alternaria alternata* in a diabetic patient. *Mycoses* 2002; 45:512–514
9. Garg P, Mahesh S, Bansal AK, Gopinathan U, Rao GN. Fungal infection of sutureless self-sealing incision for cataract surgery. *Ophthalmology* 2003; 110:2173–2177
10. Tu EY. *Alternaria* keratitis: clinical presentation and resolution with topical fluconazole or intrastromal voriconazole and topical caspofungin. *Cornea* 2009; 28:116–119
11. Mahdy RA, Nada WM, Wageh MM. Topical amphotericin B and subconjunctival injection of fluconazole (combination therapy) versus topical amphotericin B (monotherapy) in treatment of keratomycosis. *J Ocul Pharmacol Ther* 2010; 26:281–285
12. Ando N, Takatori K. Keratomycosis due to *alternaria alternata* corneal transplant infection. *Mycopathologia* 1987; 100:17–22
13. Konidaris V, Mersinoglou A, Vyzantiadis T-A, Papadopoulou D, Boboridis KG, Ekonomidis P. Corneal transplant infection due to *alternaria alternata*: a case report. *Case Rep Ophthalmol Med* Vol. 2013. Article ID 589620. Available at: <http://downloads.hindawi.com/crim/ophmed/2013/589620.pdf>. Accessed September 23, 2013
14. Verma K, Vajpayee RB, Titiyal JS, Sharma N, Nayak N. Post-LASIK infectious crystalline keratopathy caused by *Alternaria*. *Cornea* 2005; 24:1018–1020
15. Kocaturk T, Pineda R II, Green LK, Azar DT. Post-LASIK dendritic defect associated with *Alternaria*. *Cornea* 2007; 26:1144–1146
16. Kelkar U, Bal AM, Kulkarni S. Fungal contamination of air conditioning units in operating theatres in India. *J Hosp Infect* 2005; 60:81–84
17. Ramsay A, Lightman S. Hypopyon uveitis. *Surv Ophthalmol* 2001; 46:1–18
18. L-j Xu, Song X-s, Zhao J, Sun S-y, Xie L-x. Hypopyon in patients with fungal keratitis. *Chin Med J* 2012; 125:470–475. Available at: http://www.cmj.org/ch/reader/create_pdf.aspx?file_no=20122337461790&flag=1&year_id=2012&quarter_id=3. Accessed September 23, 2013
19. Bunya VY, Hammersmith KM, Rapuano CJ, Ayres BD, Cohen EJ. Topical and oral voriconazole in the treatment of fungal keratitis. *Am J Ophthalmol* 2007; 143:151–153



First author:

Evangelina Espósito, MD

Department of Ophthalmology, University Clinic Reina Fabiola, Catholic University of Cordoba, Cordoba, Argentina