CASE REPORT

Candida keratitis after Descemet stripping with automated endothelial keratoplasty

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Purpose: *To report a case of Candida albicans keratitis after Descemet stripping with automated endothelial keratoplasty (DSAEK) due to fungal contamination of the donor cornea.*
Methods: *Case report.*
Results: *A 73-year-old woman underwent phacoemulsification with intraocular lens (IOL) implantation and DSAEK with 1 week difference. Ten days after DSAEK surgery, the culture of the donor corneoscleral rim revealed Candida albicans contamination and a small whitish infiltrate was noted within the interface. Despite conservative treatment with oral and systemic voriconazole, the infection was present outside the interface and inside the anterior chamber. Hot penetrating keratoplasty (PKP) was performed and the infection was eradicated. However, due to uncontrolled high intraocular pressure, a new PKP had to be performed, the IOL was removed, and an Ahmed valve was implanted (by pars plana vitrectomy). The anterior cap of the same donor cornea was used to perform a tectonic superficial anterior lamellar keratoplasty and the recipient did not have any problem related to fungal infection.*
Conclusions: *The diagnosis of fungal keratitis should be taken into account once a small infiltrate is seen in the interface of any kind of lamellar keratoplasty. It is not clear whether it is better to treat it conservatively or aggressively.*

Keywords: *DSAEK, Candida keratitis, Fungal infection*

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INTRODUCTION

Candida keratitis is a rare but recognized complication of corneal transplantation and has been described after both penetrating and lamellar keratoplasty (1).
Infection may result from either fungal contamination of the donor cornea or from secondary infection of an epithelial defect by ocular surface flora (2). The present report describes a patient who developed *Candida albicans* keratitis after Descemet stripping with automated endothelial keratoplasty (DSAEK) due to fungal contamination of the donor cornea.

Case Report

A 73-year-old woman was referred to the cornea/external disease department due to cataract and advance Fuchs endothelial syndrome in both eyes. Her corrected distance visual acuity (CDVA) was 0.30 in both eyes. She underwent phacoemulsification with intraocular lens (IOL) implantation and DSAEK with 1 week difference in her right eye, and her CDVA was 0.85.
Four months later, she was scheduled to receive the same surgery in the left eye. Phacoemulsification and IOL implantation was performed without any problem and, 1 week later, a donor corneoscleral rim stored in Optisol media was brought from the eye bank (4 days after donor death from respiratory failure). Donor serologic tests, which include HIV, hepatitis B surface antigen, hepatitis C virus, and rapid plasma reagin, were all negative. Donor endothelial cell count was 2,242 cells/mm^2. Donor corneoscleral rim was mounted on an artificial anterior chamber (Ziemer Ophthalmic Systems AG, Port, Switzerland) and a

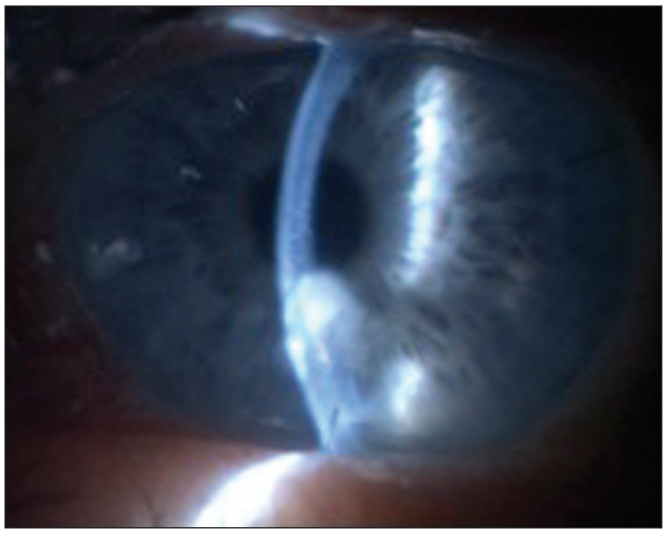

Fig. 1 - *A small whitish infiltrate was noted within the interface 10 days after Descemet stripping with automated endothelial keratoplasty.*

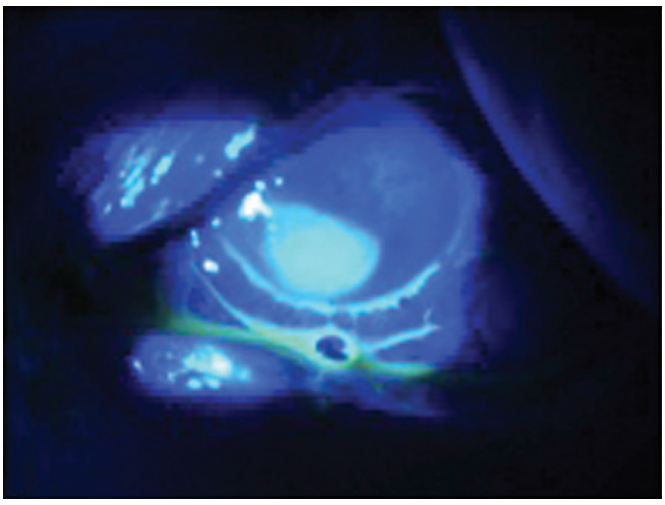

Fig. 2 - *Fourteen days after Descemet stripping with automated endothelial keratoplasty, the infiltrate was larger and an epithelial defect appeared.*

free cap was created with the Amadeus II microkeratome using the 500-µm blade holder. The posterior lamellar graft was punched from the endothelial side with an 8-mm Hessburg-Barron trephine, folded, and inserted with the pull-through technique using a Busin glide through a 4.50-mm clear cornea inferior incision.

On the first postoperative day, the donor disc was well attached and the patient was instructed to instill tobramycin/dexamethasone drops (TobraDex; Alcon, Fort Worth, Texas, USA) to be used 4 times daily. The third postoperative day, slit-lamp examination demonstrated a well-positioned donor lenticule and a soft overlying stromal edema. The patient was instructed to continue with the same treatment and to return in a week. On the 10th postoperative day, the culture of the donor corneoscleral rim revealed *C albicans* contamination and a small whitish infiltrate was noted within the interface (Fig. 1). The patient did not complain of blurred vision and the eye was quiet. An infectious infiltrate without clinical endophthalmitis was suspected, and treatment with topical voriconazole 1% every hour and oral voriconazole 200 mg/d were prescribed.

We do not routinely perform fungal cultures for the scleral-corneal rings; only for the presence of bacteria. Once the infiltrate was clinically diagnosed, a request for fungal culture was send to the laboratory, due to the high clinical suspicion of fungal contamination. *C albicans* was detected in 48 hours.

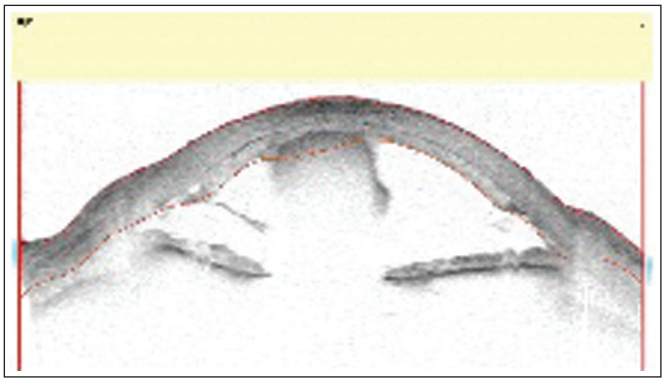

Fig. 3 - *Time-domain anterior segment optical coherence tomography (Visante, Zeiss, Gena, Germany) 21 days after Descemet stripping with automated endothelial keratoplasty shows that the infection was outside the interface and inside the anterior chamber.*

Fourteen days after DSAEK, the infiltrate was larger and an epithelial defect appeared (Fig. 2). The patient complained of pain and blurred vision and intracameral voriconazole 0.1% (0.2 mL) was injected inside the anterior chamber (AC). The patient continued with the same topical and systemic treatment with voriconazole. Twenty-one days after surgery, the infection was present outside the interface and inside the AC (Fig. 3), so a penetrating keratoplasty (PKP) was performed in order to eliminate the infection. Intrastromal, intracamerular, and intravitreal 0.1% voriconazole was injected. The recipient cornea was sent to pathology and the examination revealed spores and hyphae by using periodic acid–Schiff (PAS) staining and Grocott technique.

Interestingly, the anterior cap of the same donor cornea was used to perform a tectonic superficial anterior lamellar keratoplasty on another patient, and the recipient did not have any problem with fungal infection.

Culture of the *C albicans* revealed sensibility to voriconazole and to other antifungal agents (amphotericin, fluconazole, ketoconazole, and itraconazole), but, due to the lack of response to voriconazole, we decided to stop systemic voriconazole treatment. However, we continued with topical voriconazole 1% every hour and, empirically, we added topical amphotericin 5 mg/mL each hour and oral fluconazole 100 mg each 12 hours for 1 week, tapering the topical treatment over 1 month. Despite the anatomic alterations (poor position of the cornea, IOL near the endothelium, angle closure almost 360º), there were no signs of active infection (good fundal glow, B-mode echography without particles in vitreous cavity, and quiet eye). Therefore, only topical amphotericin 5 mg/mL every 8 hours and oral fluconazole 100 mg each day were prescribed for the next 3 months, adding tobramycin/dexamethasone drops twice a day. Four months later, intraocular pressure (IOP) was uncontrolled. A new PKP was performed, the IOL was removed, and an Ahmed valve was implanted (performing pars plana vitrectomy to clean any remnants of possible infection). The cornea was sent to pathology and the PAS staining did not identify fungi. One year later, the aphakic eye was quiet, the IOP was controlled, and the cornea was clear (Fig. 3). Nevertheless, the optic nerve was damaged and CDVA was hand movements.

DISCUSSION

Fungal keratitis after any form of corneal transplantation is a relatively rare event. Risk factors for postkeratoplasty keratomycosis include contaminated donor corneal tissue and chronic epithelial defects, loose sutures, and topical corticosteroids. Fourteen percent of patients receiving donor corneas contaminated with *Candida* developed postoperative clinical intraocular infection (3). In spite of the belief that positive corneoscleral rim cultures are poor predictors of subsequent clinical infection, they may foretell severe intraocular infection in patients with donor rims contaminated with *Candida* species.

Candida keratitis after lamellar keratoplasty is infrequent, although these types of infections in anterior and posterior lamellar keratoplasty have been reported (2, 4). Some authors have adopted the practice of empirically treating all patients who have fungal positive donor corneoscleral rims with topical amphotericin B 0.15% 4 times per day, and with oral fluconazole 200 mg orally twice a day for 4 weeks (5). The use of systemic antifungal treatment is important, especially in lamellar or endothelial keratoplasty, because the penetration of amphotericin B is poor through intact epithelium. Removal of the surface epithelium may improve the penetration of topical amphotericin B.

The source of the infection in our patient seems to be caused by donor corneal contamination. The donor rim culture was first reported positive for yeast 10 days after DSAEK. Potential predisposing donor risk factors for fungal contamination include cardiac disease as the cause of death (5), alcohol abuse (5), and prolonged death-to-preservation time greater than 12 hours (6). The initial microbiologic diagnosis was confirmed by pathologic study of the corneal piece when the hot PKP was performed. The study showed the presence of hyphae and spores with PAS and Grocott techniques.

We carefully evaluated the options of conservative or aggressive treatment for our patient. Because the infiltrate was confined to the interface without signs of ocular spread, we favored nonaggressive treatment (instead of removing the donor lamella and/or PKP) in order to prevent dissemination of the fungal infection. This was the wrong decision because the infection penetrated inside the AC, and the decision to perform hot therapeutic PKP had to be urgently made. Over the subsequent months, IOP was uncontrolled, but surgical treatment could not be performed until we had complete certainty that the infection was eradicated. After 4 months of the adequate treatment (topical amphotericin and oral fluconazole), and once the eye was quiet and without any signs of fungal infection, we decided to perform a second PKP (the cornea was edematous) with pars plana vitrectomy to clean all the remaining vitreous, removing the IOL and implanting an Ahmed valve to reduce the IOP.

This report describes the only patient in our practice who has ever developed infectious keratitis after more than 300 consecutive DSAEK procedures. During this procedure, a microkeratome is used to excise an anterior lamellar cap from the cornea and its scleral rim. It is possible that ocular surface flora adherent to the cornea and/or conjunctival remnants of the corneoscleral rim may lead to contamination of the donor lenticule. Careful excision of limbal conjunctiva during donor corneal harvest and

vigorous irrigation of the ocular surface with balanced salt solution may reduce the risk of donor lenticule contamination in donor corneas designated for DSAEK (3). We do not have a clear explanation why the anterior cap of the same donor cornea used to perform a tectonic superficial anterior lamellar keratoplasty on another recipient did not produce any problem related to fungal infection. We can only speculate about the key factor in this situation, such as the immune status of the patient or the different concentration of germs that may exist in every part of the cornea.

Given the possible risk of donor-to-host transmission of fungal keratitis or endophthalmitis after corneal transplantation, the question arises as to whether or not antifungal agents should be added to Optisol GS. Ritterband et al (7) evaluated the rates of fungal culture–positive donor rims by comparing donor rims that had been stored in Optisol GS plus voriconazole (100 mg/mL) with rims stored in standard Optisol GS. None of the rims stored with Optisol GS fortified with voriconazole had positive fungal cultures, compared with 1.3% of the rims stored in Optisol GS, and this difference was statistically significant. In addition, there was no difference in cellular morphology or percentage of nonviable endothelial cells for those corneas stored in Optisol GS plus voriconazole compared with those corneas stored in Optisol GS (7). Voriconazole (1%) added to Optisol GS retained its antifungal efficacy for 6-7 days, which is typically the length of time that donor corneas are stored in Optisol GS before use.

In conclusion, once a small infiltrate is seen in the interface of any kind of lamellar keratoplasty, the diagnosis of fungal keratitis has to be taken into account. It is not clear whether it is better to treat this conservatively or more aggressively (i.e., removing the lenticle and/or PKP). To add voriconazole to any cornea preservation media (such as Optisol) could be a good practice to avoid the small but devastating possibility of fungal keratitis/endophthalmitis.

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REFERENCES

1. Sutphin JE, Pfaller MA, Hollis RJ, Wagoner MD. Donor-to-host transmission of *Candida albicans* after corneal transplantation. Am J Ophthalmol 2002;134:120-1.
2. Koenig SB, Wirostko WJ, Fish RI, Covert DJ. *Candida* keratitis after Descemet stripping and automated endothelial keratoplasty. Cornea 2009;28:471-3.
3. Keyhani K, Seedor JA, Shah MK, Terraciano AJ, Ritterband DC. The incidence of fungal keratitis and endophthalmitis following penetrating keratoplasty. Cornea 2005;24:288-91.
4. Chew ACY, Mehta JS, Li L, Busmanis I, Tan DT. Fungal endophthalmitis after Descemet stripping automated endothelial keratoplasty—a case report. Cornea 2010;29: 346-9.
5. Rehany U, Balut G, Lefler E, Rumelt S. The prevalence and risk factors for donor corneal button contamination and its association with ocular infection after transplantation. Cornea 2004;23:649-54.
6. Kloess PM, Stulting RD, Waring GO III, Wilson LA. Bacterial and fungal endophthalmitis after penetrating keratoplasty. Am J Ophthalmol 1993;115:309-16.
7. Ritterband DC, Shah MK, Meskin SW, et al. Efficacy and safety of voriconazole as an additive in Optisol GS: a preservation medium for corneal donor tissue. Cornea 2007;26: 343-7.