Candida albicans interface infection after deep anterior lamellar keratoplasty

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The clinical features of interface *Candida* keratitis after deep anterior lamellar keratoplasty (DALK), may imitate rejection or crystalline keratopathy. We report here an 18-year-old woman presented with red eye, 4 months after undergoing DALK. Slit lamp examination revealed keratic precipitates (KPs) and cojunctival injection. She was prescribed corticosteroid treatment for endothelial rejection by another ophthalmologist because of misdiagnosis, but suffered a recurrence of symptoms after reduction of the corticosteroid treatment. At that time, she was referred to our office. The recurrence persisted despite antibiotic and antifungal therapies. Ten days after treatment with interface irrigation with amphotericin, the infiltration and hypopyon were resolved. Topical steroid was added after 3 months of antifungal monotherapy. Irrigant cultures confirmed the presence of *Candida albicans*. The corneal graft appeared semi-clear with no signs of infection at 17-month follow-up. We recommend a close follow-up and a timely intervention to prevent the need for more invasive treatment such as penetrating keratoplasty.

Key words: *Candida albicans*, corneal interface infection, corneal interface irrigation, lamellar keratoplasty

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Deep anterior lamellar keratoplasty (DALK) has been introduced as a less invasive surgical alternative to penetrating keratoplasty for the treatment of corneal diseases not affecting the endothelium.[1] Infection is a serious complication for any kind of corneal transplant as it may result in graft failure and poor visual outcome. A variety of treatments have been suggested for corneal interface infection. Medical therapy by antibiotic could be safe and effective if it was used in proper approach, but just penetrating keratoplasty (PK) was tested for treatment of interfaces infection in DALK.[2,3] PK should be considered as an invasive treatment. We report here a case of *Candida albicans* interface infection after DALK and its management by a new, effective and less invasive treatment other than PK.

Case Report

An 18-year-old woman presented with a red eye, 4 months after undergoing DALK as a treatment for keratoconus. Anterior segment examination revealed keratic precipitates (KPs) and conjunctival injection [Fig. 1]. She was treated for endothelial rejection with 1 mg/kg daily oral prednisolone (Iran Hormon company, Tehran, Iran) and topical 1% prednisolone acetate (PRECORD®, Sina Darou, Tehran, Iran), applied 6 times per day. This was recommended by another ophthalmologist because of his misdiagnosis.

According to the recommendation of the first physician, the corticosteroid was tapered off when the patient showed a favorable treatment response. Upon tapering, however, she experienced a recurrence with crystalline keratopathy features [Fig. 2a] and she was referred to our office. The recurrence was treated with topical fortified vancomycin (50 mg/ml) (VANCO®, Jaber Ebne Hayyan Pharmaceutical Mfg. Co., Tehran, Iran), a Gram-positive bacterial antibiotic, and the corticosteroid

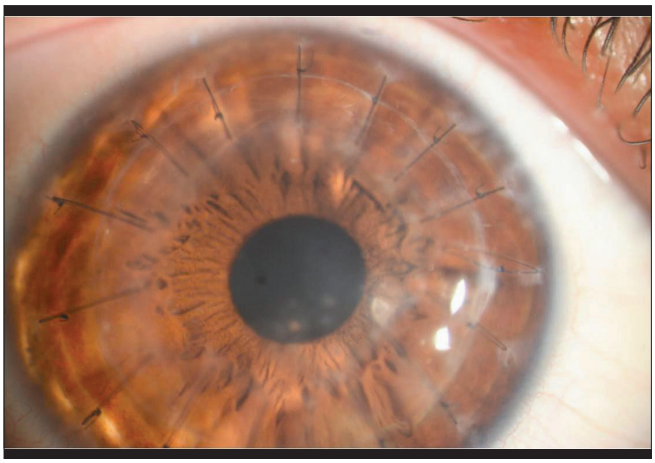

Figure 1: Slit-lamp photograph demonstrating multiple keratic precipitates and conjunctival injection in the right cornea of an 18-year-old woman, 4 months after deep anterior lamellar keratoplasty. We have borrowed the picture from the ophthalmologist who first treated her

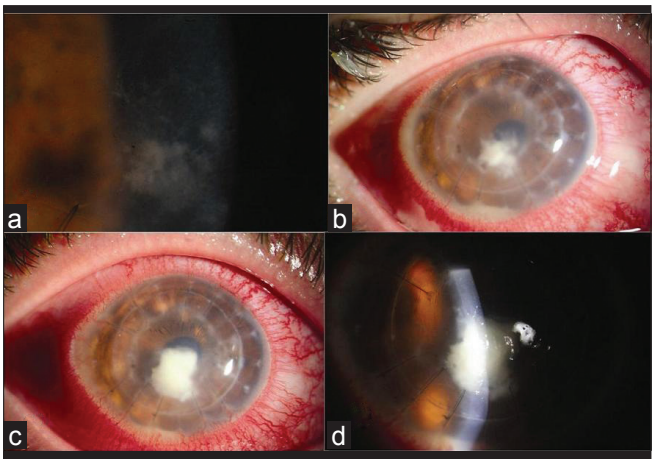

Figure 2: (a) After the tapering off of topical corticosteroid, the clinical features converted to those of crystalline-like keratopathy. (b) Non-necrotizing suppurative keratitis and hypopyon, 1 week after the use of fortified topical vancomycin. (c) Worsening of the infection with development of a necrotizing ulcer despite use of combined fortified topical vancomycin and ceftazidim; associated slit photograph is shown in (d)

regimen was discontinued. After 1 week, she came back with the clinical appearance of non-necrotizing suppurative keratitis and hypopyon [Fig. 2b]. Topical fortified ceftazidim (50 mg/ml) (CEFTAZID®, Jaber Ebne Hayyan Pharmaceutical Mfg. Co., Tehran, Iran) was commenced immediately, in addition to the vancomycin. Unfortunately, however, the keratitis progressed to a necrotizing ulcer within a week [Fig. 2c, d].

Hourly 5% natamycin suspension (NATACYN®, Alcon Inc., Texas, USA) was started. Corneal ulcer margin and surface infiltration samples, submitted to culture analysis, were negative. It is worth mentioning here that the microbial assessment of the donor tissue was negative at the time of DALK.

In the following week, interface irrigation was performed. The interface was further irrigated with amphotericin B (0.15%) during the procedure (Cipla Ltd., India). Unfortunately, a posterior perforation occurred during the irrigation procedure, and the anterior chamber was formed by an air bubble. Topical natamycin was continued postoperatively. Culture and smear tests from the irrigated material confirmed the presence of *C. albicans*.

Ten days after the irrigation treatment, the patient's infiltrations and hypopyon had resolved, but we observed a double chamber formation due to the posterior perforation [Fig. 3a]. Three weeks later, the double chamber had resolved completely without any further intervention [Fig. 3b]. After 3 months of natamycin monotherapy, the patient was prescribed topical corticosteroid, 3 times a day for 8 weeks. Follow-up examination done 17 months after the patient's initial presentation, the graft appeared semi-clear. There was no Descemet's scar at the site of infection and rupture, with no evidence of recurrence and her uncorrected visual acuity was 20/30 [Fig. 3c].

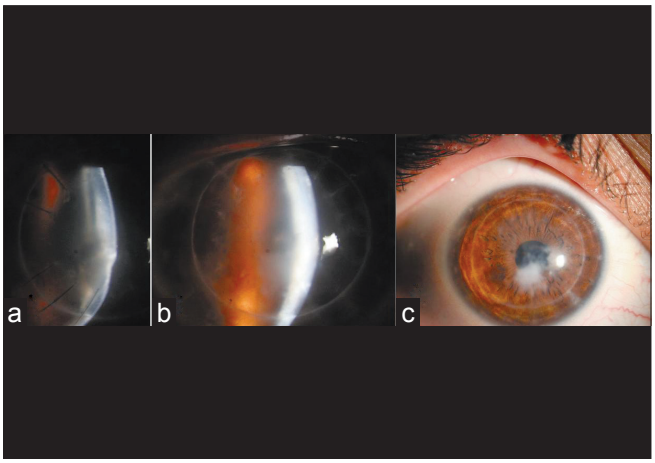

Figure 3: (a) Double chamber formation and resolution of hypopyon and infiltrates, 10 days after interface irrigation and topical natamycin therapy. (b) Completely resolved double chamber, 3 weeks after its formation with no intervention. (c) Clear graft, no infiltration, no recurrence and no double chamber, 17 months after first presentation; uncorrected visual acuity:20/30

Discussion

Candida species are the most common fungal cause of post keratoplasty endophthalmitis. The onset of such infections has been reported to occur as soon as 1 week or as long as several months after surgery.[4] *C. albicans* presence may be limited to the graft–host interface following DALK due to the barrier role of the Descemet's membrane. Corneal interface infection has been reported after laser-assisted *in situ* keratomileusis (LASIK),[5] epikeratoplasty,[6] endokeratoplasty[7] and DALK.[2,3]

The first-line treatment for early stage of fungal keratitis consists of topical and oral antifungal medications. In the treatment of the severe cases or failure of treatment by medical therapy, surgical procedures such as PK and conjunctival flap have been used.[8] However, PK is an aggressive treatment and has its own complications.[9] Intracameral antifungal medication has been used as an adjunctive therapy for fungal keratitis after PK.[10]

Graft infection can be acquired at any time following

operation, but most of it occurs during the first 6 months postoperatively.[11] Preoperative corneal button contamination, insufficient aseptic conditions during surgery, or recipient factors such as corneal anesthesia, ocular surface problems, eyelid abnormalities, persistent epithelial defect and suture-related complications may result in such infections.[12]

Furthermore, eyes with corneal grafts are susceptible to infection because of long-term topical corticosteroid use and corneal sutures. The late infections are usually acquired from the environment.[12]

Development of endophthalmitis can be prevented by the corneal layers separating the infection site from intraocular spaces in DALK, but penetration of topical, intraocular and systemic drugs may not be adequate to reach the infection site, so surgery is always the only treatment.[10] Furthermore, obtaining enough material for reliable culture tests may be more difficult with the layers intact. In prior reports of *Candida* interface infection following DALK, the infection was treated by PK.[2,3] Antibiotic irrigation of the interface following LASIK has been reported.[13] Here, we report evidence of therapeutically efficacious interface irrigation with amphotericin in the treatment of interface *Candida* infection after DALK.

Culture carried out on liquefied irrigation material may help in the timely and effective treatment of interface infection when culture tests of marginal and superficial infiltrations are negative.

The confocal microscopy could give useful information for diagnosis of bacterial, fungal or acanthamoeba corneal ulcers.[14] There are different reports of successful use of *in vivo* confocal microscopy in early detection, evaluation of the effectiveness of treatment and healing process of microbial corneal infections, especially in fungal ones.[15] Unfortunately, it was not accessible in our city at the time of our report.

In summary, the clinical features of interface keratitis after DALK may imitate endothelial rejection, crystalline keratopathy or epithelial downgrowth. Therefore, *Candida* keratitis should be considered in cases involving interface deposits and recurrent inflammation after the tapering off of steroid therapy for presumed graft rejection, following any kind of lamellar keratoplasty. Interface irrigation combined with topical antifungal administration can preserve the graft and may result in good vision without the need for more invasive treatments like PK.

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