Management of *Candida glabrata* infectious crystalline keratopathy with endophthalmitis following penetrating keratoplasty

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A 33-year-old male underwent an optical keratoplasty elsewhere in the right eye following which he developed endophthalmitis and subsequently underwent a pars plana vitrectomy and lensectomy. At presentation, he had a deep stromal crystalline infiltration along the graft–host junction. A large therapeutic keratoplasty was performed, and the excised corneal button was evaluated. Histopathology revealed gram-positive round-to-oval budding structures and microbiology identified the organism as *Candida glabrata.* He was treated with antifungals in the postoperative period. At 4 months after therapeutic keratoplasty, the patient developed recurrent endophthalmitis, following stoppage of antifungals. The treatment was reinstituted for another year, and the patient did well with a clear graft at 18-month-follow-up period after the recurrence episode. Management of infectious crystalline keratopathy with endophthalmitis is a challenging situation and requires long-term treatment.

Key words: *Candida*, endophthalmitis, infectious crystalline keratopathy, penetrating keratoplasty

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Postkeratoplasty infections although uncommon can cause serious complications. Donor tissue is a potential source of infection since it cannot undergo a usual sterilization process. Postkeratoplasty endophthalmitis rates vary from 0.1% to 0.4%.[1] Among the implicated yeasts, *Candida albicans* is the most common reported species. The non-*C. albicans Candida* species implicated include *Candida glabrata*, *tropicalis, and parapsilosis.* These infections are often linked to contaminated donor tissues as opposed to bacterial infections, where patient's own flora is implicated to be the source.[2,3] Herein, we report a case of infectious crystalline keratopathy (ICK) in a graft caused

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by *C. glabrata* with underlying endophthalmitis, which was successfully managed with surgical and medical treatment.

Case Report

A 33-year-old male presented to our clinic with whitish appearance of his right eye for 2 months. He had undergone an optical keratoplasty 8 months previously for keratoconus and a pars plana vitrectomy with lensectomy 3 months ago at a medical center overseas, for postkeratoplasty fungal endophthalmitis. He was using topical Amphotericin B, timolol maleate 0.5% twice per day from the time since vitrectomy was performed. At this presentation, the patient was systemically healthy, and as per the available records, there was no history suggestive of immunocompromised status in the past. Best-corrected visual acuity (BCVA) in the right eye was 20/40 with + 10 dioptre (D) correction and in the left eye was 20/40p. Examination of the right eye showed lid edema, conjunctival congestion with subconjunctival silicone oil, and a full-thickness graft secured with four interrupted and continuous sutures. Graft showed circumferential, dense white, mid-to-deep stromal crystalline infiltration spanning along the suture tracts of the graft–host junction [Fig. 1a]. Anterior chamber (AC) and vitreous cavity were quiet, and the retina was attached. Left eye showed corneal ectasia with Vogt's striae, a clear crystalline lens, and normal posterior segment. Intraocular pressure was 16 mm Hg in the right eye and 12 mmHg in the left eye.

A clinical diagnosis of ICK was made, and a large therapeutic penetrating keratoplasty was planned. A full-thickness host trephination of 10.75 mm was done, and 11.25 mm donor tissue was secured with 24 interrupted sutures. Microbiology of corneal button showed creamy-white, smooth colonies on chocolate agar after 48 h incubation at 37°C [Fig. 2a and b], which on gram stain revealed gram-positive yeast-like fungus. A negative germ tube test ruled out *C. albicans*. Results of yeast reagent card on VITEK 2 identified the species as *C. glabrata*. Histopathology also revealed gram-positive round-to-oval budding structures staining positively on Grams and Gomori methenamine silver staining [Fig. 2c and d]. The patient received eye drop voriconazole 1% every 1 h and oral voriconazole 200 mg twice daily and did well. At 1 week, epithelial rejection line was noted, and eye drop prednisolone acetate 1% was given 4 times/day [Fig. 1b]. At 2 weeks, the BCVA was 20/60 with a clear graft and quiet eye. The patient was advised to continue with topical and oral antifungals and topical corticosteroids and follow-up at his native place. The need for long-term antifungal treatment at least for 6-month duration was emphasized.

After 4 months, the patient returned with complaints of blurred vision and pain, following stoppage of antifungal medications due to their nonavailability at his native place. The BCVA in the right eye was 20/60. Graft had small white fluffy infiltrates on the endothelial surface with a clear posterior stroma [Fig. 1c]. A clinical impression of recurrence of infection in AC was made, and a diagnostic paracentesis was planned along with intracameral Amphotericin B (AMB) injection. Oral and topical antifungals were restarted, and corticosteroids were withheld. AC paracentesis revealed gram-positive budding yeast cells on direct microscopy [Fig. 2e], with confluent growth of smooth, cream-colored colonies on all culture media [Fig. 2f] identified as *C. glabrata* by VITEK 2. The patient received 5 doses of intravitreal AMB every 2- to 3-day-interval followed by reinstitution of corticosteroids at a frequency of four times a day. At 6 weeks, the graft was clear with a quiet AC and vitreous cavity. Subsequently, the patient received topical voriconazole 1% every 3 hourly for 2 months, every 6 hourly thereafter and oral voriconazole tablets 200 mg twice daily, and prednisolone acetate 1% eye drops twice daily for about a year and did well. At 18 months following recurrence episode, the graft was clear and compact with all sutures out and a quiet eye [Fig. 1d]. His BCVA was 20/60. He was asked to discontinue antifungals and continue with corticosteroids twice daily.

Discussion

ICK is a pauci-inflammatory chronic keratopathy, characterized by crystalline stromal opacities, representing colonies of the causative organism.[4] The origin is thought to be an infection by weak pathogens in an immunocompromised cornea. Surface adhesion proteins, biofilm formation, and production of hydrolytic enzymes all are known to contribute toward its pathogenesis.[5] *C. glabrata* differs from the *albicans* species in being a nondimorphic yeast, existing only as blastoconidia without forming hyphae or pseudohyphae and having a reduced pathogenicity and virulence.[6] Hence, 13 cases of postkeratoplasty endophthalmitis attributed to *C. glabrata* have been reported in the literature with the majority having a 100% concordance with the donor rim cultures.[7,8] Our patient had keratoplasty done overseas; hence, the donor corneal rim culture details

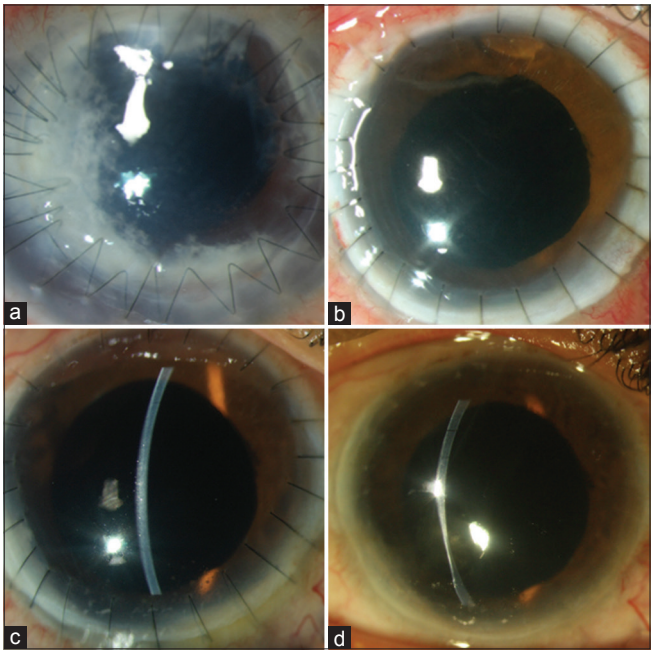

Figure 1: (a) Diffuse image of the right eye at presentation showing full-thickness graft with dense white crystalline infiltration along the suture tract at the graft–host junction. (b) Diffuse image of the right eye at 1 week showing clear graft with intact 24 sutures and an epithelial rejection line superiorly. (c) Slit view of the right eye at 4 months' follow-up showing small whitish infiltrates stuck to the endothelial surface of the graft inferiorly, suggestive of anterior chamber recurrence. There was no infiltration in the graft. (d) Slit view of the right eye at 18 months' follow-up after the recurrence episode showing a compact graft with all sutures removed

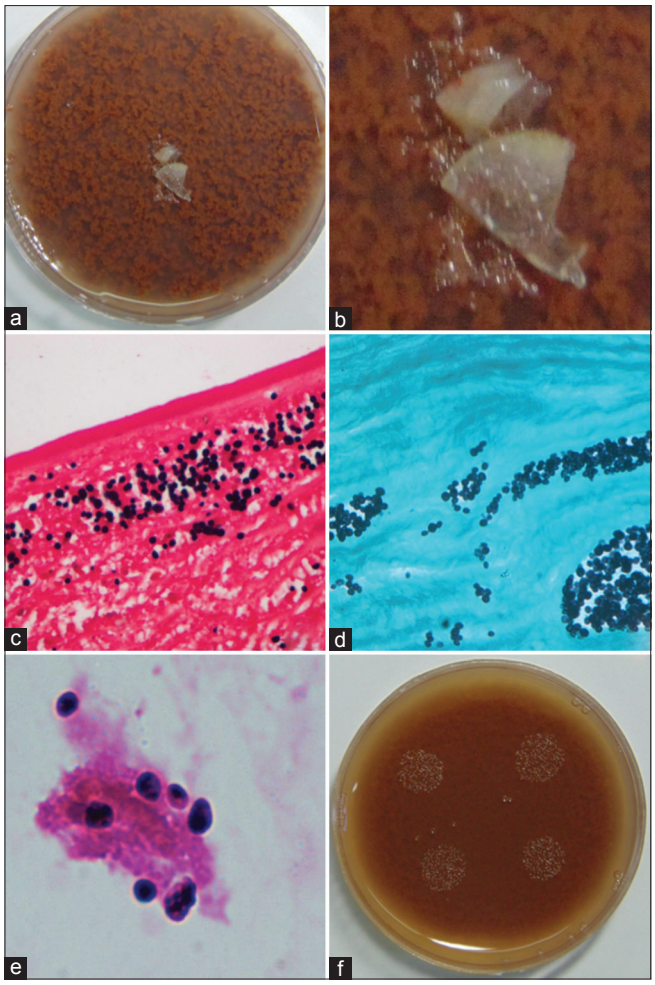

Figure 2: (a) Chocolate agar plate showing confluent growth of smooth, creamy-white colonies around the half corneal button after 48 h of incubation at 37°C. (b) High magnification image of the same chocolate agar plate shown in Figure A showing creamy-white, smooth raised colonies suggestive of *Candida* spp. from half corneal button. (c) Photomicrograph at ×40 magnification of tissue section stained with Grams stain showing gram-positive budding yeast cells. (d) Photomicrograph at ×40 magnification of tissue section stained with Gomori methenamine silver staining showing black budding yeast cells. (e) Gram-stained smear from anterior chamber tap fluid showing gram-positive budding yeast cells under ×100. (f) Chocolate agar plate with confluent growth of glistening, creamy-white, smooth colonies at the sites where anterior chamber tap fluid was inoculated after 48 h of incubation at 37°C

were not available to us, even though his treatment records suggested that his graft infection was attributed to the donor contamination.

C. glabrata is known to have higher MIC values for all azoles compared to the *albicans* species.[9] Amphotericin B resistance has not been described yet, although the MIC values are higher compared to the *albicans* species.[10] In this case, the infection responded to intraocular Amphotericin B along with oral and topical voriconazole 1%, although we did not demonstrate the drug sensitivity pattern and MIC values. *C. glabrata* is known to persist in a latent state for prolonged periods and gets reactivated in favorable conditions, contributing to recurrences. Detection of same species of *Candida* from the corneal button as well as from the AC tap fluid following recurrence supports the hypothesis. In view of this, long-term therapy with antifungals is needed to eradicate the infection. In this case, the antifungal treatment was continued close to a year after the recurrence was noted followed by successful recurrence-free interval of 6 months.

Conclusion

Patients who develop unfortunate complication of *C. glabrata* endophthalmitis and ICK need to be adequately counseled regarding the protracted disease course and prolonged course of therapy and need to maintain a regular follow-up even after the achievement of clinical cure.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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