

LETTER TO THE EDITORS

Donor-to-host transmission of infection: contrasting outcomes of lamellar and penetrating keratoplasty

Massimo Busin^{1,2,3}, Giuseppe Giannaccare^{4,5} , James Myerscough^{1,2,6}, Cristina Bovone^{1,2,3}, Vincenzo Scorgia⁴ & Emilio C. Campos⁵

1 Department of Ophthalmology, Ospedali Privati Forlì, Forlì, Italy

2 Istituto Internazionale per la Ricerca e Formazione in Oftalmologia (IRFO), Forlì, Italy

3 Department of Morphology, Surgery and Experimental Medicine, University of Ferrara, Ferrara, Italy

4 Department of Ophthalmology, University of "Magna Graecia", Catanzaro, Italy

5 Ophthalmology Unit, S.Orsola-Malpighi Hospital, University of Bologna, Bologna, Italy

6 Department of Ophthalmology, Southend University Hospital, Southend, UK

E-mail: giuseppe.giannaccare@gmail.com

Dear Editors,

Donor-to-host transmission of infection is a rare complication of corneal transplantation. Recent evidence reported an increasing trend in the incidence of fungal infection after endothelial keratoplasty compared with penetrating keratoplasty (PK), although neither observation reached statistical significance [1]. The main reason is the creation in lamellar techniques of a donor–host interface that provides a hypoxic sequestered environment for microorganisms to thrive protected from the host immune response [2–7]. We describe herein the contrasting outcomes of two patients who received tissues from the same donor contaminated with *Candida albicans*: the first patient underwent Descemet's stripping automated endothelial keratoplasty (DSAEK), while the second one underwent PK.

Both patients underwent surgery 1 day apart with grafts recovered from the same donor without any potential predisposing risk factors for fungal contamination [8]. Two days postoperatively, the eye bank noticed that donor broth of both corneas had tested culture positive for *C. albicans*. Patients were recalled for an unscheduled visit and informed of the exposure incident. On examination, both patients had clear grafts, without any signs of infection.

Patient #1 (69-year-old woman with Fuchs endothelial dystrophy) underwent DSAEK using a precut graft. Early postoperative course was unremarkable until four weeks when fluffy infiltrates were observed in the graft–host interface (Fig. 1a). In vivo corneal confocal microscopy revealed the presence of high-contrast elongated particles resembling *Candida* pseudofilaments (Fig. 1b). Amphotericin B (5 mg/ml) and voriconazole (10 mg/ml) eye drops were commenced and corticosteroids were withdrawn. The infiltrates worsened over the following week with corneal edema and 3-mm hypopyon (Fig. 1c). Daily intracameral and intrastromal injections of amphotericin B and voriconazole were performed. After 72 h, there was no clinical improvement so excisional PK was performed. Both the anterior chamber culture and the excised cornea tested positive for *C. albicans*. The patient was kept on topical amphotericin B and voriconazole for 4 months with no sign of recurrence, although at 6 months, secondary glaucoma required surgery. Currently, 1 year postoperatively, vision corrects to 20/200 and the graft is slightly edematous (Fig. 1d).

Patient #2 (60-year-old woman with aphakic bullous keratopathy and scarring) underwent PK. Postoperative course has been satisfactory with no signs of infection. Currently, 1 year postoperatively, vision corrects to 20/30 and the corneal graft is clear.

Our case report provides a unique head-to-head comparison between lamellar and full-thickness techniques using grafts recovered from the same infected donor. Since both recipients were immune-competent, the occurrence of the infection only in the case undergoing lamellar keratoplasty supports the hypothesis that this closed environment increases the viability of infection transmission. We did not start antifungal therapy until clinical evidence of infection (Patient #1) and this could have potentially influenced the outcomes. However, the use of empiric antimycotic prophylaxis in case of positive rim cultures and the

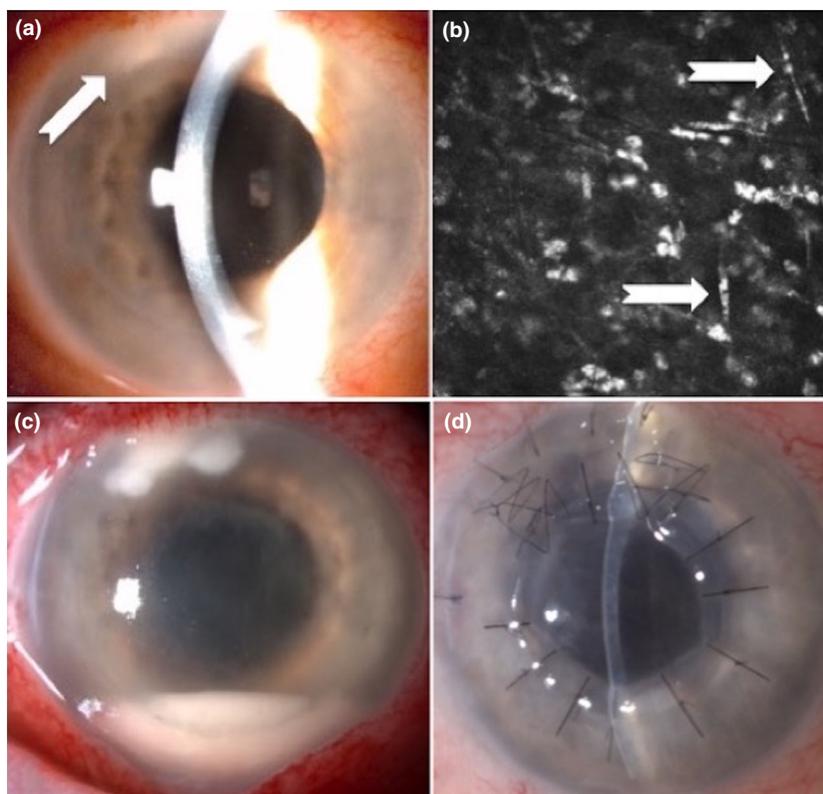


Figure 1 Slit-lamp and in vivo confocal microscopy images of patient who developed infectious keratitis. (a) Slit-lamp photograph taken 1 month after Descemet's stripping automated endothelial keratoplasty at the time of presentation of keratitis in Patient #1, showing a 1.5 mm by 1.0 mm area of infiltrate at the graft–host cornea interface (arrow). (b) *In vivo* confocal microscopy (Heidelberg Retina Tomograph III-Rostock Cornea Module) images ($300 \times 300 \mu\text{m}$) of the *Candida albicans*-infected cornea showing high-contrast elongated particles resembling *Candida* pseudofilaments (arrows) in the posterior stroma at $480 \mu\text{m}$ depth. (c) Slit-lamp photograph taken 1 week after the initiation of topical targeted therapy, showing a 4.5 mm by 2.0 mm area of infiltrate with a 3-mm hypopyon. (d) One year after therapeutic penetrating keratoplasty, the graft is slightly edematous with no signs of recurrent infection. Note that the graft is “keyhole-shaped” to allow the excision of the superior corneal infiltrate.

addition of antifungal medication to the preservation media represent unanswered issue that should be addressed by future studies.

Funding

The authors have declared no funding.

Conflicts of interest

The authors have declared no conflicts of interest.

Acknowledgements

None.

REFERENCES

1. Aldave AJ, DeMatteo J, Glasser DB, *et al.* Report of the Eye Bank Association of America medical advisory board subcommittee on fungal infection after corneal transplantation. *Cornea* 2013; **32**: 149.
2. Fontana L, Moramarco A, Mandarà E, Russello G, Iovieno A. Interface infectious keratitis after anterior and posterior lamellar keratoplasty. Clinical features and treatment strategies. A review. *Br J Ophthalmol* 2019; **103**: 307.
3. Holz HA, Pirouzian A, Sudesh S, Holsclaw DS, Chandra NS. Simultaneous interface candida keratitis in 2 hosts following Descemet Stripping Endothelial Keratoplasty with tissue harvested from a single contaminated donor and a review of clinical literature. *Asia Pac J Ophthalmol (Phila)* 2012; **1**: 162.
4. Kitzmann AS, Wagoner MD, Syed NA, Goins KM. Donor-related candida keratitis after Descemet stripping automated endothelial keratoplasty. *Cornea* 2009; **28**: 825.
5. Nahum Y, Russo C, Madi S, Busin M. Interface infection after Descemet

- stripping automated endothelial keratoplasty: outcomes of therapeutic keratoplasty. *Cornea* 2014; **33**: 893.
6. Palioura S, Sivaraman K, Joag M, *et al.* Candida endophthalmitis after Descemet stripping automated endothelial keratoplasty with grafts from both eyes of a donor with possible systemic candidiasis. *Cornea* 2018; **37**: 515.
7. Brothers KM, Shanks RMQ, Hurlbert S, Kowalski RP, Tu EY. Association between fungal contamination and eye bank-prepared endothelial keratoplasty tissue: temperature-dependent risk factors and antifungal supplementation of optisol-gentamicin and streptomycin. *JAMA Ophthalmol* 2017; **135**: 1184.
8. Rehany U, Balut G, Lefler E, *et al.* The prevalence and risk factors for donor corneal button contamination and its association with ocular infection after transplantation. *Cornea* 2004; **23**: 649.