Inadvertent Donor Button Inversion During Big-Bubble Deep Anterior Lamellar Keratoplasty

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Purpose: The aim of this study was to describe clinical outcomes and histopathologic findings in a case of repeat deep anterior lamellar keratoplasty (DALK) performed because of inadvertent inversion of the donor button at the time of primary surgery.

Methods: A 34-year-old woman underwent big-bubble DALK for keratoconus in her right eye; 4 days postoperatively, slit-lamp examination revealed the presence of several inclusions in the interface, whereas anterior segment optical coherence tomography (AS-OCT) showed pathologically marked wrinkling of the posterior stroma; inadvertent intraoperative inversion of the graft was diagnosed and the interface inclusions were assumed to be of epithelial origin. Repeat surgery was performed: donor tissue was removed and submitted to histological examination, marking the external surface of the lamella; the recipient residual bed was carefully washed and a new lamellar graft was sutured into position. Three months postoperatively, the patient underwent a complete ophthalmologic examination, including best-spectacle corrected visual acuity testing, refraction, biomicroscopy, AS-OCT, and endothelial microscopy.

Results: Histological examination confirmed that the donor button had been implanted with the epithelium facing the residual bed. Three months postoperatively, normal corneal curvature was visible at AS-OCT, the best-spectacle corrected visual acuity was 20/25, and the interface appeared perfectly clear. Endothelial cell density had not been substantially affected by the 2 surgical procedures.

Conclusions: Inadvertent inversion of donor tissue at the time of DALK is reported for the first time. Prompt exchange of the lamellar graft was instrumental in avoiding epithelial colonization of the interface, as well as in restoring excellent vision.

Key Words: cornea, keratoconus, deep anterior lamellar keratoplasty, inverted corneal graft, epithelial downgrowth

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In recent years, deep anterior lamellar keratoplasty (DALK) has emerged as an alternative procedure to penetrating keratoplasty (PK) for the surgical treatment of stromal diseases.1–3 As opposed to PK, DALK leaves the recipient endothelial in place, thus eliminating the risk of immunological endothelial rejection.4 However, for many surgeons DALK is still a time-consuming procedure with a very steep learning curve; in particular, Stromal dissection of the recipient bed poses the main challenge and is often complicated by micro- or macro-perforations requiring conversion to PK; instead, preparation and positioning of donor tissue are usually uneventful.

We report the first case of inadvertent inversion of donor tissue transplanted at the time of DALK, as well as successful management of this complication.

CASE REPORT

In April 2014, a healthy 34-year-old woman with advanced keratoconus underwent DALK in her right eye because of contact lens intolerance. Surgery was performed by an experienced corneal surgeon (V.S.) under peribulbar anesthesia (a mixture of lidocaine hydrochloride 2% and bupivacaine hydrochloride 0.5%) according to the classic big-bubble technique described by Anwar and Teichmann.1 After completing Stromal excision, donor tissue was removed from the storage medium and appeared whitish and “creased” when inspected under the microscope; several attempts were made to strip endothelium and Descemet membrane, but no intact layer could be identified, and only thin fragments could be removed from the overlying edematous stroma. Tissue was punched with an 8.2-mm Barron donor punch (Katena Products Inc, Denville, NJ) and the lamella obtained was sutured into the recipient bed with one 10-0 nylon running suture; no particular difficulty was encountered during this surgical step except for increased stiffness of donor tissue. Postoperatively, tobramycin 0.3% and dexamethasone phosphate 0.1% were given 4 times a day.

On the first day after DALK, biomicroscopic examination showed a totally de-epithelialized, slightly edematous graft; the interface between donor stroma and recipient bed appeared relatively clear and the best-spectacle corrected visual acuity (BSCVA) was 20/100 with a refraction of −1 sphere combined with −5 cylinder at 5 degrees. On the fourth day after surgery, the epithelium started to grow onto the peripheral part of the graft, whereas white granular inclusions had developed in the interface (Figs. 1A, B). Anterior
Segment optical coherence tomography performed with the SS-1000 CASIA (Tomey, Kyoto, Japan) revealed the presence of many deep folds of the donor lamella and a thin highly reflective band in the innermost corneal layer (Fig. 1C); the BSCVA had decreased to 20/200 with a refraction of -1.5 sphere combined with -4 cylinder at 5 degrees.

These finding suggested that the donor button might have been inadvertently inverted during surgery; and therefore 2 days later, the anterior lamella was exchanged for a new one. Maximal care was taken to minimize surgical trauma to the recipient bed both while removing the inverted lamella and while rinsing off all possible debris with irrigation of copious amounts of balanced salt solution (BSS) through a 25-gauge blunt cannula. In particular, all inclusions seen at the slit-lamp were found to adhere rather firmly to donor tissue and no residual material seemed to be attached to the residual bed. The inverted graft was marked on its anteriorly placed surface and submitted for histological examination. A Barron donor punch was used to prepare a full-thickness graft, 8.2 mm in diameter, from which Descemet membrane and endothelium were stripped off using a dry Weck-Cel sponge; finally, donor tissue was fixated with 2 running 10-0 nylon sutures.

On the first postoperative day, the new graft was completely transparent and epithelized; no inclusions were seen in the interface. No epithelial downgrowth or other complications were seen up to 3 months after repeat DALK (Figs. 1D, E). At this examination time, with both sutures still in place, the BSCVA was 20/25 with a correction of +1.8 sphere and -2.5 cylinder at 100 degrees. Endothelial cell density measured using specular microscopy (EM-3000, Tomey, Japan) had decreased from 2564 cells per square millimeter before initial surgery to 2512 cells per square millimeter.

Light microscopy (periodic acid-Schiff stain) of the explanted donor button demonstrated a multilaminar epithelial layer on the surface believed to be posterior and was therefore placed against the residual bed; in addition, a single layer of epithelium in the absence of any endothelial cells was found on the surface of the graft believed to be anterior (Figs. 2A, B). The epithelial origin of the 2 cell layers was confirmed by positive reactivity to immunocytochemical evaluation.
with 2 selective cytokeratin markers, the pan-cytokeratin (MNF116) and cytokeratin CK3 antibodies (Fig. 2C).

**DISCUSSION**

In the past, inadvertent inversion of a corneal button during PK has been reported in very rare cases\(^5\)–\(^7\) and laboratory experiments have confirmed the possibility of spontaneous inversion of corneoscleral tissue during storage and/or preparation of the donor button.\(^6\)

Transplantation of an inverted full-thickness graft at the time of PK not only results in primary failure but also carries the threat of intraocular epithelial downgrowth and its subsequent complications up to complete vision loss. For this reason, prompt exchange of the inverted graft is combined with treatment of all the structures possibly affected by the epithelial downgrowth. Cryotherapy is usually used for this purpose, as chemical agents, such as alcohol, may diffuse and cause unintentional damage to healthy tissue.\(^8\)

As the recipient endothelium is left in place, inversion of donor tissue at the time of DALK should be compatible with postoperative clearing, and 20/100 vision was indeed achieved in our case, early after surgery. However, epithelial downgrowth, although necessarily limited to the host–donor interface, could soon complicate the postoperative course. In addition, our case demonstrated that tissue inversion also has architectural consequences, that is, “crowding” of the anterior stroma placed posteriorly, as the creases shown by anterior segment optical coherence tomography clearly document.

Similarly to that reported for PK, in our DALK case, early exchange of inverted tissue proved instrumental in restoring excellent vision and preventing possible complications. In particular, although we obviously could not treat the descemetic residual bed with cryo-applications, careful but abundant irrigation with BSS was sufficient to prevent recurrence of interface inclusions. In addition, despite repeat surgery, endothelial cell density was not substantially affected in the short term, which should also warrant graft survival in the long term.

Although inversion of donor tissue at the time of DALK can be dealt with successfully, prevention of this type of complication is certainly preferable. To identify possible clues for detection of tissue inversion, we have reviewed video recording of the procedure and realized that the presence of residual uveal tissue attached to the internal surface of the corneoscleral rim could easily serve this purpose. Checking the corneoscleral rim rather than manipulating corneal tissue offers the advantage of leaving the endothelium untouched and therefore perfectly suitable for transplantation. In conclusion, the inversion of donor cornea is a rare complication of DALK surgery; quick exchange of the inverted graft combined with copious BSS irrigation of the recipient bed restores excellent vision while preserving endothelial function in the absence of epithelial interface downgrowth.

**REFERENCES**