Case Report: Primary graft failure due to a reversed lenticule in Descemet Stripping Automated Endothelial Keratoplasty [version 2; peer review: 3 approved]

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Abstract

Introduction and importance: This report details the clinical features and management in a case of Descemet stripping automated endothelial keratoplasty (DSAEK) which had primary graft failure (PGF) due to an inverted yet attached lenticule.

Presentation of case: A 66-year-old gentleman had poor visual recovery in the right eye after undergoing cataract surgery 12 years prior to presentation. The visual acuity was counting fingers and examination revealed endothelial decompensation. The patient underwent a DSAEK and postoperatively had a well attached lenticule. However, the cornea was edematous three weeks after the surgery and optical coherence tomography (OCT) revealed a reversed lenticule. The patient underwent a repeat DSAEK and had an uneventful postoperative course. The visual acuity was 20/40 after 7 months with a clear cornea and a well attached graft.

Discussion: PGF is a rare complication following DSAEK which occurs due to poor endothelial function of the donor graft. Insertion of a reversed lenticule may get overlooked as a cause of PGF unless the graft edge profile is examined on an OCT scan. The graft in the current case was well attached despite its inverted position suggesting that graft adherence is perhaps not a function of the corneal endothelial pumps in isolation and may be driven by factors such as the intraocular pressure.

Conclusion: A reversed DSAEK lenticule may have normal adherence to the host stroma and must be considered in cases with PGF. OCT of the graft edge is required for diagnosis before performing a repeat keratoplasty.

Keywords

Endothelial keratoplasty, Descemet stripping automated endothelial keratoplasty, inverted lenticule, graft adhesion, primary graft failure
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Author roles: Kate A: Data Curation, Methodology, Visualization, Writing – Original Draft Preparation; Basu S: Conceptualization, Data Curation, Funding Acquisition, Investigation, Methodology, Project Administration, Supervision, Validation, Visualization, Writing – Review & Editing

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Introduction
The advent of endothelial keratoplasties (EK) has revolutionised the treatment of corneal endothelial disorders and has enabled the restoration of a near normal corneal anatomy and physiology. Also, the complications associated with a conventional penetrating keratoplasty (PK) such as suture related infections, vascularization and risks of an open sky procedure are drastically decreased with these lamellar surgeries. However, these procedures are not completely risk free and suboptimal results can ensue from graft detachment, rejection, chronic endothelial attrition, etc. Primary graft failure is one such complication that can occur following Descemet stripping automated endothelial keratoplasty (DSAEK) and is defined as corneal stromal edema which does not clear despite the presence of a well apposed graft. A donor graft with decreased endothelial count or loss of endothelial cells due to traumatic surgical manoeuvring are the most common causes of primary graft failure. This intraoperative manipulation of the graft is done primarily to ensure the correct orientation of the lenticule. Although several approaches exist to facilitate the same, it may still get attached in an inverted fashion, especially with very thin lenticules or in eyes with significant corneal scarring. Insertion of an inverted graft has not been reported as a cause of primary failure and so this report intends to describe the clinical features and management of primary graft failure in an eye with an attached yet reversed DSAEK lenticule.

Case presentation
A 66-year-old gentleman had complaints of intermittent pain and watering in the right eye after having undergone a small incision cataract surgery with a posterior chamber intraocular lens twelve years before presenting to us. This complaint had exaggerated in the three months prior to presentation and was now associated with a decrease in vision. There was no past history of any prior interventions, and the patient did not give any relevant family history. At presentation, his visual acuity in the right eye was counting fingers, while that in the left eye was 20/25. Slit lamp examination revealed an edematous cornea with epithelial bullae in the periphery. The anterior chamber was hazily seen and appeared normal with a stable intraocular lens. The posterior segment was hazily visible and revealed no abnormalities. The left eye had a visual acuity of 20/20 with a clear cornea and no guttate changes. A cataractous lens was present. Rest of the anterior and posterior segment examination was within normal limits. Specular microscopic examination revealed a healthy endothelial morphology and count in the left eye. A diagnosis of pseudophakic bullous keratopathy was made and the patient was planned for a DSAEK.

The surgery was carried out under local anesthesia and followed a standard technique. Briefly, the central 9 mm of the host Descemet’s membrane was stripped. An 8mm trephination was carried out on a pre-cut donor tissue with an endothelial count of 2508 cells/mm². The graft was inserted with a Sheets glide and apposed to the host stroma with a full chamber air tamponade of ten minutes. Postoperatively the visual acuity was counting fingers and the graft was edematous but well attached on the optical coherence tomography (OCT) scan. The patient was started on topical corticosteroids (prednisolone acetate 1%, six times/day) and antibiotics (moxifloxacin 0.5%, 4 times/day).

Figure 1. (A, B) Slit lamp image of the right eye at presentation depicting corneal edema with Descemet membrane folds and peripheral bullae which are also visible on the optical coherence tomography scan (OCT). (C, D) Image captured one month after the Descemet stripping automated endothelial keratoplasty (DSAEK) showing primary graft failure with a well attached graft. (E, F) Clear cornea with an attached DSAEK lenticule 2 weeks after the repeat endothelial keratoplasty.
The patient was reviewed again after three weeks and no improvement in either the visual acuity or the corneal clarity was noted. The OCT was repeated, and the graft edge was included in the scan which showed a reversed orientation of the graft with the longer endothelial side adherent to the stroma (Figure 2). Furthermore, the irregular donor stromal surface facing the anterior chamber was also observed (Figure 2).

The patient underwent a repeat DSAEK, 6 weeks after the primary surgery. After the previous donor tissue was detached and removed, a new DSAEK lenticule, 7.5 mm in diameter, with an endothelial count of 2457 cells/mm² was inserted. The rest of the surgical technique was similar to that of the first procedure. On the first postoperative day, the patient had a visual acuity of 20/60 with a well attached graft and a significant decrease in the corneal edema. The correct apposition and orientation of the graft was confirmed on OCT (Figure 2). The patient was continued on topical antibiotics and a tapering dose of topical corticosteroids. At the 7th month postoperative visit, the corrected visual acuity was 20/40 in the right eye. The cornea was clear with an attached lenticule, and the patient was maintained on a once daily dose of topical steroids (Figure 1). Figure 3 details the timeline of the patient from presentation to the last follow up.

Discussion

Several studies have investigated the factors that affect graft attachment following a DSAEK.5,9,10 One of the key elements that facilitates good adherence of the lenticule is the endothelial pump action. A well-functioning endothelium also helps to clear the corneal edema. Hence primary graft failure and graft detachment is observed in eyes with a poor quality donor tissue or excessive intraoperative manipulation.11–13 Dislocation of the graft in such cases is probably
mediated by the presence of fluid in the interface, which the dysfunctional endothelium is unable to overcome. And so, various modifications of the DSAEK technique have been employed which provide an additional means for graft apposition until the functional pumps can take over. These include surface massage to displace the interface fluid, use of venting incisions and roughening of peripheral stromal fibers to create stronger adhesions.5,9,10

The use of air tamponade and increase in intraocular pressure (IOP) has also been described for the same purpose. Vaddavalli et al and Bhogal et al independently studied the role of IOP in graft adherence.5,10 Both studies did not find a significant correlation between the two although Vaddavalli et al found an increasing rate of graft attachment with higher IOP. However, the experimental set up was devised to test the attachment under normal and high pressures and the role of hypotony was not assessed. Thus, IOP probably significantly contributes to good attachment of the donor lenticule as seen in the current case where a well attached graft was seen despite its inverted position. This also highlights the fact that there may be several other factors besides the endothelial pump action which bring about the binding of the two stromal surfaces. This needs to be taken into consideration especially in eyes which have a higher rate of graft dislocation such as aphakic eyes, vitrectomised eyes or eyes with glaucoma filtering surgery.1,3 Ensuring a watertight globe at the end of the surgical procedure will help prevent postoperative hypotony and decrease the risk of graft detachment.

Primary graft failure is a rare complication following DSAEK, with a reported rate of around 1%.3 The diagnosis of this entity is made in the presence of persistent corneal edema following a DSAEK. The normal time taken for the recovery of graft clarity following DSAEK ranges from three weeks to three months which can cause a delay in establishing the diagnosis of primary failure.3 As a result, the subsequent interventions required to visually rehabilitate the patient will also get stalled. However, a reversed lenticule is an exception to this as it can be detected in the early postoperative period and promptly managed. Several measures have been advocated to help ensure the insertion and attachment of the graft in its correct position. These include marking of the stromal surface, use of the double ring sign, intraoperative OCT, etc.4,11 However, the lenticule may get inverted despite these safeguards especially in cases with very thin grafts or in eyes with suboptimal clarity of the anterior chamber structures due to corneal scarring. And thus, caution must be exercised in such cases during graft insertion and more than one safeguard should be employed to ensure the correct graft orientation especially by novice EK surgeons.

As highlighted by the current case, judicious use of an OCT in the weeks following the surgery can help identify the improper orientation of the lenticule in eyes with slow recession of corneal edema. Although documentation of an attached lenticule with an AS-OCT scan is a routine practice following endothelial keratoplasty, it is essential to include the peripheral graft area when capturing such images. An acute angle configuration of the graft edge has been described which indicates a stroma-to-stroma apposition with correct positioning of the endothelial layer.4 Alternatively, in centers with limited access to AS-OCT, slit lamp examination of the graft edge may also help assess its orientation in relatively clear corneas. This additional information is vital as the mere presence of an attached lenticule does not signify its correct orientation. Future studies that look into different insertion techniques and the associated rates of graft reversal can help identify the safest surgical procedure in eyes where a graft reversal is anticipated. Although a repeat EK was carried out for the reversed lenticule in our case, this option may not be available in areas where corneal grafts are a scare resource. In such scenarios, reversal of the graft can be attempted within a short interval from the primary surgery especially in grafts with excellent preoperative endothelial cell counts.

**Conclusion**
The current report highlights a reversed DSAEK lenticule as a cause of primary graft failure. This clinical entity can be diagnosed early with the help of an AS-OCT in eyes with slow resolution of the corneal edema and a repeat intervention can be planned subsequently. Adhesion of the graft in DSAEK may depend on factors beyond functional endothelial pumps and an improved understanding of the same will help improve outcomes in eyes which are at a greater risk of having graft detachments.

**Consent**
Written informed consent was obtained from the patient for publication of this case report and accompanying images.

**Author contributions**
SYB contributed to the study conceptualization, study investigation, methodology, manuscript editing and revision. AK contributed to the original draft preparation, study methodology and revisions.

**Data availability**
All data underlying the results are available as part of the article and no additional source data is required.
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The authors describe an interesting case of Primary graft failure due to reversed lenticule in Descemet Stripping Automated Endothelial Keratoplasty and a very valuable use of the anterior segment OCT.

Slit-lamp biomicroscopy may not be as precise in edematous corneas as details may be easily missed, even by expert clinicians. Anterior Segment Tomography is a very useful tool in searching for clinical cues that may guide the clinician in the diagnosis. As clearly demonstrated by the authors in this case report, OCT of the graft edge may demonstrate the reversed position of the lenticule a detail that would be overlooked by biomicroscopy.

Is the background of the case's history and progression described in sufficient detail?  
Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?  
Yes

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?  
Yes

Is the case presented with sufficient detail to be useful for other practitioners?  
Yes

**Competing Interests:** No competing interests were disclosed.
**Reviewer Expertise:** Cornea, Corneal Transplant.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

**Author Response 04 Jan 2023**

**Sayan Basu**, L V Prasad Eye Institute, Hyderabad, India

We thank the reviewer for their comments

**Competing Interests:** None

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**Reviewer Report 01 November 2022**

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**Jaime D. Martinez**

Anne Bates Leach Eye Center, Bascom Palmer Eye Institute, Department of Ophthalmology, University of Miami Miller School of Medicine, Miami, FL, USA

**Summary**

Interesting paper. This case presents a patient who had primary graft failure after a DSAEK graft. Graft failure was secondary to reverse graft tissue. The patient had a repeat DSAEK graft after surgery with the correct corneal graft position with a successful outcome. I like how they describe what to look for in these specific situations on OCT images to confirm the diagnosis. I think this is important as many cases are difficult to distinguish if the graft is in the correct position even with the reference maker.

It will be helpful for the surgeon to picture the different findings on OCT by doing the following:

- Add in the Figure 2 legend the different types of angle configurations between cases.
  - Maybe consider adding a geometrical line on the edges with acute and obtuse angles on OCT images.

**Is the background of the case's history and progression described in sufficient detail?**

Yes

**Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?**

Yes

**Is sufficient discussion included of the importance of the findings and their relevance to**
future understanding of disease processes, diagnosis or treatment?
Yes

Is the case presented with sufficient detail to be useful for other practitioners?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Ophthalmology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 04 Jan 2023
Sayan Basu, L V Prasad Eye Institute, Hyderabad, India

We would like to thank the reviewer for reading and commenting on our submission. The required change has been made to the figure 2

Competing Interests: None

Reviewer Report 25 October 2022
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Ka Wai Kam
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The authors reported a patient who underwent DSAEK and developed persistent corneal oedema after transplantation despite graft adherence.

In addition to the use of ASOCT, an attentive slit lamp examination with a narrow light beam and focusing on the graft edge may alert the clinician about a potential graft reversal. This may be highlighted as ASOCT may not be readily available in every eye centre.

In the report, the authors mentioned the use of Sheets glide in implanting the lenticule. Unlike in DMEK where some surgeons would use an S-stamp or an asymmetrical triangle mark at the graft periphery, graft orientation in DSAEK relies on a careful preparation and insertion process. It would be interesting to compare the different insertion techniques (Sheets glide, Busin glide, Endoglide) and look at the rate/risk of graft lenticule reversal - but in reality, there are multiple
factors that could interfere with the final outcome.

Similarly, the authors may wish to elaborate on what in their opinion contributed to the graft reversal during the first transplantation, and what special precaution was taken during the second transplantation in order to avoid the same complication. This would be beneficial to novice EK surgeons in ensuring a correct graft insertion.

In places where grafts are scarce, reversal of a flipped endothelial keratoplasty may be attempted if the reversal had been noted earlier. In our experience, we had treated two flipped DSAEK buttons on postoperative day 1 by reversing the graft in the operating theatre. One of the two grafts cleared up after the reversal. This option may be considered especially in areas where corneal grafts are not as abundant.

Is the background of the case's history and progression described in sufficient detail?
Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?
Yes

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?
Yes

Is the case presented with sufficient detail to be useful for other practitioners?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Cornea

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 04 Jan 2023

Sayan Basu, L V Prasad Eye Institute, Hyderabad, India

1. In addition to the use of ASOCT, an attentive slit lamp examination with a narrow light beam and focusing on the graft edge may alert the clinician about a potential graft reversal. This may be highlighted as ASOCT may not be readily available in every eye centre.

We thank the reviewer for their comment and agree that slit lamp examination can provide an understanding of the graft orientation especially in eyes with limited scarring and a good view of the anterior chamber. This point has been added to the discussion.

2. In the report, the authors mentioned the use of Sheets glide in implanting the lenticule.
Unlike in DMEK where some surgeons would use an S-stamp or an asymmetrical triangle mark at the graft periphery, graft orientation in DSAEK relies on a careful preparation and insertion process. It would be interesting to compare the different insertion techniques (Sheets glide, Busin glide, Endoglide) and look at the rate/risk of graft lenticule reversal - but in reality, there are multiple factors that could interfere with the final outcome.

We concur with the reviewer that understanding the rates of graft reversal in different insertion techniques will help identify the one associated with the least risk of graft reversal and this procedure can be adopted in eyes where in a higher risk of reversal is anticipated. This has been added to the discussion.

3. Similarly, the authors may wish to elaborate on what in their opinion contributed to the graft reversal during the first transplantation, and what special precaution was taken during the second transplantation in order to avoid the same complication. This would be beneficial to novice EK surgeons in ensuring a correct graft insertion.

The first procedure was performed by a surgeon with relative inexperience and marking of the graft was not carried out. This could have resulted in the inversion of the graft during its insertion. This point along with measures to prevent the same has been added to the discussion to help surgeons early in the course of their training.

4. In places where grafts are scarce, reversal of a flipped endothelial keratoplasty may be attempted if the reversal had been noted earlier. In our experience, we had treated two flipped DSAEK buttons on postoperative day 1 by reversing the graft in the operating theatre. One of the two grafts cleared up after the reversal. This option may be considered especially in areas where corneal grafts are not as abundant.

We agree that attempting a graft reversal is a viable option in low resource settings provided a reasonable time interval exists between the primary EK and the secondary procedure. This point has been added to the discussion.

**Competing Interests:** None
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