Descemet membrane detachment after penetrating keratoplasty for keratoconus

[1]Vivienne Kit MBBS BSc, [1]Jaime Kriman Nunez MD, [1]Alfonso Vasquez-Perez MD FRCOphth, [1]Kirithika Muthusamy FRCOphth, [2]Caroline Thaung FRCOphth FRCPath, [1]Stephen Tuft MD FRCOphth

Running header: Descemet detachment

[1]Moorfields Eye Hospital, 162 City Road, London EC1V 2PD

[2]UCL Institute of Ophthalmology, 11-43 Bath Street, London EC1V 9EL

Corresponding author: Mr Stephen Tuft

Email: Stephen.tuft@nhs.net

Tel: 0044 207 253 3411

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Abstract

Purpose: To describe risk factors, management and outcome of delayed Descemet membrane (DM) detachment following penetrating keratoplasty (PK) for keratoconus.

Methods: We report seven eyes and combine this data with seven previous case reports identified by a search of PubMed.

Results: DM detachment occurred at a median of 25 years (range, 7 to 33 years) following PK. One individual had bilateral detachments. There was typically mild ocular discomfort accompanied in some cases by a rapid onset of visual blur. Cases were often treated for allograft rejection before a DM detachment was suspected and confirmed by optical coherence tomography. Detachments were limited to the donor tissue in eleven eyes, but a DM break was identified at the time of onset in only two eyes. Thinning of the host corneal rim with ectasia was reported in eight eyes (57%). In three eyes the detachment resolved spontaneously, but in two eyes a detachment was still present at 12 months. Gas tamponade to reattach the DM was performed in nine eyes and was effective in five eyes. Five eyes had a repeat PK or endothelial keratoplasty. Histology showed fibroblastic proliferation on the stromal surface of the folded DM.

Conclusion: The cause for DM detachment many years after PK is unknown, although progressive thinning of the host cornea and secondary graft ectasia may be implicated. Gas tamponade can be effective, but a repeat keratoplasty may be necessary. DM detachment should be included in the differential diagnosis for late onset corneal oedema after PK.

Introduction

Keratoconus is progressive thinning and ectasia of the cornea that results in visual loss from irregular corneal astigmatism. Contact lenses are often required to correct the vision, and approximately 12% to 20% of cases eventually require corneal transplantation for visual rehabilitation.[1] Corneal collagen cross-linking can arrest the course of keratoconus, and it may reduce the proportion of eyes that progress to contact lens wear or corneal transplantation.[2] Penetrating keratoplasty (PK) is still the most common transplantation procedure for keratoconus worldwide, but deep anterior lamellar keratoplasty is an alternative.[3]

The probability of graft survival following a PK for keratoconus is approximately 85% to 88% at 20 to 25 years after surgery.[4-6] Late complications include irreversible graft oedema from endothelial cell loss, allograft rejection, and progressive astigmatism associated with peripheral corneal thinning. Late-onset Descemet membrane (DM) detachment has also been described.[7-11] We report an additional seven eyes that developed an acute DM detachment several years after a PK for keratoconus, including an individual with bilateral detachments, and one case that resolved spontaneously. DM detachment was identified at slit lamp examination and confirmed with anterior segment optical computerized tomography (AS-OCT, Casia2, Tomey Corporation, Japan). Corneal tomography (Pentacam, Oculus Optikgeräte GmbH Wetzlar, Germany) taken before the DM detachment had occurred is included for comparison. Tissue from two eyes that had a repeat PK was available for histological examination. We then combined data from these seven eyes with data from a further seven eyes described in previous published case reports to identify common aetiological factors, management options and outcome. We excluded a similar case of acute corneal oedema following PK in which the original pathology was unknown,[12] and a further case in which a DM detachment was not identified before a repeat PK.[13] Cases with acute onset oedema at the graft interface in which a DM detachment was not confirmed were also excluded.[14-16] Four of our cases with important features are described in more detail.

Case reports

Case 1

A 51-year-old male with severe atopic keratoconjunctivitis (AKC) had a right PK for keratoconus twenty-seven years previously with a repeat PK for herpes keratitis ulceration after eleven years, and a left PK nine years previously (Table 1). He had also had bilateral cataract surgeries. His visual acuity with scleral contact lenses before DM detachment was 6/9 bilaterally. He developed a right allograft rejection that was treated with topical dexamethasone 0.1%, with signs of improvement after one week. Four weeks later he developed sudden and painless blur of the vision in his left eye to count fingers. On examination there was diffuse oedema of the left graft without inflammation (Figure 1A). He was treated empirically with hourly topical dexamethasone 0.1%, but after two days a total left DM detachment was confirmed (Figure 1B). There was no sign of a DM break and no DM detachment in the right eye. The peripheral cornea was thinned inferiorly with slippage of the graft interface (Figure 1B). The detachment did not resolve after tamponade with 20% sulfur hexafluride (SF6) gas, but there was subsequently an obvious DM break (Figure 1C). Because there was interface malposition and high astigmatism, a repeat PK rather than an endothelial keratoplasty was performed. Histology of the excised tissue showed that the DM detachment originated just central to the graft interface (Figure 1D). There was a central DM break with fibrosis on the anterior surface of the detached membrane associated with DM folds. The endothelial cell density was moderate with no evidence of inflammation. After ten months both grafts were clear with corrected visual acuities of 6/9.

CASE 2

A 49-year-old female with severe asthma and atopic dermatitis had a right PK for keratoconus 27 years previously and a left PK 25 years previously. Ten years after the left graft she had bilateral surface laser refractive surgery to reduce astigmatism. Despite multiple bilateral allograft rejections (Table 1), the grafts remained clear with a corrected visual acuity of 6/9 right eye and 6/6 left eye with scleral contact lenses. She described a sudden and painless blur of her left eye to count fingers, and there was oedema of the

inferior half of the graft. This was initially managed as an allograft rejection with hourly topical dexamethasone 0.1%, but an AS-OCT confirmed an inferior DM detachment but with no DM break. She declined treatment and the vision gradually improved to 6/60. Ten months after the episode in the left eye she had a similar sudden reduction of the vision in the right eye to count fingers due to a total DM detachment and a DM break was identified (Figure 2A and 2B). This did not resolve with 20% SF6 gas tamponade combined with corneal compression sutures.[17] Because there was poor wound apposition and high astigmatism, a repeat right PK was performed that improved the unaided vision to 6/36. After 12 months the vision in the left eye had improved to 6/60, but with poor binocular vision. Gas injection with 20% SF6 was therefore performed. This reattached the DM but the vision remained at 6/60 due to stromal haze. Histology of the right cornea showed a folded DM detachment with fibrosis and pigment deposition on the anterior (stromal) surface of the membrane.

Case 3

A 43-year-old male with severe AKC, atopic dermatitis and asthma had a right PK for keratoconus 20 years previously and a left PK 16 years previously. Right astigmatic keratotomies were performed after 10 years. With scleral lenses his visual acuities were 6/9 in both eyes, and recent graft endothelial cell densities were recorded to be 1006 cells mm^2 right eye and 1312 cell mm^2 left eye. He developed an acute and painless blur of his left eye to 6/60 with diffuse graft oedema. He was treated for two days with topical dexamethasone 0.1% for a presumed allograft rejection before an AS-OCT demonstrated a partial DM detachment limited to the inferior half of the graft (Figure 2C). No DM break was identified but the space between the DM and stroma appeared to contain filaments of stromal collagen. After nine days, and without any additional treatment, the detachment had resolved although the graft was still oedematous (Figure 2D). After 11 months the corneal graft was clear with an attached DM and his visual acuity had returned to 6/9 with a scleral contact lens.

Case 4

A 57-year old female had a right PK for keratoconus 14 years previously with a recent visual acuity of 6/9 with a rigid contact lens. The left eye had a history of acute corneal hydrops and had no surgery as it was thought to be amblyopic with a potential acuity of 6/36. She experienced a sudden painless reduction of vision in the right eye with vision reduced to 6/60. There was superior graft oedema (Supplementary Figure 1B), and an AS-OCT demonstrated a partial DM detachment based at the graft interface. Again, there appeared to be filaments between the DM and stroma (Supplementary Figure 1B). Because of poor health she declined surgical intervention. In the subsequent 12 months the sector of oedema reduced, but an area of DM detachment has persisted but reduced (Supplementary Figure 1C and 1D). She has not returned to contact lens wear and the right spectacle corrected acuity is 5/60, with the visual loss in part due to cataract.

When we include previous case reports, there were thirteen individuals (median age at onset 49 years, range 29 to 73 years) who had fourteen episodes of DM detachment at a median of 25.0 years following PK (range 7 to 33 years), affecting the right eye in 7 cases (50%). Ten of the 13 individuals were male (Table 1). In no case was trauma or eye rubbing reported to be the precipitating factor. Any loss of vision was typically described as sudden, with the degree of loss dependant on whether the central cornea was involved. In two eyes the detachment was total, with partial detachments based at the host/graft interface and involving any portion of the graft. In two eyes the DM detachment crossed the graft interface.[7] In three eyes there was spontaneous resolution, while in three eyes that were untreated the detachment persisted for at least six months. Peripheral corneal thinning or interface wound slippage was noted in ten eyes but there was no comment on this feature for three eyes. A DM tear present before gas injection or keratoplasty was only reported in three eyes. Nine eyes had tamponade of the detached DM membrane with gas, which was successful in four eyes. In four eyes, in addition to gas tamponade, there was an attempt to relieve tension on the detached DM membrane to facilitate reattachment. In three of these eyes the procedure was unsuccessful and the DM remained detached; one eye (case 2) had

corneal compression sutures, one eye had an intracameral incision of the graft interface,[7] and one eye had a descemetorhexis.[11] However, the DM reattached in one eye following a 270^{o} full thickness wound revision with gas tamponade.[8] Finally, two eyes had a PK and a three eyes had a DSAEK.

Discussion

Descemet membrane (DM) detachment is a rare late complication following a PK for keratoconus, typically occurring one to three decades after surgery. It is characterised by minor symptoms of discomfort and conjunctival redness without intraocular inflammation. There may be a sudden onset of visual blur if the area of detachment crosses the central cornea, but patients with peripheral detachment may be visually asymptomatic.[7] The presence of corneal oedema can lead to a mistaken diagnosis of allograft rejection, and the presence of a DM detachment may not be obvious without AS-OCT. In this report we describe an additional seven eyes of six patients with late DM detachment, as well as the first report of a bilateral case. To identify potential risk factors we have also reviewed the seven cases described since the first report in 2007,[7-11] including one cases in which the area of detachment was limited to the host cornea.[10] For consistency we excluded four cases with a sudden onset of host corneal oedema in which a DM detachment was not confirmed.[14-16] We also excluded two similar cases with late DM detachment, one in which the detachment was only identified at histology after a repeat PK,[13] and a second case in which the original pathology of keratoconus could not be confirmed.[12]

In this series the natural history of DM detachment was variable. One eye had a total DM detachment that resolved over one week without surgical intervention, and in two other cases there was complete resolution over several months.[9] In contrast, two eyes had partial DM detachments that did not fully resolve with up to 12 months of observation. A partial DM detachment could involve any quadrant of the graft, although the wedge of detachment was typically based at the graft interface. In almost all cases the DM detachment was limited to the donor tissue, although extension beyond the interface could occur,[7] and in one report the

DM detachment was entirely limited to the host tissue.[10] In only three of the fourteen reported eyes was a DM break identified clinically before intervention.[9] In contrast, histology in two cases demonstrated a break in the Descemet membrane with secondary scrolling from fibroblastic proliferation. In one of these cases the break may have been iatrogenic following gas injection. Peripheral host corneal thinning or wound disparity was commented in eight eyes, and six eyes had been fitted with a scleral contact lens for optimal visual correction, which is suggestive of a highly abnormal corneal contour in these eyes.

The mechanism of late DM detachment after a PK for keratoconus has been the subject of speculation, centred on the progressive change in corneal shape associated with increasing astigmatism that can occur in the decades after a PK for keratoconus. This type of change has been referred to as recurrence of keratoconus, which is disease specific as it is a feature of PKs for keratoconus but not Fuchs endothelial corneal dystrophy.[18] Secondary ectasia is characterised by an increase in both average keratometry and astigmatism.[19] Thinning of the host and wound attenuation can cause corneal flattening in the meridian of maximal host thinning, which is usually inferior but can occur in any quadrant.[20] In this study we identified thinning of the host rim with wound slip in six of the seven additional eyes that we have reported, while in one eye the mean keratometry was abnormally flat although there were 12 dioptres of astigmatism. Changes in the anatomy of the graft interface from stretching and progressive ectasia could then cause mechanical traction on the relatively weak anchoring structures of the pre-Descemet layer,[21] or emphasise differences between the elasticity of the DM and posterior stroma.[22] In contrast to acute corneal hydrops, a primary break in the central DM was usually not present in eyes with late detachment,.

Another potential mechanism for late DM detachment is endothelial cell failure. Although a recent measurement for endothelial cell density was only available in three of the eyes, the figures were compatible with a long-term PK rather than corneal decompensation.[23] Finally, keratoconus is associated with chronic allergic eye disease, and four of the six individuals in our series were severely atopic. However, individuals in this study usually specifically denied

eye rubbing immediately prior to their loss of vision.[8] Unfortunately, none of the previous reports contained details of associated disease. There was also insufficient data to comment on the effect of an acute corneal hydrops prior to the PK as a proxy for severity of keratoconus before surgery.

The prefered management in this series was generally an attempt at DM reattachment by gas tamponade, followed by keratoplasty if this failed. The DM was reattached by gas tamponade in four of nine eyes in which it was attempted. Interestingly, it was successful in one eye after almost ten months of DM detachment. There was no clear benefit of most adjunctive procedures to alleviate DM traction (corneal compression sutures, internal wound incision, or Descemetorhexis), although 270^{o} wound revision was successful in one case. A DSAEK was performed in three eyes and a PK in two eyes for visual rehabilitation when there was persistent DM detachment after tamponade. A PK is an option to potentially correct wound disparity, reduce astigmatism and high refractive error that had previously meant scleral lens wear was required for visual correction. High astigmatism is likely to persist Following DSAEK unless the surgery is combined with wound revision, and continued scleral lens wear may be necessary following a DSAEK.[7,11]

In conclusion, the aetiology of this condition is unknown, although it is strongly associated with peripheral corneal thinning, wound slippage and ectasia consistent with recurrence of keratoconus. However, we have not included a control group and, potentially, these changes may be common in PKs for keratoconus after 20 years, with only a minority progressing to DM detachment for unrelated reasons. Another weakness of this study is the poor recording of potential risk factors in previous publications. However, the study highlights that a DM detachment should be excluded in patients who present with a sudden onset of visual blur and corneal oedema many years following a PK for keratoconus. Although some cases will resolve spontaneously, and intracameral tamponade with gas can reattach the membrane, an endothelial keratoplasty or repeat PK may be required.

Legends

Figure 1.

(A) Clinical image of Patient #1 showing diffuse graft oedema with details of the detached Descemet membrane (DM) visible within the anterior chamber (arrow). (B) Anterior segment optical coherence tomography (AS-OCT) shows complete DM detachment across the posterior surface of the graft. There is minor thinning of the host peripheral cornea inferiorly without wound slippage. (C) Following tamponade with gas the DM detachment is still present with a probable secondary DM tear (arrow). (D) Histology shows the DM attached to the posterior interface between the graft and host. There is fibroblastic proliferation on the posterior surface of the DM with secondary folds (PAS 4x objective).

Figure 2.

(A) Anterior segment ocular coherence tomography (AS-OCT) of the right eye of Patient #2 demonstrates a complete Descemet membrane (DM) detachment that extends across the presumed graft interface (asterisk). There appear to be fibrous adhesions between the DM and the stroma, a DM break centrally, and oedema of the host cornea (arrow). (B) An AS-OCT taken of the same eye one week later and at a meridian 90^{o} to (A). There appears to be a fluid cavity within the stroma at the wound and the DM is less folded. (C) Partial DM detachment of Patient #3. The space between the DM and stroma was not optically transparent and may contain filaments of stroma (inset, arrow). (D) After one week the DM detachment of Patient #3 had spontaneously resolved, although there is some persistent swelling of the graft that resolved over the subsequent months.

Supplementary Figure 1.

(A) Vertical Scheimpflug image taken from Patient #4 one year prior to Descemet membrane (DM) detachment. There is thinning of the host cornea at the superior graft interface (arrow) that corresponds to the segment of subsequent DM detachment. (B) Clinical photograph showing oedema of the superior graft that corresponded to an area of DM detachment demonstrated by anterior segment optical coherence tomography (AS-OCT), which

extended to the graft interface superiorly (C). Similar to Patient #3 (Figure 2C), there appear to be filaments of material within the space between the DM and stroma. After twelve months the area of corneal oedema had reduced clinically (D), with a reduction both in the extent of DM detachment and associated corneal thickening.

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