

Intracameral tissue plasminogen activator to mitigate anterior chamber fibrin reaction in pediatric DMEK

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Abstract

A 4-year old male was referred for corneal edema and blurry vision. Initial exam findings were notable for bilateral, visually significant cornea edema, worse in the left eye with decreased vision bilaterally.

Patient's exam and family history were consistent with a diagnosis of Posterior Polymorphous Corneal Dystrophy (PPCD). Visually significant corneal edema and risk of amblyopia prompted the discussion for corneal transplantation and the family elected to proceed with Descemet Membrane Endothelial Keratoplasty (DMEK). This case describes successful, bilateral DMEK surgery in a 4-year old with PPCD facilitated by the use of intracameral tPA (tissue plasminogen activator) to mitigate the anterior chamber (AC) fibrin reaction that can occur in DMEK. To our knowledge, this is the youngest reported successful DMEK procedure and also the first case report describing the use of intraoperative tPA to combat the fibrinoid reaction.

History

A 4-year-old male was referred for corneal edema and blurry vision. Patient's mother noted the patient was experiencing difficulty reading and not tolerating the prescribed glasses. Patient's mother noted she had several family members with corneal disease that required a corneal transplant.

Examination

Initial cycloplegic refraction revealed mild hyperopic astigmatism with BCVA of 20/150 and 20/400 in the right and left eye, respectively. Right and left eye baseline IOP measurements were 19 and 18 mmHg, respectively. Anterior segment exam (Figure 1) revealed broad areas of thickened, irregular endothelium in both eyes with overlying edema and posterior corneal haze, slightly worse in the left eye. Endothelial cystic changes and "snail tracks" were present bilaterally. Pupils were round and there was no evidence of iris synechiae.

The exam findings were consistent with PPCD. Incidentally, the patient's mother was also examined and demonstrated similar findings as well as focal areas of peripheral anterior synechiae, confirming the diagnosis of PPCD.

Discussion and diagnosis

PPCD is a rare, autosomal dominant, corneal endothelial dystrophy; the pathogenesis of the disease entails an irregular differentiation of the endothelium with transformation into epithelial-like cells.^{1,2} In rare instances, this disease can manifest early in life with visually

significant corneal edema and may require corneal transplantation to reduce the risk of amblyopia.^{2,3}

DMEK has emerged as an excellent option for diseases targeting the endothelium owing to rapid visual rehabilitation and decreased risk of rejection.⁴ Moreover, although the cases were performed in adults, prior studies have demonstrated favorable DMEK outcomes in PPCD.^{6,7} DMEK in pediatric patients, however, may be more challenging attributable to difficulty stripping the host endothelium, more aggressive intraocular inflammation (including a predisposition to generate fibrin) and challenges with postoperative compliance. A prior case report by Strungaru et al⁵ described an unsuccessful DMEK attempt in a 4-month old infant necessitating subsequent DSAEK.

After extensive discussion, the patient's family elected to proceed with DMEK surgery. For the first eye (left), a backup pre-cut DSAEK tissue was available if the DMEK graft could not be successfully unscrolled. A sterile solution of intracameral tPA (0.1 mL of 12.5 µg/0.1 mL) was also prepared in anticipation of a possible anterior chamber fibrinoid reaction.^A

DMEK was performed under general anesthesia according to a prior, published standardized technique with modifications.⁸ To prevent pupillary block, a small inferior peripheral iridectomy was created by excising a small segment of peripheral iris through a separate incision. Owing to equipment availability, graft orientation was confirmed using two different methods (S-stamp for the first eye and intraoperative OCT for the second eye).

For the first eye, despite insertion of the DMEK tissue in an optimal configuration, the graft could not be unscrolled due to rapid fibrin formation in the AC causing the graft to diffusely adhere to the iris. Shortly after, tPA was injected into the AC. Although initially there was no discernible response, the tissue behavior improved dramatically within 15 minutes, permitting successful graft attachment after 21 minutes of manipulation. For the second eye, tPA was injected 10 minutes prior to graft insertion. No fibrinoid reaction occurred and the DMEK scroll was unscrolled uneventfully in under 3 minutes.

Postoperatively, the first DMEK graft was fully attached on postoperative day 1 and all subsequent visits (Figure 2). For the second eye, a thin, temporal detachment with symptomatic edema developed 1-week postoperatively (Figure 3). The graft was successfully re-bubbled on postoperative day 10. At 1 month postoperative, both grafts remained fully attached with improved edema (Figure 4).

Conclusion

As an intraocular injection, tPA has demonstrated efficacy for treating fibrinous exudates encountered in uveitic patients.⁹ Moreover, it has been demonstrated to be of value in the postoperative setting for treating fibrinoid reactions with prior studies describing its use¹⁰⁻¹² in pediatric cataract surgery to attenuate the amplified inflammatory response.¹³⁻¹⁵ However, there has been scant discussion regarding its use in the intraoperative setting, and no prior usage in DMEK surgery.

Our case highlights the potential value of intracameral tPA intraoperatively to treat, or, optimally prevent, the spontaneous fibrinoid reaction that may complicate DMEK in pediatric eyes. The significantly improved intraoperative behavior of the second eye signifies the value of pre-treating eyes at high risk for intraoperative fibrin.

Given that this is an isolated case report, further research is warranted to further evaluate the use of intraoperative tPA. The high cost of tPA may be cost prohibitive for some institutions and the short shelf-life (<24 hrs) of prepared, intracameral tPA complicates its potential as a rescue therapy. Use of an alternative, lower cost fibrinolytic such as heparin may circumvent some of these issues and prior studies have highlighted it's anti-inflammatory properties in pediatric cataract surgery.¹⁶ Finally, although it was not observed in this case, the use of any anti-thrombotic agent may enhance the risk of intraocular hemorrhage.

To our knowledge, this case represents the youngest patient to undergo successful DMEK surgery. This is also the first report describing the use of intracameral tPA intraoperatively to both treat, and prevent, anterior chamber fibrinoid reaction during DMEK surgery. Although further investigation is warranted, this case supports the use of intracameral tPA to facilitate DMEK surgery for patients at high risk of an intraoperative fibrinoid reaction.

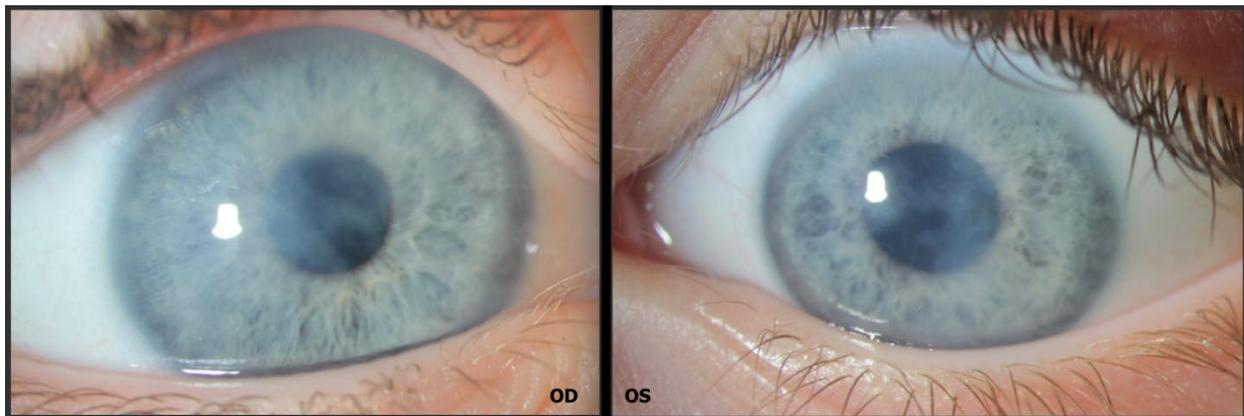


Figure 1. Slit-lamp photo from initial visit depicts the bilateral, visually significant corneal edema present bilaterally at the initial exam.

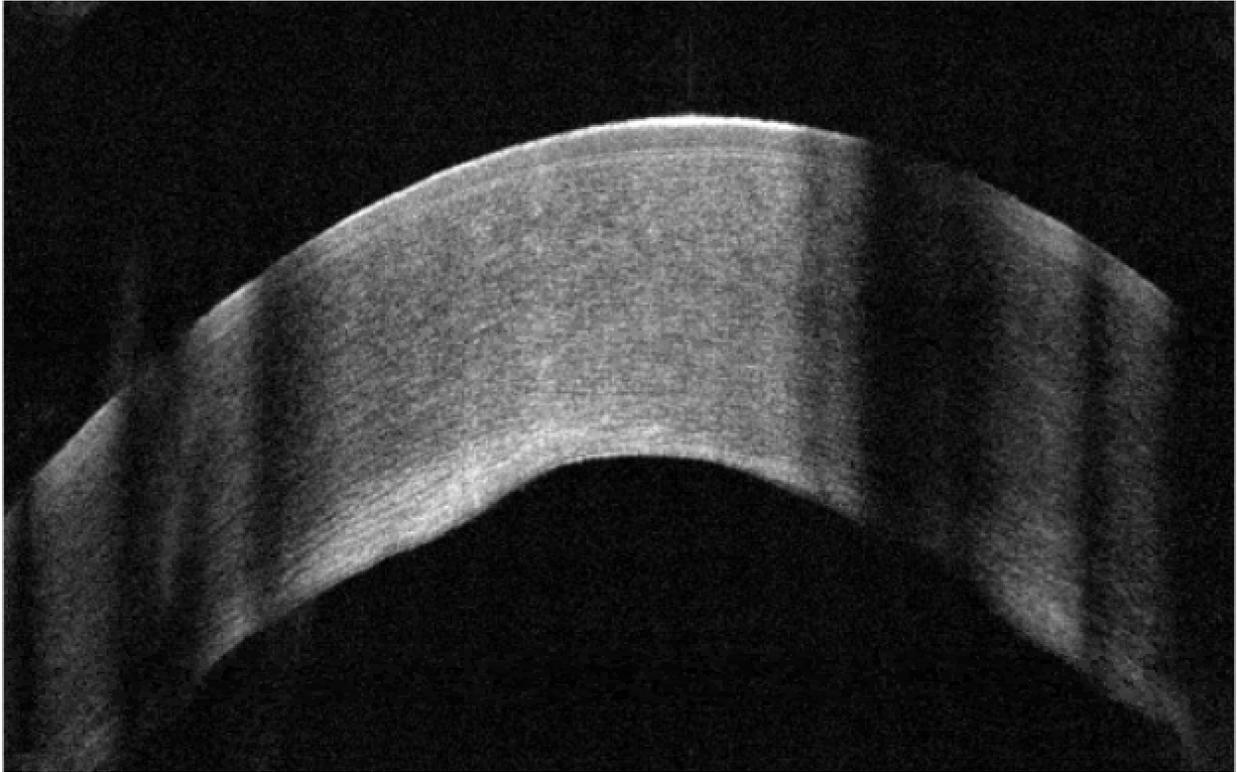


Figure 2. Anterior segment OCT photo taken 5 days postoperatively in the first operative eye (OS). Image demonstrates fully attached DMEK graft with mild-moderate stromal edema.

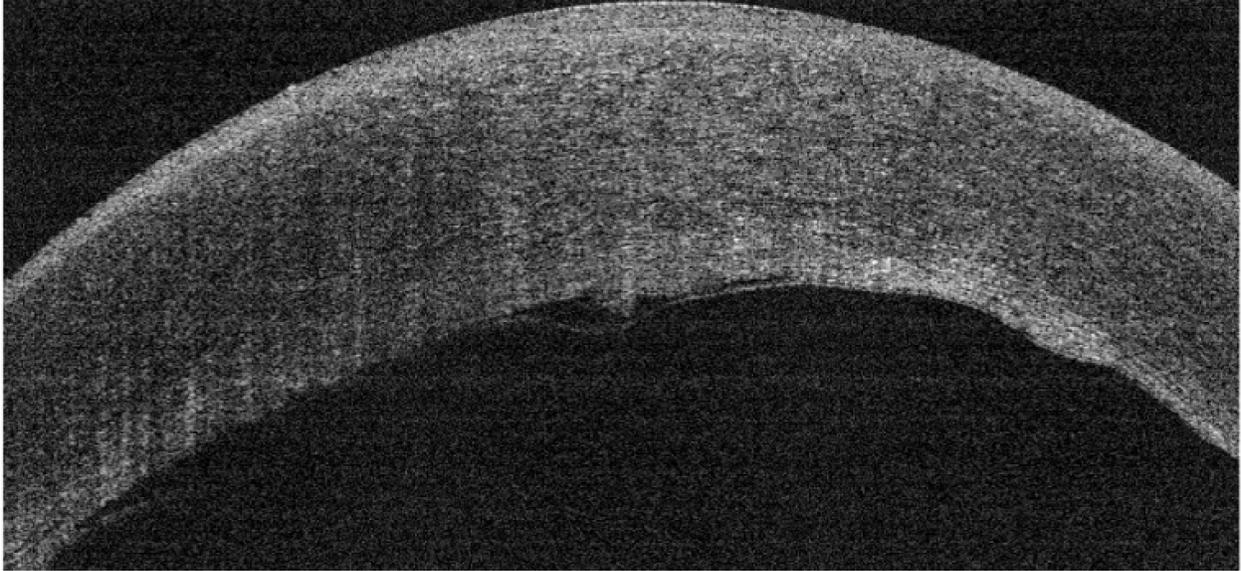


Figure 3. Anterior segment OCT photo captured at 1-week postoperative in the second eye (OD). Image demonstrates a thin detachment temporally with overlying edema. Posterior stromal irregularities are visible centrally which may have contributed to poor adherence. Re-bubbling was performed successfully at 10 days postoperative and the graft remained fully attached at 1 month postoperative.

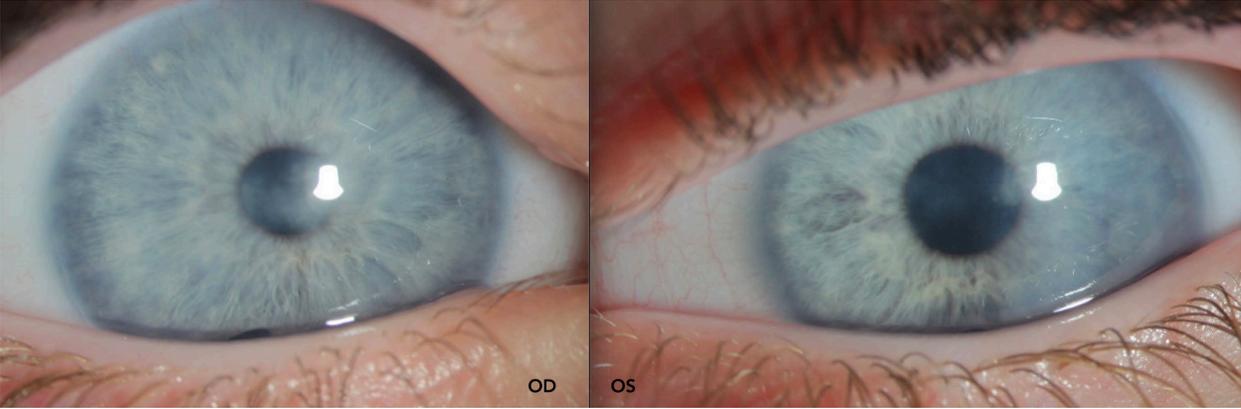


Figure 4. Slit-lamp photo captured at 1 month postoperative in the second eye (OD) and 2 months postoperative in the first eye (OS). Left eye shows significant improvement in haze and corneal edema. Right eye (OD) demonstrates residual stromal haze with overall improvement in corneal edema.

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