

Stromal graft rejection after uneventful deep anterior lamellar keratoplasty with a misleading manifestation similar to viral endotheliitis: A case report

Reza Soltani-Moghadam¹, Mitra Akbari²

Department of Ophthalmology, Eye Research Center, Guilan University of Medical Sciences, Rasht, Iran

CASE STUDY

Please cite this paper as: Soltani-Moghadam R, Akbari M. Stromal graft rejection after uneventful deep anterior lamellar keratoplasty with a misleading manifestation similar to viral endotheliitis: A case report. AMJ 2018;11(1):14–17. <https://doi.org/10.21767/AMJ.2017.3250>

Corresponding Author:

Mitra Akbari MD

Assistant Professor of Ophthalmology, Eye Research Center, Guilan University of Medical Sciences, Rasht, Iran

Email: mitra.akbari20@gmail.com

ABSTRACT

We describe an unusual and misleading manifestation of stromal graft rejection after uneventful deep anterior lamellar keratoplasty (DALK). A 25-year-old healthy man with advanced keratoconus underwent uneventful DALK. After a few months, developed recurrent graft oedema, acute and diffuse epithelial and stromal oedema, few very fine keratic precipitates (KPs) in the allograft and not seen in the recipient bed, anterior chamber (AC) inflammation with cells and flair, without any vascularization in the graft and recipient bed, and without any infiltration or loosening of the sutures. Polymerase chain reaction (PCR) analysis was performed on an aqueous sample, which was negative for herpes simplex virus (HSV) and cytomegalovirus (CMV). Management with topical and systemic steroids led to complete resolution of the problem. Although there is no endothelial immune reaction after uneventful DALK, stromal graft rejection after DALK can present with the same features as endothelial graft rejection and should be differentiated from other similar demonstrations such as viral induced endotheliitis.

Key Words

Deep anterior lamellar keratoplasty, endothelial rejection,

stromal graft rejection, endotheliitis

Implications for Practice:

1. What is known about this subject?

Allograft rejection is one of the most important complications after any transplantation procedure.

2. What new information is offered in this case study?

Unusual and misleading presentation of stromal rejection after DALK with similar features with endothelial rejection or viral endotheliitis can occur.

3. What are the implications for research, policy, or practice?

Strong clinical suspicion and prompt recognition with aggressive treatment is necessary in order to achieve a good visual outcome after stromal rejection in DALK.

Background

In corneal transplantation, an advantage of deep anterior lamellar keratoplasty (DALK) over penetrating keratoplasty (PKP) is the elimination of endothelial rejection.¹ The preservation of a healthy host endothelium in DALK prevents the possibility of endothelial rejection, which is considered as a primary factor in both early and late graft failure following PKP. There are three types of rejection (including stromal, epithelial, and subepithelial), which may occur in cases of DALK using the big-bubble technique.² There are reports that discriminated the stromal rejection after DALK and presented typically with graft stromal oedema and stromal haze occurring specially near the blood vessels and interface neovascularization.²

In this case report, we describe an unusual and misleading presentation of stromal rejection after DALK without neovascularization and had a similar features with endothelial graft rejection versus viral endotheliitis.

Case details

A 25-year-old healthy man with advanced keratoconus in

both eyes underwent DALK in his right eye. An uneventful DALK with 8.25mm graft size was performed using the standard big-bubble technique.³ During this procedure, the Descemet membrane of the donor cornea was removed completely and 16 interrupted 10-0 nylon sutures were applied.

After surgery, a topical antibiotic agent, chloramphenicol 0.5 per cent (Chlobiotic, Sina Darou, Tehran, Iran) and steroid eye drop, betamethasone 0.1 per cent (Betasonate, Sina Darou, Tehran, Iran) were started four times a day. The topical antibiotic was continued until corneal epithelialization was completed. Also, topical steroid was tapered during three months according to ocular surface inflammation. The ocular surface was continuously lubricated using topical preservative-free artificial tears (Artelac; Bausch and Lomb, France). Best spectacle-corrected visual acuity (BSCVA) was 20/25 in the right eye at three months after operation.

Five months after surgery, the patient was referred with the complaints of red eye and decreased vision in the right eye. Slit lamp examination revealed the presence of acute corneal graft epithelial and stromal oedema, diffuse stromal oedema involving the entire graft, few and very fine keratic precipitates (KPs) limited only to the graft location without evidence of any vascularization in the graft and recipient bed. No infiltration and loosening of the sutures were seen. There was also anterior chamber (AC) inflammation with cells and flair. The intraocular pressure was 14mmHg using applanation tonometer. Diagnostic AC tap was performed and aqueous fluid was sent for polymerase chain reaction (PCR) analysis for herpes simplex virus type-1 (HSV-1), herpes simplex virus type-2 (HSV-2) and cytomegalovirus (CMV). PCR was negative for those viruses. The patient was managed with betamethasone 0.1 per cent eye drops hourly, levofloxacin (OFTAQUIX 5mg/ml očni kapky, roztok) four times per day, and systemic prednisolone 50mg per day that was soon tapered after the clinical response. The stromal oedema was reduced markedly after five days and was resolved within 10 days accompanied with regression of KPs and AC inflammation. After one month, there was a clear graft with uncorrected visual acuity (UCVA) and best-corrected visual acuity (BCVA) of 20/60 and 20/25, respectively. The topical corticosteroid was tapered and continued for three months.

Nine months after the first episode, the patient was referred again with the same signs and symptoms with graft oedema and KPs limited to the graft location (Figure 1). The BCVA was 5/60 in his right eye. The graft was oedematous

and there was moderate congestion with fresh KPs and 2+ cells in the anterior chamber of the affected eye. The KPs were fine in size and were localized to the area of stromal oedema of the graft. He underwent medications with topical betamethasone 0.1 per cent eye drops hourly; topical levofloxacin eye drops four times a day and oral steroid 1mg/kg/day again. Reduction in the graft oedema and resolution of the AC reaction and KPs occurred rapidly with this management. After two weeks, the clinical response was optimal and clear graft was achieved (Figure 2).

Discussion

Allograft rejection is one of the most important complications after any transplantation procedure. The occurrence of rejection following corneal transplantation may lead to focal or global corneal dysfunction, which is occasionally irreversible. The resulting level of dysfunction depends on the magnitude, location, and duration of the alloimmune response before proper recognition and treatment as well as the location and density of target antigens within the donor tissue layers.⁴ To improve graft survival and reduce the risk of endothelial graft rejection, corneal surgeons recommend anterior lamellar keratoplasty (LK), which involves targeted substitution of damaged corneal tissue and retention of intact healthy corneal tissue. The avoidance of rejection is the important factor influencing surgical outcomes after keratoplasty.⁵ Due to retaining a healthy endothelium of the host, DALK has become the preferred surgical approach for corneal diseases not involving the endothelium. Thus there is no endothelial immune reaction after DALK. However, the three types of stromal, epithelial, and subepithelial rejections may occur after DALK with the big-bubble technique.⁶ Chances of irreversible vision loss caused by stromal rejection are always present after DALK.⁷

The contributing factors for stromal rejection after DALK are dependent on sutures, so that loose sutures incite peripheral vascularization and suture infiltration. Previous vascularization and vernal keratoconjunctivitis are other reported risk factors for graft rejection after the big-bubble technique.⁸ Other risk factors include PKP in fellow eye and atopic keratoconjunctivitis.⁹

Stromal rejection following DALK may present as corneal oedema, hazy or partial stromal infiltration with accompanying neovascularization limited to the graft area. Patients with stromal rejection have bothersome eye symptoms (e.g., ocular discomfort and redness) that may be misdiagnosed. But a prompt response is observed to the

initiation of the correct treatment. If this complication is left untreated or undiagnosed, the persistence of signs and symptoms may jeopardize visual outcomes. Permanent stromal scarring may lead to the profound visual loss in these cases.⁶ Timely diagnoses of stromal rejection after DALK and its prompt and meticulous management is mandatory in order to prevent the consequences of untreated stromal rejection including vascularization and opacification of the graft.¹⁰

In our case, atypical stromal rejection appeared with stromal oedema without neovascularization. The oedema gradually spread over the entire stroma. Stromal inflammation may be disturbed endothelial function and cause stromal oedema. The inflammatory reaction of the anterior chamber may be secondary to the occurrence of stromal inflammation and its spillover.

Our patient had no previous history of allergic keratoconjunctivitis and herpes simplex virus keratitis. Herpes simplex virus can present with endotheliitis after keratoplasty such as previously reported after Descemet membrane endothelial keratoplasty (DMEK).¹¹ Our diagnosis of stromal rejection was based on PCR analysis of an aqueous sample, which was negative for herpes simplex virus types-1, type-2 and CMV. Also the clinical examination and dramatic response to topical and systemic steroids were helpful.

It is probable that true episodes of stromal rejection have been misclassified as “endothelial rejection” in studies that have examined rejection patterns in PKP.⁵ This phenomenon can occur for DALK such as our case that stromal rejection appeared similar to endothelial rejection or endotheliitis. Evaluation of stromal rejection after Femto-DALK with in-vivo confocal microscopy revealed cellular inflammatory infiltrates in the subepithelial and middle stroma of the donor lamella without an involvement of the endothelium.¹⁰

In conclusion, the clinical presentation of stromal graft rejection, in this case, did not resemble those of previously published case reports, which had prominent corneal neovascularization without significant anterior chamber reaction and KPs. This unusual presentation of stromal graft rejection should be differentiated from similar presentation such as HSV and CMV endotheliitis. Stromal graft rejection remains as a significant complication after DALK but is associated with a good recovery, because the endothelium is spare.

Conclusion

Strong clinical suspicion and prompt recognition with aggressive treatment is necessary in order to achieve a good anatomic and visual outcome after stromal rejection in DALK.

References

1. Shimazaki J, Shimmura S, Ishioka M, et al. Randomized clinical trial of deep lamellar keratoplasty vs penetrating keratoplasty. *Am J Ophthalmol*. 2002;134(2):159–165.
2. Watson SL, Tuft SJ, Dart JK. Patterns of rejection after deep lamellar keratoplasty. *Ophthalmology*. 2006;113(4):556–560.
3. Anwar M, Teichmann KD. Big-bubble technique to bare Descemet's membrane in anterior lamellar keratoplasty. *J Cataract Refract Surg*. 2002;28(3):398–403.
4. Noble BA, Agrawal A, Collins C, et al. Deep Anterior Lamellar Keratoplasty (DALK): visual outcome and complications for a heterogeneous group of corneal pathologies. *Cornea*. 2007;26(1):59–64.
5. Panda A, Vanathi M, Kumar A, et al. Corneal graft rejection. *Surv Ophthalmol*. 2007;52(2):375–396.
6. Olson EA, Tu EY, Basti S. Stromal rejection following deep anterior lamellar keratoplasty: implications for postoperative care. *Cornea*. 2012;31(9):969–973.
7. Fontana L, Parente G, Tassinari G. Clinical outcomes after deep anterior lamellar keratoplasty using the big-bubble technique in patients with keratoconus. *Am J Ophthalmol*. 2007;143(1):117–124.
8. Feizi S, Javadi MA, Javadi F, et al. Deep anterior lamellar keratoplasty in keratoconic patients with versus without vernal keratoconjunctivitis. *J Ophthalmic Vis Res*. 2015;10(2):112–7.
9. Epstein AJ, de Castro TN, Laibson PR, et al. Risk factors for the first episode of corneal graft rejection in keratoconus. *Cornea*. 2006;25(9):1005–1011.
10. Mosca L, Fasciani R, Mosca L, et al. Graft rejection after femtosecond laser-assisted deep anterior lamellar keratoplasty: report of 3 Cases. *Cornea*. 2011;30(8):912–916.
11. Zarei-Ghanavati S, Alizadeh R, Yoo SH. Herpes simplex virus endotheliitis following descemet's membrane endothelial keratoplasty. *J Ophthalmic Vis Res*. 2015;10(2):184–186.

PEER REVIEW

Not commissioned. Externally peer reviewed.

CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

FUNDING

None

PATIENT CONSENT

The authors, *Soltani Moghadam R, Akbari M*, declare that:

1. They have obtained written, informed consent for the publication of the details relating to the patient in this report.
2. All possible steps have been taken to safeguard the identity of the patient.
3. This submission is compliant with the requirements of local research ethics committees.

Figure 1: Total graft edema without vascularization 14 months after DALK

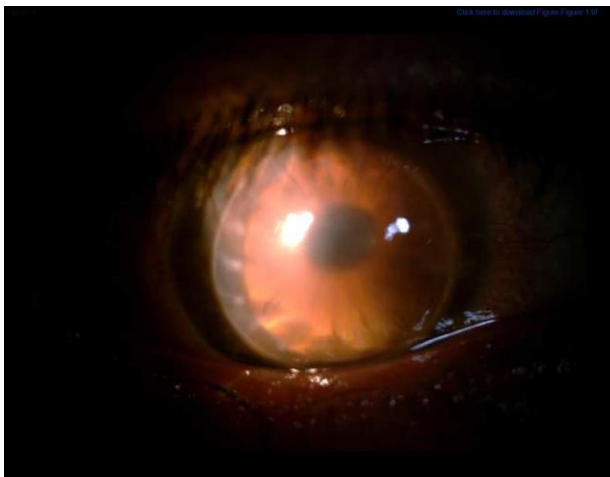


Figure 2: Clear graft one month after graft edema resolution

