Presumed herpes simplex virus endotheliitis following ultra-thin Descemet's stripping automated endothelial keratoplasty

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A 78-year-old male underwent ultra-thin DSAEK for PBK (OS) and achieved BCVA 6/12 at 9 months. The patient developed allograft rejection 10 months postoperatively and was treated with IV methyl prednisolone, systemic, and topical steroids. The patient then improved and achieved 6/18 BCVA at 8 weeks. Topical prednisolone 1% twice daily was continued. Six weeks later, the patient developed fever and diminished vision and had high IOP, corneal edema, and keratic precipitates on endothelium. Considering it to as second episode of graft rejection, IV methyl prednisolone and topical steroids were given. Seeing no response, presumed HSV endotheliitis was considered as diagnosis and treated with steroids, oral acyclovir. The patient improved and achieved BCVA 6/24 with no subsequent recurrence during 11 months follow-up.

Key words: Descemet's stripping automated endothelial keratoplasty, endothelial keratoplasty, herpes simplex virus, HSV endotheliitis, viral endotheliitis

In recent years endothelial keratoplasty (EK) has emerged as a standard of care for the management of pseudophakic corneal edema (PBK). Both Descemet's membrane endothelial keratoplasty (DMEK) and Descemet's Stripping Automated Endothelial Keratoplasty (DSAEK) have advantages over penetrating keratoplasty (PKP) including, non-compromised wound strength, elimination of suture related complications, less post-surgery astigmatism, and early visual rehabilitation.[1] In addition lower incidence of allograft rejection following DSAEK is a major advantage.[1] From clinical standpoint, it is important to differentiate allograft rejection from Herpes simplex virus (HSV) endotheliitis as the treatment is different and antiviral prophylaxis to prevent recurrence is needed.[2] We report an unusual case, who developed HSV endotheliitis after successful treatment of allograft rejection following ultrathin DSAEK performed for PBK.

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Case Report

An immunocompetent 78-years-old male presented with pain, redness, watering and diminished vision (DV) in OS, 7 months following cataract surgery. Patient did not reveal any history of recurrent redness. His BCVA in the OD was 6/6 and 6/60 OS. Intra ocular pressures in OD and OS were 17 and 16 mm Hg, respectively. Slit lamp biomicroscopy revealed clear cornea and pseudophakia OD and marked corneal edema OS. There were no keratic precipitates (KPs), no synechiae and well centered PCIOL in either eye. Retina examination did not reveal any abnormality OD. B scan of the OS was normal. Diagnosis of PBK was considered and ultrathin DSAEK in OS was planned.

An uneventful ultrathin-DSAEK was performed on 28th Dec 2017. A clear corneal incision with 2.8 mm disposable keratome was made. Two side ports were prepared. Descemets membrane was stripped off using a reverse sinskey hook. Donor lenticule 8.0 mm diameter was punched out from the pre-cut donor cornea. Donor cornea had 2870/mm^2 endothelial cell density and 92 microns thick donor lenticule. Donor lenticule was loaded into the Endosaver (SightLife surgical, Winston-Salem,

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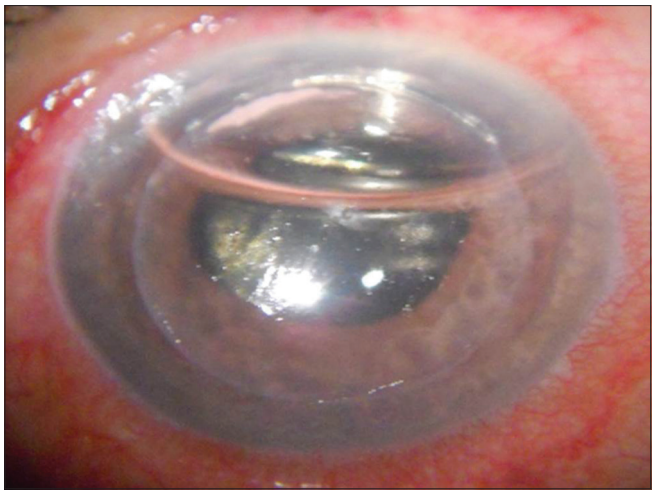

Figure 1: DSAEK 72 hour post op, Clear cornea, well centered and firmly attached donor lenticule with partially absorbed air bubble

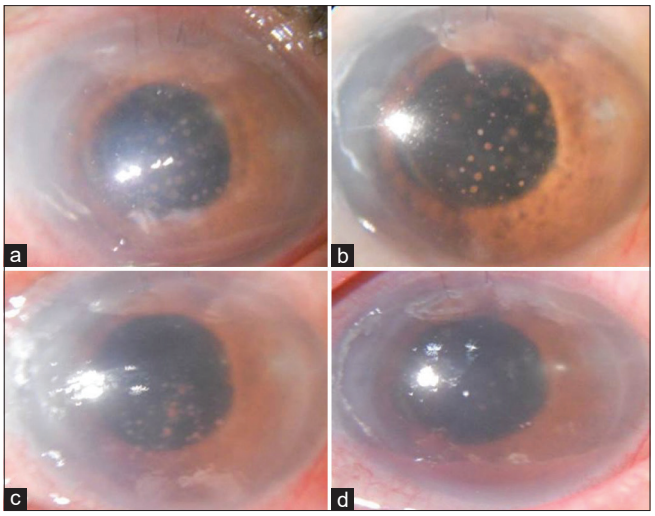

Figure 2: (a) Corneal edema and KPs on donor lenticule (Graft rejection post DSAEK, active) (b) Clear cornea and old KPs (Graft rejection, healed at 8 weeks) (c) Corneal edema with KPs on donor lenticule (HSV endotheliitis) (d) Clear cornea with few old KPs (HSV endotheliitis healed. Positive response to Acyclovir and Steroid)

NC 27101 USA) and was delivered into the anterior chamber. An air bubble was placed in the anterior chamber and the lenticule was centered. Patient was made to lie down for 20 minutes. After 1 hour 20% of air was removed. Patient was put on moxifloxacin 0.5% (Vigamox 5 mg/ml; Alcon Laboratories, USA, Inc.), prednisolone accetate 1% suspension (Pred Forte, 10 mg/ml Allergan USA, Inc.) and cyclopentolate hydrochloride 1% (Cyclate 10 mg/ml ZydusCadila Healthcare Ltd, India) each thrice daily. Post-operative period was uneventful [Fig. 1. Patient achieved BCVA 6/24 at 1 month and further improved to 6/18 (-1.25/-2.50 × 80^0) at 3 months. IOP was normal. Topical steroid was tapered to prednidolone 1% twice daily. Patient achieved BCVA 6/12 at 9 months follow-up.

Patient developed sudden DV in OS 10 months after surgery. He had corneal edema and medium sized KP's on donor lenticule and was diagnosed as allograft rejection [Fig. 2a]. He was given I/V methyl prednisolone (IVMP) I gm daily for 3 days and topical prednisolone acetate 1% every 1 hour. Patient improved, steroids were tapered and achieved BCVA 6/18 at 8 weeks [Fig. 2b]. Topical prednisolone 1% twice daily was continued. Six weeks later patient had fever and again developed DV in OS. His IOP in OD and OS were 18 and 29 mm Hg. Slit lamp biomicroscopy revealed corneal edema, KP's on donor lenticule [Fig. 2c]. Considering second episode of graft rejection patient was given I/V methyl prednisolone 1 gm daily for three days in addition to topical prednisolone 1% 1 hourly. Patient did not show any response at 1 week. Then diagnosis of presumed HSV endotheliitis was considered and was given oral acyclovir 400 mg 5 times a day in addition to steroids. Patient improved and achieved 6/24 at 6 weeks [Fig. 2d]. Topical prednisolone 1% was gradually reduced to twice daily. Patient was kept on acyclovir 400 mg twice daily and did not develop any recurrence during 11 months follow-up.

Discussion

Post DSAEK allograft rejection has been reported in 0.6% patients. HSV-1 DNA has been isolated from 2 of 51 (4.0%) failed DSAEK grafts.[3] Preoperative diagnosis was HSV endotheliitis in the first and failed PKP for keratoconus in second.[3] HSV endotheliitis after successful treatment of graft rejection following DSAEK for PBK has not been reported. Clinical differentiation between the two is necessary as HSV endotheliitis needs acyclovir during treatment and prophylaxis.

The second episode made us suspicious whether we are dealing with graft rejection or HSV endotheliitis. Episode of fever before onset of DV is characteristic of HSV recurrence. Patient developed recurrence of inflammation, while he was still on topical steroids. Fresh KPs on the graft and raised IOP indicated more of HSV endotheliitis. It is possible that due to prior topical steroid instillation KPs on host cornea were not seen. Three consecutive doses of IVMP as in optic neuritis, were given to achieve maximum anti-inflammatory response and to reset the aberrant immune response.[4,5] Patient did not respond to steroids alone, but responded to combination of steroids and oral acyclovir. Patient did not develop any recurrence during 11 months of follow-up while on acyclovir prophylaxis. Clinical presentation, response to oral acyclovir, and no recurrence during acyclovir prophylaxis confirm the diagnosis of presumed HSV endotheliitis.[2]

Corneal endotheliitis may also occur due to varicella zoster virus (VZV) and cytomegalo virus (CMV).[6] Post DSAEK endotheliitis patients not responding to combined acyclovir and corticosteroids, have been advocated confocal microscopy and aqueous tap for viral DNA PCR.[7] Coin shaped KP's on confocal microscopy indicate CMV endotheliitis and positive PCR test is confirmatory.[8,9] For CMV endotheliitis treatment gancyclovir is preferred.[10]

Conclusion

A high index of suspicion is needed in cases with post DSAEK recurrent endotheliitis and suboptimal response to steroids. An aqueous tap for viral PCR may be performed in such a scenario for an early diagnosis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have

given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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