CASE REPORT

Successful management of immunological rejection following allogeneic simple limbal epithelial transplantation (SLET) for bilateral ocular burns

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SUMMARY

A 41-year-old woman presented with bilateral total limbal stem cell deficiency, one year after chemical injury. She underwent allogeneic simple limbal epithelial transplantation (SLET) from a cadaveric donor in her right eye. One month later her unaided visual acuity (VA) improved to 20/100 from hand-motions. The corneal surface was avascular and epithelialised. Three months later, she presented with acute pain in right eye with peripheral corneal neovascularisation encircling the transplants, engorged and tortuous perilimbal vessels and diffuse epithelial haze. For a diagnosis of allograft rejection, pulse doses of intravenous methyl prednisolone with intensive topical steroids were administered. Her symptoms resolved in a week, confirming the diagnosis. She recovered her pre-rejection VA. She was maintained on systemic immunosuppressive agents. Her ocular surface continues to be stable. This case describes hitherto unknown clinical features of allograft rejection following SLET and emphasises the importance of continued immunosuppression in allogeneic limbal transplantation.

BACKGROUND

Simple limbal epithelial transplantation (SLET) is a novel surgical technique of limbal stem cell transplantation (LSCT), which combines the benefits of cultivated and conventional LSCT.[1] SLET obviates the need for a stem cell biology laboratory and requires minimal amount of donor limbal tissue.[1] This case reports the first application of allogeneic SLET using a cadaveric donor to treat bilateral corneal blindness due to LSCD, highlighting the unique clinical features of immune rejection and its management.

CASE PRESENTATION

A 41-year-old woman presented with bilateral and total LSCD, 1 year after sustaining extensive ocular surface damage following accidental alkaline burns. Unaided visual acuity was light perception in both eyes, without further improvement on refraction. Slit lamp biomicroscopy showed bilateral absence of limbal palisades, conjunctivalised corneal surfaces with extensive symblepharon formation (figure 1A,B). Intraocular pressure appeared normal on digital palpation in both eyes and ultrasound B scan showed normal posterior segment findings.

The treatment options of allogeneic limbal stem cell transplantation (SLET or cultivated) and autologous oral mucosal epithelial transplantation were discussed with the patient. As a suitable living donor was not available and her oral hygiene was not deemed appropriate for obtaining oral mucosa, she underwent an allogeneic SLET in her right eye from a cadaveric donor in June 2012. Briefly, this procedure involved removing the vascularised pannus from the cornea; placing a human amniotic membrane (hAM) graft on the bare ocular surface with fibrin glue; transplanting small bits of limbal tissue obtained from a fresh corneo-scleral rim on the cornea covered with the hAM graft in a circular fashion avoiding the visual axis; placing a layer of fibrin glue to fix the transplants and placing a soft bandage contact lens over the eye at the end of the procedure.

She was continued on tapering doses of oral and topical corticosteroids. At the 2-month post-operative visit, her vision had improved to 20/100 in right eye. The central cornea was well epithelialised, but showed residual deep stromal scarring (figure 1C). She was advised to continue oral prednisolone 5 mg daily and topical prednisolone acetate 1% eye drops twice daily. Three months following surgery she presented with complaints of acute pain and decreased vision in right eye. Examination showed circum-corneal congestion with engorged and tortuous perilimbal vessels and 360° peripheral superficial corneal neovascularisation (figure 1D). Fine vascular ingrowth was noted from the perilimbal area encroaching onto the peripheral limbal transplants (figure 1E). In the infero-temporal area two layers of vessels could be clearly differentiated. These included superficial vessels due to localised conjunctivalisation and vessels passing beneath that encroaching onto the limbal transplant lying ahead of the conjunctivalisation. Corneal examination in the right eye showed diffuse epithelial haze and stippled staining of epithelium.

DIFFERENTIAL DIAGNOSIS

Allograft rejection after LSCT can be confused with recurrence of LSCD. It is important to differentiate the two as the first is reversible with systemic immunosuppression and the second requires repeat surgery. However, failing to make this distinction can result in either a patient with acute immune rejection receiving a second graft, which is doomed to fail, or a patient with recurrence of LSCD being unnecessarily immune-compromised.

TREATMENT

Allograft rejection was suspected based on the acuteness of symptoms, presence of circum-ciliary

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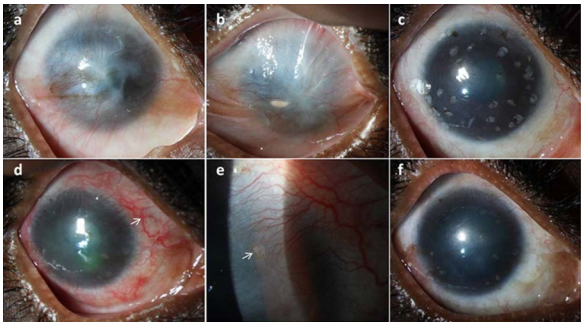

Figure 1 (A and B) Clinical photograph of right and left eye showing conjunctivalised ocular surface with extensive symblepharon and stromal scarring in the left eye. (C) Right eye well epithelialised central cornea with residual deep stromal scarring and few limbal transplants persisting over the cornea. (D) Circumcorneal congestion with engorged, tortuous perilimbal vessels (arrow) and 360° peripheral superficial corneal neovascularisation. (E) Fine vascular ingrowths from the perilimbal area approaching the peripheral limbal transplants (arrow). (F) Well epithelialised ocular surface with decrease in congestion and persistence of neovascularisation following systemic immunosuppression.

congestion, corneal vascularisation directed specifically towards the transplants and absence of generalised conjunctivalisation or large epithelial defects. The patient received a single pulse dose of intravenous methylprednisolone (500 mg) and hourly topical prednisolone acetate 1% eye drops. Within 3 days of therapy the patient's pain was relieved and within a week her visual acuity returned back to 20/100 with decrease in circum-corneal congestion.

OUTCOME AND FOLLOW-UP

She was discharged on 50 mg of oral prednisolone daily along with topical prednisolone acetate 1% eye drop 10 times a day in tapering doses. At the last follow-up in December 2012 (6 months); her unaided visual acuity was 20/100 in the right eye. Ocular surface was completely epithelialised and stable with persistent corneal stromal haze. Peripheral neovascularisation was still persisting but had not progressed (figure 1F). She was continued on 5 mg of oral corticosteroids and twice daily topical prednisolone acetate 1% eye drop.

DISCUSSION

The utility of SLET in treating unilateral LSCD has been established.[1] However, its use in bilateral LSCD has been unexplored. For allogeneic SLET living donors may be preferable as limbal cells obtained from cadavers have a lower proliferative rate in vitro[2] and a poorer corneal epithelialisation rate in vivo.[3] However, in our case a living donor tissue was not available and we compensated for the possibility of poorer cell viability by using more donor tissue. SLET using cadaveric limbal tissue was successful in restoring a stable corneal surface and improvement in vision. However, because of the allogeneic nature of graft, it experienced immunological rejection. Clinical signs of presumed immunological rejection in allogeneic limbal transplantation have been previously described in literature. Tsai *et al*.[4] proposed engorged and tortuous perilimbal vessels as an early sign of allograft rejection following conventional cadaveric limbal transplantation. In their cases fine vascular ingrowths were noted from perilimbal area encroaching cadaveric limbal transplants sutured at the recipient limbus. These vessels could be arrested with systemic cyclosporine treatment. Rao *et al*.[5] also reported engorged perilimbal vessels at the site of limbal grafts as a sign of allograft rejection in their cases of limbal allografting form related live donors. In our case, as the limbal transplants were placed over the cornea, fine vessels were noted approaching the individual transplants along with engorged and tortuous perilimbal vessels. These perilimbal vessels disappeared after pulsed intravenous steroids with persistence of fine vascular ingrowths approaching transplants. Engorged and tortuous perilimbal vessels along with fine vascular ingrowths approaching limbal transplants might represent an early sign of allograft rejection after allogeneic SLET. If recognised and treated promptly these can avoid failure of allograft following rejection. As this case is the first report of allogeneic SLET, signs of allograft rejection need to be further defined. This case also emphasises the fact that more aggressive immunosuppression than used may be required to avoid allograft rejection.

Learning points

- Allogeneic simple limbal epithelial transplantation is a viable option for the treatment of bilateral limbal stem cell deficiency.
- It is necessary to recognise early signs of allograft rejection in limbal transplants for the prompt treatment of rejection.
- Sustained immunosuppression is necessary for allograft survival in allogeneic limbal transplantation.

Competing interests None.

Patient consent Obtained.

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