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Case report

Allogeneic simple limbal epithelial transplantation for bilateral limbal stem cell deficiency in chronic vernal keratoconjunctivitis: A case report

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ABSTRACT

Introduction and importance: This report describes the management of bilateral limbal stem cell deficiency (LSCD) in vernal keratoconjunctivitis (VKC) with allogeneic simple limbal epithelial transplantation (allo-SLET).
Presentation of case: A 22-year-old female presented with bilateral VKC with total LSCD. A thick fibrotic pannus was present in both eyes, with visual axis involvement in the right eye. The central cornea in the left eye was clear. The patient underwent a cadaveric allo-SLET in the right eye to restore the ocular surface. Systemic immunosuppression with oral cyclosporine was administered following the surgery. The corrected visual acuity with scleral contact lenses (SCL) was 20/20 in both eyes which was maintained until the last follow-up visit, one year after the surgery. No recurrence of LSCD was observed in the right eye and the ocular surface was well epithelialized.
Discussion: Allo-SLET is a simple and efficacious surgical technique for bilateral LSCD. Eyes with VKC have a wet ocular surface, relatively clear corneal stroma, and minimal adnexal involvement. Thus, allo-SLET is the ideal procedure to address LSCD in such cases. The systemic immunosuppression that is given for ensuring graft survival can also help control the underlying allergy. Scleral contact lenses improve the visual acuity and their long-term usage does not affect the functioning of the SLET transplants.
Conclusion: VKC with bilateral LSCD can be successfully managed with allogeneic SLET. Post-operative systemic immunosuppressants are essential to maintain viable grafts. The use of SCL can improve vision and they do not pose any risk to the SLET transplants.

1. Introduction

Allergic conjunctivitis accounts for 29.5% of cases with bilateral LSCD [1]. In VKC, inflammatory cells and eosinophils produce toxins that damage LESC at sclerocorneal junction manifesting as partial or total LSCD depending upon the severity of damage [2–4]. This may result in corneal epithelial dysfunction, clinically characterized by progressive vascularization, conjunctivalization and corneal scarring [3]. In eyes with bilateral LSCD, an allogeneic source of LESCs is required and systemic immunosuppression is necessary in such cases. Stable long-term results with well epithelialized ocular surfaces have been described following procedures such as allogeneic CLET, CLAL and KLAL [5,6,17]. SLET is a novel surgery for transplantation of LESC and has been garnering popularity on account of its simple technique and effective outcomes. However, there is scarcity of literature on the outcomes of allo-SLET with a majority of existing reports pertaining to LSCD due to ocular burns [2,8,10,16]. Hence, in the current report we describe a case of VKC with bilateral LSCD which was managed with allo-SLET. The postoperative immunosuppressive regimen employed and the use of scleral lenses for visual rehabilitation has also been discussed. This report is as per the SCARE-2020 criteria [9].

Abbreviations: LSCD, limbal stem cell deficiency; VKC, vernal keratoconjunctivitis; SLET, simple limbal epithelial transplantation; SCL, scleral contact lens; LESC, limbal epithelial stem cells; CLET, cultivated limbal epithelial transplantation; CLAL, conjunctival limbal allograft; KLAL, kerato-limbal allograft; AS-OCT, anterior segment Optical coherence tomography; PROSE, prosthetic replacement of the ocular surface ecosystem; BCL, bandage contact lens; LSCT, limbal stem cell transplantation; CsA, cyclosporine A; AM, amniotic membrane.

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2. Case presentation

A 22-year-old female who was a known case of chronic VKC presented to our clinic with diminution of vision which was greater in the right eye. She also complained of redness and irritation which had increased in the two years prior to presentation. At presentation, the patient was on topical corticosteroids (fluorometholone 0.1%, twice daily), cyclosporine 0.05% (twice daily), and lubricants (carboxymethylcellulose 0.5%, 4 times/day). There was no significant family history. The visual acuity was hand movements and 20/25 in the right and left eye respectively. Slit-lamp examination revealed a thick fibrotic pannus with superficial and deep vascularization, covering the entire corneal surface including the visual axis in the right eye (Fig. 1). The deeper structures could not be visualized. In the left eye, a 360-degree conjunctivalization of the cornea was observed with a central clear 4x4mm island (Fig. 1). Both eyes had a wet ocular surface with normal adnexa. The intra-ocular pressure was normal in both eyes. The b-scan ultrasonography in the right eye and the fundus examination in the left eye revealed no abnormality. The AS-OCT line scan of the right eye depicted a thick hyper-reflective epithelial layer with normal thickness of the underlying stroma (Fig. 1). The patient was diagnosed to have VKC with total LSCD in both eyes and was continued on topical medications. A PROSE lens trial was given in the left eye with which the vision improved to 20/20. The right eye was planned for an allogeneic SLET to address the LSCD.

The surgical procedure was performed by an experienced surgeon under general anesthesia as per a standardized protocol [2]. In brief, a 360-degree peri-limbal conjunctival peritomy was carried out and the pannus was separated from underlying cornea by blunt dissection and excised. An AM was secured over bare area with fibrin glue (Tisseel Kit, Baxter AG, Vienna, Austria). Limbal stem cells were harvested by snip biopsy from a cadaveric donor with a healthy limbus. The biopsied tissue was cut into multiple smaller bits and placed concentrically in the mid-periphery and secured with fibrin glue (Fig. 2). A BCL was placed at the end of the surgery. A temporary tarsorrhaphy was performed with a 6-0 polyglactin suture.

On the first post-operative day, vision in the right eye was 20/250. On slit lamp examination, the AM and the overlying limbal transplants were noted to be in place. Oral prednisolone (20 mg, once daily) and CsA (50 mg, once daily) were started along with topical antibiotics (moxifloxacin 0.5%) and corticosteroids (prednisolone acetate 1%, 8 times/day). Topical steroids were tapered weekly for 5 weeks after which a twice daily maintenance dose was continued. Antibiotic-steroid (chloramphenicol+polymyxin B + dexamethasone) ointment once at night, and lubricants (hydroxypropylmethylcellulose 0.3%, 3 times/day) were given for both eyes. Over subsequent visits, her vision improved in both eyes and the ocular surface was quiet with progressively increasing corneal clarity. Systemic investigations including complete blood counts, liver and renal function test were advised as the patient was on oral CsA. One year following the procedure, the patient was asymptomatic, and the ocular surface was stable. A clear cornea was seen in the right eye and no progression of the LSCD was noted in the left eye (Fig. 3). With PROSE lenses the patient had a visual acuity of 20/20, N6 in both eyes. Oral CsA was continued along with the topical medication regimen mentioned above.

3. Discussion

Bilateral LSCD is usually accompanied by significant adnexal involvement as seen in cases of Stevens-Johnson syndrome or mucous membrane pemphigoid. Thus, LSCT is often not feasible in these eyes or is performed in conjunction with extensive surface reconstruction. LSCD due to ocular allergy is an exception to this as the conjunctival and lid involvement is rarely severe enough to affect the surgical technique or the outcome. Additionally, stromal involvement is uncommon in eyes with VKC, making them the ideal cases for allogeneic LSCT. Of the allogeneic procedures, the lack of conjunctival cicatrization renders a CLAL redundant in eyes with VKC. The required regulatory approval and

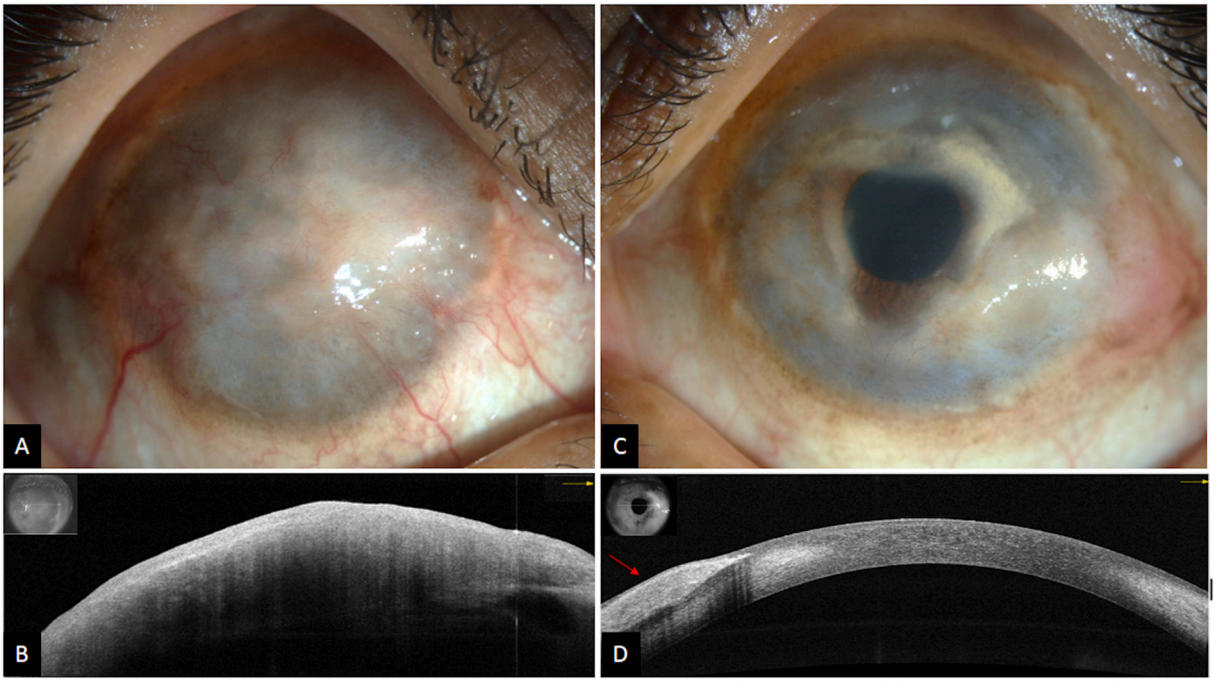

Fig. 1. Collage of images depicting the clinical picture at presentation. (A) Right eye shows a thick fibrotic pannus covering the entire cornea including the visual axis. Total limbal stem cell deficiency is present. (B) Anterior segment optical coherence tomography (AS-OCT) of the right eye with a thick hyper-reflective epithelial layer with normal thickness of the underlying stroma can be seen. Anterior chamber and iris details are visible hazily on the infra-red image (inset). (C) Left eye showing 360-degree corneal conjunctivalization with a central 4 mm clear corneal island. Limbal thickening can be noted temporally. (D) AS-OCT of the left eye with a thick hyper-reflective epithelial layer with normal thickness underlying stroma can be seen nasally (red arrow). The vertical black bar represents 250 μm of corneal thickness. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

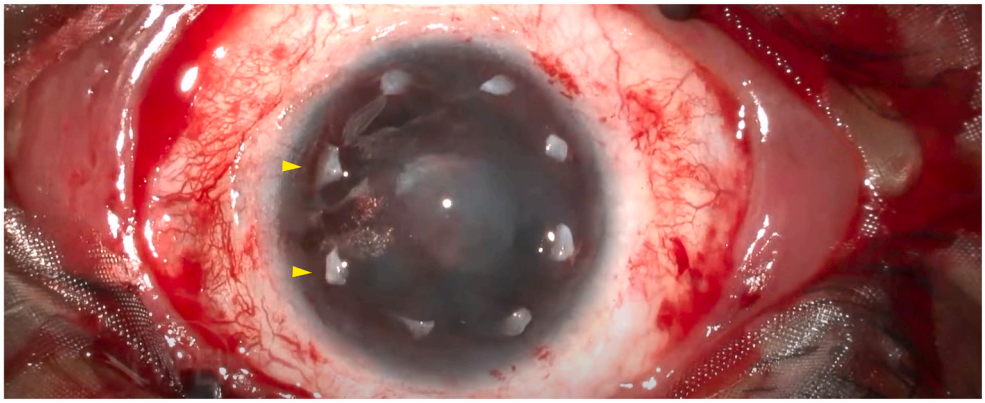

Fig. 2. Image of cornea captured at the end of the surgical procedure depicting the circumferentially placed donor limbal transplants (yellow arrowheads). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

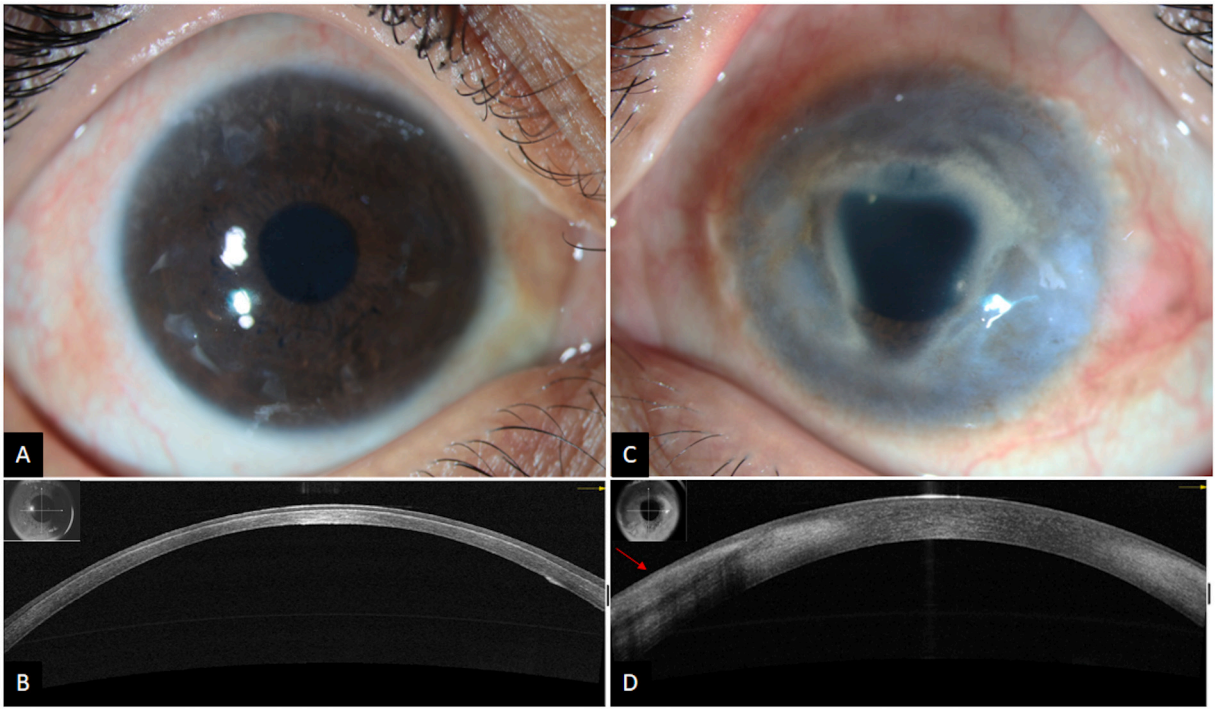

Fig. 3. Collage of images depicting the clinical presentation at the 1-year postoperative visit. (A) Right eye shows a clear, well epithelized corneal surface which is also seen on the optical coherence tomography scan. (B) (C) Left eye depicting a quiet ocular surface with no progression of LSCD. (D) Anterior segment optical coherence tomography of the left eye showing resolution of the pannus and a regular anterior corneal contour nasally (red arrow). The vertical black bar represents 250 μm of corneal thickness. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

laboratory set up restricts the adoption of CLET as the preferred procedure. Allo-SLET circumvents these issues and offers a single step, effective modality of re-establishing a stable ocular surface in eyes with ocular allergy. The stable outcomes seen in our case is similar to that reported by Shanbhag et al. who described four cases of VKC managed with allo-SLET with good long-term results [2]. They reported a similar rate of visual recovery in living-related and cadaveric allo-SLET and the 5-year cumulative survival probability was 90 ± 4% and 82 ± 7% for the two types respectively.

The expected risk of rejection is lower in SLET as the limbal tissue is placed on the mid-peripheral avascular stroma. However there are more antigen presenting cells in the limbal area and so rejection and subsequent failure of the procedure can occur without immunosuppression [2,6,10]. This rejection in allogeneic limbal grafts is considered to be mediated through T-cells and thus CsA, which inhibits T-cell activation through its effect on interleukin 2, is the most commonly used immunosuppressant [6,11]. Mycophenolate mofetil and tacrolimus are also gradually being used either in conjunction with CsA or as a monotherapy [6,11,13]. These agents are given along with oral or intravenous corticosteroids. Shanbhag et al. have described a long term schedule for the administration of pulse methylprednisolone following allo-SLET [2]. Topical immunosuppression with corticosteroids is also necessary with a maintenance dose of 1–2 times/day [2]. A similar protocol was followed in the current case. Since VKC is an immune mediated disorder, the systemic oral immunosuppressants in such patients will also help control the ocular allergy in both eyes. By preventing further inflammatory episodes in the current patient, these agents may have also helped arrest the progression of LSCD in the contralateral eye.

Scleral lenses in LSCD serve a dual purpose by correcting the visual dysfunction arising from the irregular corneal surface and by addressing

the concurrent aqueous deficiency that is usually present in these eyes. Ensuring proper fit of the lenses is essential in such cases as ill-fitting lenses can cause mechanical compression at the limbus and can thus affect the health of the stem cells [15]. In the present case, improvement in the quality of vision was noted, along with a stable LSCD in the left eye. In the right eye, the use of the lenses did not affect the functioning of the limbal transplants, and a stable ocular surface was observed until the last follow up visit.

4. Conclusion

This report describes a case of bilateral VKC with advanced LSCD which was successfully managed with allo-SLET. Systemic immunosuppression is essential in these cases to ensure the functioning of the allogeneic grafts and has the additional benefit of controlling the ocular allergy. PROSE lenses can improve the visual acuity in eyes with corneal irregularities secondary to VKC. Our case highlights the long-term stability of the SLET transplants and non-progression of LSCD with the use of these lenses.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Patient perspective

I have had multiple interventions for my allergy and was very concerned about vision especially in my right eye. With this surgical intervention I have regained my visual function and I am also happy about the cosmetic outcomes.

Ethical approval

Ethics committee approval was not required for this manuscript because it is a clinical case report.

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Declaration of competing interest

The authors have no conflicts of interest to declare.

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