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Automatized large diameter lamellar keratoplasty and stem cell transplantation for the treatment of ocular surface diseases with limbal insufficiency

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PURPOSE. *To report a new surgical procedure for the treatment of ocular surface diseases associated with severe limbal insufficiency.*

METHODS. *A retrospective review of four patients with severe ocular surface disease who required stem cell transplantation and keratoplasty for the correction of limbal insufficiencies. They underwent large diameter lamellar keratoplasty with microkeratome. When limbal dysfunction was associated with limited alteration of the ocular surface and transparent deep corneal stroma only the anterior corneal stroma was transplanted. When the entire corneal thickness was compromised, both anterior and deep donor buttons were transplanted.*

RESULTS. *Patients remained stable and improved their visual acuity after surgery. Best-corrected visual acuity ranged from 20/200 to 20/30. No corneal graft rejections were found. The main complication found in one of our patients was a central stromal opacity which required a secondary penetrating keratoplasty.*

CONCLUSIONS. *Automatized large diameter lamellar keratoplasty provides a safe and successful alternative to limbal transplantation for limbal insufficiency associated with corneal opacity. This technique enables a single-stage surgical procedure and the use of a single donor which reduces the risk of rejection. In addition, better refractive results are achieved due to the quality of the interface and the absence of corneal sutures. (Eur J Ophthalmol 2008; 18: 641-4)*

KEY WORDS. *Automatized large diameter lamellar keratoplasty, Stem cell transplantation, Ocular surface disease, Limbal insufficiency, Microkeratome*

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INTRODUCTION

Stem cells responsible for the regeneration of the corneal epithelium are thought to be located in the basal layers of the corneoscleral limbus (1). In eyes with significant alteration of the corneal epithelial surface and compromised corneoscleral limbus, anatomic recovery of the corneoscleral limbus can only be achieved by stem cell transplantation, with keratoepithelioplasty (2), limbal transplantation (3), or by transplanting cultivated epithelial stem cells (4). More recently, Vajpayee et al suggested a manual technique of large-diameter lamellar keratoplasty (LDLK) including corneoscleral limbus (5). Later, a new ring and head were designed for the microkeratome system (Moria®, France) which made it possible to obtain lamellar grafts of 11.4–12.8 mm for limbal stem cell transplantation (6).

Four patients with chronic limbal stem cell deficiency were treated with the automatized large diameter lamellar keratoplasty. Patients were prospectively evaluated.

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METHODS

Patients

Four eyes of four patients with severe ocular burns (grade III/IV in Thoft's scale) were included. All patients exhibited signs and symptoms consistent with chronic limbal stem cell deficiency.
Patients 1, 2, and 3 had a severe ocular alkali burn, whereas Patient 4 was a contact lens wearer who had limbal dysfunction caused by abuse of topical anesthetic. After initial anti-inflammatory treatment and amniotic membrane transplantation, complete limbal insufficiency and anterior stromal opacification were evident. Deep stroma was transparent in two eyes whereas the other two eyes had a full corneal thickness involvement. Visual acuity was less than counting fingers in all cases.

Surgical technique

Informed consent for the intervention was obtained from all the patients and ethics committee approval was obtained. Surgery was performed with peribulbar anesthesia by a single experienced surgeon (J.M.).
Large-diameter lamellar keratoplasty was performed in all eyes using a new head and ring of the ALTK® (Moria®, France) microkeratome system (6). With this new head, larger than the regular heads, we have obtained lamellar grafts of 13–14 mm in diameter and 100–150 µm in thickness including limbal area over 360° with the presence of stem cells as previous authors suggested (6).
From the donor eye, a 13–14 mm diameter lamellar graft was harvested using the microkeratome, ensuring that limbal stem cells were included in the graft. Perilimbal conjunctival dissection was previously performed to avoid obstruction in the passing of the microkeratome. A deep corneal button was also trephined to be used in cases where deep stromal opacification was evident on the injured eye.
After conjunctival peritomy an 8–10 mm central stromal bed was cut in the recipient eye using a 130–150 µm head of the ALTK System® (Moria®, France), or a 250 or 350 µm head when corneal stromal opacification was deeper. A 13 or 15 mm in diameter trephine with a stop device (Moria®, France, references 18186/13.5 and 18186/15) was used to mark the outer margin (150 µm in depth). A crescent scalpel (Alcon®, USA reference 28065-940002) was used to connect the edge of the keratectomy to the scleral bed.
The graft was then sutured to the host with eight interrupted radial 10-0 nylon sutures and the conjunctiva was secured to the episclera with 6-0 Vicryl sutures.

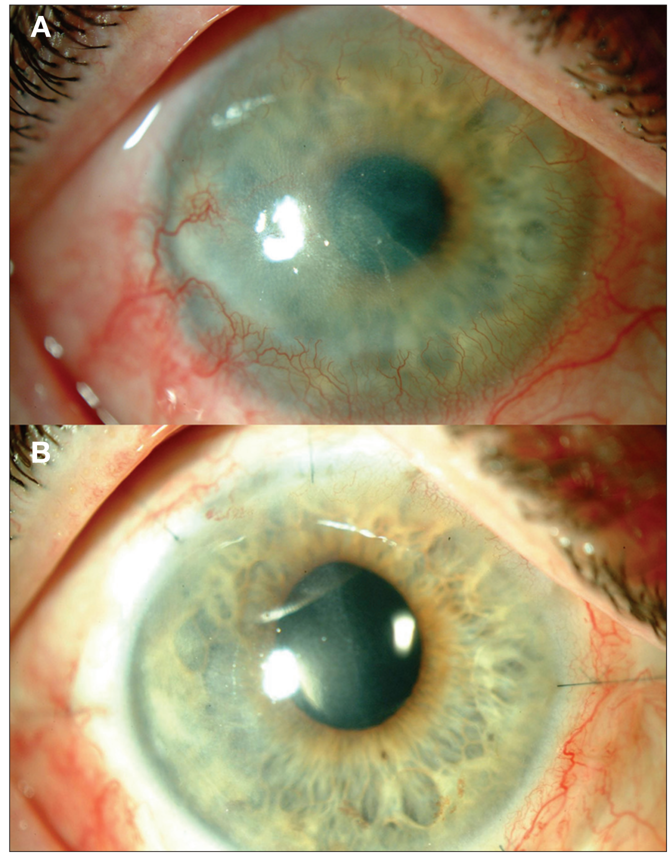

Fig. 1 - *Patient 1.* **(A)** *Preoperative situation.* **(B)** *One year after large diameter lamellar keratoplasty.*

When opacification was observed in the deep corneal stroma, the deep recipient cornea was also trephined with a 7.5-8mm trephine and the deep donor button was sutured to the recipient's stroma with eight 10-0 nylon sutures. The large-diameter lamellar graft was then sutured on top of this.
Postoperatively, all patients received 0.1% dexamethasone sodium phosphate eyedrops four times a day, tobramycin eyedrops four times a day for 1 month, and preservative-free artificial tears. Systemic cyclosporine and dexamethasone was given in all cases.

RESULTS

Patient 1 (Fig. 1)

A 55-year-old man attended our hospital in 1996 with a severe ocular alkali burn in his left eye (grade III). Initially, a limbal allograft transplantation was performed but failed

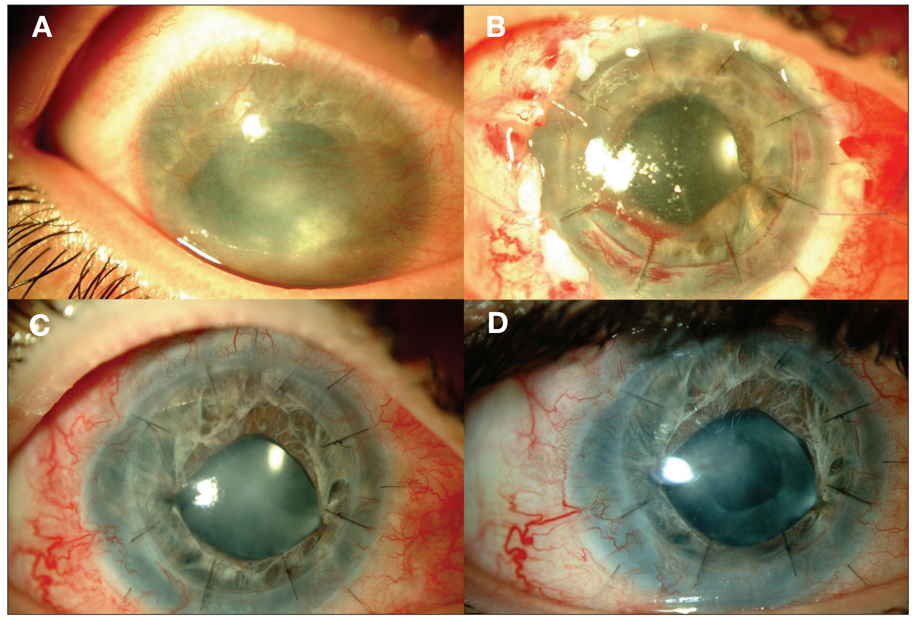

Fig. 2 - *Patient 3.* **(A)** *Preoperative situation.* **(B)** *Early postoperative period.* **(C)** *One year after large diameter lamellar keratoplasty.* **(D)** *After cataract removal and YAG laser capsulotomy.*

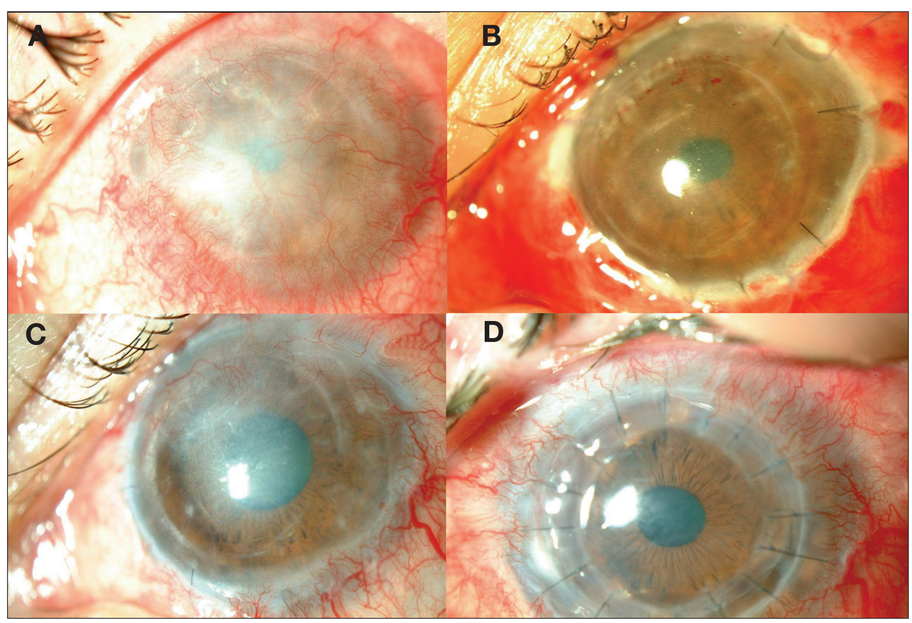

Fig. 3 - *Patient 4.* **(A)** *Preoperative situation.* **(B)** *Early postoperative period.* **(C)** *One year after large diameter lamellar keratoplasty.* **(D)** *After secondary penetrating keratoplasty.*

to succeed, leading to extensive epithelial damage and anterior stromal opacification.

In 2003, an automatized large diameter lamellar keratoplasty (ALDLK) preserving the deep stroma was performed. One month after surgery, a clear cornea could be seen on slit-lamp examination. One year after surgery, unaided visual acuity (UVA) was 20/40 and best-corrected visual acuity (BCVA) was 20/30 with a manifest refraction of –4.0 x 110° and corneal epithelium and stroma remained transparent and stable.

Patient 2

A man aged 52 years had a chemical injury caused by a strong alkali on his left eye (grade IV). On slit-lamp examination a severe limbal insufficiency with corneo-conjunctival epithelial defects and deep corneal scarring were evident and an ALDLK was performed. As the entire corneal thickness was compromised, deep corneal button was also transplanted. One year after surgery, a clear cornea could be seen on slit-lamp examination and UVA was

20/60 and BCVA was 20/40 with a manifest refraction of +2.0 –2.0 x 160º.

Patient 3 (Fig. 2)

A 25-year-old man attended our hospital with a severe alkali burn in his right eye (grade IV). He had been previously treated in another hospital and was sent to our hospital with stromal opacification and complete breakdown of the limbal barrier associated with cataract and paralytic mydriasis. As the entire corneal thickness was compromised, the deep corneal button was also replaced. Open sky extracapsular cataract extraction and pupilloplasty were performed at the same surgical procedure.

Months after surgery, and despite a favorable initial evolution, a central corneal opacity was noticed and a penetrating graft was performed to restore visual acuity. One year after the procedure and a YAG laser capsulotomy, corneal stroma and epithelium remain transparent and BCVA is 20/70 with a manifest refraction of +4.0 –5.0 x 15º.

Patient 4 (Fig. 3)

A man aged 42 years had a chemical injury caused by topical anesthetic abuse on his left eye. On examination, severe stromal opacification and complete breakdown of the limbal barrier were seen.

A superficial ALDLK was performed. One year after the initial procedure, a central corneal opacity was observed on slit lamp examination and a penetrating keratoplasty was performed. At the present time, the corneal surface remains stable and BCVA is 20/200.

DISCUSSION

Limbal transplantation attempts to correct the deficit in cases of stem cell deficiency (3). In cases of superficial scarring, this procedure can lead to visual improvement. However, when deeper opacification is present, limbal transplantation will have to associate penetrating or lamellar keratoplasty (3).

Performing a large-diameter lamellar keratoplasty offers certain advantages when treating limbal insufficiencies associated with corneal opacity, particularly if we compare it with limbal transplantation associated with keratoplasty. Both limbal transplantation and keratoplasty are performed in a single-stage surgical procedure, a suture-free corneal surface is obtained, and the risk of infection is reduced (7). Therefore, the resulting refractive corneal surface is more uniform and surgical recovery is faster.

In addition to these benefits, performing a large-diameter lamellar keratoplasty with microkeratome (ALDLK), compared to the manual technique (5), offers further benefits such as smoother surfaces with better refractive results.

With this new technique, limbal insufficiency and corneal opacity can be resolved in a single-stage surgical procedure using a single donor, irrespective of the depth of the corneal scarring. This avoids the increased risk of corneal rejection more common when performing both techniques in two separate operations, which would require two different donor corneas. The main disadvantage regarding this procedure is the need for a specific technology, which is not always available or affordable.

Our experience demonstrates that ALDLK is a valid management option for patients with chronic limbal stem-cell deficiency. However, long-term follow-up is needed to determine if this technique is comparable to limbal transplantation with additional keratoplasty.

None of the authors has financial or proprietary interest in any material or method mentioned.

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