Limbal Stem Cell–Sparing Lamellar Keratoplasty for the Management of Advanced Keratoglobus

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Purpose: To describe the technique and outcomes of limbal stem cell–sparing lamellar keratoplasty (LSCS-LKP) for the management of advanced keratoglobus (KGB).

Methods: In a sequential interventional case series from March 2010 to December 2012, 8 eyes of 6 patients with advanced KGB underwent an LSCS-LKP. Three patients had isolated KGB, 2 were affected with the Ehlers–Danlos syndrome, and the other subject had osteogenesis imperfecta. Epithelial healing, anatomical results (corneal thickness and keratometry), and visual outcomes were evaluated after this intervention.

Results: Three of the 6 patients were male. Complete epithelial healing occurred in 7 eyes during 2 weeks. Refractory persistent epithelial defect and graft melting occurred in 1 eye. Corneal thickness increased and central keratometry decreased after the LSCS-LKP was performed in all the patients. The patients were followed up for at least 6 months. Visual acuity improved in all eyes except 1.

Conclusions: LSCS-LKP is an effective procedure for preserving ocular integrity and for improving visual acuity in patients with advanced KGB. Early surgical intervention can be considered before the occurrence of vision-threatening traumatic corneal rupture.

Key Words: keratoglobus, limbal stem cell sparing, lamellar keratoplasty

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Keratoglobus (KGB) is a rare, bilateral condition characterized by generalized limbus-to-limbus globular corneal thinning.[1] The congenital form presents at birth and is associated with Ehlers–Danlos syndrome type VI, Lebers congenital amaurosis, and the blue sclera syndrome.[2] The acquired form, which presents in adulthood, may evolve from preexisting pellucid marginal degeneration (PMD) or keratoconus.[3] The etiology of KGB remains unknown; however, associations have suggested defective collagen synthesis as the cause.[4,5] Patients may present with stable or deteriorating bilateral visual impairment as a result of extreme myopia, irregular astigmatism, and corneal scarring caused by previous hydrops.[6]

Surgery is indicated when visual needs are no longer satisfied, or when there is a risk of occurrence of corneal rupture.[7] Various techniques have been proposed, but there is no consensus on an optimal method. The main problem in the surgical treatment of KGB is the extreme thinning and extensive area of anomalous corneal protrusion, creating unfavorable conditions for conventional keratoplasty techniques such as penetrating or lamellar keratoplasty (LKP) and epikeratophakia.[7,8] Significant postoperative astigmatism after a penetrating keratoplasty (PKP) and an LKP is likely, which results in poor visual outcomes. Other potential complications include the higher risk of wound leakage, traumatic wound dehiscence, graft rejection, delayed reepithelialization, and postoperative glaucoma.[9] Alternative procedures including eccentric PKP and staged surgery such as an LKP followed by a PKP have been described.[10,11] The overall prognosis for KGB is poor, with suboptimal final visual outcomes.[12,13] Here, we describe a modified surgical technique of limbal stem cell–sparing LKP (LSCS-LKP) for the management of advanced KGB.

METHODS

In a sequential interventional case series, patients with advanced KGB underwent an LSCS-LKP. Before operation, all the patients had severe corneal thinning and bulging with excessive steepness (evaluated by Orbscan II, Bausch and Lomb, Germany). The study was conducted from March 2010 to December 2012. The study protocol was based on the tenets of the Declaration of Helsinki. It was approved by the Ethics Committee of the Ophthalmic Research Center, Shahid Beheshti University of Medical Sciences. Other possible risks and benefits inherent to the nature of the condition and the possibility of reoperations were explained to the patients before enrollment, and informed consent was obtained from all the subjects or their legal guardians. During the postoperative period, the duration of epithelial healing, anatomical results, changes in corneal thickness and central keratometry, and visual outcomes were evaluated.

Surgical Technique

All the procedures were performed under general anesthesia (Fig. 1). Using a 15-degree blade (Sharpoint, Somerset, United Kingdom) a 360-degree beveled lamellar corneal incision was made 1.0 to 1.5 mm anterior to the vascular arcade of

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the limbus. Using a crescent knife (Alcon, TX) the primary incision was made and extended about 2 mm beyond the limbus at half thickness plane into the sclera. Care was taken to preserve the limbal stem cells. After creating the 360-degree corneoscleral pocket, corneal epithelial debridement was performed using 20% ethanol touch for 30 seconds and preventing direct contact with host stem cells. Manual dissection of the donor corneoscleral rim was performed to fit it into the dissected recipient corneoscleral pocket. The donor tissue was prepared from a fresh whole globe or an eye bank prepared corneoscleral rim. The margins of the donor tissue were trimmed to create a tapered edge for better stability and apposition into the pocket, and the Descemet membrane was peeled off. Donor size ranged from 16 to 18 mm. A paracentesis was made to decompress the anterior chamber. Peripheral iridectomy was performed through the same incision, which was sutured thereafter. By vigorous irrigation with balanced salt solution (BSS) and gentle rubbing using hydrated methylcellulose spears over the interface usually no significant interface debris remained. The donor corneoscleral graft was positioned into the corneoscleral recipient pocket and fixed (using at least 16 interrupted 10/0 nylon sutures or more as required). Thereafter, the dissected limbal area was repositioned and sutured over the donor corneoscleral graft using several 10-0 nylon sutures. All steps were performed manually using no special instruments.

Postoperative Management

The patients were examined on postoperative days 1, 3, 7, 14, and 28 and every 2 weeks until 3 months, then monthly until 1 year, and every 3 months thereafter. After the surgery was performed, oral prednisolone 1 mg/kg/d was started and tapered off by 2 to 3 weeks. A topical antibiotic agent (chloramphenicol 0.5%) and steroid drops (betamethasone 0.1%) were started 4 times a day after the surgery took place. The former was discontinued when corneal epithelialization was complete, whereas the latter was tapered off according to ocular surface inflammation. The ocular surface was continuously lubricated using topical preservative-free artificial tears (Artelac; Bausch and Lomb, France). No topical or systemic immunosuppressive agent was used. Suture removal was considered 6 months after the operation was done, except in cases with early suture loosening.

RESULTS

Eight eyes of 6 patients including 3 male and 3 female subjects whose age ranged from 2 to 23 years were operated (Table 1). Three patients had isolated KGB, 2 patients had the Ehlers–Danlos syndrome, and 1 patient had osteogenesis imperfecta. Three patients had nearly visually lost contralateral eyes because of previous minor trauma.

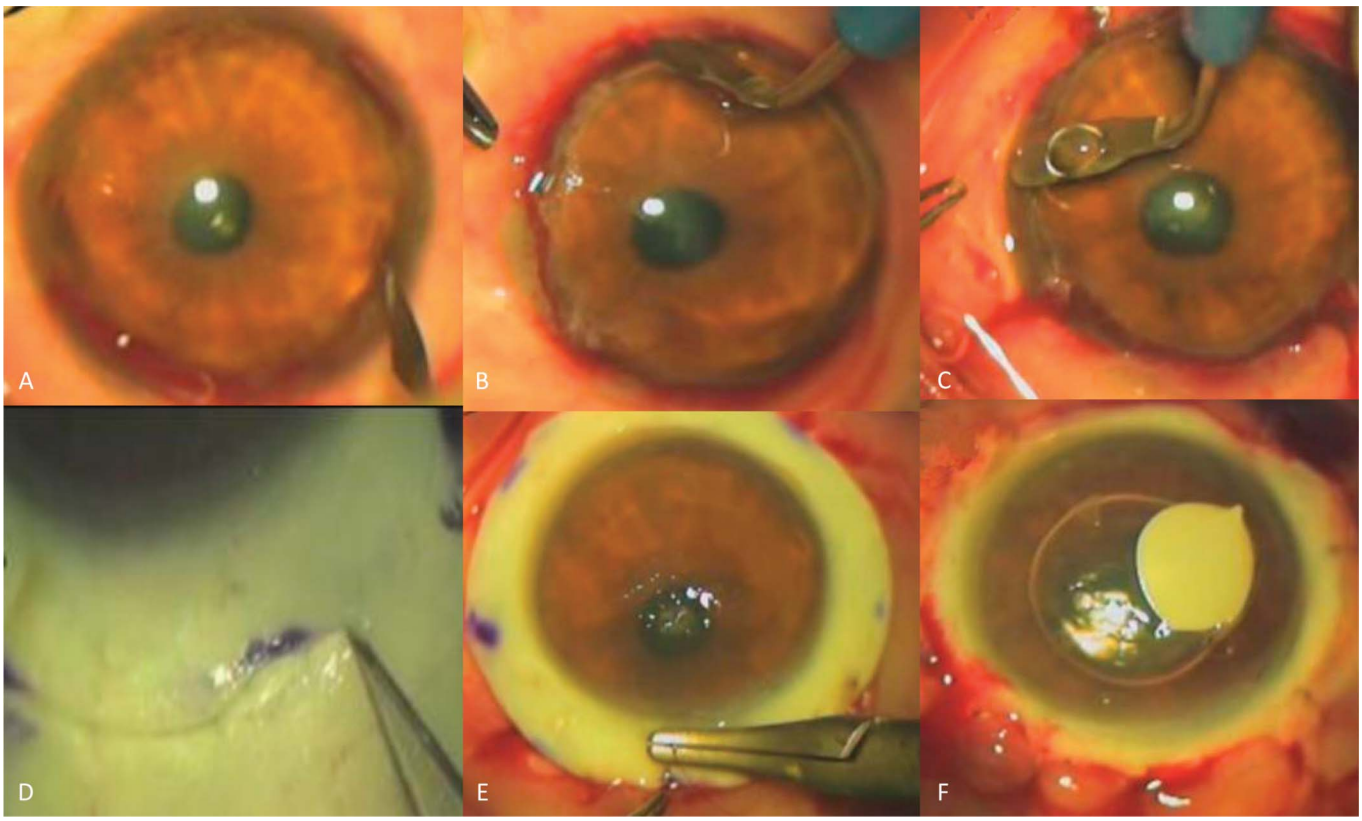

FIGURE 1. Surgical steps: A, Annular beveled incision over the cornea 1 to 1.5 mm anterior to the vascular arcade of the limbus. B, Lamellar dissection under the limbus into the sclera with a crescent knife. C, 360-degree extension of lamellar dissection into the sclera. D, Manual preparation and beveled cutting of donor corneoscleral rim. E, Separate suturing of the donor graft. F, End of the surgery with an air bubble in the anterior chamber enhancing recipient to donor adhesion.

TABLE 1. Preoperative and Postoperative Data of Patients Who Underwent the LSCS-LKP

Case	Age (yrs)	Sex	Eye	Vision		Refraction		Complications
				Preop	Postop	Preop	Postop	
1	2	Male	OS	NCSM*	CSM*	Not possible	−6.00/−5.00 × 60	None
2	12	Female	OU	OU: CF*	OD: 20/60 OS: 20/30	Not possible	OD: −5.00/−3.00 × 170 OS: −6.00/−4.00 × 10	None
3	5	Female	OS	CF	20/40	Not possible	−6.00/−3.00 × 110	Localized stable and regressed epithelial cyst
4	14	Male	OD	CF	CF	−18.00/−6.00 × 80	Not possible	Graft melting
5	23	Male	OD	20/200	20/25	−8.00/−3.00 × 140	−4.00/−6.00 × 20	None
6	14	Female	OU	OD: 20/200 OS: 20/160	OD: 20/40 OS: 20/60	OD: −14.00/−4.50 × 150 OS: −12.00/−6.00 × 80	OD: −5.00/−3.00 × 30 OS: −7.00/−2.00 × 20	None

*CF, counting fingers; CSM, central, steady, maintained; NCSM, not central, steady, maintained; OD, oculus dexter; OS, oculus sinister; OU, both eyes; Postop, postoperative; Preop, preoperative.

Preoperatively, all the patients had severe generalized corneal thinning with the thinnest pachymetry ranging from 220 to 350 μm. The thinnest pachymetry was increased considerably after operation (range, 630–780 μm). Before the procedure was carried out, excess central corneal keratometry steepness ranging from 50 to 78 Diopters (D) flattened (range, 40–52 D) after the operation.

Before the operation, the best-corrected vision in all patients was <20/160. Refraction in 3 patients was not possible, and in the other 3 patients, high myopic astigmatism was present. After the surgery, vision was markedly improved in all patients except 1 (Table 1).

There was no significant interface foreign body, debris, or haziness. There was only a single case of epithelial cyst formation (case 3), which remained stable and regressed after 2 years, with no surgical intervention. There were only 2 transient episodes of epithelial rejection, which was easily controlled by applying topical steroids. There was no case of postoperative traumatic wound dehiscence, corneal laceration, or ectasia recurrence in this series. Because the patients were satisfied with their postoperative vision, none of them required a later central optical PKP.

SELECTED CASE REPORTS

Case 1

A 2-year-old boy was referred to the emergency department because he had a traumatic globe rupture with corneal tissue loss and crystalline lens extrusion on the right side. The rupture had not been repaired completely. He was a known case of the Ehlers–Danlos syndrome with blue sclera, joint hyperextensibility, pectus excavatum, and the result of consanguineous marriage. He also had a severely protruding cornea with a generalized thinning in his left eye. An LSCS-LKP was performed for the left eye to provide tectonic support. Epithelial healing was complete after 8 days, and an excellent structural integrity was achieved.

Case 5

A 23-year-old man was referred to the cornea clinic with severe decreased vision. His best spectacle-corrected visual acuity in each eye was 20/200. There was severe thinning and protrusion of both corneas. The right eye underwent an LSCS-LKP. The preoperative thinnest corneal thickness increased from 297 to 756 μm and central 3-mm keratometry decreased from 54.8 to 45.1 D after an operation was performed (Fig. 2).

DISCUSSION

Various surgical techniques including PKP, LKP, "tuck-in" LKP, epikeratoplasty, and corneoscleroplasty have been described for the management of KGB.[7,8] Because of severe generalized corneal thinning and protrusion, PKP and LKP are demanding procedures with a high risk of wound leakage, wound instability and malposition, high astigmatism, delayed epithelial healing, and recurrence of the ectatic disorder leading to poor visual outcomes. Further, a large PKP entails an increased risk of rejection.[9,14] Although, an LKP, in comparison with a PKP, may result in lower levels of vision (because of graft–host interface diffraction problems), it

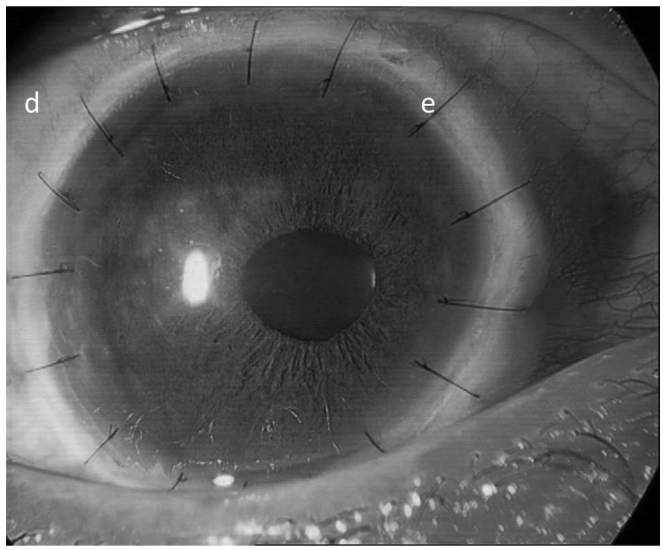

FIGURE 2. Case 5, 3 months after the surgery.

offers advantages including wound stability, epithelial healing, and lower risks of postoperative complications.

A "tuck-in" LKP is a partial-thickness corneal transplantation technique that has been described for patients with advanced peripheral corneal thinning disorders, such as KGB, PMD, or patients with a combination of keratoconus and PMD.[12,15] This procedure involves removing a central lamellar corneal stromal button that is 8.5 mm in diameter followed by the creation of a peripheral pocket in the recipient cornea into which the thinned peripheral rim of a 12-mm donor corneal button is tucked and sutured.[16] This procedure is technically demanding because it involves the lamellar dissection of a thin host bed, which may be difficult or sometimes impossible to perform. Similar surgical procedures with limited modifications have also been described.[12,17] Jones and Kirkness[11] described a 2-stage procedure especially when there is a significantly opacified host cornea or host–donor interface abnormality, in which an LKP is done as a tectonic procedure followed by a later central PKP.[12] Recently, the application of a femtosecond laser for making incisions into the peripheral cornea and dissecting the corneal part of the corneoscleral pocket (eg, in a keratolimbal allograft) has been reported.[18] Whether this technique can be applied in extremely thin and steep corneas requires further experience.

The current technique of LSCS-LKP does not involve any lamellar dissection in the central cornea, thereby decreasing the risk of perforation. The lamellar pocket is dissected into the peripheral cornea and sclera, thus preventing limbal stem cell damage and later epithelial healing problems. Postoperatively, a normal, healthy, and functional limbus was observed in 7 of 8 eyes as evidenced by a stable, smooth, and normal looking corneal epithelium. Visual acuity and refraction showed improvement in most cases after the surgery was done, and the corneal thickness was increased significantly. Good tectonic support and avoidance of damage to the limbal tissue are the main advantages of the present surgical approach. There was no episode of epithelial breakdown and vascularization in the donor corneas, and there was no recurrence of ectasia up to 2 years.

The only significant postoperative complication was persistent epithelial defects in the only patient with osteogenesis imperfecta. The cause of this complication was probably intraoperative limbal stem cell trauma and deficiency.

One patient had a small but stable paracentral interface epithelial cyst. The complete removal of the corneal epithelium is important to prevent this complication, which may lead to the melting of the donor graft. The technique may not "eliminate" the risk of traumatic wound dehiscence and/or rejection. These complications may be reduced, because the recipient thinned corneal stroma and endothelium are preserved.

In summary, the LSCS-LKP seems to be a practical technique for restoring the structural integrity of the cornea in KGB without jeopardizing the limbal stem cells. Early intervention before the development of corneal scarring or hydrops, in addition to providing tectonic support, may lead to better visual results and reducing the need for a further central PKP. This will eliminate the inherent risks of performing a PKP including traumatic wound dehiscence and graft rejection in such a setting of an extremely thin cornea.

REFERENCES

1. Krachmer JH, Feder RS, Belin MW. Keratoconus and related noninflammatory corneal thinning disorders. *Surv Ophthalmol.* 1984;28:293–322.
2. Jacobs DS, Green WR, Maumenee AE. Acquired keratoglobus. *Am J Ophthalmol.* 1974;77:393–399.
3. Cameron JA, Al-Rajhi A, Badr IA, Corneal ectasia in vernal keratoconjunctivitis. *Ophthalmology*. 1964;58:678–682.
4. Meghpara B, Nakamura H, Vemuganti GK, et al. Histopathologic and Immunohistochemical studies of keratoglobus. *Arch Ophthalmol.* 2009; 127:1029–1035.
5. Baillif S, Garweg JG, Grange JD, et al. Keratoglobus: review of the literature [in French]. *J Fr Ophtalmol.* 2005;28:1145–1149.
6. Kanellopoulos AJ, Pe LH. An alternative surgical procedure for the management of keratoglobus. *Cornea*. 2005;24:1024–1026.
7. Cameron JA, Cotter JB, Risco JM, et al. Epikeratoplasty for keratoglobus associated with blue sclera. *Ophthalmology*. 1991;98:446–452.
8. McDonald MB, Koenig SB, Safir A, et al. On-lay lamellar keratoplasty for the treatment of keratoconus. *Br J Ophthalmol.* 1983;67:615–618.
9. Hallermann W. Technique and results of an operative treatment of keratoglobus (author's transl) [in German]. *Klin Monbl Augenheilkd.* 1975; 166:593–598.
10. Kodjikian L, Baillif S, Burillon C, et al. Keratoglobus surgery: penetrating keratoplasty redux. *Acta Ophthalmol Scand.* 2004;82:625–627.
11. Jones DH, Kirkness CM. A new surgical technique for keratoglobus-tectonic lamellar keratoplasty followed by secondary penetrating keratoplasty. *Cornea*. 2001;20:885–887.
12. Vajpayee RB, Bhartiya P, Sharma N. Central lamellar keratoplasty with peripheral intralamellar tuck: a new surgical technique for keratoglobus. *Cornea*. 2002;21:657–660.
13. Vymazal M, Penetrating keratoplasty in keratoglobus [in German]. *Klin Monbl Augenheilkd.* 1988;192:237–238.
14. Javadi MA, Kanavi MR, Ahmadi M, et al. Outcomes of epikeratoplasty for advanced keratoglobus. *Cornea*. 2007;26:154–157.
15. Kaushal S, Jhanji V, Sharma N, et al. "Tuck in" lamellar keratoplasty (TILK) for corneal ectasias involving corneal periphery. *Br J Ophthalmol.* 2008;92:286–290.
16. Vishal J, Rasik B, Vajpayee MS. Surgical management of ectatic corneal disorder: review article. *HK J Ophthalmol.* 2010;14:20–25.
17. Watson SL, Rauz S, Dart JK. Limbal sparing lamellar keratoplasty. Video report. *Br J Ophthalmol.* Feb 2005; available at http://bjo.bmjjournals.com/cgi/content/full/89/2/DC1/1.
18. Choi SK, Kim JH, Lee D, et al, A new surgical technique: a femtosecond laser-assisted keratolimbal allograft procedure. *Cornea*. 2010;29:924–929.