·Letter to the Editor·

Central corneal epithelium self-healing after ring-shaped glycerin-cryopreserved lamellar keratoplasty in Terrien marginal degeneration

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Dear Sir,

I am Dr Yan-Long Bi, from the Department of Ophthalmology, Tongji University Affiliated to Tongji University School of Medicine, Shanghai, China. I write to present a case report of total limbal stem cells deficiency after treatment with ring-shaped lamellar keratoplasty secondary to Terrien marginal degeneration. During 3 years observation, the central epithelial island showed a self-healing capacity.

A generally accepted opinion is that unipotent corneal epithelial precursor cells with stem-cell (SC) properties are located in the basal cell layer of the limbus. But Majo and colleagues reported the identification of oligopotent stem cells throughout the entire corneal surface in rodents [1]. However, this is a subject of ongoing debate [2]. One is inclined to accepted the view that there are some cells among the central corneal epithelium that have characteristics closer to the parent SC, Dua *et al* [3] termed these conceptual cells 'transient cells'. Under the circumstances of total limbal stem cell deficiency (LSCD), what would happen to the corneal surface, should the central island of the healthy epithelium be damaged by injury or disease, remains an important and unanswered question.

A 76-year-old man presented with a 2-week history of sudden decreased vision in his right eye. He had a 1-year history of recurrent symptoms of ocular irritation on a background of 30 years of rheumatoid arthritis. His left eye was enucleated after trauma. At the initial examination, Best-corrected visual acuity (BCVA) was 20/40, and intraocular pressure was 7mmHg. Slit-lamp examination showed approximately 320 degrees of circular peripheral corneal thinning. The nasal corneal stroma was almost dissolved with a 2mm^2-sized perforation at 3 o'clock (Figure 1A). Fluorescein staining demonstrated a positive Seidel's sign. The anterior chamber was shallow with iris anterior synechiae. Hematological screening for systemic vasculitis was normal. A diagnosis of Terrien marginal degeneration (TMD) with spontaneous corneal perforation was made. A ring-shaped lamellar keratoplasty (RSLP) was undertaken immediately. Perilimbal resections were made on the recipient bed at a width of 2-3mm on the cornea and 1.5mm on the sclera, and at a depth about 150μm thickness. The resection range was 320 degrees, and only 40 degrees of superior normal limbal area was left (Figure 1B). Around the nasal perforation, only abnormal corneal epithelium and/or fibrovascular pannus were stripped away. A trimmed ring-shaped glycerin-cryopreserved corneoscleral graft, which was about 1mm larger than the recipient lesion, was fixed to the recipient bed with interrupted 10-0 nylon sutures at the cornea side and 8-0 vicryl sutures at the sclera side. Two months later, the TMD had progressed and erosion had extended to the superior corneolimbal region; the graft was partly dissolved and was beginning to detach from the recipient bed (Figure 1C). Iris anterior synechiae and hypotony had also reoccurred, accompanied by the formation of scattered central corneal epithelial bullae. The central corneal thickness was 658μm. Specular microscopy showed an edematous endothelial appearance with blurred cell boundaries. A therapeutic bandage contact lens was given immediately. Methotrexate and sulfasalazine were started after a rheumatology consultation and systemic immunosuppression combined with topical cyclosporine were also administered. Two weeks later, a second ring-shaped lamellar corneoscleral tissue was regrafted, followed with cryopreserved amniotic membrane transplantation to the superior limbus and patching on the whole cornea. During surgery, the pathological tissue on the corneoscleral rim was further resected and complete hemostasis was also done using

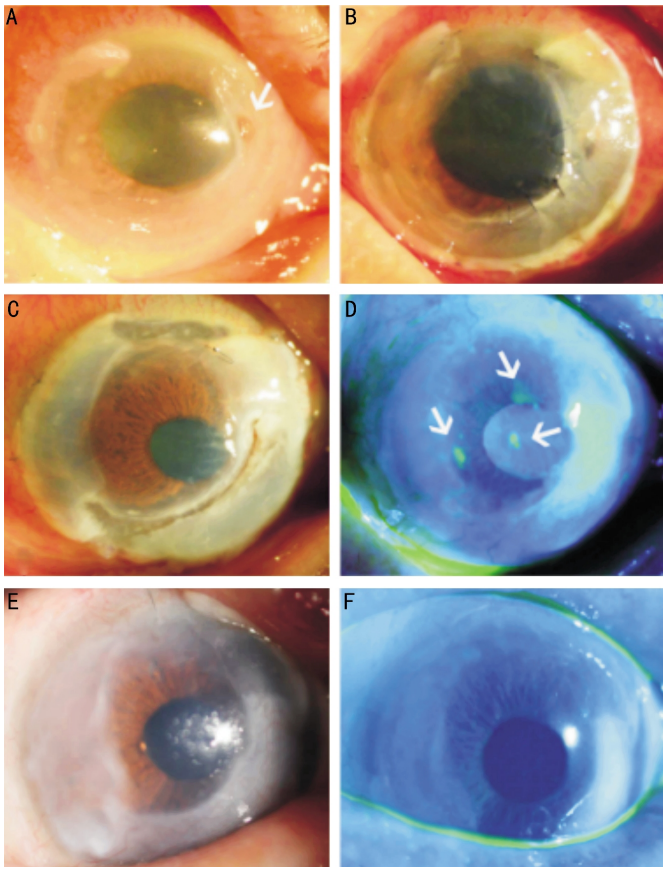

Figure 1 A: A corneoscleral erosion extends 320 degrees of the limbus with a 3 o'clock perforation (arrow); B: A 320-degree ring-shaped acellular lamellar graft was transplanted; C: Two months after the first RSLP, the erosion enlarged into the whole limbus; D: Detached flakes of epithelium in the central cornea after the second RSLP (arrows); E: Corneal endothelial temporary failure after cataract surgery with epithelial bullae formation; F: Thirty-two months after cataract surgery, the central corneal epithelium maintained an intact and smooth surface.

diathermocoagulation. The shallow anterior chamber gradually deepened, and 1 month after the amnion had dissolved the graft seemed to integrate with the recipient bed border smoothly. But at the same time, fluorescein staining showed 3 areas of epithelial defect. Furthermore, Phacolytic glaucoma had formed and the patient's visual acuity had decreased to hand movements (Figure 1D). Surprisingly, after only a short course (5 days) of topical bFGF treatment, complete reepithelialization covered the epithelial defects. Four months after the second RSLP, uncomplicated phacoemulsification and implantation of a posterior chamber intraocular lens was performed. However, the epithelial bullae appeared again on the first day after surgery (Figure 1E), and on the third day the bullae ruptured leaving an epithelial defect of about 2mm^2. Corneal endothelial decompensation was diagnosed and treated with 5% sodium chloride eye drops six times/day and 20% mannitol two times/day. In the following week, the corneal edema gradually subsided and the detached epithelium re-epithelialized with negative fluorescein staining. During the next 32 months, the ring-shaped graft remained translucent and stable with neovascularization mainly at the nasal region; the central corneal epithelium stayed smooth and transparent (Figure 1F).

In this case, about 89% of the peripheral limbal SCs have been resected during the first RSLP. In theory, the residual 11% of normal limbal SCs would be insufficient to keep a normal ocular surface intact[4]. A further erosion extending to the superior 40 degrees corneal limbus and the extent debridement during the second RSLP lead to an anatomical total LSCD. And both lamellar grafts were long-term glycerin-cryopreserved tissue containing no living cells [5]. So even if there are some limbal stem cells left, it is unlikely for them to penetrate through the graft and have any effect. Similar to Dua's report[3], the central corneal epithelium island remained intact for a long period of time. But unfortunately, this patient had anterior chamber collapse on two occasions and phacolytic glaucoma, and these lead to a notable decrease in corneal endothelial cell count (ECD), from 2432/mm^2 to 550-600/mm^2 after the second RSLP. Also after the cataract surgery, the endothelial cells faced another high risk of decompensation. When ECD drops too low, the pump starts to fail; as fluid accumulates between the basal epithelium cells, bullae may undergo painful ruptures leaving flakes of epithelial detachments[6]. In this case, bullae ruptures happened twice, but amazingly, all these defects quickly re-epithelialized. At the last follow-up, except for the nasal peripheral area, the corneal graft at other regions and the central cornea were all transparent, covered by epithelium with negative fluorescein staining. To our knowledge, this is the first report showing the *in vivo* self-healing ability of the human corneal central epithelial cells under pathological damage without supporting by LSCs[7].

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