CASE REPORT

Autologous simple limbal stem cell transplantation: a case series

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Abstract

This case series reviewed medical records of eight patients who underwent autologous simple limbal epithelial transplantation (SLET) for total limbal stem cell deficiency (LSCD) secondary to chemical injury (n=5), thermal injury (n=2), or autoimmune disorder (n=1) between 2016 and 2019 at the Caritas Medical Centre. The mean time from injury to SLET was 67 months (range, 3 weeks to 30 years). The mean time to re-epithelialization was 20 (range, 13-42) days. The follow-up duration ranged from 1 to 6 years. At the 1-year follow-up, the success rate of SLET was 37.5%, and visual gain among the three successful cases ranged from <1 line to >6 lines. Patients with Dua grade V or VI chemical injury and patients with systemic causes of LSCD had poorer prognosis, as did those with cicatricial lid changes, anterior segment necrosis, glaucoma, sterile cornea ulceration, superimposed infections, or tobacco usage. SLET should be a reconstructive procedure for chronic LSCD rather than for acute injury or inflammation.

Key words: Corneal injuries; Limbus corneae; Stem cell transplantation

Introduction

Limbal stem cell deficiency (LSCD) is caused by the loss of healthy limbal stem cells and the lack of regenerative power of the corneal epithelium and results in conjunctivalization and neovascularization of the corneal surface.[1] LSCD can be acquired or hereditary; acquired LSCD is more common in Hong Kong. Common causes of LSCD include chemical and thermal injury, severe blepharokeratoconjunctivitis, topical and systemic drug toxicity, and systemic diseases such as Steven Johnson syndrome, mucous membranous pemphigoid, graft versus host disease, and severe allergic ocular surface disease.[2-4] Treatment strategies involve replenishing limbal stem cells and include keratolimbal autografting, conjunctival-limbal autografting, ex-vivo cultivated limbal epithelial transplantation, cultivated oral mucosal epithelial transplantation, and simple limbal stem cell transplantation.[5] The latter does not require extensive laboratory support and has comparable results.[6] This case series reviewed medical records of eight patients who underwent autologous simple limbal epithelial transplantation (SLET) for LSCD to determine factors associated with successful outcome.

Case presentation

This study was approved by the Kowloon West Cluster Research Ethics Committee [KWC-REC Reference: KW/EX-22-012(169-01)]. Medical records of eight patients who underwent autologous SLET for total LSCD secondary to chemical or thermal injury or autoimmune disorder between 2016 and 2019 at the Caritas Medical Centre were retrospectively reviewed. Patients with unidentifiable causes or bilateral total LSCD were excluded. Chemical burns were classified using the Dua classification. Data recorded included the extent of LSCD, time from injury to SLET, time to re-epithelialization, and best-corrected visual acuity before and after SLET. Successful SLET was defined as complete epithelialization, stable corneal surface, and absence/recession of corneal neovascularization at 6 months.[7,8]

Patients were under general anesthesia. For the recipient eye, vascular pannus over the cornea was removed after 360° peritomy at 2 mm after the limbus (**Figure 1**).

Hemostasis was achieved with cautery. The amniotic membrane was transplanted to bare ocular surface with fibrin sealant (Tisseel; Baxter Healthcare) and tucked under surrounding healthy conjunctiva. For the donor eye, the conjunctiva was incised and subconjunctival dissection was performed using a crescent knife until 1 mm into clear cornea. The 2×2 mm block limbal tissue was excised into 15 to 20 blocks on wet nitrocellulose paper with No. 15 surgical blade. The small limbal tissues were then placed circularly on the amniotic membrane along the peripheral cornea and the epithelial side-up and were secured with fibrin sealant. Soft bandage contact lens (Air Optix Night & Day Aqua; Alcon) was inserted. Eye patch was removed on day 1. The recipient eye received prednisolone acetate 1% eye drop every 2 hours tapered over 8 weeks and chloramphenicol eye drop four times a day until epithelialization, whereas the donor eye received a 1-week course of dexamethasone 0.1% and chloramphenicol 0.5% eye drop. Preservative-free lubricants were applied as needed. The bandage contact lens was removed upon complete epithelialization.

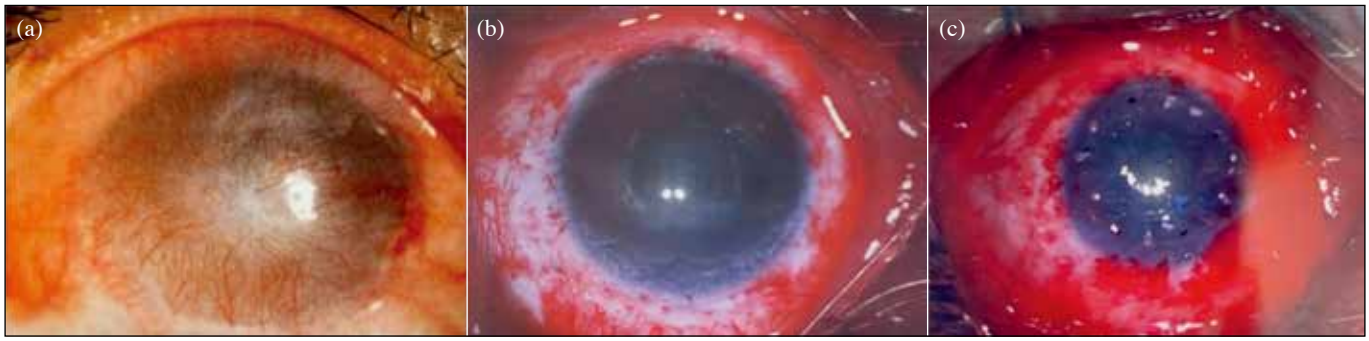

Figure 1. (a) An eye with total limbal stem cell deficiency for autologous simple limbal epithelial transplantation. (b) The overlying fibrovascular membrane is dissected at 2 mm after the limbus. (c) The amniotic membrane is tucked under conjunctival edges and secured with fibrin sealant, and the transplanted tissues are placed in a circular manner and secured with fibrin sealant.

Table. Clinical characteristics and treatment outcomes of eight patients who underwent autologous simple limbal epithelial transplantation (SLET) for total limbal stem cell deficiency

Patient	Age/ sex	Cause of injury	Dua classification	Symblepharon	Time from injury to SLET, m	Eye with SLET	Time to reepithelialization, days	Best-corrected visual acuity, logMAR			Visual gain, lines	Outcome			Latest cornea/eye status	Additional procedures after SLET	Follow-up, y
								Preop	Month 3	Latest follow-up		Month 6	Year 1	Latest follow-up			
1	49/F	Cement (alkaline)	IV	No	31	Left	27	2.4	0.7	0.4	>6	Success	Success	Success	Static conjunctivalization at 2 o'clock area	Phacoemulsification, intraocular lens	6
2	33/M	Thermal	-	No	360	Right	12	0.5	0.5	0.2	3	Success	Success	Success	No epithelial defect, superficial corneal scars	-	4
3	40/M	Thermal	-	Yes	9	Right	12	2.4	2.4	2.0	<1	Success	Success	Success	No epithelial defect, static inferior symblepharon 1.5 mm onto cornea	Multiple tarsorrphaphies, hard palate grafting, inferior labial mucosal grafting, fornix reconstruction	3.5
4	58/M	Sodium hydroxide (alkaline)	VI	No	0.75	Left	No healing	2.4	Light perception	No light perception	-	Failure	Failure	Failure	Phthisis	Penetrating keratoplasty, anterior chamber washout, pars plana vitrectomy, silicone oil injection	1
5	66/F	Lichen planus	-	Yes	54	Left	42	0.3	2.1	1.8	-	Failure	Failure	Failure	No epithelial defect, corneal stromal scars	Symblepharon lysis, fornix reconstruction, pseudopterygium excision, multiple amniotic membrane transplantations	5.5
6	41/M	Fosroc Polyurea (alkaline)	V	No	6	Right	14	1.0	0.4	0.4	6	Failure	Failure	Failure	Conjunctivalization over superior half of cornea	2nd SLET 3.5 years after 1st SLET	5
							13 (2nd SLET)	2.4	0.4	0.4	>6	Success	Failure	Failure		Subconjunctival Eylea	
7	53/M	Cement (alkaline)	V	No	1.5	Left	No healing	2.1	Light perception	Light perception	-	Failure	Failure	Failure	Vascularized corneal scar	Multiple amniotic membrane transplantations and tarsorrphaphies	3
8	55/M	Cement (alkaline)	V	Yes	72	Right	No healing	Light perception	2.1	2.4	<1	Failure	Failure	Failure	Vascularized corneal scar	Amniotic membrane transplantation	3

Of the eight patients, five had chemical injury, two had thermal injury, and one had lichen planus (**Table**). All had total LSCD. The mean time from injury to SLET was 67 months (range, 3 weeks to 30 years). The mean time to re-epithelialization was 20 (range, 13-42) days. The follow-up duration ranged from 1 to 6 years. At the 1-year follow-up, the success rate of SLET was 37.5%, and visual gain among the three successful cases ranged from <1 line to >6 lines.

Patient 1

In January 2014, a 49-year-old woman presented with a Dua grade IV chemical injury by cement to her left eye, which was amblyopic. One week later, the pH value in the eye remained raised, and the patient underwent emergency removal of the embedded cement and conjunctival resection. To facilitate epithelial healing, bandage contact lens, autologous serum, and temporary median tarsorrhaphy were applied. In July 2016, she underwent SLET. In March 2018, she underwent phacoemulsification and intraocular lens implantation, and her vision improved significantly. At the 6-year follow-up, the cornea remained clear with only limited conjunctivalization over the inferotemporal limbus area (**Figure 2**).

Patient 2

In August 2013, a 33-year-old man presented with persistent ocular discomfort of the right eye. He had a history of thermal injury by coal powder to the eye at the age of 3. The affected eye, which was likely amblyopic, showed 360° pannus with central stromal scar, with a refraction of +1.00/-3.00× 65. Nonetheless, the patient opted for SLET. The best-corrected visual acuity remained the same at logMAR 0.5 before and after SLET, whereas postoperative refraction was -1.50/-5.00× 165. Two months later, the pannus recurred at the superior cornea and remained static (**Figure 3**), which is not unusual in successful cases.[7,9,10] Nonetheless, the patient was satisfied with the much improved ocular comfort and tear film stability.

Patient 3

In November 2016, a 40-year-old man presented with a third-degree periocular burn of the right eye associated with severe periorbital swelling after a welding accident. The injured eye showed severe chemosis, total limbal ischemia, and a completely opacified cornea (**Figure 4**). Parts of the conjunctiva were also burnt away exposing bare sclera underneath. Intraocular pressure was 34 mmHg. The patient was treated with daily rodding, maximal glaucoma medications, topical and systemic antibiotics, oral vitamin C, and autologous serum. One week after injury, distichiasis and early lagophthalmos developed, and the patient underwent paramedian tarsorrhaphy for epithelial healing. However, the tarsorrhaphy broke off and showed a lower lid defect after raw lid tissues sloughed off. The patient underwent repeat paramedian tarsorrhaphy, but symblepharon occurred. In August 2017, the patient underwent symblepharon lysis and fornix reconstruction combined with SLET and amniotic membrane transplantation (AMT). However, there was progressive obliteration of the superior and inferior fornix and lagophthalmos. This necessitated further hard palate

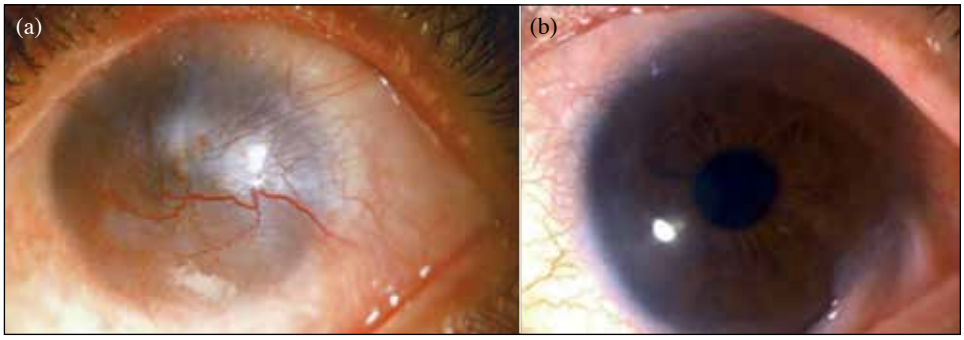

Figure 2. Patient 1: (a) Conjunctivalization of the cornea of the left eye at 4 months after chemical injury by cement. (b) Static and limited conjunctivalization after successful autologous simple limbal epithelial transplantation and intraocular lens implantation.

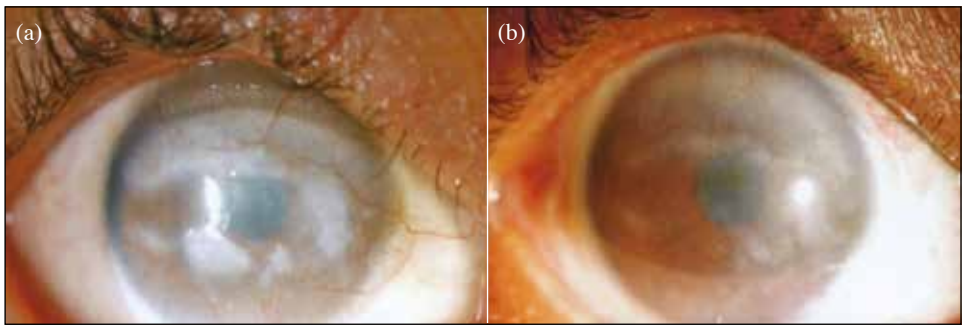

Figure 3. Patient 2: (a) Irregular corneal surface and conjunctivalization of the right eye before simple limbal epithelial transplantation. (b) Smoother ocular surface and static pannus at the superior cornea after simple limbal epithelial transplantation.

Figure 4. Patient 3: (a) Total limbal ischemia, opacified cornea, and bare sclera of the right eye after thermal injury. (b) Tarsorrhaphy breaking off prematurely owing to necrotic lid tissues and cicatricial lid changes. (c) Formation of symblepharon after repeat tarsorrhaphy. (d) Simple limbal epithelial transplantation combined with fornix reconstruction. (e) Repeat inferior fornix reconstruction with hard palate and inferior labial mucosal grafts. (f) Complete eye closure. (g) Recurrence of symblepharon.

grafting and inferior labial mucosal grafting for inferior fornix reconstruction to achieve complete eye closure. In October 2017, the cornea remained epithelialized and stable. Corneal transplantation (for stromal scarring with deep vascularization) was deferred for 4 months, owing to the recurrence of symblepharon and insufficient forniceal space. In January 2022, the cornea condition remained unchanged.

Chemical or thermal injury is usually associated with severe eyelid injury. Distichiasis, entropion, and tissue loss may affect corneal surface recovery.[11] Joint management of lid problems with oculoplastic surgeon is advised.

Patient 4

In June 2017, a 58-year-old man presented to the emergency department with a caustic injury to the face and eyes by sodium hydroxide when cleaning an air conditioner. He had minimal irrigation on the site of injury. Three hours later, he was admitted to the intensive care unit for inhalation injury and airway management. At 8 hours after injury, eye assessment revealed a pH value of 12 for both eyes. The left eye showed a Dua grade VI injury, complete opacification of the cornea, total epithelial defect, total limbal involvement, necrotic conjunctiva and tenon, absence of anterior chamber and fundal views, and severe periorbital soft tissue swelling (**Figure 5**). Applanation and tonometry failed to measure the intraocular pressure; digital palpation of the globe was high. The right eye showed Dua grade I injury, which was completely epithelialized at week 1 and had no clinical evidence of limbal ischemia. The left eye was treated with intensive lubrication, topical prednisolone 8 times per day, topical antibiotics, oral doxycycline, and high-dose Vitamin C. On day 2, digital pressure over the left globe remained high, and maximal anti-glaucomatous drugs were administered. On day 4, early symblepharon was noted, and daily glass rodding was performed in addition to daily normal saline irrigation. Nonetheless, upper lid entropion and distichiasis developed. Bandage contact lens was inserted to aid epithelialization and to protect the ocular surface, and autologous serum was prescribed for round-the-clock usage.

In view of the persistent denuded ocular surface, at 3 weeks after injury, the patient underwent AMT for the entire conjunctival surface and cornea combined with autologous SLET. The left upper lid entropion was corrected with everting sutures. However, healthy tissue was inadequate for tenoplasty or conjunctival flap, and the patient declined conjunctival autograft harvest from the completely

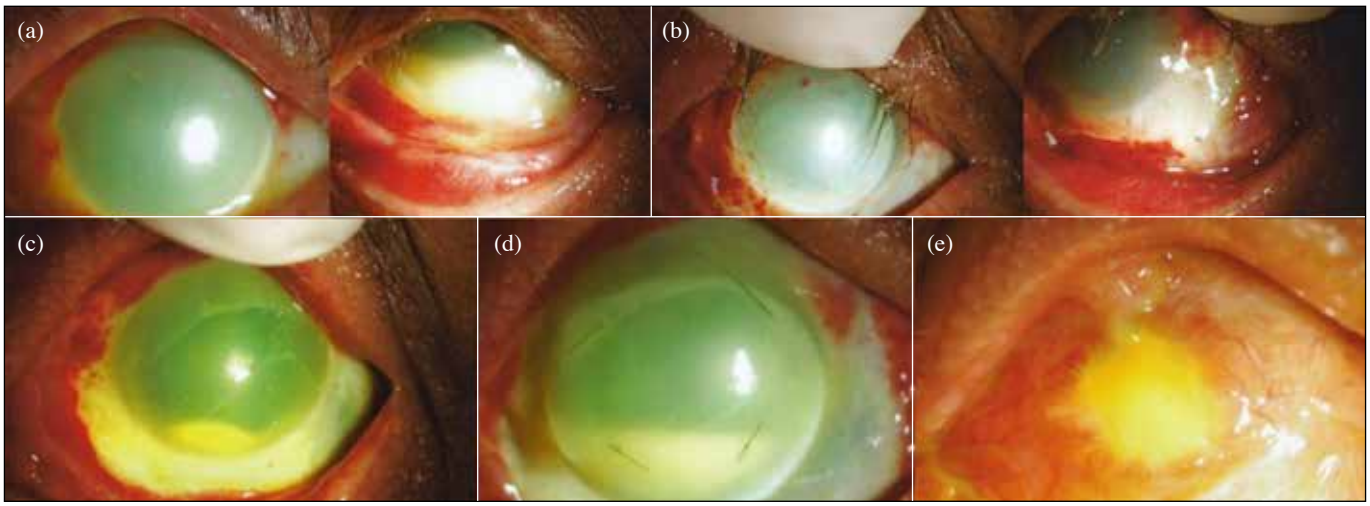

Figure 5. Patient 4: (a) Dua grade VI injury to the left eye, with total limbal and conjunctival involvement, complete corneal opacification, and scarring of forniceal conjunctiva. (b) No conjunctival reperfusion after the amniotic membrane dissolved. (c) Persistent epithelial defect, reactive hypopyon, conjunctival loss, and non-reperfusion after the amniotic membrane dislodged prematurely. (d) Double-layered amniotic membrane transplantation, with the inner layer secured with 10-0 nylon sutures. The outer layer is dissolved on day 5 and the inner layer is dislodged after 2 weeks. (e) Development of phthisis bulbi.

recovered right eye. On day 5, the transplanted limbal tissues and bandage contact lens dislodged. On day 6, the amniotic membrane showed early melting but no evidence of conjunctival reperfusion. On day 10 after the first AMT, the patient underwent the second AMT; the amniotic membrane was secured with fibrin sealant to the corneal and conjunctival surface, but it dislodged again 2 days later. The third AMT was performed, with the inner layer secured to the corneal surface with 10-0 nylon stitches, and the outer layer secured to the bare sclera, and the entire cornea overlaid the first layer with 8-0 vicryl. However, the outer layer dissolved 5 days later, and the inner layer was out of position 2 weeks later. Anterior segment optical coherence tomography showed left eye hyperechoicity throughout the entire cornea and 4-mm hypopyon secondary to persistent inflammation (**Figure 6**). After scheduled for a temporary tarsorrhaphy, the patient consulted another ophthalmologist and underwent large-sized penetrating keratoplasty, anterior chamber washout, pars plana vitrectomy, and silicone oil injection. However, the epithelial defect persisted, and the eye became phthisical and progressed to no light perception.

After chemical injury, the time to first irrigation and early normalization of pH are very important.[12] Sodium hydroxide is strongly alkali and may cause high-grade chemical injury with poor visual prognosis. Early referral to anterior segment ophthalmologists for evaluation is important. Despite early SLET, surgical outcome of patient 4 was suboptimal owing to persistent inflammation and 'marbalization' of the ocular surface.[13] Integration of the transplanted amniotic membrane to the avascular host surface was difficult despite the use of fibrin sealant and sutures. Eyes with high-grade chemical injury are at risk of phthisis, uncontrollable glaucoma, and superimposed infection. The use of free autologous conjunctival flap from the contralateral eye can be a viable option for reperfusion of the cornea, and further rehabilitative surgery can be considered in the long run.

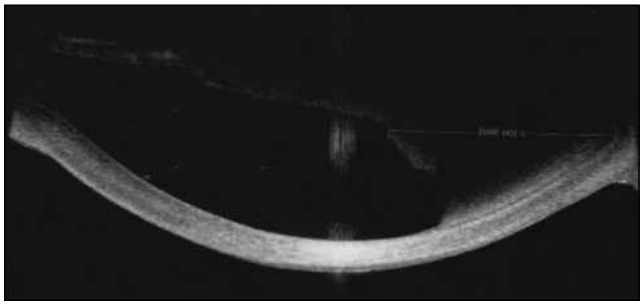

Figure 6. Patient 4: Anterior segment optical coherence tomography showing left eye hyperechoicity throughout the entire cornea and 4-mm hypopyon secondary to persistent inflammation.

Patient 5

In May 2005, a 55-year-old woman presented with occasional redness and grittiness of both eyes, which were relieved with topical lubricants. In 2007 to 2009, she developed bilateral upper and lower eyelid trichiasis that required regular epilation. In March 2012, she presented with similar symptoms and was diagnosed to have inferior fornix shortening of the right eye. She also complained of frequent oral and genital ulcers. Buccal mucosa biopsy revealed lichenoid inflammation. Microscopic examination of the buccal mucosa revealed subepidermal bullous formation and a layer of parakeratosis. Dermis showed

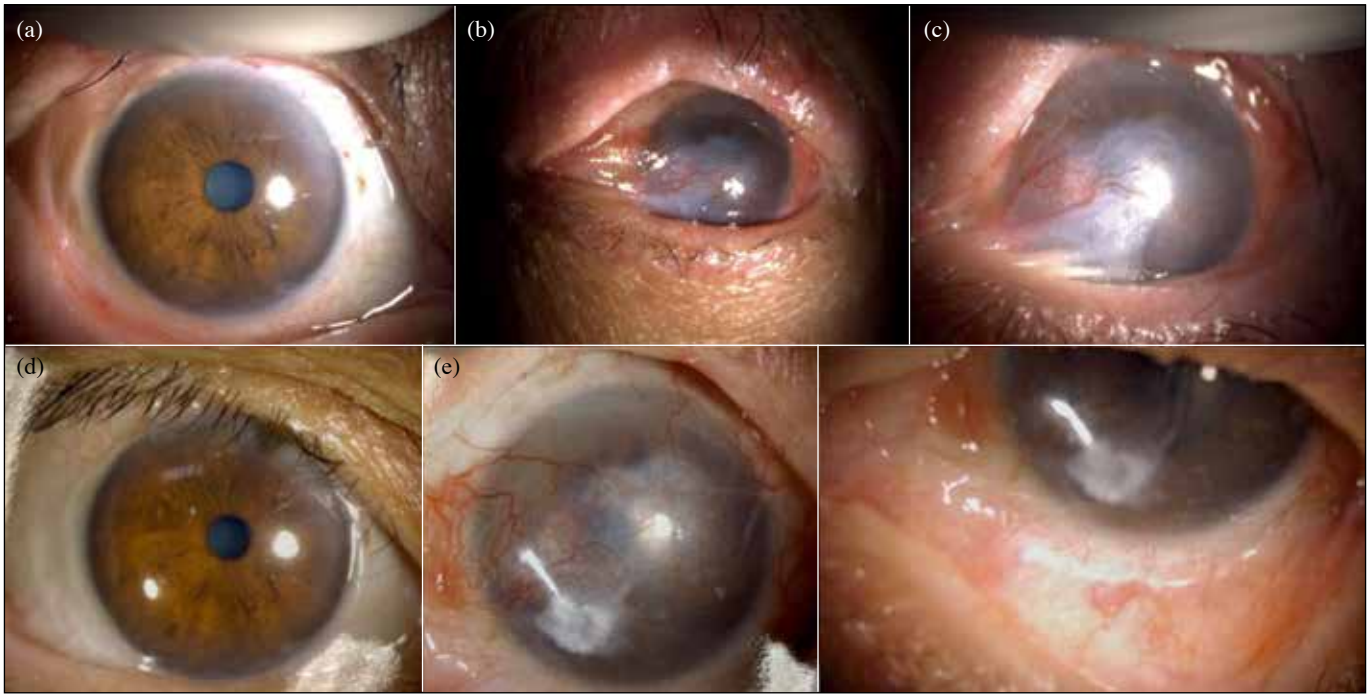

Figure 7. Patient 5: (a) The donor right eye. (b) Lower eyelid symblepharon and limbal stem cell deficiency of the left eye before simple limbal epithelial transplantation. (c) Recurrence of symblepharon causing complete gaze restriction. At the 6-month follow-up, (d) the donor right eye remains healthy, and (e) the left eye showing successful symblepharon lysis

a dense band-like lymphoplasmacytic infiltrate with occasional eosinophils. Immunofluorescent study showed no staining of immunoglobulin (Ig) G, C3, IgA, and IgM at the dermoepidermal junction.

In May 2013, the patient underwent symblepharon lysis of the right eye lower lid and AMT with fornix forming sutures, with perioperative steroid cover. Pathology of the lysed conjunctiva showed discontinuous bland non-keratinized stratified squamous epithelium. Subepithelial stroma was collagenous, mildly edematous, and chronically inflamed. In June 2014, she underwent grey line splitting follicles removal for bilateral upper eyelid trichiasis, which recurred continually and necessitated regular epilation. In October 2014, symblepharon of the left eye lower lid progressed and caused upgaze restriction. There was progressive lid margin keratinization, corneal neovascularization, and LSCD. In September 2015, she had an episode of infective corneal ulcer of the left eye that resulted in more stromal vascularization and scarring; her visual acuity decreased to logMAR 0.3. In November 2016, she underwent symblepharon lysis and fornix reconstruction with AMT and SLET of the left eye (**Figure 7**).

Pathology report showed stratified squamous epithelium lining fibrous stromal tissue with mild mixed acute and chronic inflammatory cells infiltration. There was focal parakeratosis in the surface epithelium but no subepidermal bulla. Immunofluorescence studies were negative of IgA, IgG, IgM, C3, C1q, and fibrin. Thus, the rheumatologist did not prescribe systemic immunosuppression medications despite years of ocular inflammation. In April 2017, SLET failed and symblepharon recurred, and the pseudopterygium covered three-quarter of the cornea. In March 2018, based on the first buccal mucosa biopsy, the patient was treated for lichen planus with high-dose oral steroid for systemic control of the condition. However, the patient was unable to tolerate oral steroid despite rapid tapering and had palpitations, rapid weight gain, and raised lipid levels. She was then treated with methotrexate.

In November 2018, she underwent another symblepharon lysis, pseudopterygium removal, AMT, and fornix forming sutures for the left eye. Recovery was complicated with persistent epithelial defects necessitating another AMT. The defect healed with time but a tuft of symblepharon recurred and encroached onto cornea surface. In April 2019, her visual acuity was logMAR 2.00. In October 2021, she had complete gaze restriction and underwent extensive pseudopterygium excision, symblepharon lysis, AMT, temporary spacer, and fornix forming sutures. In March 2022, she had unrestricted gaze movement and no recurrence of symblepharon, with visual acuity improved to logMAR 1.80.

Early and repeat conjunctival biopsy is useful after inconclusive biopsy results for buccal mucosa. Without a tissue diagnosis or other rheumatological symptoms, initiating immunosuppression is debatable. In Hong

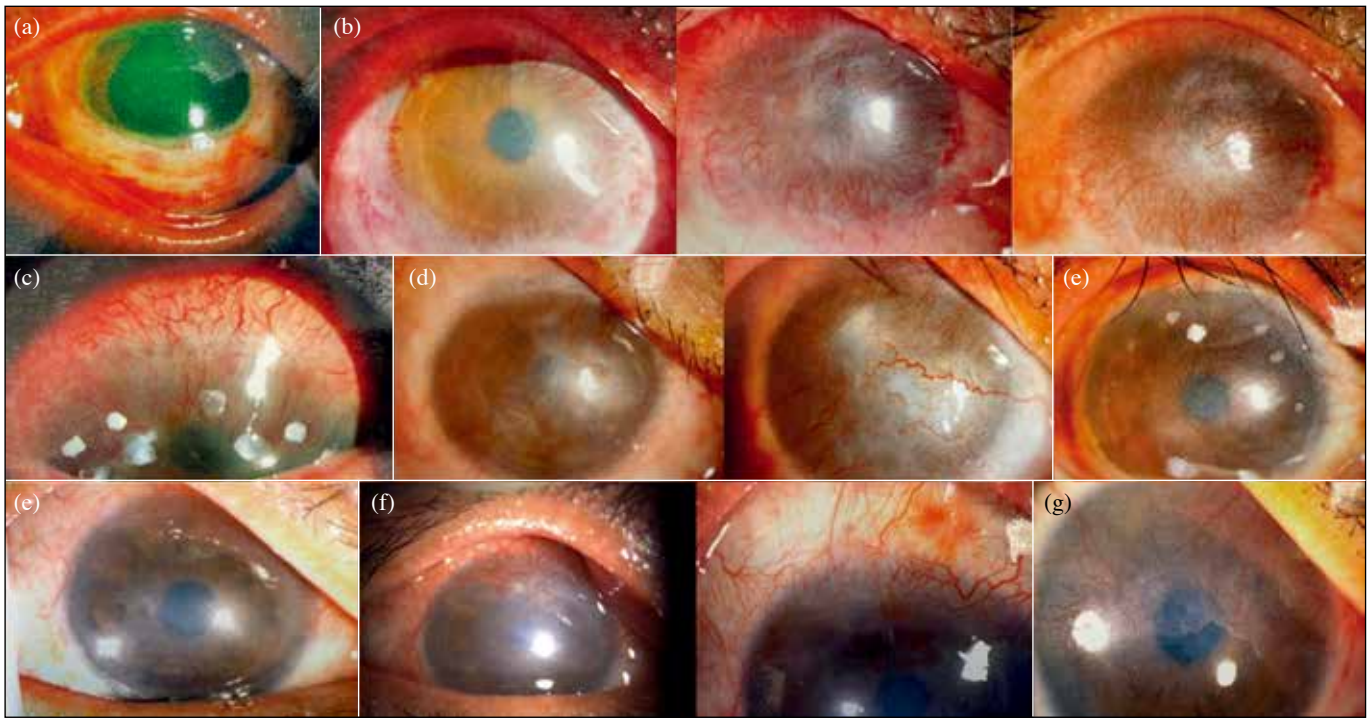

Figure 8. Patient 6: (a) Near total limbal stem cell deficiency and 80% conjunctival involvement of the right eye after Dua grade V injury. (b) Early formation and then progression of conjunctivalization. (c) Early vascularization at the superior cornea after the first simple limbal epithelial transplantation. (d) Recurrence of fibrovascular membrane. (e) The epithelium is stable after the second simple limbal stem cell transplantation. (f) Superior vascularization recurs 8 months later and is halted by subconjunctival aflibercept. (g) Conjunctivalization recurs 2 months later and obscures the superior half of the cornea.

Kong, the decision to initiate immunosuppression when patients have no rheumatological diagnosis is usually made by ophthalmologists. Early immunosuppression may decrease the degree and complexity of cicatricial changes. Reconstructive procedures can achieve better outcome when underlying inflammation is adequately controlled. Cornea and oculoplastic specialists should work together to manage recurring lid and eyelash problems because lid margin health affects cornea surface health and visual outcome.

Patient 6

In November 2016, a 41-year-old man presented with chemical injury by Fosroc Polyurea WPE liquid to the right eye (Dua grade V) and left eye (Dua grade II). The pH value of both eyes was 11. The patient was treated with daily irrigation, intensive topical steroid, antibiotics, lubrication, oral vitamin C, and doxycycline. One week later, autologous serum and bandage contact lens were added for treating persistent total epithelial defect of the right eye, whereas the left eye cornea healed without LSCD. In January 2017, the right eye developed total LSCD. In April 2017, the right eye was treated with SLET (**Figure 8**). One month later, the right eye showed early failure with progressive 360° revascularization and conjunctivalization. In September 2018, the patient underwent second SLET. Eight months later, the cornea surface showed superior vascularization, and subconjunctival aflibercept 2 mg was injected to halt the vascularization. Bandage contact lens was used to prevent breakdown of epithelium. However, in July 2019, conjunctivalization recurred. In June 2022, conjunctivalization and visual acuity remained static.

Patient 7

In December 2018, a 52-year-old man presented with a Dua grade V chemical injury by cement to the left eye. The patient underwent removal of the cement embedded in fornices and was treated with daily irrigation with Morgan lens for 1 week. 11 days after injury, AMT was performed, but residual epithelial defect and progressive corneal neovascularization persisted (**Figure 9**). In January 2019, the patient underwent SLET. Two days later, the donor limbal tissues and the amniotic membrane were shifted downwards after the patient rubbing the eye. Two weeks later, the epithelial defect and corneal vascularization persisted, despite transplantation of the AmnioTek-C. The patient underwent total tarsorrhaphy after multiple limited tarsorrhaphies for an unhealing neurotrophic ulcer. In April 2021, the tarsorrhaphy was released and the ocular surface was found to have epithelialized with dense scarring. The patient opted for conservative treatment. Eye rubbing causes early dislodgement of the amniotic membrane and transplanted tissues.

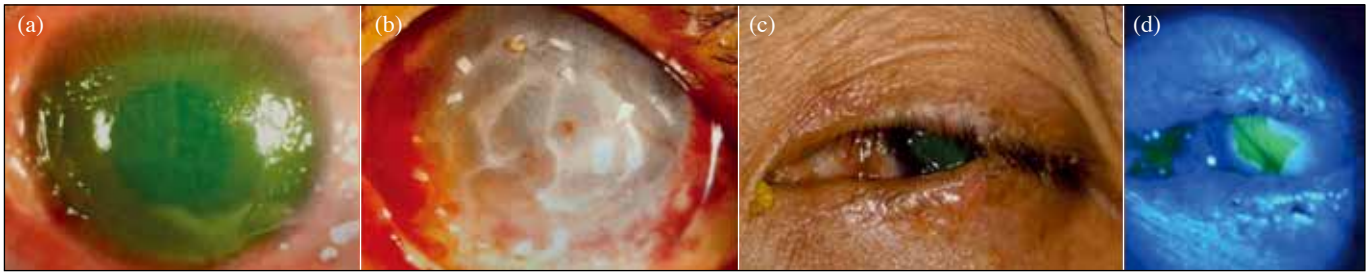

Figure 9. Patient 7: (a) Large epithelial defect despite amniotic membrane transplantation with 360° corneal vascularization. (b) The amniotic membrane and limbal tissues shift downwards secondary to eye rubbing. (c) Persistent epithelial defect necessitates lateral tarsorrhaphy to aid epithelial healing. (d) Complete tarsorrhaphy is performed as repeat limited tarsorrhaphies fail to aid epithelialization.

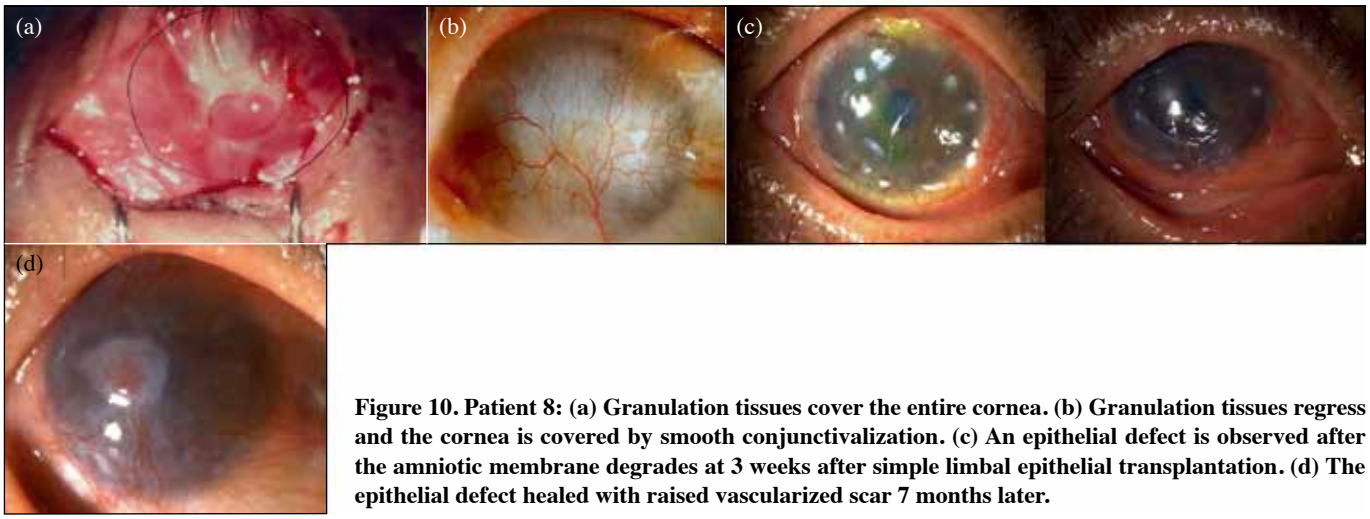

Figure 10. Patient 8: (a) Granulation tissues cover the entire cornea. (b) Granulation tissues regress and the cornea is covered by smooth conjunctivalization. (c) An epithelial defect is observed after the amniotic membrane degrades at 3 weeks after simple limbal epithelial transplantation. (d) The epithelial defect healed with raised vascularized scar 7 months later.

Patient 8

In August 2013, a 55-year-old man presented with infectious keratitis and persistent epithelial defect of the right eye secondary to a Dua grade V chemical injury by cement. One month after injury, the patient underwent paramedian tarsorrhaphy. However, 1 month later, the cornea healed with conjunctivalization and granulation tissues (**Figure 10**). Granulation tissues regressed with time, and the cornea was covered by smooth conjunctivalization. In April 2019, the patient underwent SLET. Three weeks later, an elliptical epithelial defect was observed after the amniotic membrane degraded. Amniotic membrane overlay was performed, but the cornea showed revascularization and conjunctivalization, which is suspected to be caused by heavy tobacco consumption (two packs a day) during the perioperative period.

Discussion

According to the consensus on classification and diagnosis of LSCD,[14] symptoms of LSCD include ocular discomfort, foreign body sensation, redness, tearing or dryness, photophobia, decreased vision, and pain. Patients with partial LSCD may remain asymptomatic. Early clinical signs can be detected by slit lamp examination with the aid of fluorescein stain and include sectoral and curve-like punctate epitheliopathy at the peripheral cornea, which later evolved into a whorl-like pattern and spreading into the central cornea. Clinical signs at later stages include tongue-like hazy opaque or grayish epithelium, superficial vascularization, and pannus formation. Advanced stage of LSCD may show subepithelial fibrosis, conjunctivalization, stromal scarring, neovascularization, and recurrent epithelial defects. Diagnostic tools include impression cytology and/or immunohistochemistry, in vivo confocal microscopy, and anterior segment optical coherence tomography.[15] However, these are not considered as quantitative tools. Quantification of severity of LSCD enables better preoperative counselling for patients.

The success rate of SLET may be higher in cases of thermal injury than of chemical injury, likely owing to the

extent of initial injury being more localized. Chemicals may stay in the fornices or conjunctivae for a prolonged period and hence a longer duration of insult. Higher grades of chemical injury have poorer prognosis. Cicatricial lid changes and symblepharon formation worsen treatment outcomes. The success rate of SLET is lower in patients with systemic causes, as in patient 5, owing to questionable quality of transplanted autologous limbal tissues and ongoing systemic inflammation, particularly when immunosuppression is not achieved before and during recovery.

The amniotic membrane has anti-inflammatory and wound-healing properties. However, these properties may not work in cases that require longer time to achieve normal pH or in cases with alarmingly raised intraocular pressure. The transplanted tissue may hinder accurate intraocular pressure measurement and decrease absorption of topical intraocular pressure–lowering and anti-inflammatory agents. As in patients 3 and 4, we opted for topical autologous serum and/or temporary tarsorrhaphy rather than an early AMT.

The time from injury to SLET is associated with treatment outcome. SLET is a reconstructive procedure for chronic LSCD rather than acute injury or inflammation.[16] For acute cases, treatment options of free conjunctival autografting from the contralateral eye, tenonplasty,[17] and conjunctival flap should be considered for reperfusion of avascular corneal surface and prevention of corneoscleral melting. Tarsorrhaphy should be considered for persistent epithelial defect. Selective cases may benefit from allogenic stem cell transplantation from cadaveric eyes for temporary epithelial healing during early post-injury period.[18] Limbal stem cells of the contralateral eye should not be harvested for treating acutely inflamed eye because of the high failure rate, as in patient 4. In contrast, in patients 1, 2, and 3 with stable chronic LSCD, SLET was successful.

Patient 7 rubbed his eye after SLET and displaced the amniotic membrane and transplanted tissue on postoperative day 3. He developed persistent epithelial defect and required further AMT and tarsorrhaphies.

Patient 8 was thought to be a good candidate for SLET because of the long time since injury, stable ocular surface, and healthy contralateral limbus. However, he had persistent epithelial defect and recurrence of conjunctivalization despite the amniotic membrane overlay. The patient smoked heavily perioperatively. Delayed epithelial healing has been reported in smokers.[19]

The success rate of SLET has been reported to be 70% at 1.1-year follow-up,[7] 76% at 2.96-year follow-up,[10] 66% at 6.2-month follow-up,[20] and 83% at 1-year follow-up.[9] When smaller studies are included, the success rate can vary from 25%[21] to 100%.[22] In our cohort, the success rate was lower (37.5%) because all our patients had total LSCD (other studies include patients with partial LSCD); in addition, three had severe symblepharon, one had displacement of implants secondary to eye rubbing, and one had lichen planus. The criteria to define success, partial success, and failure vary among studies; thus, comparison of outcomes among different studies is difficult.

In patients with bilateral injuries or asymmetrical involvement of the eyes from systemic disease, all donor eyes showed no clinical evidence of limbal stem cell damage preoperatively and did not develop iatrogenic LSCD postoperatively. We opted for autologous SLET because prior to 2019 the evidence of success of allogenic SLET and the consensus of immunosuppressant usage were limited. With local eye bank updating donor suitability for allogenic SLET and better understanding of risk factors, allogenic stem cell transplantation is the future direction, particularly for patients with bilateral LSCD. Collaboration between ophthalmologists and immunologists is needed for the safe and prolonged usage of multiple systemic immunosuppressants.

Contributors

All authors designed the study, acquired the data, analyzed the data, drafted the manuscript, and critically revised the manuscript for important intellectual content. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

All authors have disclosed no conflicts of interest.

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Data availability

All data generated or analyzed during the present study are available from the corresponding author on reasonable request.

Ethics approval

This study was approved by The Kowloon West Cluster Research Ethics Committee [KWC-REC Reference: KW/EX-22-012(169-01)]. The patients were treated in accordance with the tenets of the Declaration of Helsinki. The patients provided written informed consent for all treatments and procedures and for publication.

References

1. *Jhagta HS, Jain P. Limbal stem cell deficiency: a review. J Clin Ophthalmol Res 2015;3:71-5.* Crossref
2. *Singh P, Tyagi M, Kumar Y, Gupta KK, Sharma PD. Ocular chemical injuries and their management. Oman J Ophthalmol 2013;6:83-6.* Crossref
3. *Sekhon A, Wang JYF, Tan JCH, Holland SP, Yeung SN. Limbal stem cell deficiency secondary to systemic paclitaxel (Taxol) for breast cancer: a case report. BMC Ophthalmol 2020;20:400.* Crossref
4. *Mehta U, Farid M. Dupilumab induced limbal stem cell deficiency. Int Med Case Rep J 2021;14:275-8.* Crossref
5. *Deng SX, Kruse F, Gomes JAP, et al. Global consensus on the management of limbal stem cell deficiency. Cornea 2020;39:1291-302.* Crossref
6. *Shanbhag SS, Nikpoor N, Rao Donthineni P, Singh V, Chodosh J, Basu S. Autologous limbal stem cell transplantation: a systematic review of clinical outcomes with different surgical techniques. Br J Ophthalmol 2020;104:247-53.* Crossref
7. *Gupta N, Joshi J, Farooqui JH, Mathur U. Results of simple limbal epithelial transplantation in unilateral ocular surface burn. Indian J Ophthalmol 2018;66:45-52.* Crossref
8. *Le Q, Chauhan T, Yung M, Tseng CH, Deng SX. Outcomes of limbal stem cell transplant: a meta-analysis. JAMA Ophthalmol 2020;138:660-70.* Crossref
9. *Vazirani J, Ali MH, Sharma N, et al. Autologous simple limbal epithelial transplantation for unilateral limbal stem cell deficiency: multicentre results. Br J Ophthalmol 2016;100:1416-20.* Crossref
10. *Basu S, Sureka SP, Shanbhag SS, Kethiri AR, Singh V, Sangwan VS. Simple limbal epithelial transplantation: long-term clinical outcomes in 125 cases of unilateral chronic ocular surface burns. Ophthalmology 2016;123:1000-10.* Crossref
11. *Shanbhag SS, Patel CN, Goyal R, Donthineni PR, Singh V, Basu S. Simple limbal epithelial transplantation (SLET): review of indications, surgical technique, mechanism, outcomes, limitations, and impact. Indian J Ophthalmol 2019;67:1265-77.* Crossref
12. *Soleimani M, Naderan M. Management strategies of ocular chemical burns: current perspectives. Clin Ophthalmol 2020;14:2687-99.* Crossref
13. *Dua HS, Miri A, Faraj LA, Said DG. Free autologous conjunctival grafts. Ophthalmology 2012;119:2189-2189.e2.* Crossref
14. *Deng SX, Borderie V, Chan CC, et al. Global consensus on definition, classification, diagnosis, and staging of limbal stem cell deficiency. Cornea 2019;38:364-75.* Crossref
15. *Le Q, Chauhan T, Deng SX. Diagnostic criteria for limbal stem cell deficiency before surgical intervention: a systematic literature review and analysis. Surv Ophthalmol 2020;65:32-40.* Crossref
16. *Dua HS, Miri A, Said DG. Contemporary limbal stem cell transplantation: a review. Clin Exp Ophthalmol 2010;38:104-17.* Crossref
17. *Kuckelkorn R, Schrage N, Reim M. Treatment of severe eye burns by tenonplasty. Lancet 1995;345:657-8.* Crossref
18. *Iyer G, Srinivasan B, Agarwal S, Tarigopula A. Outcome of allo simple limbal epithelial transplantation (alloSLET) in the early stage of ocular chemical injury. Br J Ophthalmol 2017;101:828-33.* Crossref
19. *Dhillon HK, Bahadur H, Raj A. A comparative study of tarsorrhaphy and amniotic membrane transplantation in the healing of persistent corneal epithelial defects. Indian J Ophthalmol 2020;68:29-33.* Crossref
20. *Jain R, Kanaujia V, Sahu S, Das S. Management of unilateral limbal stem cell deficiency by simple limbal epithelial transplantation: our experience. MOJ Surg 2014;1:4-7.* Crossref
21. *Mittal V, Jain R, Mittal R, Vashist U, Narang P. Successful management of severe unilateral chemical burns in children using simple limbal epithelial transplantation (SLET). Br J Ophthalmol 2016;100:1102-8.* Crossref
22. *Amescua G, Atallah M, Nikpoor N, Galor A, Perez VL. Modified simple limbal epithelial transplantation using cryopreserved amniotic membrane for unilateral limbal stem cell deficiency. Am J Ophthalmol 2014;158:469-75.e2.* Crossref