manifestations of SLE include keratoconjunctivitis sicca and rarely keratoendothelitis, corneal infiltrates, and peripheral ulcerative keratitis.[1] In 1964, Halmay and Ludwig first reported a case of band-shaped keratitis in a patient with SLE.[2] Since then, IK has been reported rarely.[3,4]

The previous case reports all involved adult patients who had either pre-existing SLE or presented with characteristic associated systemic complaints (e.g., skin rash, arthritis, or myalgias). They also had focal corneal involvement, either band shaped or localized to a quadrant. Most presented with significant ocular pain and photophobia. In contrast, our pediatric patient had not been previously diagnosed with SLE, nor did she have any of the classic systemic or ocular complaints. Her pulmonary symptoms were felt to be consistent with asthma, and she was treated accordingly for years. Her corneal pathology also featured more circumferential inflammation with deep stromal neovascularization.

Although other etiologies such as viral may be theoretically implicated, her IgM titres were negative. Over her 12-year follow-up, she did not develop any other ocular manifestations consistent with viral corneal disease. It has been also previously reported that herpes simplex virus and Epstein–Barr virus are exceedingly rare in active bilateral IK, with a prevalence of 2% and 1%, respectively.[5] In addition, the improvement of her corneal disease and stability of her ocular examination on MTX for several years also provides stronger evidence for lupus as the underlying etiology of her stromal inflammation and vascularization.

The dramatic corneal findings and relative lack of symptoms may be unique to the presentation of lupus IK in a child. The lack of symptoms, or ability for the child to identify them, may have delayed medical attention, allowing the inflammatory process to progress to a more advanced state. Additional cases are needed to further detail potential differences of this rare disease between adults and children. We present the first report of a child with lupus IK. Even though it is extremely rare, SLE should be considered in the differential diagnosis of a child with IK. Prompt recognition and treatment with topical steroids and systemic immunosuppression can prevent permanent corneal scarring and vision loss.

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Footnotes and Disclosure

The authors have no proprietary or commercial interest in any materials discussed in this article.

Simple limbal epithelial transplantation (SLET) in conjunction with keratoplasty for severe congenital corneal opacities

Congenital corneal opacities (CCO) are rare, with an incidence of 1 in 26,000 to 37,000 live births.[1,2] There is a wide spectrum of CCO disease severity from mild and small opacities to fully opaque cornea with severe lens involvement and vascularization or conjunctivalization of the cornea. The severe form of CCO is usually associated with large corneal opacity and the presence of extensive superficial corneal vascularization. Such eyes may have conjunctival epithelial ingrowth, which can increase the risk of allograft rejection.[3]

Limbal epithelial stem cells reside at the limbus and act as a barrier against the invasion of conjunctival epithelium onto the corneal surface.[3,4] The limbal stem cells are also essential for the epithelialization of the cornea.[3,4] Limbal stem cell deficiency (LSCD) can lead to a wide range of clinical problems, including recurrent or persisting epithelial defects, conjunctivalization of the cornea, scarring, localized neovascularization, chronic inflammation, and corneal perforation.[3,4] Limbal stem cells can fail in primary ocular diseases such as congenital aniridia[5] or become damaged in acquired disease as seen in chemical injuries and Stevens-Johnson syndrome.[4] There is very little in the literature on LSCD in CCOs and the mechanism is not well understood.

Nischal and Lathrop found a correlation between the absence of palisades of Vogt and failure of corneal epithelialization after penetrating keratoplasty in a patient with congenital corneal opacity.[6]

Corneal transplantation and visual rehabilitation in patients with CCO can be challenging. Ocular surface failure and loss of limbal stem cells further threatens the survival of corneal grafts and is of significant concern. Various modalities of limbal stem cell transplantation (LSCT) have been reported. The severity and laterality of the LSCD guides decision on the particular LSCT procedure chosen.[7,8] Simple limbal epithelial transplantation (SLET) is a relatively new technique described by Sangwan et al, in 2012.[9-11] The technique uses the healthy autologous stem cells from the unaffected eye to repopulate the affected eye. Clinical success rates for autologous SLET have been reported to be equal to or better than those reported with earlier techniques.[9] Also, an autologous procedure does not require immunosuppression because of a lack of immunologic rejection that can occur in allogenic LSCT.[3,10,11] Therefore, the authors feel that SLET will be useful in maintaining graft clarity in patients with congenital corneal opacity and conjunctivalized cornea with the fellow eye suitable to serve as a donor. To the best of our knowledge, this is the first report of SLET being done in conjunction with corneal transplantation in patients with congenital corneal opacities.
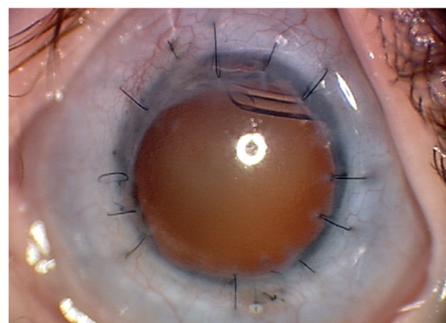
Case 1

A systemically healthy baby girl was referred in the first week of life for corneal evaluation. On slit-lamp examination and ultrasound biomicroscopy (UBM), her right eye had central corneal opacity with iridocorneal and corneolenticular adhesions consistent with type II Peters anomaly. This eye had healthy limbus without significant conjunctival override for 9 clock hours. However, B-scan ultrasound indicated severe persistent fetal vasculature with retinal detachment in the right eye.

The left cornea was completely opacified, with extensive vascularization and conjunctivalization of the corneal surface, an ill-defined limbus, and no view of the anterior chamber (Fig. 1A). UBM indicated a poorly developed anterior segment with a mildly cataractous lens adherent to cornea and rudimentary iris with a small cyst. The patient was diagnosed with left severe anterior segment dysgenesis with a phenotype consistent with type II Peters anomaly. B-scan indicated an excavation at the optic nerve head consistent with morning glory disc anomaly with an attached retina. Visual evoked potential indicated a nonrecordable response in the right eye and a positive response in the left eye. After an extensive discussion of the options with the parents, and given the better visual potential in the left eye, a decision was made to proceed with left penetrating keratoplasty (PKP) combined with right to left SLET. The

(a)

(b)

Fig. 1—Case 1. (A) Photograph of the left eye showing diffuse corneal opacity and conjunctivalization. (B) Photograph of the left eye 7 months after penetrating keratoplasty and simple limbal epithelial transplantation showing a clear graft.

decision to combine penetrating keratoplasty with SLET was to address extensive corneal conjunctivalization. The concomitant replenishing of the limbal stem cells along with the corneal graft was performed in an attempt to prevent delayed corneal epithelization and postoperative corneal neovascularization.
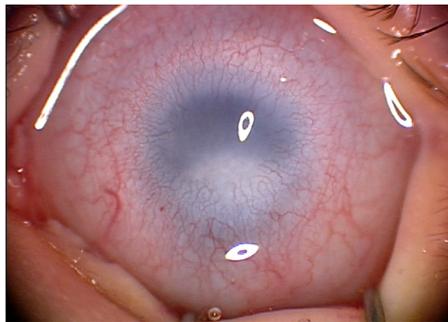
At 5 months of age, uneventful PKP and SLET were performed using a standard published technique.[12] In summary, a 360-degree conjunctival peritomy was performed to recess the conjunctiva that was inserting into the central 2 mm of the cornea. Through a paracentesis, viscoelastic (Healon; Abbott Medical Optics Inc., Santa Ana, Calif.) was injected in the anterior chamber and the adherent lens was gently separated from the cornea using a sweeping movement. A 6.0 mm trephine was used on the host cornea and 6.5 mm donor cornea secured using interrupted sutures. Two clock hours of healthy limbus from the right eye was used to harvest SLET material and applied over the left transplanted cornea using a technique published previously.[9] A first-stage Ahmed valve implantation was also performed in anticipation of the development of glaucoma. A central temporary tarsorrhaphy was then performed to ensure the SLET, amniotic membrane, and bandage contact lens were not rubbed out by patient and was opened up after 2 weeks. The seton was then inserted into the eye combined with lensectomy and anterior vitrectomy in the subsequent weeks to address high intraocular pressure and moderate lens opacification,

respectively. Pathologic analysis of the corneal button indicated classic Peters anomaly, superficial corneal vascularization, a thin layer of epithelium with no stratification, and no goblet cells. At 17 months follow-up, the graft remained clear, with healthy epithelium and no signs of corneal neovascularization or conjunctival overgrowth (Fig. 1B). The patient's vision was fixating and following the light, limited by large morning glory disc anomaly, and her intraocular pressure was 17 mm Hg.
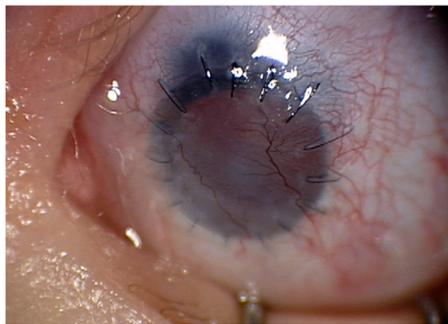
Case 2

A 6-week-old girl with a positive family history for microcornea and ocular coloboma was referred to our corneal

(a)

(b)

(c)

Fig. 2—Case 2. (A) Preoperative photograph of the left eye showing diffuse corneal opacity (worse inferiorly). (B) Photograph of the left eye 4 months after deep anterior lamellar keratoplasty. Note the conjunctivalization of the graft. (C) External photograph of the left eye 21 months after repeat deep anterior lamellar keratoplasty and simple limbal epithelial transplantation.

clinic for evaluation. On examination, her right eye was found to have an inferocentral corneal opacity with iridocorneal adhesions and an inferior iris coloboma. Her left eye examination identified diffuse corneal opacity that was worse inferiorly (Fig. 2A) and a corneal diameter of approximately 6−7 mm with an indistinct limbus. A UBM indicated iridocorneal adhesions to the corneal opacities in both eyes with normal crystalline lens, which was consistent with type I Peters anomaly. Dilated fundus examination of the right eye indicated inferior chorioretinal coloboma splitting the macula. There was a limited view to the fundus in the left eye; however, B scan ultrasound identified an optic nerve coloboma without masses or retinal detachment. The patient underwent optical iridectomy in the right eye with good clearing of the visual axis. Given the extent of the corneal opacity in her left eye, a decision was made to proceed with keratoplasty. A deep anterior lamellar keratoplasty (DALK) was considered superior to a penetrating keratoplasty in this case because it carries lower graft rejection rate despite being more technically challenging. Therefore, we performed an uneventful layer-by-layer manual dissection of the host cornea until a clear cornea was seen. The use of intraoperative optical coherence tomography provided intraoperative guidance regarding the thickness of the residual stromal bed. Pathologic analysis of the host corneal button indicated a thin layer of epithelium with no stratification and no goblet cells. The patient had a persistent epithelial defect for 6 weeks postoperatively and subsequently developed superficial haze and conjunctivalization over most of the graft, including the visual axis (Fig. 2B). Six months later, she underwent a repeat DALK with autologous SLET procedure. Histologic examination identified no epithelium consistent with surgical superficial keratectomy performed to remove the conjunctivalized graft. The patient was followed for 2 years with no evidence of corneal neovascularization or ocular surface failure (Fig. 2C). The posterior lamella of the cornea became clearer over time, allowing examination of the retina with a large macula involving coloboma and hand motions vision.

Discussion

In this paper we report long-term results in the youngest patients to have SLET procedure in the literature and the first 2 patients with congenital corneal opacities and corneal conjunctivalization.

SLET is a relatively new surgical technique, first described by Sangwan et al. in 2012 to treat unilateral LSCD.[9] In a single-center study of 125 SLET procedures for unilateral LSCD secondary to chemical injury, an 80% success rate in adults and 76% success rate in children was reported.[7] Similarly, results from a multicenter retrospective study described an 84% success rate for SLET, suggesting it to be comparable to or even better than previous techniques; specifically,

conjunctival—limbal autograft and ex vivo cultivated limbal epithelial transplantation.[10] In contrast, a case series specifically looking at SLET in 4 children after severe chemical injury reported a complete success rate of 25%.[11] Success improved to 100% after repeat SLET surgery for residual LSCD in 1 quadrant.

All published case series to date on SLET in children report on the results of SLET after acquired causes of LSCD (mostly chemical injury).[7–11] To the best of our knowledge, we report the first cases describing the use of SLET in patients with severe CCO who are known to have abnormal or absent palisades of Vogt with delayed epithelial healing after penetrating keratoplasty.[6] Clinically, patients with severe CCO have poorly differentiated limbus and conjunctivalization of cornea. Our first patient had severe corneal conjunctivalization at birth, and the second patient had a persistent epithelial defect followed by conjunctival overgrowth 6 weeks after a DALK procedure, highly suggestive of limbal stem cell disease. Furthermore, histologic examination for both patients indicated a lack of normal corneal epithelium, revealing abnormally thin and nonstratified epithelium. After SLET, both patients maintained clear corneal grafts and healthy epithelium during their follow-up periods of 17 and 24 months, respectively.

Allogenic limbal stem transplantation has been previously reported for 2 patients with congenital corneal opacities.[13] The first patient was an 8-year-old with peripheral sclerocornea in whom allograft limbal transplantation was performed and who required systemic immunosuppression for 2.5 months after the procedure. The graft remained clear for 2 years after the surgery with 20/100 vision. The second case was a 12-year-old patient with presumed PHACES syndrome and bilateral sclerocornea.[14] He underwent bilateral PKP with concomitant allogenic limbal stem transplantation. Both of his grafts remained avascular for 5 years after surgery; however, he developed graft failure in one eye after 3 years. The authors did not comment if the patient received immunosuppression postoperatively.

Our study describes the use of SLET technique in congenital corneal opacities associated with LSCD, with a fellow eye that had a healthy limbus. This is a technique that avoids the need for immunosuppression and may increase the likelihood of maintaining a clear graft in eyes with severe congenital corneal opacity.

Weaknesses of our study include the small sample size and the retrospective nature of this study, but this particular clinical presentation is rare. Results of our case study are encouraging and merit further study.

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Footnotes and Disclosure

The authors have no proprietary or commercial interest in any materials discussed in this article.

Leber hereditary optic neuropathy harboring a rare m.12811 T>C mitochondrial DNA mutation

Leber hereditary optic neuropathy (LHON) is the first hereditary disease recognized to be caused by mitochondrial DNA (mtDNA) mutation.[1] It is the most commonly inherited optic neuropathy resulting in bilateral visual impairment.[2] More than 90% of LHON cases harbor 1 of the 3 major mtDNA mutations m.11778G>A, m.3460G>A, and m.14484T>C; however, other variants have been previously identified.[3−5] We report on a case of LHON with an m.12811T>C mtDNA mutation, a rare variant mutation that has only been previously reported as a secondary mutation of LHON.[5,6] Nevertheless, its phenotypic features have not been well described in previous literature. To our knowledge, this is the first reported case of the m.12811T>C mutation in which its clinical course and features were investigated.

A 53-year-old male presented with a 2-month onset of bilateral, progressive, painless blurred vision. Ocular symptoms first appeared in the right eye followed by the left within 2 weeks. The patient had a history of hypertension and no family history of ocular disease. He was a heavy smoker (40 cigarettes daily over 25 years), a heavy drinker (liquor >750 mL/d), and had a poor diet (a bowl of instant noodles daily) before the onset of his symptoms.

Initial best-corrected visual acuity was 20/100 on the right and 20/200 on the left eye with normal intraocular pressure. Slit-lamp examination of the anterior segment was unremarkable. Pupillary light reflex remained prompt and relative afferent pupillary defect (RAPD) was not observed. Fundoscopy revealed no optic disc hyperemia or swelling. Peripapillary telangiectatic blood vessels were not observed.

Further examination showed decreased critical flicker frequency values of 13.2 Hz on the right and 13.8 Hz on the left eye. Optic coherence tomography (OCT) revealed no foveal or disc abnormalities. Central scotoma was observed bilaterally on the Humphrey Field Analyzer (HFA) 30-2 visual field test (Fig. 1). Flash electroretinography was normal. Gadolinium-enhanced orbital magnetic resonance imaging (MRI) did not reveal any inflammation around the optic nerve.

Laboratory data did not reveal any vitamin deficiency. Mitochondrial genetic analysis identified an m.12811T>C (p.Tyr159His) mutation of the mtDNA, a rare variant mutation in LHON.[3−5] The percent heteroplasmy of the patient's mtDNA was below the limit of quantification (i.e., <20% for our laboratory).

With the improvement of dietary habits as well as the cessation of smoking and alcohol consumption, the patient's best-corrected visual acuity recovered to 20/20 bilaterally within 3 months from onset. Critical flicker frequency values also improved to 28.7 Hz on the right and 28.2 Hz on the left eye after 6 months. Follow-up OCT map image after 4 months revealed thinning of the retinal nerve fiber layer (RNFL) in the temporal quadrant of the optic disc, namely the papillomacular bundle (PMB) (Fig. 2). RNFL thinning was also observed in the macula regions (Fig. 2). Follow-up visual field test showed bilateral recovery of retinal sensitivities on HFA 30-2; however, some decrease in foveal sensitivity remained on HFA 10-2 after 5 months.

LHON occurs as a result of selective degeneration of the retinal ganglion cells, especially in within the PMB, which are highly susceptible to mitochondrial dysfunction due to their high metabolic activities.[1] In the acute phase, RNFL thickening, associated with impaired axonal transport, is observed starting in the temporal quadrant.[4] Vision loss and cecocentral scotoma develops as the PMB becomes damaged due to impaired mitochondria function.[2] In the chronic phase, optic nerve pallor and temporal PMB and macular thinning can manifest after 6 to 36 weeks.[2] Light reflexes usually remain prompt and RAPD is usually negative, as seen in our patient.[2,4] Visual impairment is usually permanent; however, spontaneous recovery may occur within the first year,[2] as observed in the present case.

Typical features of LHON in the acute phase was absent in the present case, suggesting that the patient was under transition from the acute to chronic phase of the disease, the m.12811T>C mutation had a mild phenotype, or both.

Right: MD = −7.02 dB, PSD = 7.47 dB
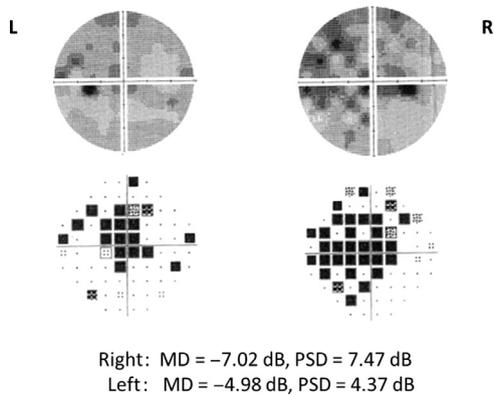Left: MD = −4.98 dB, PSD = 4.37 dB

Fig. 1—Visual field test results at initial visit. Humphrey Field Analyzer 30-2 visual field test result shown in grey scale and pattern deviation probability map. Central scotoma was observed in both eyes with overall decreased mean deviation values. MD, mean deviation, PSD, pattern standard deviation.