Clinical Case Report

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# A method to preserve limbus during penetrating keratoplasty for a case of presumed PHACES syndrome with sclerocornea

## A case report

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**Abstract**

**Background:** Sclerocornea, a congenital corneal pathology characterized by bilateral scleralization of the cornea, which can be found in few cases with posterior fossa malformationshemangiomas-arterial anomalies-cardiac defects-eye abnormalities-sternal cleft and supraumbilical raphe (PHACES) syndrome. Presence of vascularization in peripheral cornea and smaller diameter of recipient cornea correlate to poor outcome of penetrating keratoplasty (PKP) in sclerocornea. Here we report a method to preserve limbus during PKP for small, irregular, and scleralized cornea.

**Methods:** A 12-year-old boy with multiple congenital anomalies diagnosed as PHACES syndrome suffered from bilateral total sclerocornea and poor visual acuity. Due to the fact that the left eye cornea was small (6.5 mm × 10 mm), lamellar dissection and posterior recession of inferior limbus was first performed and followed by a 6 mm trephination and PKP with a 6.5 mm graft for left eye. At the same time, lens aspiration and release of peripheral anterior synechia were performed.

**Results:** After 6 years of follow-up, the cornea remained clear, and there has been no sign of inflammation and conjunctivalization. The patient maintained useful vision of 20/400 in left eye.

**Conclusion:** The stabilization of corneal surface is possible after PKP for sclerocornea if the limbus can be preserved during the operation, and epithelium can remain corneal in phenotype preventing pannas growth.

**Abbreviations:** IOP = intraocular pressure, PKP = penetrating keratoplasty.

**Keywords:** case report, limbus, penetrating keratoplasty, PHACES syndrome, sclerocornea

## 1. Introduction

Sclerocornea is a rare form of congenital corneal opacity characterized by bilateral scleralization of the cornea. The disease is due to the disorganized migration of fetal neural crest cells between the corneal epithelium and the endothelium.[1] The cases are either 50% autosomal recessive or dominant, while the remaining cases are sporadic.[2] Sometimes, sclerocornea is combined with systemic abnormalities such as mental retardation, hearing defect, and craniofacial abnormalities.[3] While among them includes the rarely seen posterior fossa malformationshemangiomas-arterial anomalies-cardiac defects-eye abnormalities-sternal cleft and supraumbilical raphe (PHACES) syndrome.

The manifestations of PHACES syndrome includes posterior fossa malformations, hemangioma, sternal defect, coarctation of the aorta, as well as anomalies of arteries, hearts, and eyes.[4] Ophthalmic abnormalities are seen in 16% of the patients with PHACES,[5] which includes Horner syndrome, exophthalmos, strabismus, sclerocornea, iris hydroplasia, glaucoma, congenital cataract, lens coloboma, optic nerve atrophy, retinal vascular abnormality, choroidal hemangiomas, and peripheral staphyloma.[4] Sclerocornera, an eye abnormality seen in PHACES, is a primary anomaly with scleralization of the peripheral part of cornea, presenting obscured boundary between sclera and cornea. Other abnormalities which involves the entire corneal tissue is called sclerocornea totalis.[6] However, similar in other

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General consideration: All patient data have been deidentified. Approval from patient and institutional review board were obtained.

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congenital corneal opacities, penetrating keratoplasty (PKP) is indicated in sclerocornea if involvement is bilateral.[7]

The patient in this case report of presumed PHACES syndrome with multiple congenital anomalies had bilateral total sclerocornea. The effort was made to preserve the limbus before performing PKP because the cornea was small and irregular. According to the best of our knowledge, this is the first report of using special technique to salvage limbus before performing PKP. The graft remained clear without pannas ingrowth for 6 years, therefore the limbal stem cell deficiency did not occur, justifying the application of this technique.

## 2. Presenting concerns

A 12-year-old boy with clouding of bilateral corneas (Fig. 1A) since birth had hemangioma over the trunk and extremities, ectopic kidney, patent ductus arteriosus, tethered cord syndrome, communicating-type hydrocephalus, cerebral palsy, leg length discrepancy, and flat feet according to his medical history. By judging from the skin, eye (Fig. 1B) and coarctation of the aorta (Fig. 1C), he was therefore, diagnosed as a case with PHACES syndrome.

### 2.1. Clinical findings/diagnostic focus and assessment

As for the ocular examination, it revealed bilateral total corneal opaque, blending of cornea with sclera, and superficial vascularization. His visual acuity was counting fingers less than 1 m in both eyes. However, while there was no clear view of anterior chamber in right eye due to total opacity of cornea; aniridia, irregular pupil, markedly opaque cornea, and cataract of left eye were found under slit-lamp biomicroscopy. Furthermore, intraocular pressure (IOP) was measured as 29 mm Hg in right eye and 24 mm Hg in left eye, yet the light perception and color sensation were intact bilaterally. B-scan ultrasonography presented normal structure in posterior pole of both eyes without vitreoretinal pathology. First, to improve his vision, we decided to perform PKP in the left eye.

### 2.2. Therapeutic focus and assessment

The operation was performed under general anesthesia. In order to control the IOP in advance, antiglaucoma agents including Latanoprost eye-drop every night in the bedtime, Timolol eye-drop twice daily and intravenous 20% D-mannitol 180 mL for once were given preoperatively. The cornea was oval and

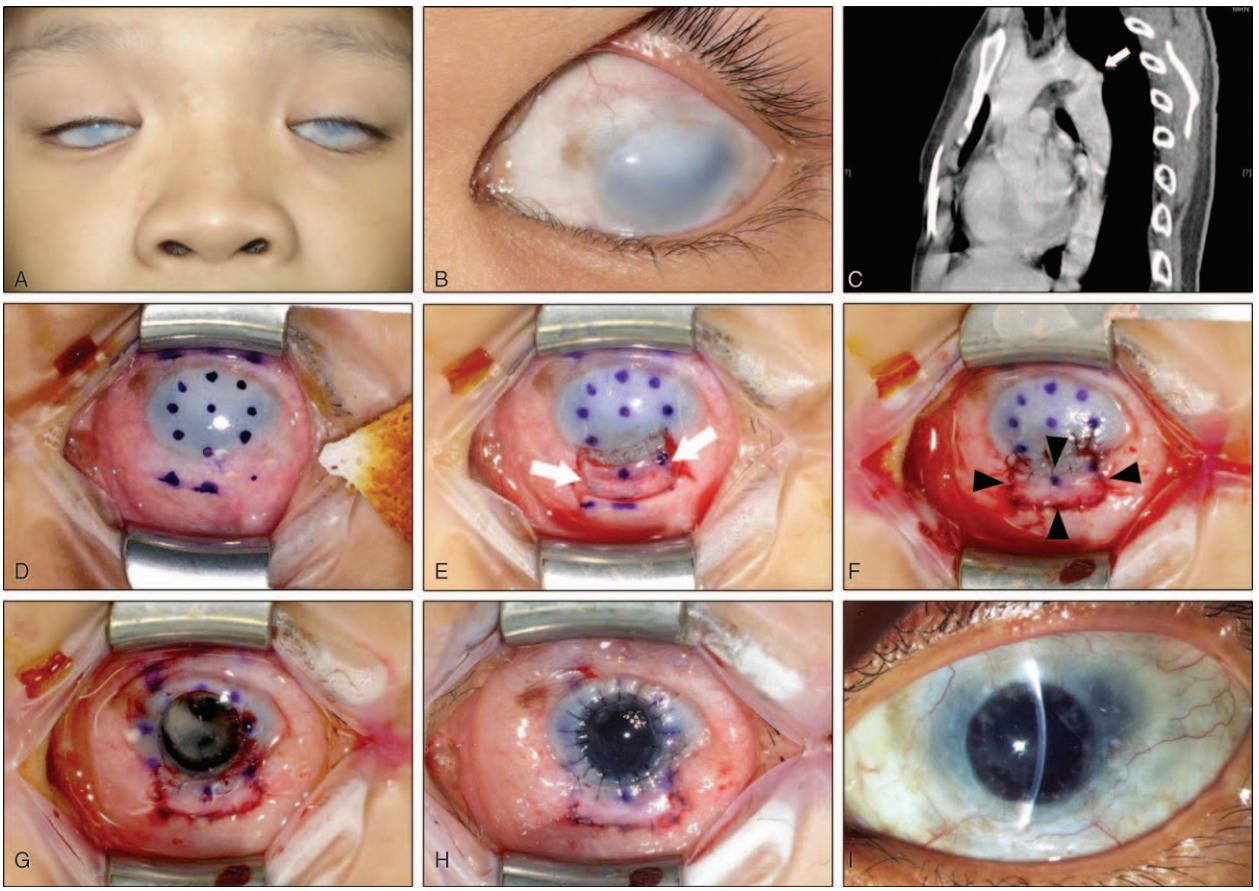


**Figure 1.** (A) The 12-year-old male patient with PHACES-like syndrome manifested with bilateral sclerocornea. (B) The preoperative photo of left eye revealed diffuse corneal opaque and superficial vascularization. (C) Coarctation of aorta was noted in computed tomography sagittal film (white arrow) (D) The cornea measured 6.5 mm × 10.0 mm in diameter, and a 6.0 mm circle was demarcated with a marking pen. (E) Five to 7 o'clock limbus was recessed posteriorly for 1.6 mm by lamellar dissection followed by posterior placement of limbal tissue (white arrows). (F) A crescent shape peripheral donor cornea (black arrow heads) was sutured to the defect with 10-0 nylon sutures (G) A Barron vacuum punch was used to cut a recipient bed 6.0 mm in diameter, which showed the absence of iris and membranous cataract. (H) A 6.5 mm donor cornea was sutured with 16 stitches of interrupted 10-0 nylon sutures. (I) The graft was clear without edema or pannas ingrowth. Photograph was taken 6 years after PKP. PHACES = posterior fossa malformationshemangiomas-arterial anomalies-cardiac defects-eye abnormalities-sternal cleft and supraumbilical raphe syndrome, PKP = penetrating keratoplasty.

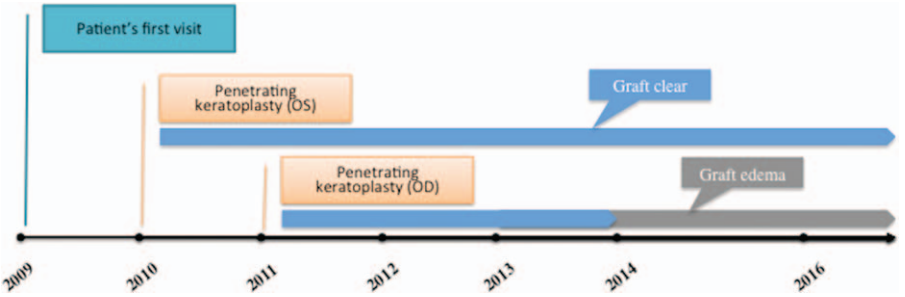


**Figure 2.** Timeline demonstrates clinical course from patient's first visit to the last time follow-up, including bilateral PKP and condition of cornea grafts. PKP = penetrating keratoplasty.

measured 6.5 mm vertically and 10.0 mm horizontally in diameter. The horizontal diameter of the cornea is appropriate for a 6.0 mm trephine, but the trephine may inevitably cut the limbus at 12 and 6 o'clock. During trephination, to avoid inadvertently excising the limbus, a 6.0 mm circle was demarcated by a marking pen (Fig. 1D). Then the 5 to 7 o'clock limbus was recessed for 1.6 mm by lamellar dissection, followed by posterior placement of limbal tissue (Fig. 1E, white arrow). The excessive bulbar conjunctiva was excised, and the graft was sutured with 8-0 vicryl sutures. The limbal defect created will then interfere with the suction of vacuum trephine, therefore, to overcome this, the crescent-shaped peripheral donor cornea was sutured to the defect with 10-0 nylon sutures (Fig. 1F, black arrow heads). This step can be omitted if hand-held punch is used instead. Afterwards, a 6.0 mm Barron vacuum trephine was used to punch the central cornea. After excising the cornea, total absence of the iris was noted, and the lens was opaque and membranous (Fig. 1G). The lens material was removed meticulously by aspiration, and the posterior capsule was left intact. A 6.5 mm donor cornea was sutured with 16 stitches of interrupted 10-0 nylon sutures (Fig. 1H). Postoperatively, dexamethasone 1 mg/mL per hour, 0.2% ciprofloxacin 4 times a day, and Tobradex ointment (Alcon) twice a day were given.

### 2.3. Follow-up and outcomes

The preoperatively elevated IOP, which was commonly found among sclerocornea,[2] returned to normal range after PKP, suggesting that previous IOP measurement might be falsely high due to originally thicken and rigid cornea. The best-corrected vision improved to 20/400 postoperatively, while suboptimal visual acuity might be attributed to preexisting amblyopia. The graft remained its clarity for over 6 years (Fig. 1I). The optic nerve head remained normal, without cupping enlargement. The patient received similar surgery for the right eye cornea a year later, but the graft failed with edematous change three years after surgery. Interventions from patient's initial visit were illustrated with timeline (Fig. 2). As the vision stayed still within counting fingers range, the patient declined advice of regrafting the right eye cornea. Since pannas invasion never happened in both eyes, we assumed that PKP-induced limbal stem cell deficiency never occurred to this patient.

## 3. Discussion

Sclerocornea is a relatively uncommon cause of congenital corneal opacity. It is characterized by a flattened cornea with varying degrees of corneal opacification, which resembles sclera in appearance. The earlier surgical outcome was poor due to vascularization of peripheral cornea, smaller recipient cornea sizes[8] and glaucoma[2] but because the eyes were not always associated with glaucoma, PKP was performed successfully to some patients with sclerocornea.[9] In this case of presumed PHACES syndrome, whose cornea is oval-shaped and scleralized, a novel technique was adopted to preserve this patient's limbus. Since without doing so, a 6.0-mm-sized PKP trephine may accidentally remove part of the limbus, not only would it induce partial limbal deficiency, but it may also jeopardize the donor cornea survival, resulting in graft failure due to close contact with limbal vasculature.

Moreover, to clarify the corneal structure in sclerocornea, there were several reports emphasizing the ultrastructure of sclerocornea by light microscopy,[10] electron microscopy,[7] and ultrasound biomicroscopy.[9] In regards to histopathology, the authors concluded that the architecture of the anterior scleralized cornea resembled sclera, with disorganized stroma and vascularization, abnormal Bowman layer, abnormal Descemet membrane and endothelium. However, Young et al found that through the study of proteoglycan content in sclerocornea, scleralized cornea expresses highly sulfated keratan sulfate proteoglycans in pattern, which can be found in cornea rather than in sclera. The above findings proved that sclerocornea is a congenital dysgenesis with failure of corneal type. In other words, sclerocornea resembles cornea rather than sclera.[11] In addition, more supporting evidence indicated that the majority of stromal collagen in the scleralized cornea is type I collagen, similar to normal cornea instead of sclera, which is predominantly type III collagen. The lumican content in the scleralized cornea is reduced, while that of aggrecan is increased.[12]

In previous studies, it remained unclear whether the epithelium of scleralized cornea is corneal or conjunctival in phenotype. Recently, using immunoconfocal microscopy to examine the expression of keratin 3, 12, 13, and 19 as well as goblet cell mucin MUC5AC in scleralized corneas, we found positive K3/12, negative K13/19, and MUC5AC staining in these corneas, indicating that the scleralized cornea preserves the corneal but not the conjunctival epithelial phenotype.[13] Thus, following keratoplasty, normal corneal epithelium can repopulate the corneal surface, and the risk of conjunctivalization is minimal. Though, rejection and glaucoma due to the presence of stromal blood vessels and abnormal iris-anterior chamber structures are more commonly encountered after operation. Therefore, close follow-ups and meticulous caring of the patient is essential.

In conclusion, we reported a technique to avoid damaging the limbus during PKP in a case of presumed PHACES syndrome with total sclerocornea. There were no signs of limbal stem cell deficiency occurrence for more than 6 years postoperatively (Fig. 1I), justifying that the application of this technique is effective. Still, such technique might also be useful for small and irregular opacity caused by other corneal pathologies.

### *3.1. Informed consent*

Written informed consent was given to the patient for the publication of this case report and any accompanying images. A copy of the written consent can be available for review by editor of this journal.

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