

# Uncommon Giant Corneal Keloid: A Case Report and Literature Review

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## Case Report

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# Abstract

**Background:** Corneal keloid is a rare kind of clinical disease. Surgery is the only treatment in the end, but the literature reports vary. This is a case study of the diagnostic and treatment course for a patient with giant corneal keloid.

**Case presentation:** A 36-year-old young man was admitted to the hospital because of a large mass on the surface of the left cornea. A slit lamp examination revealed that the lesion covered the entire cornea and protruded from the surface of the eyeball, so that the left eyelid could not be closed normally. B-scan of the eye showed that the internal structure of the left eye was normal. The mass was surgically removed and sent for pathological examination, and then the ocular surface reconstruction was taken by deep anterior lamellar keratoplasty. Histopathologic study showed irregular epithelium, the absence of Bowman's layer and hyperplastic collagen fibers, which are consistent with the diagnosis of corneal keloid. Immunohistochemical revealed positive staining for vimentin in lesion subject and smooth muscle actin (SMA) in vascular wall. The corneal graft remained clear 4 months after surgery and the patient was satisfied with the visual outcome. A final diagnosis of giant corneal keloid was reached.

**Conclusion:** Corneal keloid should be suspected in cases of enlarging white glistening corneal nodule after trauma. Deep anterior lamellar keratoplasty is one of the effective surgical option for corneal keloids.

## Background

Corneal keloid is a rare kind of clinical disease, which is easily misdiagnosed as a corneal dermoid tumor(1). Corneal keloid was first reported by Szokalski in 1865. It is clinically manifested as a white mass, which gradually increases, bulges on the corneal surface, and invades the corneal stroma(2). Most reports secondary to corneal trauma or surgery, which may be due to the proliferation of fibroblasts in the corneal stroma caused by inflammation(3). Surgery is the only treatment in the end, but the literature reports vary. We herein reported a giant corneal keloid including clinical features, histopathology, and surgical outcome.

## Case Presentation

A 36-year-old young man was admitted to the hospital because of a large mass in his left cornea. He had been delivered by vaginal birth at full-term after an uncomplicated pregnancy and denied having a family history of genetic diseases. When the patient was 6 years old, his left eye was hit by a thick rope. Since then, the left eye was recurrent redness with a foreign body sensation. In 2015, white scars were found on the surface of the left cornea and there is a tendency to get bigger. The mass has grown rapidly in the past two years, showing a porcelain white color and protruding from the surface of the eyeball, so that the left eyelid cannot be closed normally. The patient provided two unclear appearance photos in 2007 and 2015 (Fig. 1A and B).

His uncorrected visual acuity was LP/30 cm in the left eye and 1.0 in the right eye; the left eye could not be corrected. Slit-lamp examination revealed a round-like mass was located in the center of the cornea and covered almost entire cornea surface. The size of the corneal mass was 7 mm in height and 9 mm in width. The swollen material was tough, white in color, and tiny blood vessels grew on the surface, highlighting the surface of the eyeball. The iris texture can be seen from the upper and lower corneal limbus, but the lens, vitreous and retina were unclear (Fig. 2A). Anterior segment optical coherence tomography (AS-OCT) displayed the irregular epithelial tissue, dense subepithelial tissue with low-density of blood vessel invasion, similar to a honeycomb-like structure (Fig. 2C). B-scan showed that the internal structure of the left eye was normal. The fellow eye showed normal structure under slit lamp and AS-OCT examination (Fig. 2B and D).

The patient underwent deep anterior lamellar keratoplasty in her left eye. After electrocoagulation of superficial abnormal vessels, a large amount of fibrous connective tissue hyperplasia was found inside (Fig. 3A and B). The 9.0 mm corneal trephine was performed in the cornea. The lesion was easily removed from the base of mass and sent for histopathological examination (Fig. 3C). The corneal stromal opacity was exposed and neovascular grew into it (Fig. 3D). Then we dissected the corneal stroma layer by layer until approaching the Descemet's membrane (Fig. 3E). The donor corneal graft was 9.25 mm, which preserved by anhydrous calcium chloride from our hospital eye bank. The corneal graft was removed endodermis and then sutured into the recipient bed with 10 - 0 nylon sutures (Fig. 3F). After the operation, an antibiotic steroid ointment was administrated.

Postoperatively, the patient was advised topical steroids, antibiotics and lubricants. On the first day after surgery, the uncorrected vision was 0.02. One week after surgery, the ocular surface had completely re-epithelized. Histopathological examination revealed irregular hyperplastic epithelium, the absent Bowman's layer, abundant subepithelial collagen fibers with irregular proliferation and degenerative changes, fibroblasts and vascular cavities within (Fig. 4A and B). Immunohistochemical revealed positive staining for vimentin in lesion subject and SMA in vascular wall (Fig. 4C and D). At follow up 4 months later, there were no signs of recurrence of the lesion and other complications occurred (Fig. 5A). AS-OCT showed that the corneal graft is closely attached to the bed (Fig. 5B). The patient was satisfied with his appearance.

## Discussion And Conclusions

Corneal keloid are not a common disease in the clinic, which mainly manifested as white lesion that protrude from the corneal surface and involve the entire corneal stroma(4). The differential diagnosis of corneal keloid mainly include dermatoid tumor, myxoma and fibrous histiocytoma. Corneal dermoid is a congenital disease with yellowish white lesions involving the bulbar conjunctiva and corneal stroma(5). It characteristically occurs near the corneoscleral limbus and has hair tissue on the surface. Corneal dermoid may occur as an isolated lesion or accompany with Goldenhar's syndrome(6). HE staining showed that the corneal surface was covered with stratified squamous epithelium. A large amount of collagen fiber tissue and adipose tissue were seen in the lesion(7). Corneal myxoma appears as

avascular translucent subepithelial mass white within the stroma(8). Histopathology examination reveal subepithelial myxomatous tissue. Electron microscope show spindle shaped and stellate cells embedded in a loose stroma(9). Corneal fibroma can also appear as white tumors with intralesional blood vessels. The histopathological examination reveal the corneal epithelium was intact over the mass and subepithelial spindle cells in “featherstitched” or storiform pattern(10). However, some scholars have classified fibroma, keloid, and hypertrophic cicatrix as fibrous tumors of the ocular surface, which maybe represent different nodes of corneal tissue healing(11). In addition, it should be distinguished from the following diseases: sclerocornea, Salzmann’s nodular degeneration, Peter’s anomaly, congenital hereditary endothelial dystrophy, congenital glaucoma, familial band-shaped keratopathy, spheroidal degeneration, squamous cell carcinoma, juvenile xanthogranuloma, birth trauma, infection and metabolic disease(12, 13).

Histopathology is the gold standard for confirmed diagnosis(14). Epithelium hyperplasia, absence of the Bowman layer, irregular collagen fibers are considered to be a characteristic pathological manifestation(4), which is consistent with our inspection results. The histogenesis of keloid can be divided into four stages of early inflammatory, fibroblastic, fibrous and hyaline stages(12). In the early stages, there is a predominance of type III collagen, abundant fibroblasts, and new vessel formations. In the later hyaline stages, there is a predominance of disordered type I collagen with involution of blood vessels, giving a whitish rigid scar appearance(2, 4, 12, 15). Immunohistochemical studies of keloids showed vimentin was positive staining in active fibroblasts and SMA was positive staining in myofibroblasts(4, 13). Our result revealed vimentin was staining in keloid lesion subject and SMA only in vascular wall, which was consistent with Palko JR’s study(16). Light and electron microscopy are also important for discovering hyalinized collagen, activated fibroblasts and myofibroblasts(3). The younger fibroblasts contain rough endoplasmic reticulum, numerous mitochondria and prominent nucleoli(2). The mature myofibroblast showing numerous thin filaments and fusiform densities(13). But not every patient has the conditions to do electron microscopy and immunohistochemistry, so HE staining is still the main method for the diagnosis of disease.

Corneal keloid can be divided into primary and secondary according to the etiology(2). Primary keloid are more common in congenital diseases, such as Lowe’s syndrome and Rubinstein-Taybi syndrome (RTS) (17, 18). In Lowe’s syndrome, increased levels of amino acids such as tyrosine leaking from abnormal new corneal vessels or the anterior chamber through defective endothelium, which stimulate fibroblast proliferation(17). Other ocular anomalies associated with congenital keloid include peripheral iridocorneal adhesions, anterior segment mesenchymal dysgenesis, aniridia and cataract with anophthalmia(2). Secondary corneal keloid are mostly caused by inflammation, trauma or surgery. Unlike a hypertrophic scar, a keloid outgrows its initial boundaries from several months to a many years after the initial injury(19). In our case, the formation of the lesion took thirty years after initial corneal trauma. The previous view was that when corneal perforation with iris incarceration, the keloids originated from stromal cells of the iris. However, Mejia and O’Grady believe that excessive hypertrophy of the scar is due to corneal epithelial damage releasing too many cytokines(20, 21). Dhooge et al further research found the high levels of BMP4 inhibit the normal activation of TGF- $\beta$ , leading to overstimulating fibroblastic

growth during corneal wound healing(22). In addition, new vessel growth or partial limbal stem cell deficiency might be involved in the pathogenesis of corneal keloid development or recurrence(23).

Because corneal keloid are benign lesions and are prone to recurrence after surgery, if the lesions are small, they may not be treated temporarily. However, surgical treatment is necessary when the appearance is affected or the eyelids cannot be closed. Surgical methods currently reported include superficial keratectomy, lamellar keratoplasty, penetrating keratoplasty and enucleation(16). Enucleation is considered only when the eyeball is non-functional, painful or unsightly(12).It is reported that superficial keratectomy combined with amniotic membrane transplantation can easily remove the lesion and control the recurrence of the disease, which maybe due to its antifibrotic and anti-inflammatory properties(14, 24). But Lee HK et al found the lesion recurred in three of four cases treated with superficial keratectomy and amniotic membrane. And then the mitomycin C (MMC) was applicated to suppress activated fibroblasts and keratocytes in the residual stroma during secondary surgery without lesion recurrent(23). Because residual aberrant nerves and myofibroblasts in the corneal stroma maybe cause it, the lesion is considered to be removed completely by penetrating keratoplasty (PK). In 2012, Alkatan HM reported a patient with corneal keloid underwent a PK. The graft remained clear and vision outcome was satisfactory at 6 months after surgery. However, the recurrent epithelial breakdown or persistent epithelial defect can easily lead to the failure of graft after PK(18). In recent years, deep anterior lamellar keratoplasty is considered to be a better choice, with a lower rejection rate than PK. Bakhtiari P reported that no recurrence of corneal stromal opacification is noted in a 21-year-old child 8 months after the deep anterior lamellar keratoplasty (25). In our case, the lesion involved the entire corneal layer during the operation, which can also be confirmed by postoperative AS-OCT. However, the surgical method of deep lamellar corneal transplantation is adopted, and the thickness of stroma left about 100  $\mu\text{m}$  during the operation. On the one hand, we considered that oversize graft can easily lead to rejection after surgery. On the other hand, we have exposed enough central optical areas during the surgery to ensure vision recovery. If necessary, we can do another central PK in the second phase. Fortunately, the lesion has not recurred so far, and the patient is satisfied with his vision.

## Abbreviations

SMA

smooth muscle actin

AS-OCT

Anterior segment optical coherence tomography

RTS

Rubinstein-Taybi syndrome

MMC

mitomycin C

PK

penetrating keratoplasty

## Declarations

**Informed Consent:** This study was conducted from Beijing Tongren Hospital in accordance with the Helsinki Declaration. The case report was approved by the Ethics Committee of Beijing Tongren Hospital, and informed consent form was signed by the participant.

**Availability of data and materials:** The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

**Competing interests:** The authors declare that they have no competing interests in this section.

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**Authors' contributions:** LS accepted this patient and performed a detailed ophthalmic examination. XXL pathologically examined the specimen. JY participated in the design of the study, performed the operation. LJ analyzed the results and drafted the manuscript. YK conceived the study, participated in its design and coordination, and helped draft the manuscript. All authors have read and approved the final manuscript.

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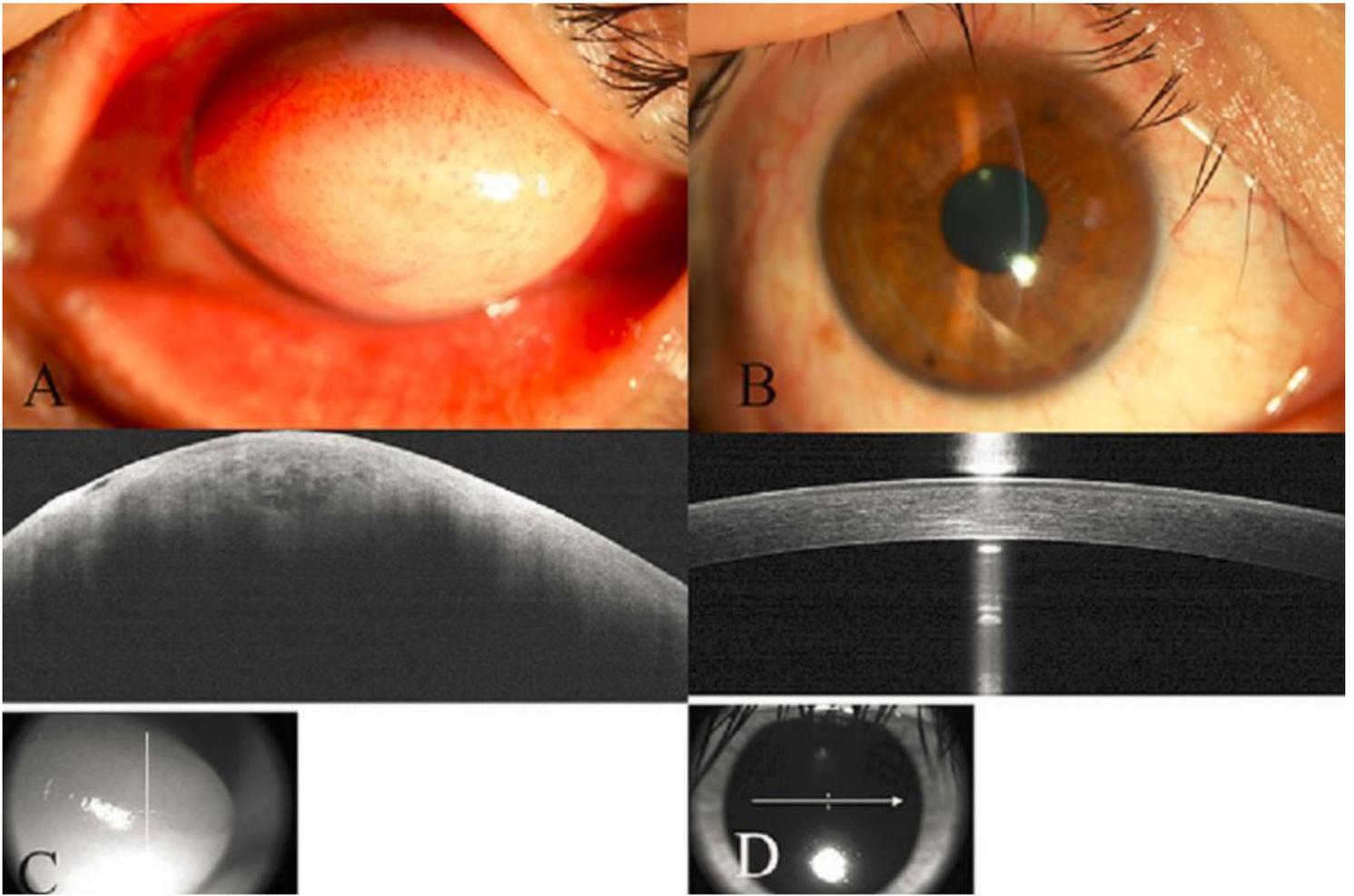
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## Figures



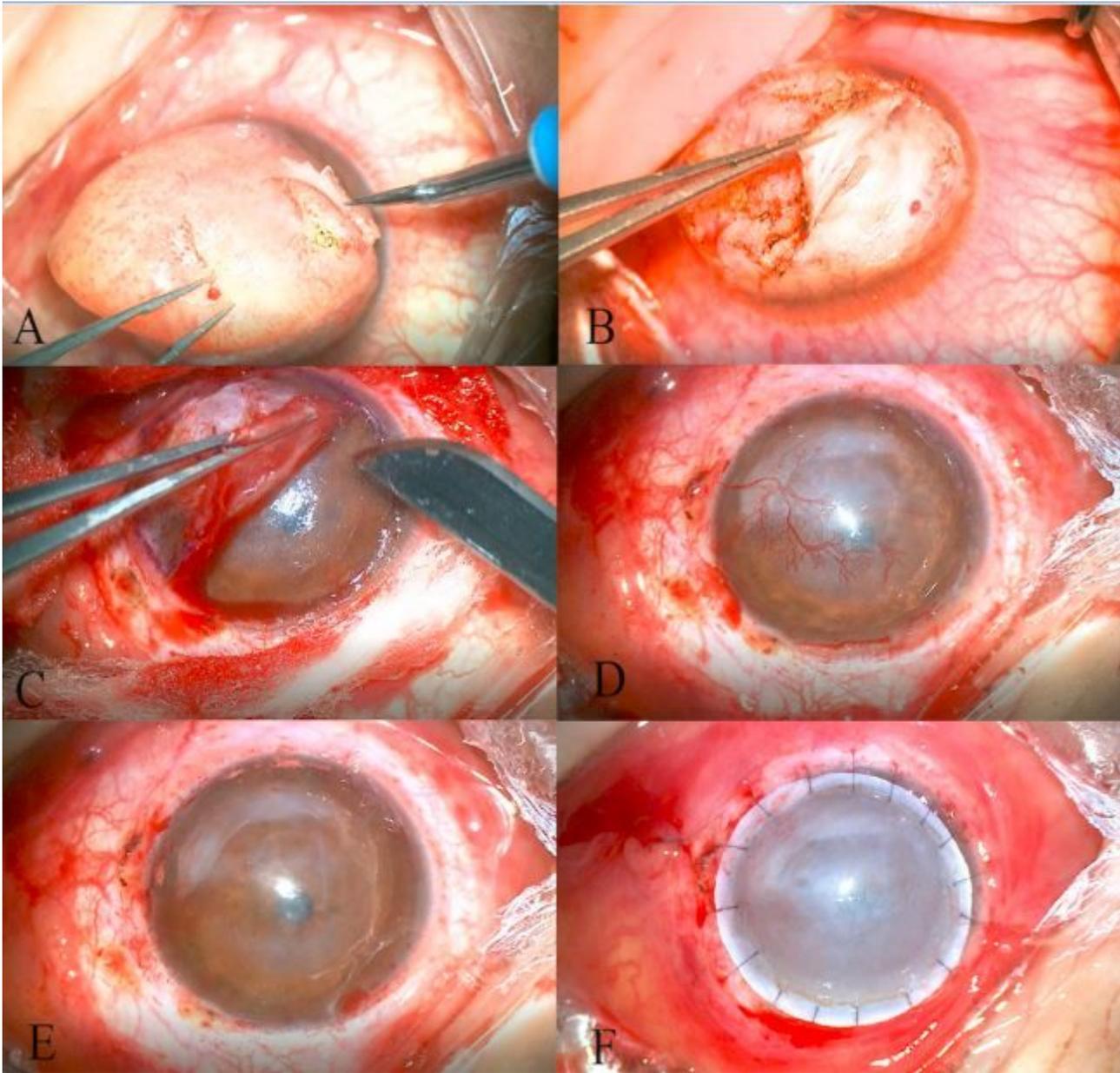
**Figure 1**

The patient provided two unclear appearance photos in 2007 and 2015



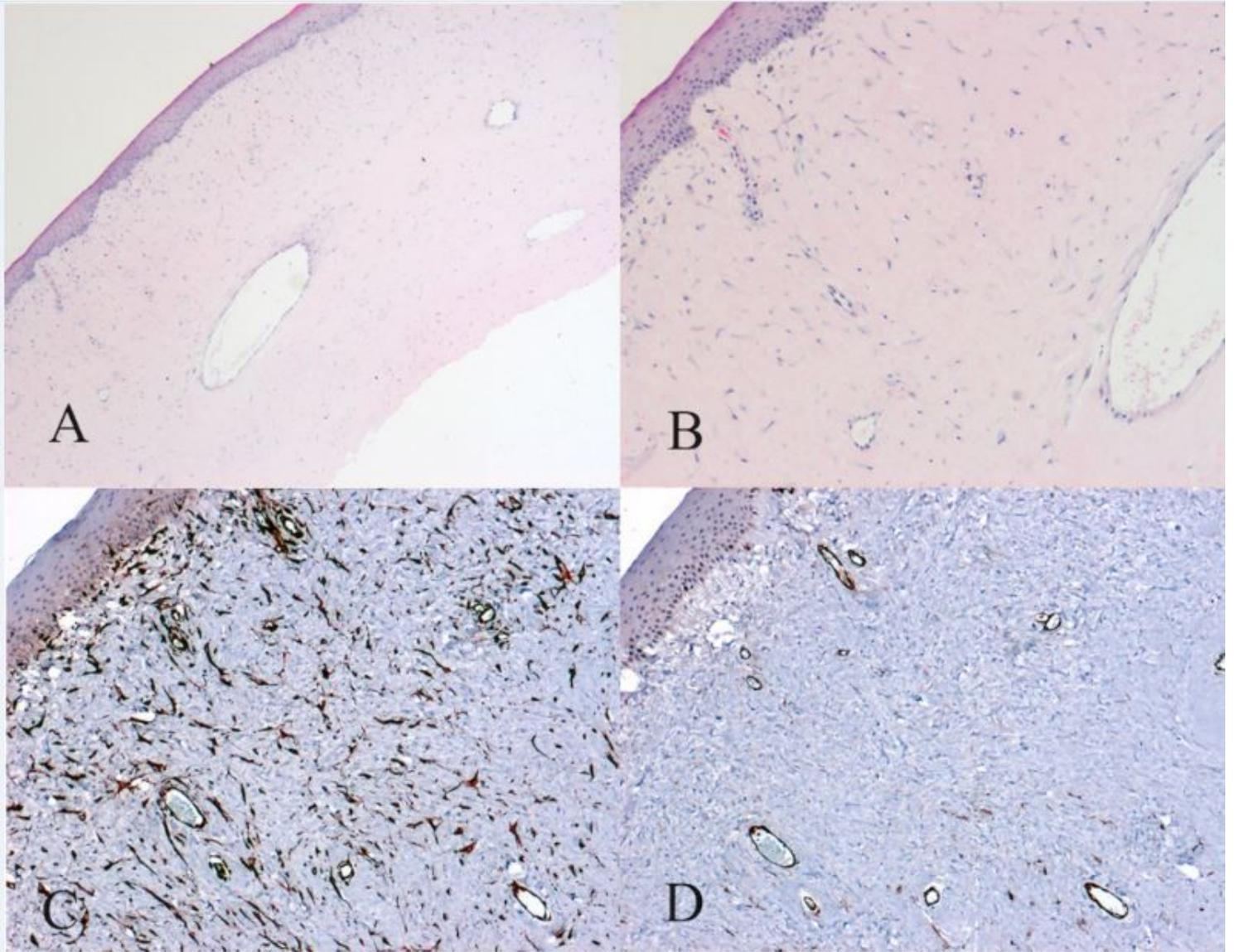
**Figure 2**

Anterior segment optical coherence tomography (AS-OCT) displayed the irregular epithelial tissue, dense subepithelial tissue with low-density of blood vessel invasion, similar to a honeycomb-like structure (Fig 2C). B-scan showed that the internal structure of the left eye was normal. The fellow eye showed normal structure under slit lamp and AS-OCT examination (Fig 2B and D).



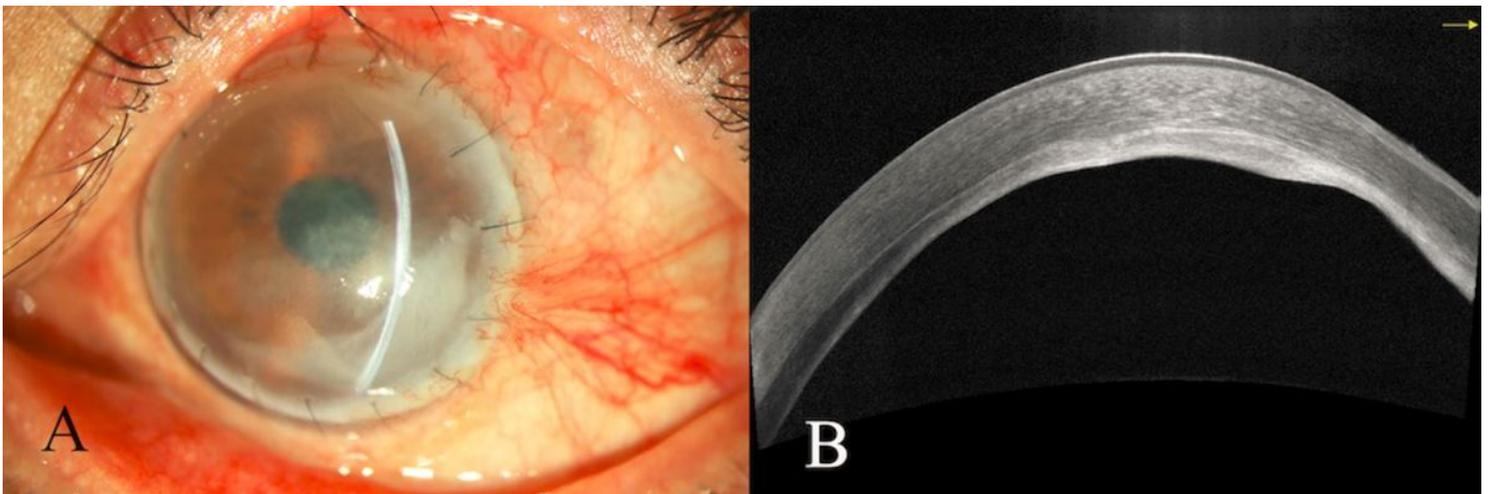
**Figure 3**

The 9.0 mm corneal trephine was performed in the cornea. The lesion was easily removed from the base of mass and sent for histopathological examination (Fig 3C). The corneal stromal opacity was exposed and neovascular grew into it (Fig 3D). Then we dissected the corneal stroma layer by layer until approaching the Descemet's membrane (Fig 3E). The donor corneal graft was 9.25mm, which preserved by anhydrous calcium chloride from our hospital eye bank. The corneal graft was removed endodermis and then sutured into the recipient bed with 10-0 nylon sutures (Fig 3F).



**Figure 4**

Immunohistochemical revealed positive staining for vimentin in lesion subject and SMA in vascular wall (Fig 4C and D ).



## Figure 5

At follow up 4 months later, there were no signs of recurrence of the lesion and other complications occurred (Fig 5A). AS-OCT showed that the corneal graft is closely attached to the bed (Fig 5B). The patient was satisfied with his appearance.

## Supplementary Files

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