



# Corneal keloid caused by persistent atopic eye disease and chronic eyelid closure

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## ABSTRACT

**Purpose:** This report aimed to present a case of corneal fibrosis with prolonged atopic blepharitis caused by psychological resistance to steroid treatment.

**Observations:** A 49-year-old woman presented with atopic dermatitis and a history of panic attack and autism spectrum disorder. The upper and lower eyelid margins of her right eye became adherent, and the eyelid remained closed for several years due to refusal of steroid treatment and aggravation of blepharitis. During the initial examination, a lesion with elevated white opacity on the corneal surface was observed. Subsequently, superficial keratectomy was performed. The histopathological findings were indicative of corneal keloid.

**Conclusions and Importance:** Persistent atopic ocular surface inflammation and prolonged eyelid closure resulted in the formation of a corneal keloid.

## 1. Introduction

Corneal keloids are a rare ophthalmic disease characterized by focal white elevated lesions on the cornea.<sup>1</sup> These lesions are opaque and can be vascular or nonvascular, with well-defined borders and varying thickness and size.<sup>1</sup> Corneal keloids have been reported to form in patients without a history of surgery or corneal trauma, although most cases occur months to years after trauma or surgery.<sup>1,8–11</sup> Definitive diagnosis of corneal keloids requires biopsy and histopathology and is characterized by dysplasia of the corneal epithelium and hyperplasia of collagen fibers.<sup>1,4,9–11</sup> Here, we report a case of corneal keloid that might have developed after prolonged eyelid closure and been maintained due to severe atopic blepharitis (see [Table 1](#)).

## 2. Case report

A 49-year-old woman with vision loss in the right eye for 3 years was referred to our hospital. The patient had atopic dermatitis, and the disease in her eyelid worsened approximately 10 years ago. She refused steroid treatment because of a strong fear of steroids. The patient said that the upper and lower eyelid margins of her right eye were fused, and the eyelids had remained closed for several years because of atopic

conjunctivitis and blepharitis. She also said that her eyelid dermatitis improved with steroid-free atopic treatment (eyelid hygiene and chiropractic treatment of autonomic imbalance) during the past 3 years. She became aware of a loss of vision in her right eye and noticed that it was cloudy when she looked at the mirror with the open right eye. Notably, she has been diagnosed with atopic dermatitis since childhood and has been attending a psychosomatic medicine clinic for a panic disorder and autism. She underwent right cataract surgery and right posterior capsulotomy 9 years ago and a second posterior capsulotomy 8 years ago. Her best corrective visual acuity was 20/30 in the left eye, and light perception was present in the right eye. Furthermore, there was an elevated white opaque lesion on the central corneal surface of the right eye with vascular invasion and a dislocated intraocular lens (IOL) in the anterior chamber ([Figs. 1–](#)). Anterior segment 3-dimensional optical coherence tomography (AS-OCT) scan revealed areas of high intensity from the corneal surface to the superficial layer of stroma, with an increased central corneal thickness of 1570  $\mu\text{m}$  ([Figs. 1–2](#)). B-mode ultrasonography did not identify abnormal findings in the posterior segment.

Superficial keratectomy was performed on the right eye. Major portion of the lesion was easily detached in the Bowman's layer; however, a small portion was infiltrating into the stroma ([Fig. 2](#)).

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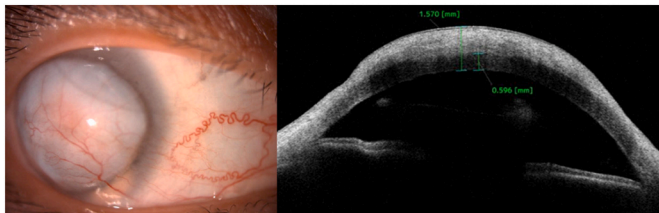
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**Table 1**  
Clinical and pathological features of corneal keloids.

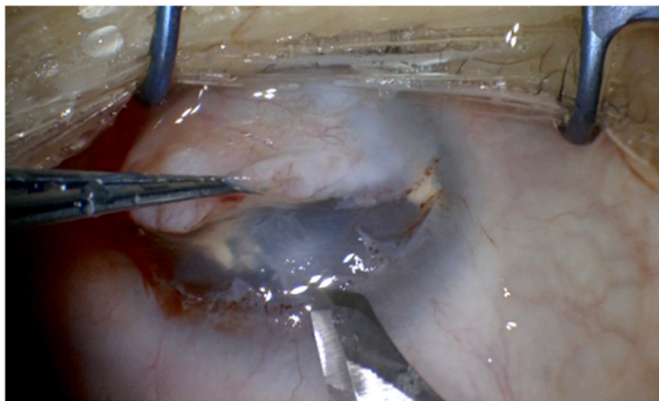
Features of corneal keloids
Clinical findings
<ul style="list-style-type: none"> <li>• Unilateral or bilateral</li> <li>• Localized white elevated lesions</li> <li>• Vascular or nonvascular</li> <li>• Clear border</li> <li>• Varying in thickness and size</li> </ul>
There was gradual expansion beyond the wound after trauma over months to years.
Pathological findings
<ul style="list-style-type: none"> <li>• Epithelium: normal or thickened and keratinized with varied thickness</li> <li>• Bowman's layer: usually absent and sometimes present in fragments</li> <li>• Substantia: proliferation of collagen fibers, fibroblasts, and myofibroblasts</li> <li>• Descemet's membrane and endothelium: normal</li> </ul>
Depending on the stage of the disease, it can involve the following:
<ul style="list-style-type: none"> <li>• Inflammatory phase: angiogenesis and inflammatory cell infiltration</li> <li>• Late stage: hyalinization within the stroma</li> </ul>
Onset triggers
<ul style="list-style-type: none"> <li>• Trauma: corneal perforation and nonperforating corneal trauma (radiation, wood chips, and nails)</li> <li>• Surgery: cataract surgery, pterygium surgery, and PRK*</li> <li>• Inflammation/infection: corneal ulcer, viral keratitis, and neonatal infection</li> <li>• Congenital</li> <li>• Primary</li> </ul>
* PRK: Photo-refractive keratectomy



**Fig. 1.** Initial examination findings

Ophthalmologic examination findings of a 49-year-old woman's right eye

- 1) An elevated white opaque lesion was observed on the central corneal surface.
- 2) Anterior segment optical coherence tomography (AS-OCT) scan demonstrated areas of hyperintensity from the corneal surface to the superficial layer of stroma and a dislocated intraocular lens (IOL).



**Fig. 2.** Surgical Treatment

Most of the fibrotic tissue was easily detached using superficial keratectomy. Superficial keratectomy enabled easy detaching of most of the fibrotic tissue.

On histopathologic examination, the majority of the excised tissue comprised thick collagen-rich tissue, with a mildly thickened stratified squamous epithelium in the superficial layer. Capillaries were formed in the collagen fibers under the epithelium, and plasma cell and lymphocyte infiltrates were seen surrounding the vessels, suggesting that the tissue was different from the original corneal stroma (Fig. 3 a, b, c). In

addition, immunohistochemical staining was performed using anti-vimentin and anti-alpha smooth muscle actin ( $\alpha$ SMA) antibodies. Both stains diffusely highlighted the stroma in the keloid lesion (Fig. 3 e, f). The patient was diagnosed with a corneal keloid based on clinical, histopathological, and immunohistochemical findings.

After carefully explaining to the patient that topical steroid treatment is safer than systemic administration and obtaining her consent, postoperative eye drops containing a 0.1% betamethasone sodium phosphate ophthalmic solution were administered until the third postoperative day; subsequently, 0.1% fluorometholone ophthalmic solution was administered until 1 month after surgery, and this was then switched to tacrolimus ophthalmic solution. Consequently, the corneal transparency improved, and the anterior chamber could be observed, but the IOL had dislocated into the anterior chamber with the completely cloudy lens capsule, and the fundus was not assessable (Fig. 4). Approximately 1 month after the surgery, IOL removal and vitrectomy were performed, and the fundus became observable, but the optic nerve papilla was pale. Postoperative best visual acuity was 20/300, intra ocular pressure was low-teen, and the residual visual field was limited. A specular microscopy could not detect endothelial cells. Finally, the patient was considered to have severe visual dysfunction due to glaucoma and bullous keratopathy. Epithelialization was achieved 2 months after the surgery, but subepithelial corneal opacification was observed at a follow-up visit after 5 months of the surgery. The lesion led to the development of an elevated opacity at another follow-up visit after 15 months of the surgery. Eventually, the patient was considered to have recurrent corneal keloid because the elevated lesion was found to be increasing in size at the final visit of 15 months after the surgery (Fig. 5). The best postoperative corrected visual acuity in the right eye was 20/300, and the final corrected visual acuity was 20/2000.

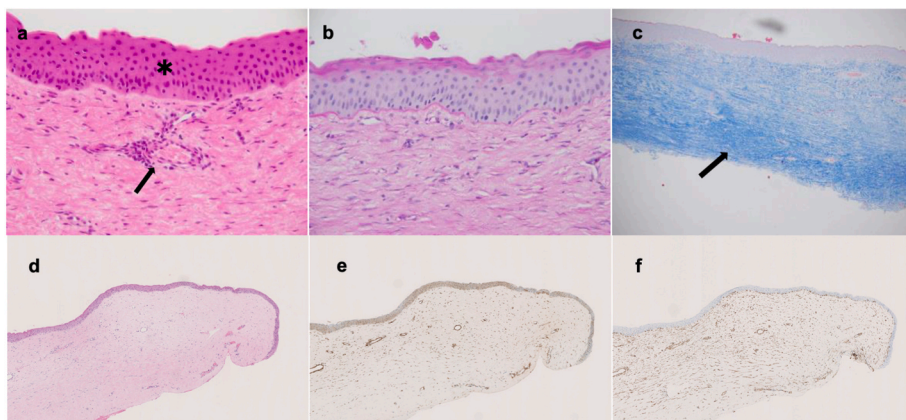
### 3. Discussion

Corneal keloids usually produce localized white elevated lesions on the corneal surface.<sup>1</sup> Although congenital cases have been reported, and some cases are associated with specific genetic syndromes, such as Lowe's syndrome,<sup>3,6,7</sup> most corneal keloids occur after trauma, surgery, or keratitis.<sup>1</sup> Differential diagnosis with similar white elevated lesions include hypertrophic scars, Salzmann's nodular degeneration, limbal dermoids, sclerocornea, myxomas, congenital glaucoma with corneal edema, and metabolic diseases, such as Peters anomaly, fibrous histiocytomas, and mucopolysaccharidosis.<sup>1,5,9</sup>

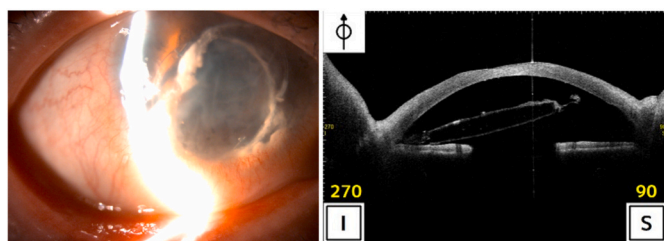
Histopathological findings of corneal keloids are characterized by a normal or thickened and keratinized epithelium, fragmented or absent Bowman's membrane, and proliferated collagen fibers.<sup>1,4,9,10</sup> Based on immunohistochemical examination of the present case, positive staining with  $\alpha$ SMA and vimentin should be expected in cases of corneal keloids. Notably, the positive  $\alpha$ SMA staining is correlated with myofibroblasts and the smooth muscle walls of the limited vasculature. Furthermore,  $\alpha$ SMA immunostaining is characteristically positive in corneal keloids, but it is negative in the normal stroma.<sup>16</sup> In contrast, vimentin staining is positive for fibroblasts as well as vascular endothelial, smooth muscle, and other cells.<sup>15-17</sup> In corneal keloids, vimentin staining is nonspecific as is positive for both the lesion and normal corneal stroma.<sup>16</sup> In such cases, the diagnosis is established based on the patient's history and clinical and histopathological findings.

In the present case, Salzmann's nodular degeneration and hypertrophic scarring were considered as differential diagnoses. In Salzmann's nodular degeneration, the lesions are multiple and elevated occurring after ocular surface diseases, such as keratitis or vernal keratoconjunctivitis.<sup>12</sup> However, the pathology of this case where there was a single large opacity with thickened overlying epithelium.

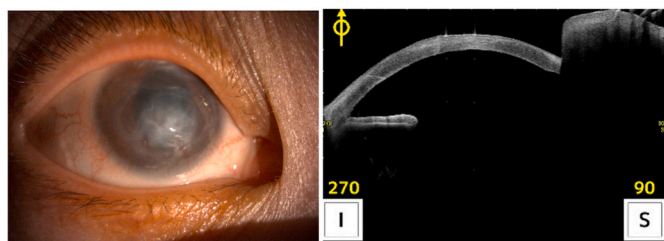
Additionally, a post-traumatic hypertrophic scar was suspected if the severe ocular abrasion was considered to be similar to trauma. Corneal keloid lesions occur months to years after trauma and expand over time, extending beyond the boundaries of the trauma, whereas hypertrophic



**Fig. 3.** Histopathological and immunohistochemical findings  
 a. Hematoxylin and eosin (HE) staining revealed a mildly thickened superficial epithelium (\*) and plasma cell and lymphocyte infiltration surrounding capillaries formed in the superficial layers of the stroma (→). b. Periodic acid-Schiff staining revealed no Bowman's layer between the epithelium and stromal tissue. c. Azan staining demonstrated thick collagen fibrils in the stromal tissue. d. HE staining. e. Vimentin staining was diffusely positive in the stromal tissue, predominantly in the anterior stroma, highlighting fibroblasts and neovascular endothelial cells. f. Alpha-SMA staining was diffusely positive in the stromal tissue, predominantly in the anterior stroma, highlighting myofibroblasts and neovascular endothelial cells.



**Fig. 4.** Findings at 1-month after surgery  
 One month after the superficial keratectomy, the IOL was dislocated into the anterior chamber with the lens capsule.



**Fig. 5.** Findings at 15 months after surgery  
 Fifteen months after the superficial keratectomy, the patient was diagnosed with recurrent corneal keloids owing to the development of an elevated corneal opacity.

scars appear immediately after trauma and do not expand beyond the initial boundaries.<sup>4,5</sup> In this case, the patient's history makes a hypertrophic scar unlikely.

Before 9 years, the patient underwent cataract surgery and Nd-YAG laser capsulotomy. We speculated that the IOL was dislocated to anterior chamber after rubbing eye lid and caused corneal edema. Moreover, this pathologic change may have caused stimulation of cytokines releasing in corneal stroma.

The pathogenesis of corneal keloids remains unknown, but several hypotheses have been proposed. Mejia et al. reported that cytokines released from the damaged epithelium might prevent normal corneal growth and differentiation, influencing fibroblasts.<sup>9</sup> Furthermore, it has been reported that in patients with atopic keratoconjunctivitis, damage to the corneal epithelium triggered by ocular abrasion or other factors stimulates fibroblasts in the corneal stroma to express chemokines and adhesion molecules in the stroma through cytokines, such as interleukin (IL)-6, tumor necrosis factor (TNF)- $\alpha$ , and matrix metalloproteinase (MMP)-13, in the tear fluid.<sup>13,14</sup>

In the present case, the patient suffered from severe atopic

blepharitis that resulted in her eyelid being closed for a prolonged period. The patient's difficulty in opening the eyelids may have been caused by blepharoconjunctivitis or an epithelial disorder. Mechanical trauma caused by eye rubbing would have resulted in corneal epithelial damage, and atopic keratoconjunctivitis might have led to chronic inflammation and corneal keloid formation as a result of cytokine-mediated fibroblast proliferation. Alternatively, inflammation due to prolonged atopic dermatitis may have affected the corneal surface.

Depending on the location, size, and depth of the corneal keloid, treatments, other than conservative treatment, have been reported; these include superficial keratectomy, lamellar keratoplasty, deep anterior lamellar keratoplasty, penetrating keratoplasty, and keratoplasty combined with amniotic membrane transplantation,<sup>2</sup> but recurrence is often observed.

In the present case, the remaining visual field was minimal, and the patient did not wish to undergo corneal transplantation.

**4. Conclusions**

This is a report of a specific case of corneal keloid following prolonged eyelid closure and eye rubbing due to severe atopic blepharitis. Prolonged eyelid closure may have resulted in prolonged ocular surface inflammation, and trauma due to ocular abrasion may have caused the fibrotic corneal hyperplasia.

**Patient consent**

Written informed consent was obtained from the patient.

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**Authorship**

R.M., T.T., and T.M. contributed to the design and conduct of the study; R.M., T.T., R.A., and S.Y. contributed to the collection, management, analysis, and interpretation of data; and T.T., Y.A., S-Y., and T.M. contributed to the preparation, review, and approval of the manuscript.

**Declaration of competing interest**

The authors have no financial disclosures.

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