Clinical Case Report

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Corneal cross-linking for keratoconus caused by compulsive eye rubbing in patients with Tourette syndrome

Three case reports

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Abstract

Rationale: Eye rubbing is an important risk factor for keratoconus progression. Tourette syndrome (TS) is a neurological disorder, and approximately 50% of individuals with TS exhibit obsessive-compulsive behaviors including eye rubbing. We report the effects of corneal cross-linking (CXL) on the progression of keratoconus combined with psychiatric treatment for 3 patients with TS.

Patients' concerns: Three cases, 24-year-old male, 14-year-old male, and 17-year-old male, were all referred to our institute, due to decreased visual acuity.

Diagnosis: All 3 patients were diagnosed with progressive keratoconus. They were found to rub their eyes, and were also diagnosed with TS by psychiatrists.

Intervention: Upon diagnosis of keratoconus, we performed CXL on 1 eye of each patient.

Outcomes: After CXL, there was no further progression. Psychiatric medication was also required.

Lessons: For patients with keratoconus caused by eye rubbing due to TS, CXL seems to be effective when done in association with psychiatric treatment.

Abbreviations: CXL = corneal cross-linking, K_s = the steepest keratometric value, TS = Tourette syndrome.

Keywords: corneal cross-linking, eye rubbing, keratoconus, progression, Tourette syndrome

1. Introduction

Tourette syndrome (TS) is a neurological disorder characterized by repetitive muscle contractions, and stereotyped movements or sounds.[1,2] Ophthalmic manifestations of TS have been reported, including eye tics, chronic blepharospasm, involuntary gaze deviations, and strabismus.[3–5] In addition, approximately 50% of individuals with TS exhibit obsessive-compulsive behaviors, including eye rubbing.[1]

Keratoconus is a noninflammatory and progressive ectasia of the cornea. The disease usually begins during puberty and progresses until the third or fourth decades of life. The etiology and mechanisms for progression have not been fully elucidated. However, it is commonly accepted that the etiology of KC is multifactorial, combining environmental and genetic factors.[6–8]

Eye rubbing is thought to be an important risk factor for the progression of keratoconus. Allergic disorders, such as atopy, asthma, and hay fever, are all associated with a higher incidence of keratoconus. Because people with allergic disorders often rub their eyes, the eye rubbing and allergic inflammation cannot be separately assessed.[9–11] However, some investigations have indicated that the eye rubbing itself may play a crucial role in the development of corneal ectasia in keratoconus.[6,7,11,12] Accidental or self-induced ocular injuries may also cause keratoconus, with 3 reports demonstrating an association between keratoconus and TS.[13–15]

Nowadays, with the development of corneal cross-linking (CXL),[16] we are able to intervene during the early stages of keratoconus. CXL is a procedure that consists of epithelial abrasion, riboflavin application as a photosensitizer, and ultraviolet-A irradiation.[17,18] This photochemical process induces the formation of CXL between corneal collagen fibers, resulting in the increase in biomechanical strength of the entire corneal stroma, stabilizing corneal configuration. Clinical trials for CXL have been conducted in many countries, and its effectiveness is well documented.

We recently experienced 3 cases of TS associated with keratoconus progression. We hypothesized that CXL may also

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Eye-Lens Pte Ltd lent us the KXL system, an instrument for corneal cross-linking without compensation.

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halt the progression of keratoconus in patients with TS. We report the effects of CXL on the progression of keratoconus-like corneal ectasia combined with psychiatric treatment for 3 patients. Patients have provided written informed consent for publication of the case details

1.1. Case 1

A 24-year-old male presented to our institute due to keratoconus-like corneal ectasia in his right eye on June 30, 2010. He was previously diagnosed with TS at a psychiatric hospital, and had tendency to rub his eyes. He previously received photocoagulation for a retinal hole by a previous ophthalmologist. He had no ocular history or allergies.

At the first visit, his uncorrected and corrected visual acuity were 0.02 and 0.4 (S -3.50D c -10.00D Ax 45) OD, and 0.1p and 1.0 (S -3.50D C -4.50D Ax 115) OS, respectively. His right eye revealed a posterior subcapsular cataract. A tomography map produced using CASIA (SS-1000, Tomey, Aichi, Japan) showed a typical keratoconus pattern in the right eye and possible keratoconus in the left eye (Fig. 1A and B).

He visited our institute regularly for 3 years. His symptoms for TS were well controlled by psychiatrists. His corrected visual acuity was 0.5 (S -8.00D C -5.50D Ax 70) OD and 1.0 (S -2,75D, c -7.70D Ax 110) OS. However, the tomography showed progression of keratoconus in both eyes (Fig. 1C and D).

We performed CXL on his right eye on August 7, 2013. The procedure was performed with epithelial debridement, 0.1 mL riboflavin in 20% dextran solution (MedioCross D, Opto Medica Oftalmologia, Roma, Italy) instillation every 2 minutes for 30 minutes, and then after the corneal stroma was swollen by instillation of hypotonic riboflavin solution (MedioCross H, Opto Medica Oftalmologia) and distilled water up to 400 μm of the thickness, subsequent ultraviolet-A irradiation with 18.0 mW/cm^2 of intensity for 5 min (KXL System, Avedro, Waltham, MA). His right cornea showed slight flattening with the steepest keratometric value (K_s) 58.0 D. ECD was 2900 $cells/mm^2$ 6 months after the surgery.

When he returned on May 14, 2014, the patient complained of increased eye rubbing and a decrease in visual acuity. His corrected visual acuity was 0.4 (S -2.00D C -3.00D Ax 100) OD and 0.3 (S -7.00D) OS. His right cornea showed no progression after the CXL (Fig. 1E and G). His left cornea revealed a mild enlargement of the protrusion accompanied with stromal scar on the temporal area (Fig. 1F and H). However, we did not perform CXL on his left eye because he was admitted to a psychiatric hospital.

The most recent corrected visual acuity measured at 4 years after CXL was 0.4 (S-8.00D C -3.50D, Ax 110) OD and 1.2 (S -3.25D, C -4.00D, Ax 100), OS, revealing no further progression of keratoconus on both eyes (Fig. 2).

1.2. Case 2

A 14-year-old male presented to our institute on February 4, 2015, due to keratoconus. He had a habit to rub his eye by hands. His left eye experienced acute hydrops in November of the previous year. His right eye also had severe keratoconus as diagnosed by CASIA (Tomey), demonstrating a K_s 78.1 D and CCT 330 μm. The uncorrected and corrected visual acuity was 0.03 and 0.08 (S -9.00D) OD, respectively. When he returned on April 28, the keratoconus-like pattern was more pronounced in his right eye (Fig. 3A). Accelerated CXL was performed June 23 on his right eye, with epithelial debridement, 0.1% riboflavin (VIBEX RAPID, Avedro) instillation for 20 minutes, and ultraviolet-A irradiation with 18.0 mW/cm^2 of intensity for 5 min (KXL System, Avedro). On November 17, his corrected visual acuity was 0.06 (S -20.0D) OD (Fig. 3B). We recommended a psychiatric consultation, although this was declined. The patient continued to compulsively rub his eyes.

On January 2016, he visited a psychiatrist and was diagnosed with TS. He was started on antipsychotic medications shortly afterward. On May 17, 2016, his right cornea had a stromal scar, with a visual acuity of 0.03p (S -20.0D) OD (Fig. 3C and D).

1.3. Case 3

A 17-year-old male was referred to our institute due to suspected keratoconus in his right eye on December 2, 2015. He had a history of pars plana vitrectomy with silicon oil tamponade due to rhegmatogeneous retinal detachment in his left eye. He had no allergic disorders, including atopic dermatitis, but was diagnosed as TS, revealing habit to rub his eyes. His uncorrected and corrected visual acuity were 0.02 and 0.5 (S -19.00D) OD and hand motion OS, respectively. He complained that the visual acuity in his right eye gradually decreased over the previous year. On examination, his tarsal conjunctiva had papillary proliferation with injection, and the right cornea showed central thinning although there were few scars. Tomography showed a keratoconus pattern in the right cornea (Fig. 4A).

He was followed for 6 months. On October 17, 2016, his visual acuity was 0.4 (S -20.0D) OD. The tomography showed that his keratoconus was rapidly progressing (Fig. 4B). We performed an accelerated CXL procedure on November 21, 2016, with an identical protocol to case 2. Nine months after the CXL, his right cornea had a stromal scar (Fig. 4C and D). The visual acuity was 0.3 (S -20.0D), correctable to 0.8 with a hard contact lens.

2. Discussion

We describe 3 cases of TS showing progressive keratoconus as diagnosed via corneal tomography. All 3 cases were successfully treated with corneal CXL using riboflavin and ultraviolet-A irradiation, combined with adequate medication from psychiatric doctors. To the best of our knowledge, this is the first report to describe cases of successfully treated keratoconus induced by TS, progressing over time along with severity of eye rubbing.

When we searched PubMed and Medline using the key words "Tourette syndrome" and "keratoconus," we found 3 manuscripts that have been published to date. Enoch et al had reported that 2 out of 12 patients with TS were diagnosed with keratoconus and another case had moderate astigmatism.[13] Mashor et al reported 3 cases of TS associated with eye rubbing behavior, and revealed unilateral keratoconus as diagnosed with corneal topography. Among the 3 patients, one had acute hydrops in the past.[14] Another case by Kandarakis et al demonstrated bilateral keratoconus showing corresponding progression due to compulsive eye rubbing. In this case, his right eye became phthisical several years after corneal hydrops occurred.[15] The authors commented that it is essential to assist patients with TS by suggesting the use of protective polycarbonate goggles, and by ensuring close surveillance in conjunction with a psychiatry service. We summarize the characteristics of the previously reported cases and our cases in Table 1.

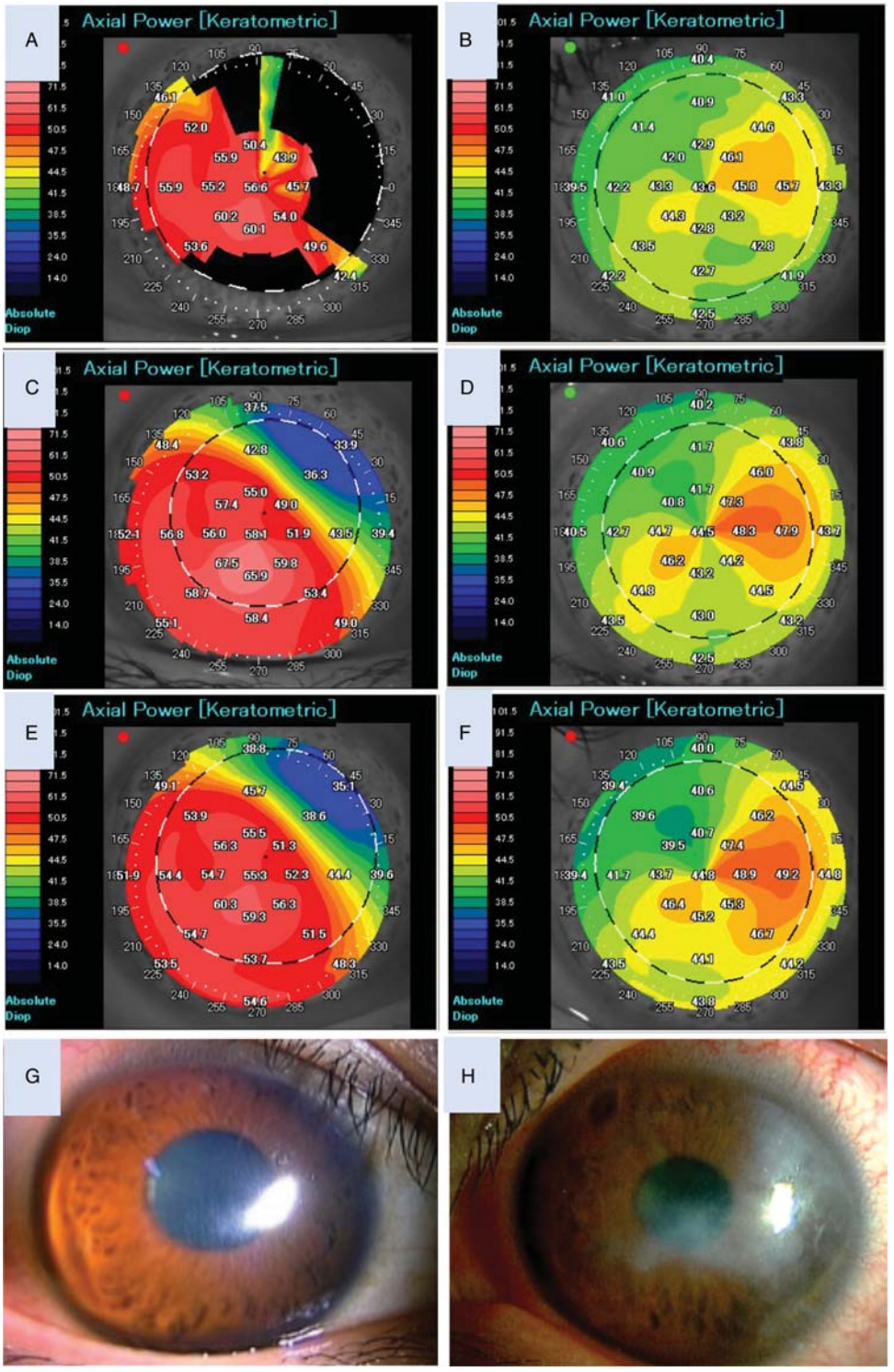

Figure 1. Change in corneal topography of case 1. At the first visit, the topography map showed a typical keratoconus pattern in the right eye (A) and forme fruste keratoconus on the left eye (B). The steepest keratometric value (K_s) was 56.6 D OD (A) and 45.4 D OS (B). Three years after the initial visit, the topography showed progression of the keratoconus pattern in both eyes, and K_s now measured 62.2 D OD (C) and 47.6 D OS (D). Nine months after CXL in the right eye, K_s of 55.9 D OD (E) and 47.6 D OS (F). The right cornea was clear (G); however, there was a stromal scar on the left cornea (H).

CXL is known to halt the progression of keratoconus, and it seemed to be effective for our cases. In case 1, the symptoms by TS were exaggerated after the CXL on the right eye, causing development of stromal scar and enlargement of the corneal protrusion on the left eye probably due to eye rubbing, although the right eye showed few changes. On the contrary, stromal scar was observed in 2 of 3 cases on the eyes underwent the CXL, and extreme flattening in case 3 was thought to be caused related to the scar formation. Whether the formation of stromal scar may be linked to the

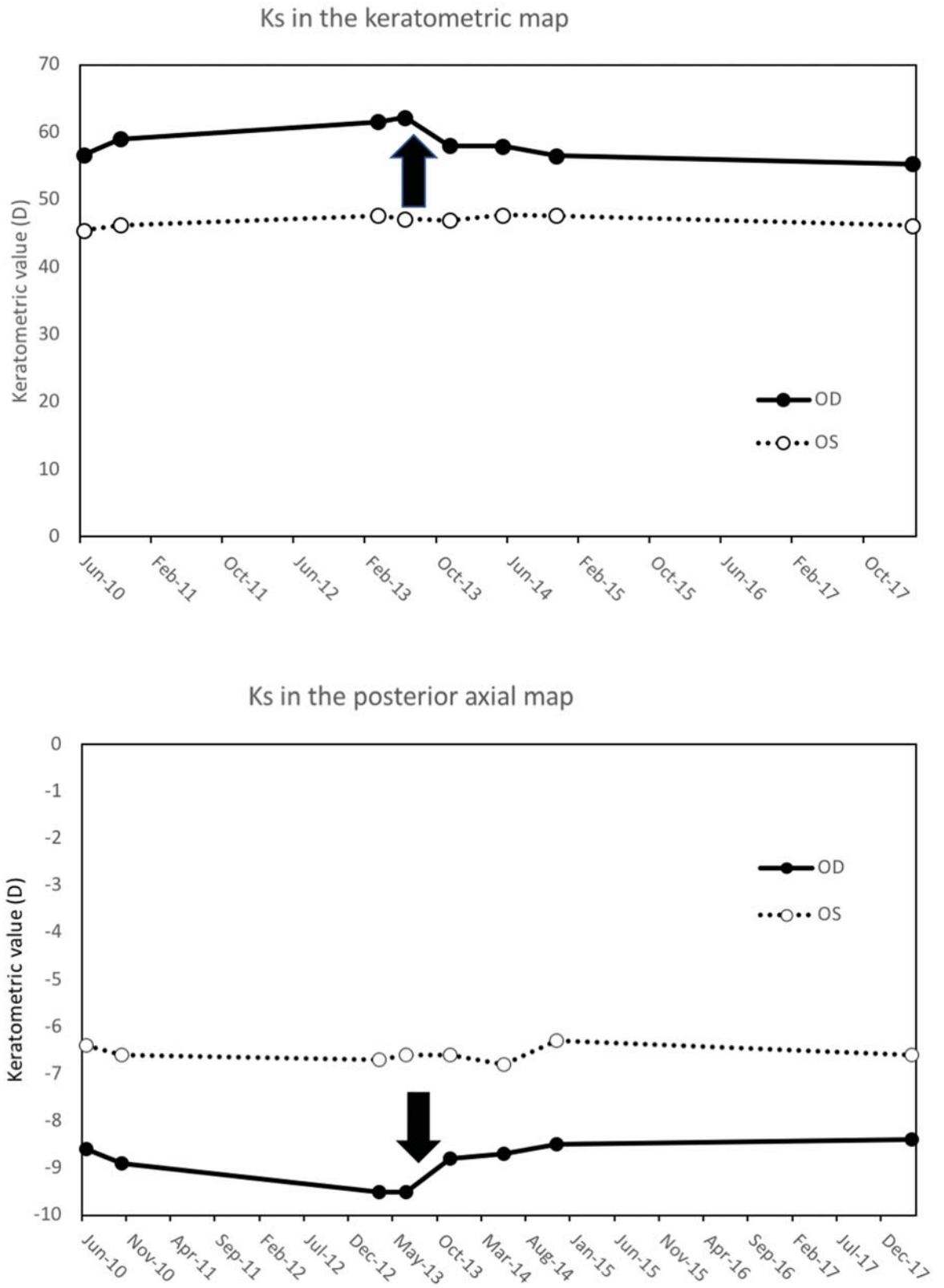

Figure 2. Change in the steepest keratometric value of case 1. The upper graph shows the change in the steepest keratometric value in the anterior keratometric map of the case 1. Before CXL, the steepest keratometric value continued to increase, but decreased after the CXL on the right eye (solid circle). The left eye showed stable keratometric value (open circle). The lower graph shows the change in the steepest keratometric value in the posterior axial map. The keratometric value continuously decreased on the right eye before the CXL, but returned and stayed stable after the CXL (solid circle). The left eye showed stable posterior keratometric value (open circle). K_s = steepest keratometric value, OD = right eye, OS = left eye. Arrow shows the timing of the CXL.

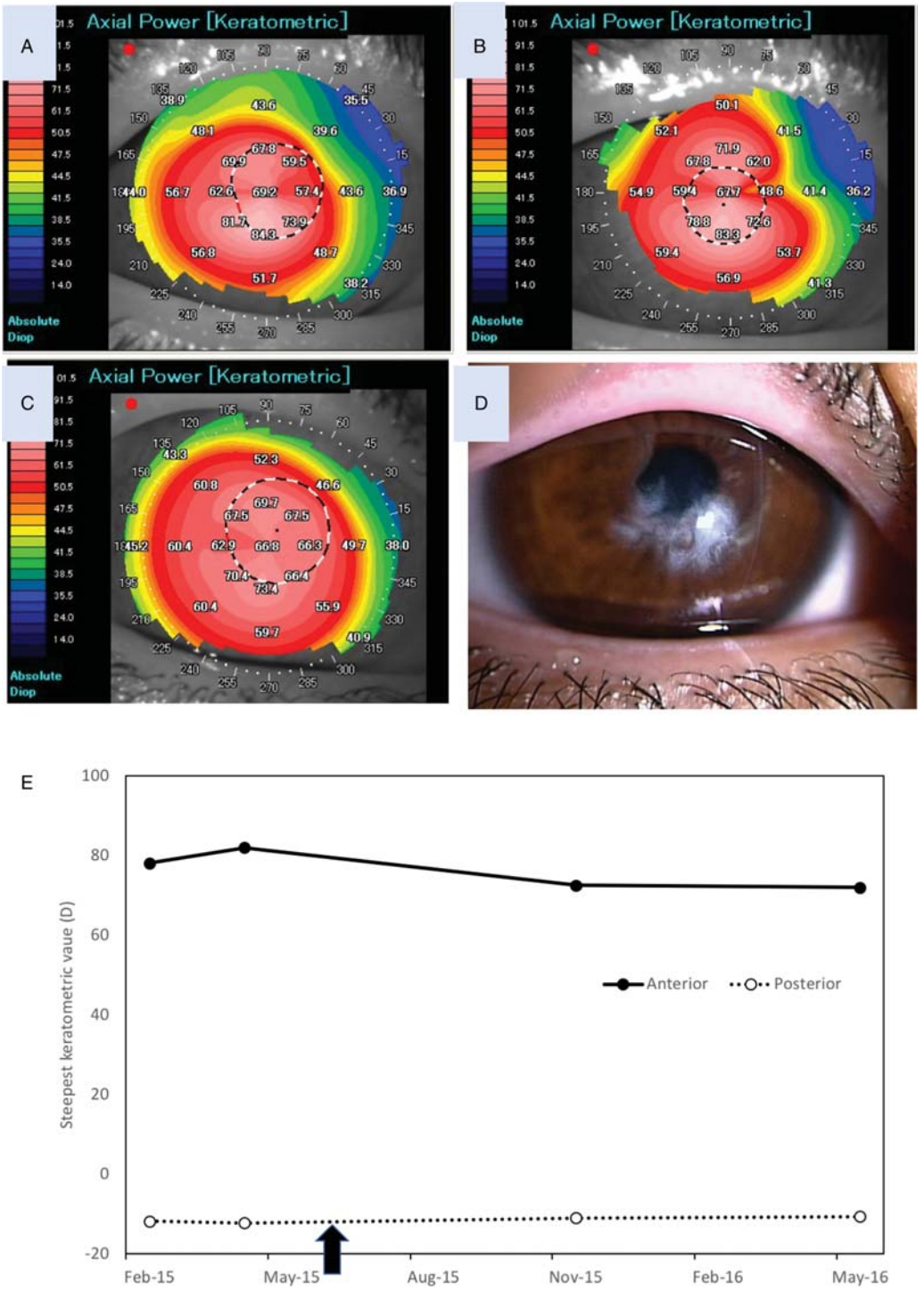

Figure 3. Change in topography and corneal thickness of case 2. Before CXL, the right eye of case 2 had a K_s of 82.9 D (A). Five months after accelerated CXL, his K_s decreased to 72.5 D (B), and at 1-year postoperative examination, his right cornea demonstrated K_s of 72.0D (C) and a stromal scar (D). The steepest keratometric values both on the anterior keratometric map and posterior axial map were stable after the CXL (E). Arrow shows the timing of the CXL.

compulsive eye rubbing is not clear, however, we should pay attention to the symptoms of TS possibly causing injuries and subsequent inflammation on the ocular surface postoperatively.

Compulsive eye rubbing may cause not only keratoconus but also more serious ophthalmic diseases such as retinal detachment.[18] In the present case series, 2 of 3 cases also suffered a retinal hole or retinal detachment that required surgical intervention. We recommend treatment of TS cases by both ophthalmologists and psychiatrists. Adequate medication in early pathological stages can prevent patients from suffering irreversible loss of visual function.

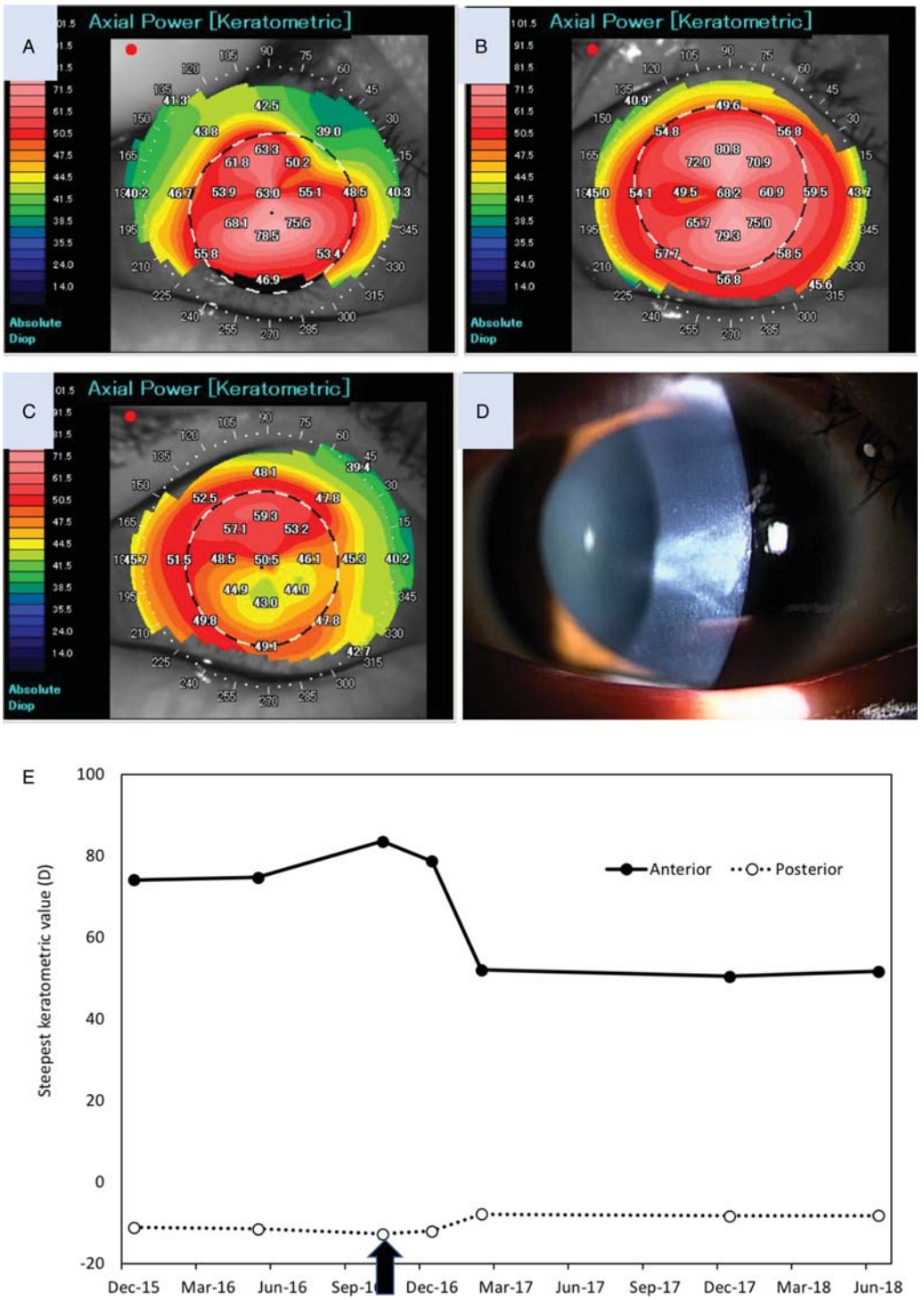

Figure 4. Change in topography and corneal thickness of case 3. At the initial visit, the corneal topography of case 3 had a K_s of 74.1 D (A) and CCT 417 μm (B) in his right eye. In 10 months, his keratoconus showed rapid progression and the K_s increased to 83.8 D (C). CCT decreased to 347 μm OD (D). Nine months after CXL, his K_s decreased to 51.7 D (E) and the right cornea showed a stromal scar (F). The steepest keratometric values both on the anterior keratometric map and posterior axial map showed extreme flattening after the CXL (arrow) and stayed stable thereafter (E).

Table 1

Characteristics and comparison of reported cases.

Authors; published year (reference number)	Characteristics of cases
Enoch et al 1989[13]	Among 12 patients with TS, 2 patients were diagnosed with keratoconus, and another patient had moderate to high astigmatism and corneal thinning but was not diagnosed with keratoconus. The authors mainly reported visual field anomaly in patients with TS. Corneal topography was not used for diagnosis of keratoconus.
Mashor et al 2011[14]	Existence of keratoconus in 3 cases with TS was shown. The first case revealed findings consistent with keratoconus as determined via Pentacam scan. The second case had corneal scar with thinning of the lower half of the cornea. The third case had corneal hydrops with significant corneal thinning.
Kandarakis et al 2011[15]	35-year-old man revealed corneal hydrops on both eyes, and the right eye became phthisic after 4 years. Two topography maps at the first visit and 4 years later were shown.
Shinzawa et al, present investigation	Three cases; 14-, 17-, and 24-year-old males. Keratoconus was identified by corneal tomography (CASIA). Keratoconus progressed over time and in accordance with severity of eye rubbing in all cases were shown by tomography. Progression of keratoconus was halted by CXL and adequate psychiatric medications.

Author contributions

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Validation: Naoko Kato, Kozue Kasai, Kenji Konomi.
Visualization: Naoko Kato.
Writing – original draft: Megumi Shinzawa.
Writing – review and editing: Naoko Kato, Kenji Konomi, Yuzhu Chai.

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