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# Clinical characteristics and topographic findings of corneal ectasia in patients with symptomatic *Demodex* blepharitis

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## Abstract:

**PURPOSE:** The purpose of this study is to present characteristics and topographic findings of patients with corneal ectasia and symptomatic ocular demodicosis.

**MATERIALS AND METHODS:** A retrospective, noncomparative study. Twenty-one patients with symptomatic ocular demodicosis and corneal ectasia since 2017 to 2019 were enrolled. Patients with dry eye syndrome and meibomian gland dysfunction were identified and treated. Demographic data, topography, and clinical data were collected. All patients underwent lash sampling to confirm *Demodex* mite infestation by direct visualization under the microscope.

**RESULTS:** Twenty-one ectasia patients (36 eyes) were enrolled with male preponderance (M:F=18:3). Mean age (years) was  $28.6 \pm 8.12$ . Of the 21 cases reviewed, the average number of topography taken was 6.8 within 43.8 months of follow-up. Corneal ectasia was characterized by focal thinning area beside central cornea, with corresponding mean thickness of  $487.1 \mu\text{m}$  and  $518 \mu\text{m}$ , respectively. All ectasia patients were combined with *Demodex* blepharitis and associated symptoms, proven by direct microscopic examination. After treatment with eyelid cleanser (OCuSOFT® Lid Scrub® PLUS), warm compress, and improved daily hygiene, ocular demodicosis and topographic changes were controlled and even reversed.

**CONCLUSION:** Our results indicated that ocular demodicosis may be potentially associated with corneal ectasia. *Demodex* blepharitis still remains an overlooked differential diagnosis in clinic; however, it may be one of the risk factors triggering eye rubbing. Comorbidity of lid infestation with eye rubbing may lead to corneal ectasia, even in elder patients with thick cornea. Therefore, meticulous examination and intensive treatment were highly recommended in this group of patients.

## Keywords:

Blepharitis, corneal ectasia, corneal topography, demodex mite, thick cornea

## Introduction

Corneal ectatic disorder is traditionally defined as a family of noninflammatory, noninfectious degenerative disorders, including Terrien's marginal degeneration, pellucid marginal degeneration, post-laser-assisted *in situ* keratomileusis (LASIK) ectasia, and keratoconus (KC). Among these corneal ectasia, KC is the most common one, mainly prevalent in adolescence and early adulthood with unknown pathogenesis.

Clinically, the incidence and prevalence rate of KC are estimated as 1 per 2000 per year and 54.5 per 100,000, respectively.<sup>[1]</sup> KC may occur unilaterally or bilaterally with progressive asymmetric bowtie pattern of astigmatism, early ectasia on posterior elevation map of topography,<sup>[2,3]</sup> focal thinning cornea at the region of bulging, progressive high myopia, and potential acute hydrops. Exacerbated ectasia tends to cause ocular pain, visual disturbance, and even acute corneal perforation, leading to potential ocular infection and requiring advanced surgical intervention.<sup>[4]</sup>

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Search for the risk factors of corneal ectasia is crucial for the prevention and management of ectatic disorder. In patients receiving refractive surgery, abnormal biomechanical properties of the cornea, including thin cornea in photorefractive keratectomy/LASIK patients,<sup>[5,6]</sup> young age and high myopia in LASIK patients, are considered as the risk factors of postoperative ectasia.<sup>[6]</sup> Otherwise, various risk factors of developing KC, such as contact lens wearing, collagen vascular disorders, Marfan's syndrome, atopy, eye rubbing, and allergic conjunctivitis have been proposed.<sup>[1,7,8]</sup> Although etiology of KC has yet been fully elucidated, the occurrence and progression of KC are frequently accompanied by allergic eyes and behavior of eye rubbing. However, underlying predisposing factors of itchy eyes and effective solutions are not completely unveiled. Since blepharitis often leads to itchy eyes and subsequent eye rubbing, it should also be considered and evaluated as predisposing factors.

Bacterial or allergic blepharoconjunctivitis may induce itchy sensation, tears film imbalance, local heat, and eye rubbing. *Demodex*, as another human skin microbiome, is a common but easily overlooked parasite, causing itching, erythematous change, and irritation. Ocular demodicosis has been found associated with blepharitis and chronic chalazion, presenting telangiectasia at lid margin, cylindrical dandruff (CD) along eyelashes, madarosis, and redness with follicular plug along lid margin and periorbita. Symbiosis between *Demodex* and bacteria had ever been proposed,<sup>[9]</sup> but its role in blepharitis is yet fully understood.

Other than blepharitis, ocular demodicosis may also induce various ocular surface diseases, such as corneal neovascularization with opacity, marginal keratitis, secondary infection, and phlyctenulosis-like conjunctivitis.<sup>[10]</sup> Since the diagnosis of ocular demodicosis, based on clinical symptoms and evidence on eyelashes, has been established,<sup>[11]</sup> it is worthy to further investigate other potential *Demodex*-related ocular diseases. The potential association between eye-rubbing behavior due to ocular demodicosis and corneal ectasia has not yet been reported. In this article, we presented a cohort of corneal ectasia patients with relatively thick cornea and ocular demodicosis, which may show another spectrum of corneal ectasia in clinical practice.

## Methods

### Participants

This study was approved by the Ethics Institutional Review Board of Chang Gung Memorial Hospital, Linkou (No. 201801086B0). All protocol adhered to the tenets of the declaration of Helsinki to retrospectively review medical records of 21 patients with coexisting

corneal ectasia and *Demodex* infestation, who had been followed up during 2017–2019. All patients underwent a thorough ocular examination such as topography and photography of the eyes, especially root of eyelashes and mid-face. Dry eye syndrome and Meibomian gland dysfunction (MGD) were surveyed according to Dry Eye Workshop II report and well treated in all patients to rule out potential impact on symptoms and presentation of topography. Corneal topography with poor quality or patients with severe, uncontrolled dry eyes/MGD were excluded in this study. Informed written consent was obtained from all the patients prior to their enrolment in this study. Patients diagnosed as *Demodex* blepharitis and corneal ectasia by clinical data, pachymetry, and topography, were enrolled. Our study design was summarized as a flowchart [Figure 1]. We excluded three patients with incomplete data and one patient with fluctuated dry eye disease.

### Clinical measures and diagnosis

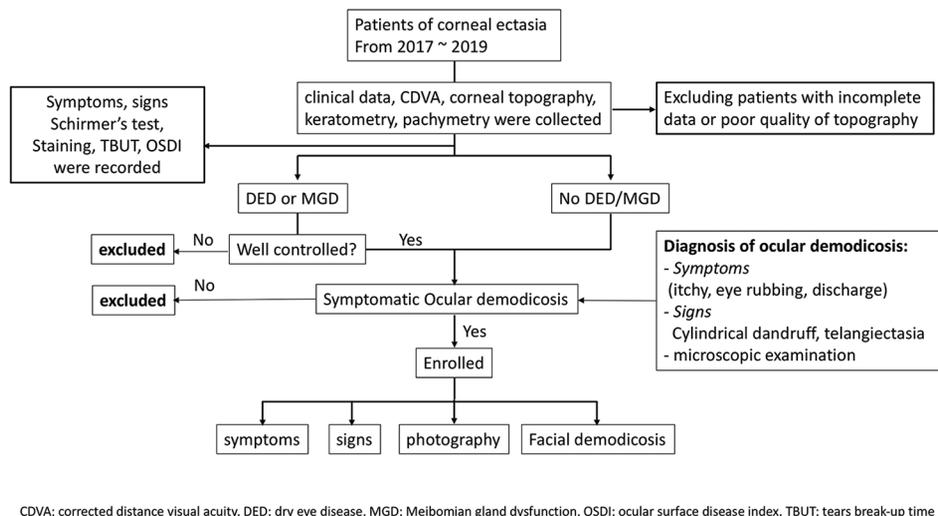
Demographic data, including age, gender, corrected distance visual acuity (CDVA), astigmatism, central corneal thickness (CCT), and thinnest corneal thickness, were collected. All patients received bilateral eyelashes sampling, external eye photography, and microscopic examination for the diagnosis of *Demodex* infestation. Briefly, three eyelashes with CD along lashes were epilated from eyelids and mounted on glass slides. The presence of *Demodex* mites, larva, eggs, and debris was documented under a light microscope by direct visualization.

### Statistics

Data were analyzed with nonparametric method were shown as median and range.  $P < 0.05$  was considered as statistically significant.

## Results

Twenty-one patients (36 eyes) diagnosed as corneal ectasia, combined with ocular demodicosis, were enrolled. Among them, 18 (86%) were male and three (14%) were female, showing a male preponderance. Seventeen eyes (47%) were right eyes and the rest (53%) were left eyes. The mean age of enrolled patients was  $28.6 \pm 8.12$  years, slightly younger than that of enrolled female (31.7 years). Of the 21 cases reviewed, average number of corneal topography taken was 6.8 within 43.8 months of follow-up. Average follow-up period in our ectasia patients before the diagnosis of ocular demodicosis was 43.5 months (nearly 3.6 years). One third of eyes had a history of wearing rigid gas permeable (RGP) contact lenses and 39% of cases had evidence of facial demodicosis. There were seven patients (12 eyes) had tried RGP and one patient (two eyes) received scleral lens fitting to control progression of corneal ectasia and improve vision. All of these patients,



**Figure 1:** Flowchart of the study, showing including, excluding criteria, and mandatory examinations of our patients. Dry eye syndrome and Meibomian gland dysfunction were surveyed before enrolment and topography

except one, tried RGP 24.9 months in average before the diagnosis of ocular demodicosis. These patients were not freshly diagnosed and had established KC or corneal ectasia, which was refractory to RGP correction. During the period, they were wearing RGP, initially improved but later fluctuated topographies were observed in all patients. However, after controlling ocular demodicosis and stopping eye rubbing, astigmatism was reducing.

Corneal ectasia was characterized by focal thinning cornea beside central cornea. Mean value of the thinnest corneal thickness and CCT presented in our patients were 487.1  $\mu\text{m}$  and 518.0  $\mu\text{m}$ , respectively. Astigmatism of 4.0 diopter (D) in average was resulted from corneal ectasia. Four out of 21 patients (1/5) were newly diagnosed corneal ectasia with concomitant ocular demodicosis. Their clinical symptoms were presented as itchy eyelids, blurry vision, dry eyes, and repeated eye rubbing. Thirty-six percent of eyes have evidence of combined dry eye syndrome in the beginning. After treatment with lid scrub, warm compress, and improved lid hygiene, ocular demodicosis and topographic changes were better controlled or reversed (33% eyes). Among patients with reversible topography, one-fourth of them were freshly diagnosed with ocular demodicosis. Demographic data of our patients are summarized in Table 1. Our patients showed improved corneal astigmatism from  $3.6 \pm 2.1$  D to  $2.6 \pm 1.2$  D ( $n = 19$ ,  $P = 0.01$ ) after the treatment for ocular demodicosis. However, both the thinnest ( $P = 0.138$ ) and CCT ( $P = 0.437$ ) did not show significant change after the management [Table 2]. Here, we presented some cases in our study.

### Case No. 1 ocular demodicosis with asymmetric changes of corneal ectasia

A 28-year-old young gentleman concerned about progressive blurred vision in both eyes since 2018. Initial

CDVA was 6/7.5 OD and 6/6 OS, with 3.1D of corneal astigmatism in the right eye and 2.4D in the left eye. The thinnest part of the cornea was 521  $\mu\text{m}$  OD and 520  $\mu\text{m}$  OS in thickness at inferior cornea with corresponding thicker apex cornea, which were 531  $\mu\text{m}$  OD and 536  $\mu\text{m}$  OS, respectively [Figure 2a and b]. The maximum refractive power of his cornea was 50.3D in the right eye and 47.9D in the left eye, with remarkable asymmetric astigmatism pattern. After 7.5 months follow-up, front difference map of corneal topography showed severer ectasia than back in both eyes [Figure 3a-d]. Difference map and average progression index exacerbated from 1.19 to 1.25 in the right eye and from 1.30 to 1.93 in the left eye. Four maps report of topography 7.5 months after his first visit are shown in Figure 2c and d.

Duration from the first visit to the diagnosis of ocular demodicosis was 7.5 months. After treatment with warm compress, lid scrub, and improved lid hygiene, blepharitis was controlled. His last CDVA was 6/6 OU, with 3.5D of corneal astigmatism OD and 2.5D OS. The thinnest part of the cornea at his last visit was 516  $\mu\text{m}$  OD and 510  $\mu\text{m}$  OS with corresponding thinning apex cornea, which were 526  $\mu\text{m}$  OD and 528  $\mu\text{m}$  OS, respectively [Figure 2e and f]. Maximum corneal refractive power was 50.5 D in the right eye and 47.5D in the left eye. Ectasia on difference map improved in the left eye; however, fluctuation was noted in the right eye [Figure 3e and f].

### Case No. 2 keratoconus with ocular demodicosis

A 20-year-old gentleman had a past history of KC in his both eyes. He experienced acute hydrops with corneal scarring in his right eye, which had undergone penetrating keratoplasty (PK) [Figure 4a and b]. Bilateral blepharitis with local redness and telangiectasia were

**Table 1: Demographics of patients with ocular demodicosis and corneal ectasia**

Age/sex	Eye	Ocular/facial demodicosis	Symptoms	Management	Ophthalmic history	Thinnest CT (µm)	Apex CT (µm)	Reversed topography
28/male	OD	+/-	Severely itchy	Nil	Allergic conjunctivitis, dry eye	519	532	+
	OS	+/-	Severely itchy	Nil	Allergic conjunctivitis, dry eye	495	515	+
20/male	OS	+/-	Blurry	PK OD	Acute hydrops, scarring OD	493	523	-
34/male	OS	+/-	Eye rubbing, blurry	LASIK OU	Dry eye OU, normal OD	425	459 <sup>a</sup>	+
39/female	OD	+/-	Blurry	RGP	Nil	510	562	+
	OS	+/-	Blurry, dry	RGP	Dry eye	503	538	+
31/male	OS	+/-	Often itchy, photophobia, eye rubbing	Nil	Allergic conjunctivitis OU HSV, KPs, uveitis OD	524	544	-
23/male	OD	+/-	Itchy	Nil	Allergic conjunctivitis	414	438 <sup>a</sup>	-
	OS	+/-	Blurry, itchy	Nil	Allergic conjunctivitis	399	444 <sup>a</sup>	-
21/male	OD	+/-	Dry, itchy	Nil	Allergic conjunctivitis, dry eye	559	577	-
	OS	+/-	Dry, itchy	RGP	Allergic conjunctivitis, dry eye	507	547	-
40/male	OD	+/+	Blurry, eye rubbing	Nil	Allergic conjunctivitis, trauma OD	478	495 <sup>a</sup>	+
	OS	+/+	Blurry, eye rubbing	Nil	Allergic conjunctivitis	470	495 <sup>a</sup>	-
20/male	OD	+/+	Blurry, eye rubbing	RGP	Allergic conjunctivitis, dry eye	498	546	-
	OS	+/+	Eye rubbing	RGP	Allergic conjunctivitis	565	583	-
21/male	OD	+/-	Eye rubbing	Nil	Allergic conjunctivitis	498	526	+
	OS	+/-	Eye rubbing	RGP	Allergic conjunctivitis	437	492 <sup>a</sup>	-
22/female	OD	+/-	Eye rubbing	Nil	dry eye	577	594	-
	OS	+/-	Eye rubbing	Nil	Nil	572	590	-
16/male	OD	+/-	Itchy	Nil	Dry eye, atopic dermatitis, allergic conjunctivitis	533	550	+
	OS	+/-	Itchy	Nil	Dry eye, atopic dermatitis, allergic conjunctivitis	536	553	-
25/male	OD	+/-	Itchy	RGP		527	531	+
	OS	+/-	Itchy	RGP		515	527	+
44/male	OD	+/+	Dry	RGP	Dry eye	449	508	N/A
	OS	+/+	Dry	RGP	Dry eye	459	504	N/A
30/male	OD	+/+	Itchy	Scleral lens	Allergic conjunctivitis, dry eye	428	460 <sup>a</sup>	-
	OS	+/+	Itchy	Scleral lens	Allergic conjunctivitis, dry eye	472	505	-
28/male	OD	+/+	Blurry	Nil	Allergic conjunctivitis, dermatitis, dry eye	431	459 <sup>a</sup>	N/A
	OS	+/+	Blurry	Nil	Allergic conjunctivitis, dermatitis	449	486 <sup>a</sup>	N/A
44/male	OD	+/-	Blurry	Nil	Nil	437	490 <sup>a</sup>	N/A
	OS	+/-	Blurry	Nil	Nil	476	515	N/A
30/male	OD	+/+	Itchy	Nil	Normal OS	465	500	N/A
26/male	OS	+/+	Itchy, blurry	Nil	Normal OD allergic conjunctivitis OU	462	519	-
24/male	OD	+/+	Blurry	RGP		500	524	+
	OS	+/+	Blurry	RGP		475	511	+
34/female	OD	+/-	Itchy	Nil	Normal OS, dry eyes OU, allergic conjunctivitis OU	480	508	-

<sup>a</sup>Thin cornea. CT=Corneal thickness, HSV=Herpes simplex virus, KPs=Keratic precipitates, PK=Penetrating keratoplasty, RGP=Rigid gas permeable, LASIK=Laser-assisted in situ keratomileusis, OS=Left eye, OD=Right eye, OU=Both eyes, (+)=Positive, (-)=Negative

**Table 2: Astigmatism and corneal thickness before and after treatment of ocular demodicosis (n=19)**

	Treatment of ocular demodicosis		P
	Before	After	
Astigmatism (D)	3.6±2.1	2.6±1.2	0.001*
Thinnest CT (µm)	507.7±43.7	475.5±122.9	0.138
CCT (µm)	539.9±32.5	539.7±31.6	0.437

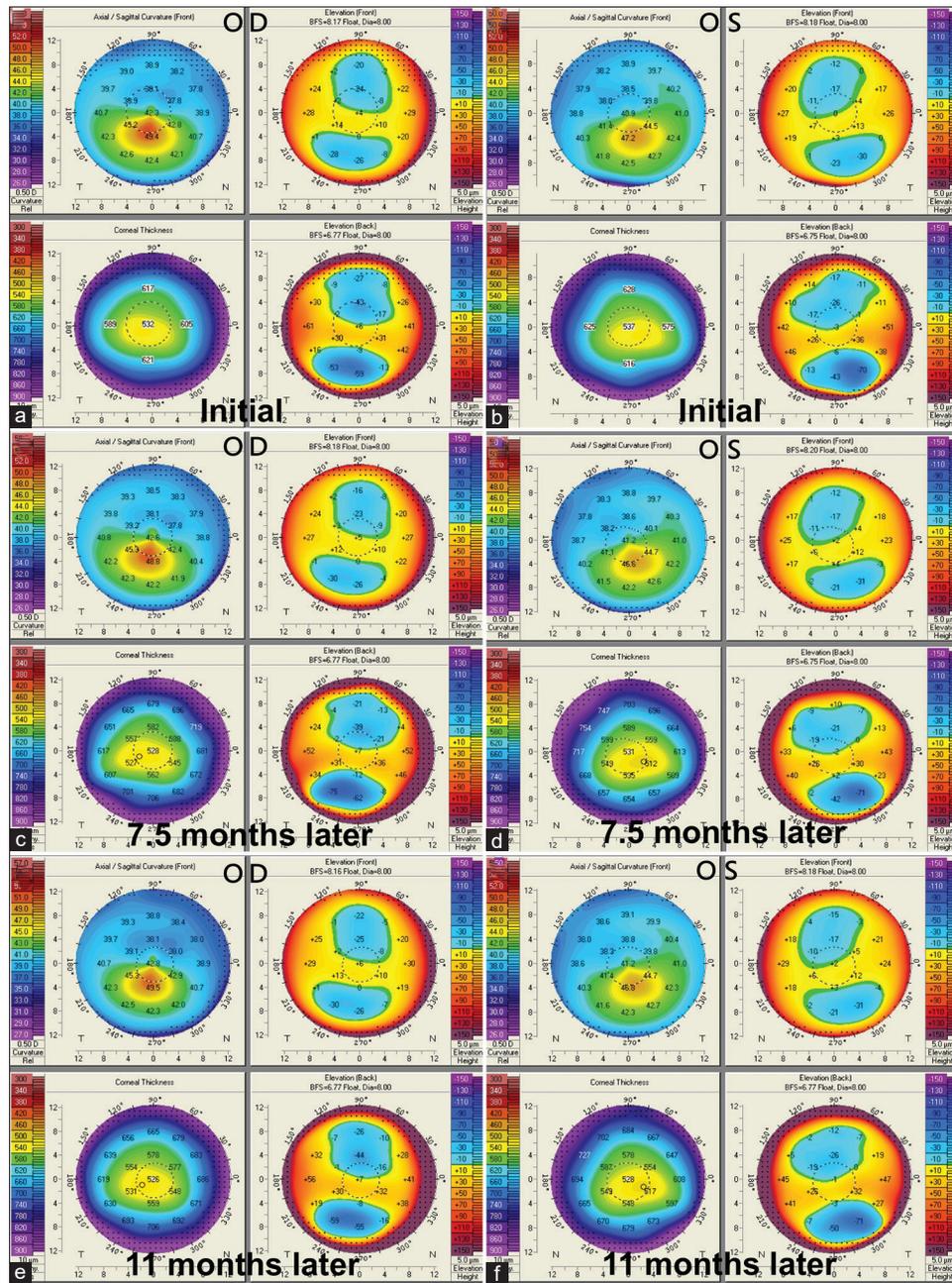
\*Statistically significant. CT=Corneal thickness, CCT=Central corneal thickness

found after PK. *Demodex* infestation with CD was identified under the microscope [Figure 4c]. At the same

time, facial demodicosis was confirmed on his skin at nasion area [Figure 4d]. Intensive treatment and warm compress were initiated after the diagnosis to eradicate mite infestation and reduce eye rubbing.

**Case No. 13 RGP-treated corneal ectasia underwent the management of ocular demodicosis**

A 25-year-old young gentleman visited our clinic for consultation of KC in his both eyes since 2013, and then, RGP contact lenses fitting had been initiated. At first, his CDVA was 6/15 in his right eye and 6/20 in

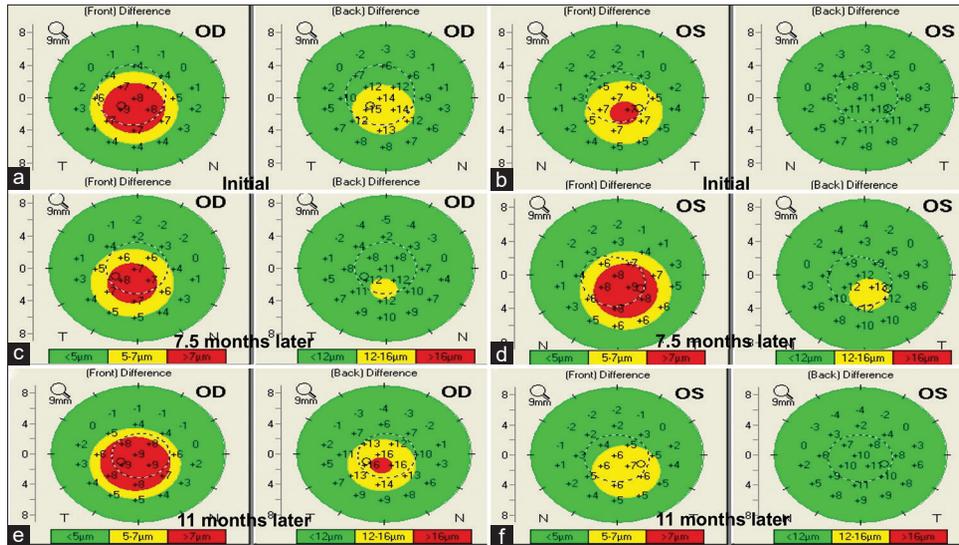


**Figure 2:** Serial four maps report of topography in patient No. 1. Asymmetric astigmatism with corresponding thinning cornea in both eyes at his first visit (a and b). Corneal condition after 7.5-month follow-up in both eyes (c and d). Four maps report of topography after treatment of ocular demodicosis at his last visit (e and f)

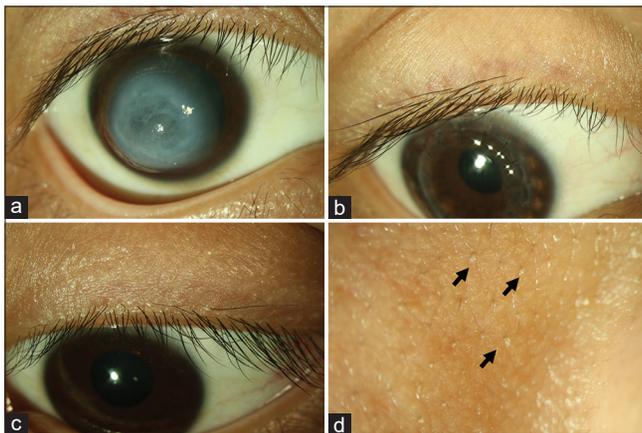
the left eye, accompanied by bilateral asymmetric high corneal astigmatism, which were 7.6D OD and 8.4D OS. The thinnest area is located at central cornea, whose thickness were 540  $\mu\text{m}$  OD and 535  $\mu\text{m}$  OS, close to apex cornea with thickness of 548  $\mu\text{m}$  OD and 546  $\mu\text{m}$  OS, respectively. Remarkable refractive power of the cornea was revealed as 57.4D in the left eye than 55.6D in the right eye [Figure 5a and b]. High astigmatism fluctuated during follow-up with decreasing corneal thickness and exacerbating corneal ectasia on the difference map. At first, severer corneal ectasia on difference map was noted in the left eye than that in his right eye, with

slightly larger area of ectasia on anterior cornea than that on posterior cornea [Figure 6a and b]. Progressive asymmetric astigmatism was also observed in his left eye. He continued to wear RGP in both eyes, 8 to 10 h per day, for a better vision during follow-up.

Ocular demodicosis was proved 6 years after his first visit, and therapeutics was administered for severe blepharitis and itchy symptoms. At the last visit, his CDVA improved to 6/12 OD and 6/10 OS. Corneal astigmatism reduced to 5.0D in the right eye and remained 8.4D in his left eye. Maximum refractive power of the cornea



**Figure 3:** Topographic changes on difference map (Belin/Ambrosio Enhanced Ectasia) in patient No. 1. Early ectasia was found on front difference map in both eyes with suspected change on back difference map OD (a and b). Ectasia 7.5 months later with enlarged area on front difference map OS with consistent lesion OD/suspected change OS on the back (c and d). Three months later, lesion on front and back difference map regressed faster in the left eye, but fluctuation was still noted on front and back difference map in the right eye (e and f)



**Figure 4:** Bilateral corneal ectasia combined with ocular demodicosis in patient No. 2. Acute hydrops with scarring was found in the right eye (a). After penetrating keratoplasty in his right eye, blepharitis was still observed at bilateral lid margins with cylindrical dandruff, redness, and marginal telangiectasia (b and c). Facial demodicosis was revealed along bilateral nasion area to medial canthal area in black arrow (d)

reduced to 48.7D in the right eye and increased to 56.0D in the left eye [Figure 5c and d]. Interestingly, prominent ectasia on front difference map in the right eye was totally resolved with residual ectasia on the back difference map in his right eye [Figure 6c-e]. Limitedly improved condition of ectasia on the difference map was observed in essentially severer left eye [Figure 6d-f].

### Case No. 19 Keratoconus patient with mood disorder and ocular demodicosis

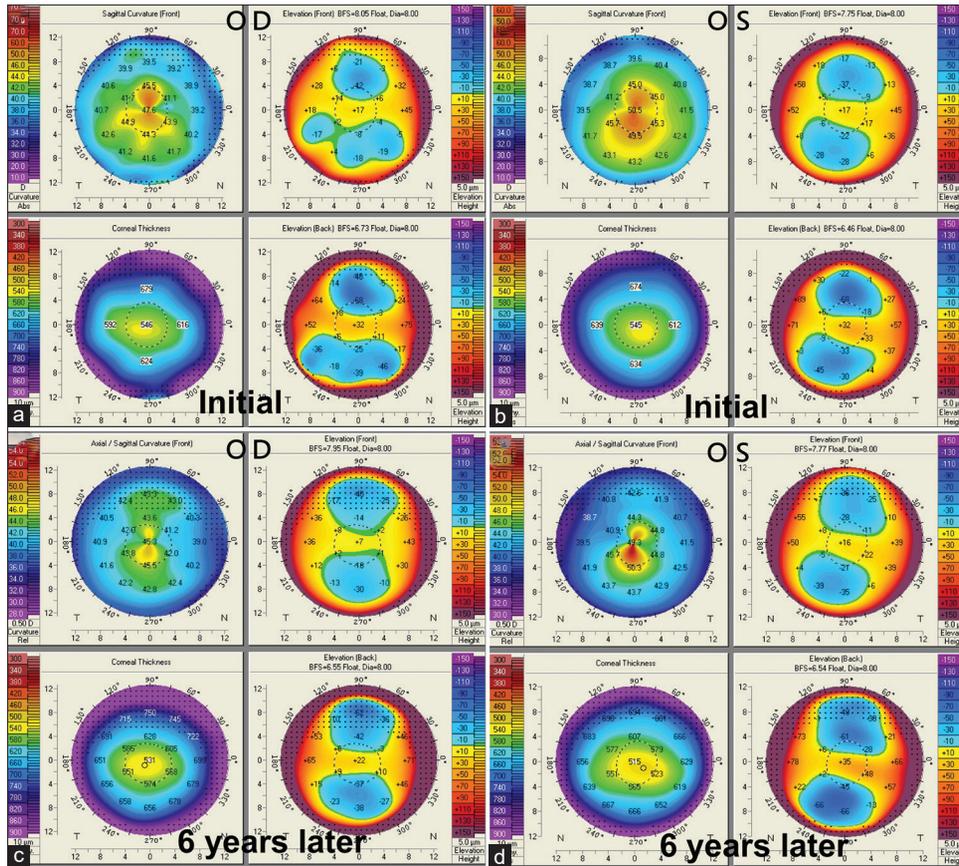
A 26-year-old gentleman has been regularly followed up for KC in his left eye since 2015. He also had a history of mood disorder under regular oral medication control. At his first visit, CDVA was 6/10 in both eyes, with 6.0D of

astigmatism in his left eye, higher than 3.45D in his right eye. Prominently, corneal refractive power was shown as 77.2D in the left eye, higher than 46.6D in the right side OD. The thinnest area of cornea was 481  $\mu\text{m}$ , close to apex cornea (495  $\mu\text{m}$ ) in his left eye [Figure 7a and b]. On difference map, larger area of ectasia was noted on the anterior surface of the cornea than that of posterior cornea. During follow-up, astigmatism, area of ectasia on front/back difference map, and corneal thickness were unstable, with remarkable corneal thinning and ectasia in the left eye. Although RGP contact lenses were fitted for patient's high astigmatism, poor compliance was noted due to patient's mood disorder in the following years.

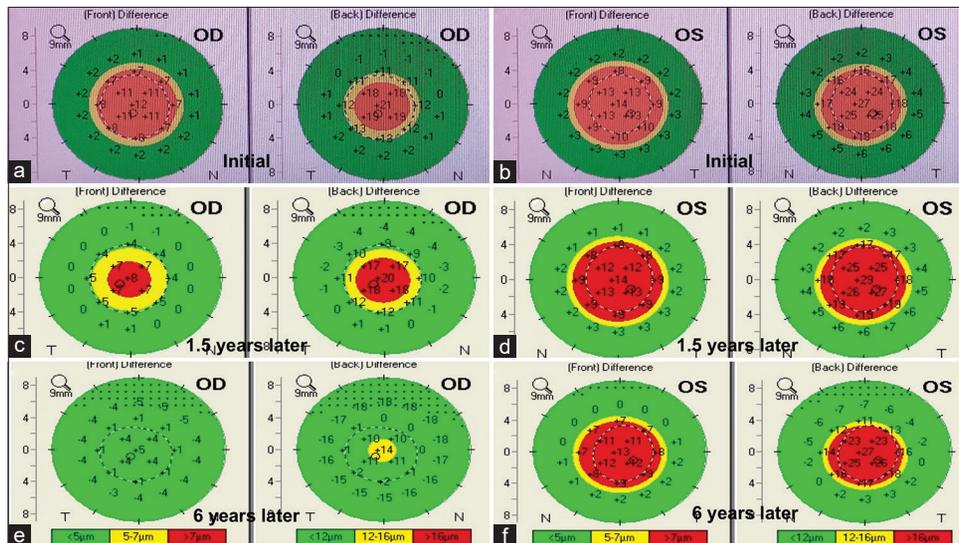
Since the patient suffered from itchy eyelids and was used to intensely rub his eyes, lashes were finally examined and ocular demodicosis was confirmed 50.3 months after his first visit. At his last visit in 2019, his CDVA improved to 6/6 OD and 6/8.6 OS, with 8.54D of astigmatism in the left eye. The thinnest part of the cornea also exacerbated to 440  $\mu\text{m}$  in his left eye, accompanied by higher corneal refractive power of 80.6 D. Area of ectasia on anterior and posterior cornea slightly reduced on difference map in the left eye [Figure 7c and d].

## Discussion

In the past, the development of corneal ectasia was considered to be associated with unstable biomechanical properties of the cornea,<sup>[12]</sup> such as thin cornea in young-age people, and further progression of this disorder could be attributed to repeated eye rubbing, which was clinically ameliorated with antihistamine drops and lubricants. Itchy symptoms and corneal



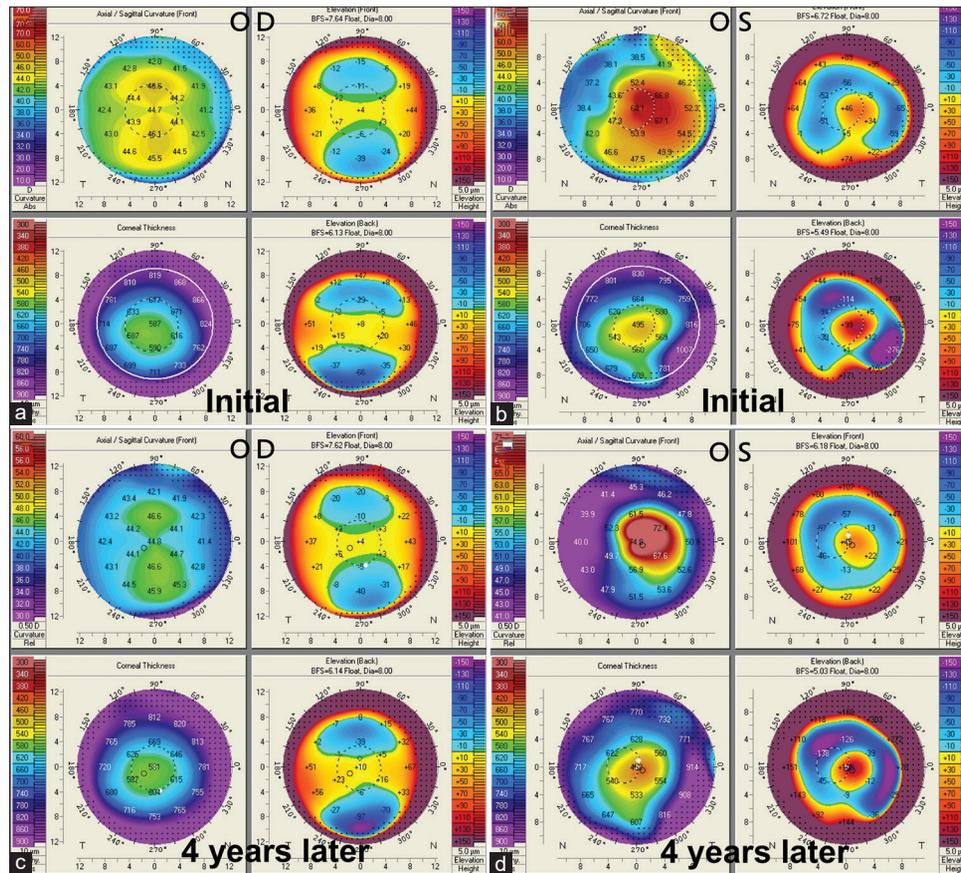
**Figure 5:** Serial four maps of topography in patient No. 13. Asymmetric astigmatism with paracentral thinning cornea OS > OD at his first visit (a and b). Corneal condition at his last follow-up in both eyes (c and d). Prominent exacerbation in the left eye was noted



**Figure 6:** Regressed corneal ectasia in the right eye of patient No. 13. At first, larger corneal ectasia was noted on front than back difference map in both eyes (a and b). Regressed corneal ectasia was noted 1.5 years later in his right eye; however, severe ectasia was still observed in his left eye (c and d). After 6 years, corneal ectasia regressed on front difference map with residual change on back difference map in the right eye. Large area of ectasia remained in the left eye with less regression (e and f)

complications from blepharitis were easily overlooked, since acquaintance with microbiology of periorbital was rather limited. In this study, we surveyed 21 patients of corneal ectasia, and found a potential association between corneal ectasia and ocular demodicosis.

*Demodex folliculorum* and *Demodex brevis* are viewed as two specific species in facial and ocular demodicosis.<sup>[9]</sup> Although *D. brevis* had been viewed as a more pivotal pathogen than *D. folliculorum* in chalazion, MGD, and keratitis,<sup>[11]</sup> there is no consensus in the leading pathogen



**Figure 7:** Progression of asymmetric corneal ectasia in the left eye of patient No. 19 after 4-year follow-up. At first, no ectasia was found in the right eye (a) and severe corneal ectasia was noted in the left eye (b). However, trace change of inferior corneal contour after repeated eye rubbing was revealed in the right eye (a). Four years later, marginal progression at inferior area was found on elevation map in the right eye, but ectasia had not yet developed (c). Ectasia was remained in the left eye (d)

of *Demodex* blepharitis. Theoretically, *Demodex*-induced anterior blepharitis tends to be derived from infestation of follicles where *D. folliculorum* often resides, and posterior blepharitis could originate from meibomitis due to local aggregation of *D. brevis*. However, clinical variation and mixed type of blepharitis lead to inconclusive results. Both species could exist along lashes in our observation. Furthermore, Chen and Plewig classified human demodicosis into primary and secondary subtype, according to whether immunocompromised status was noted.<sup>[9]</sup> Different from their definition of primary demodicosis that tends to happen in elderly people, our patients showed a young age (28.57 years) tendency, which could be attributed to bias from confounding corneal ectasia. Otherwise, around 43% (9/21) of our patients were older than 30 years old, demonstrating its different nature from primary KC which often happens before thirty.

Although migrating *Demodex* mites from skin to periorbita was mentioned before,<sup>[13]</sup> route of migration and distribution of mite infestation has not yet been disclosed. All our patients had strong itchy symptoms and corresponding behavior of eye rubbing, especially

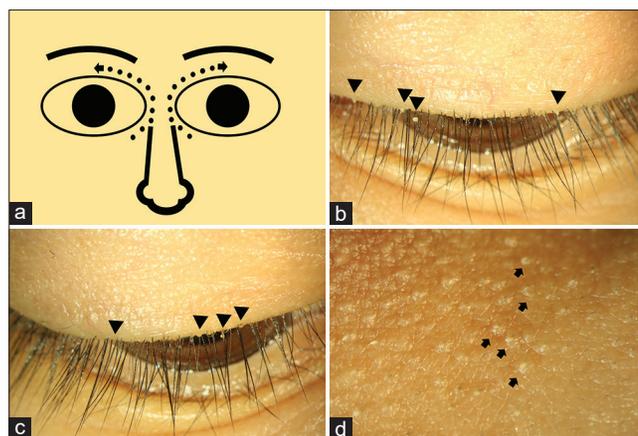
along medial canthal area to upper orbital rim. Facial demodicosis over the skin of nasal root or nasion (T zone) was found in some of our patients at the same time by direct microscopic examination of follicular plug, which was more sensitive than standard skin surface biopsy.<sup>[13]</sup> This area was linked to medial canthal area and upper eyelid/sub-brow area, where itchy sensation occurs mostly. Therefore, it is reasonable to deduce that *Demodex* mites will spread and reside along this oily route around periorbita, leaving annoying symptoms, urge of eye rubbing, and subsequent ocular complications. The presumed route of *Demodex* mites spreading, facial, and ocular findings is summarized in Figure 8.

KC generally affects patients in their second decades and seldom occurs after 40 years old.<sup>[14,15]</sup> However, our patients showed corneal ectasia with unstable topography in late twenties in average and even revealed exacerbation in their early forties, demonstrating a different clinical presentation. Repeated eye rubbing-related mechanical distortion of the cornea may in part explain this consequence. Otherwise, gender discrepancy in KC with a male/female ratio (M/F) from 1.33 to 3.34 had been reported worldwide, even

though few studies revealed a higher prevalence in females.<sup>[16-19]</sup> Young male preponderance of *Demodex* blepharitis with corneal ectasia was also noted in our patients; though, effect of androgen on corneal ectasia was still debated.<sup>[13,20,21]</sup> General ignorance of lid hygiene in males and regular removal of makeup in females, by contrast, may explain this discrepancy in part. Compared to lashes on the lower lid, those on upper lids were much easier to find CD and telangiectasia, meaning meticulous lid hygiene over these regions was worthy to be emphasized. Based on our observation, evidence of facial demodicosis along nasion requires to be identified and face wash with tea tree oil (TTO) component could be considered after warm compress. Furthermore, there was no significant difference in laterality of affected eyes implying handedness may not play an important role in developing corneal ectasia. Some multivariate study also supported this phenomenon.<sup>[22]</sup> However, if only patients with severe corneal ectasia were considered, the severity of ectasia may be related to stronger handedness.<sup>[8]</sup>

Based on clinical observation and complications after refractive surgery, corneal ectasia was closely related to thin cornea with mean CCT much  $<500\ \mu\text{m}$ ;<sup>[1-3,23,24]</sup> whereas, we found 26 out of 36 eyes (72%) in our patients had entity of thick cornea more than  $500\ \mu\text{m}$ . Thin cornea, rather than thick cornea, could hardly bear torsional force under repeated mechanical microtrauma. However, our data revealed that the cornea with CCT as thick as  $594\ \mu\text{m}$  may still lose its biomechanics under vigorous eye rubbing. On the contrary, one 34-year-old post-LASIK patient in our list presented reversible corneal ectasia only in his left eye with central thickness of  $464\ \mu\text{m}$ , compared to  $456\ \mu\text{m}$  in his right eye. This observation implied asymmetric ectatic change could still happen in a relatively thicker cornea after LASIK if the patient was under severe eye rubbing.

In the result of our study, male under their thirties with *Demodex* blepharitis tended to develop corneal ectasia. Before the diagnosis of *Demodex* blepharitis, mean follow-up period was 3.6 years in our group. However, after knowing how *Demodex* blepharitis impacts on corneal topography, freshly diagnosed patients with corneal ectasia were about one fifth on our patients list. Besides traditional therapeutics, such as lubricants, anti-histamine drops, and RGP contact lenses, for high astigmatism or visual disturbance in corneal ectasia, more intense treatments could be applied to our patients with *Demodex* infestation to acquire an earlier disease control and reduce irreversible complications. Daily usage of lid scrub with 50% TTO and 5% TTO ointment was suggested in published article for eradicating mites and blocking their life cycle at the same time.<sup>[13]</sup> In our clinical observation, daily cleaning face and root



**Figure 8:** Presumed migration route of *Demodex* mites from facial demodicosis to ocular demodicosis. According to patients' clinical symptom and rubbing habit, *Demodex* mites are presumed to migrate along inferior lid margin to medial canthus, and then superior lid margin (a). Patients with both facial demodicosis and ocular demodicosis have cylindrical dandruff (black arrowhead) along lid margin (OS: b and OD: c) and follicular plugs (black arrow) over nasion (d)

of eyelashes after warm compress for at least 10 min, combined with lid scrub is effective.

On difference map of topography, we found some patient's corneal ectasia would be earlier to appear on front elevation map or have a larger area than that on back elevation map. Furthermore, during regressed phase of ectasia, the disappearance of change on difference map was first found on either front or back elevation map, depending on severity of ectasia. This observation gave us some hints that *Demodex* blepharitis-related corneal ectasia may be reversible and occur first on front-elevation map, which meant front-elevation map could be potentially viewed as a monitoring tool for these patients. After the management of ocular demodicosis, we found astigmatism significantly improved ( $P = 0.001$ ) in our patients, but the thinnest and central part of the cornea showed no significant changes. These findings imply contour of ocular surface and associated astigmatism may be more vulnerable and reversible to mechanical distortion than eternal structural changes, i. e., thinning. Long-term follow-up after the treatment of ocular demodicosis is also required to monitor the changes of parameters in this group of patients. Other than corneal topography, tomographic data from corneal epithelial thickness mapping on optical coherence tomography (OCT) was proposed as a tool to early detect KC.<sup>[25]</sup> The correlation and serial changes between our topographic findings and potential tomographic changes on OCT in ectasia patients with ocular demodicosis are worthy to be further evaluated.<sup>[26]</sup> The drawbacks of our study were derived from small case numbers and short period of follow-up. More patients and long-term follow-up were required to consolidate our observation.

## Conclusion

We found that *Demodex* blepharitis can be a leading cause of eye rubbing and an associated corneal ectasia may potentially develop subsequently, which was reversible at an earlier stage and presented unique clinical symptoms and topographic changes. Topography is an important tool to early identify corneal ectasia and monitor changes of disease. Gross and microscopic examination of skin and lashes in particular provide important information of *Demodex* infestation, guiding us to make an adequate therapeutic strategy.

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## Conflicts of interest

The authors declare that there are no conflicts of interests of this paper.

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