Vernal keratoconjunctivitis and keratoconus

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Purpose of review
Vernal keratoconjunctivitis (VKC) is a severe allergic inflammatory disease affecting the conjunctiva in children and young adults. Keratoconus (KC) is a progressive corneal disease characterized by thinning of the corneal stroma, increased and asymmetric corneal curvature, with a potential for significant visual deterioration and is one of the most common corneal complications of VKC. We aimed to review the association of these two diseases, with focus on the mechanisms, prevalence, natural history and treatment strategies of KC associated with VKC.

Recent findings
KC is a common complication of VKC. KC prevalence can be as high as 26.8% among VKC patients, whereas abnormal corneal topography may appear in up to 71% of them. It is more severe and progresses faster in the setting of VKC ($P < 0.05$), with remarkable visual deterioration and with an increased need for keratoplasty. Crosslinking treatment and corneal transplantation appear to be as effective for KC patients with VKC as compared to the patients without VKC. However, postoperative complications are higher in patients with VKC and demand close monitoring, tight control of local inflammation and prompt awareness with consequent restrain of eye rubbing.

Summary
Patients with VKC should be closely monitored for KC. Prompt recognition of VKC and KC allows tight control of KC pathogenesis mechanisms, timely management of KC progression and preservation of vision and quality of life of young patients.

Keywords
allergic inflammation, eye rubbing, keratoconus, vernal keratoconjunctivitis

INTRODUCTION

Vernal keratoconjunctivitis (VKC) is a chronic bilateral, severe allergic inflammatory disease of the ocular surface in children and young adults. It usually affects male patients, starting during the first decade of life, and has a self-limiting course, resolving after puberty. The disease involves mainly the tarsal and bulbar conjunctiva and it is characterized by upper tarsal papillae and limbal hypertrophy, infiltrates or nodules. Symptoms include eye rubbing, hyperemia, tearing and photophobia [1,2▪▪]. In the severe form, the cornea might be affected as a result of mechanical injury promoted by the rough surface of the macro papillae, constant eye rubbing and inflammatory mediators [3].

Keratoconus (KC) has long been associated with VKC [4]. KC is a bilateral, asymmetric, progressive corneal disease, characterized by progressive thinning and increased curvature. It usually starts in the first to second decade of life and progresses until the late thirties. The etiology and pathogenesis of KC are multifactorial, sharing common features with VKC [5]. VKC which coincides with KC can significantly induce progression and deterioration of KC. Although both of the diseases, VKC and KC, are self-limited, with progression predominantly in childhood and early adulthood, they can be debilitating and may critically impact a young patient's social and educational development.

PATHOPHYSIOLOGY

The etiology of VKC is complex. No evidence of genetic predisposing factor [1] has been identified yet for VKC. However, some disease particularities indicate that VKC may have a genetic component, and may be a phenotypic model of upregulation of

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KEY POINTS

- Keratoconus (KC) is a frequent corneal complication of vernal keratoconjunctivitis (VKC) and is a result of frequent eye rubbing and tissue degradation by inflammatory mediators.
- KC is more severe and progresses faster in patients with VKC than in patients without it, with remarkable visual deterioration and with increased need for keratoplasty. Both KC and VKC affect young patients and can negatively impact their quality of life.
- Corneal collagen cross-linking (CXL) can halt KC progression in VKC patients as effectively as in non-VKC patients. Corneal transplantation outcomes are comparable between eyes with and without VKC. However, postoperative complications appear to be more frequent in VKC patients, demanding close monitoring.
- Patients with VKC should be screened for KC. Prompt recognition of KC could allow early treatment and preservation of vision and quality of life in children and young adults.

the cytokine gene cluster on chromosome 5q [6]. Those include: the high prevalence of VKC in Asia and Africa, along with the persistence of this predilection in migrated African and Asian populations [7]; the association with familiar atopic diseases in up to 49% in patients suffering from VKC [8] and the local and systemic inflammatory features of VKC.

Both type I and IV hypersensitivity reactions play important roles in the pathogenesis of VKC [2▪▪,9▪]. The predominant cell types involved in VKC include eosinophils, mast cells, T lymphocytes, basophils and macrophages. Eosinophils, the dominant cell type found in tears in the active phase of VKC [10], and its proinflammatory enzymes are in particular responsible for the corneal complications of VKC. Upon degranulation, this cell type release Eosinophil Cationic Protein, Major Basic Protein, Eosinophil Peroxidase and Matrix Metalloproteinase 9, which are toxic to the corneal epithelium and degrade the epithelial basement membrane and corneal stroma [11]. The disruption of the corneal epithelium promotes activation of fibroblasts, increasing the expression of receptors for Th2 mediators, IL-4, and IL-13, contributing to the cascade of inflammatory reactions and tissue damage, sustaining conjunctival inflammatory reaction and leading to corneal complications of VKC [12].

KC is a well-known complication of VKC. In a large series of patients, Naderan *et al.* [13]. reported that patients with VKC were at increased risk of KC with an odds ratio (OR) of 7.841. Merdler *et al.* [14] reported an OR of 6.0 for developing KC in patients with a combination of allergic conjunctivitis, chronic blepharitis, and VKC. KC is characterized by corneal steepening and thinning, leading to progressive optical distortion and visual loss. Though it is considered one of the leading causes for corneal transplantation in the developed world [15], its pathogenetic mechanisms are still unknown. The high occurrence rate in first-degree relatives, the concordance and greater similarity of phenotypes between monozygotic twins and the high prevalence among certain populations suggest a strong genetic component [15–17]. In addition, genetic studies have identified significant association with 36 genomic loci that implicate both dysregulation of corneal collagen matrix integrity and cell differentiation pathways as primary disease-causing mechanisms [18▪]. It is believed that KC occurs as a result of genetic predisposition triggered by inflammatory and environmental factors [5].

Eye rubbing is one of the important risk factors for KC. A recent meta-analysis found that the OR of developing KC was 3 times higher in subjects who abnormally rubbed theirs eyes compared with those who did not have this habit [19]. Especially in VKC, eye rubbing is a consequence of allergen trigger immune-mediated mechanisms. Allergens bind to immunoglobin E on the surface of mast cells, stimulating the release of histamine, known as a potent eye rubbing stimulus. Eye rubbing damages the corneal surface by both inducing mechanical trauma and the release of inflammatory substances [20▪▪]. Repetitive mechanical trauma can cause corneal weakening, by increasing apoptosis and oxidative damage, due to cyclic shear stress on corneal microstructures [21]. Secondary increased activity of inflammatory mediators can lead to keratocyte apoptosis, increase of fibroblast activity, increase of proteolytic enzymes, decrease of proteinase inhibitor levels, and decrease of stromal collagen [22]. In VKC, the characteristic papillae in the upper tarsal conjunctiva can produce further physical trauma and secondary inflammation upon eye rubbing, intensifying the relationship between both diseases.

KERATOCONUS PREVALENCE AMONG VERNAL KERATOCONJUNCTIVITIS PATIENTS

The prevalence of KC in VKC varies greatly among studies depending on the geographical area and diagnostic test used (Table 1) [23–29]. KC advanced signs are only detected on slit-lamp examination. Computer-assisted topographic and tomographic devices increase the diagnostic sensitivity and make early KC diagnosis possible [28].

Table 1. KC prevalence among VKC patients in different studies

Author (Ref.)	Location	KC diagnostic criteria	Device	VKC			Controls			Comments
				Patients	Mean age ± SD (range)	KC prevalence (%)	Patients	Mean age ± SD (range)	KC prevalence	
Totan [23]	Turkey	Placido disc-based videokeratography	Humphrey Master Vue (Humphrey Instruments, Optical Radiation Corp., CA)	82	15.04 ± 6.11 (8–22)	26.8	N/A	N/A	N/A	KC prevalence associated with male gender, long-standing disease, mixed and palpebral forms, and advanced corneal lesions. When biomicroscopy or keratometry used: prevalence was of 8.5% and 18.3%, respectively.
Lapid-Gortzak [24]	Israel	Videokeratography	EyeSys (EyeSys Laboratories, Houston, TX)	40	10.13 ± 3.22 (N/A)	15.0	36	11.98 ± 4.88 (N/A)	0	VKC patients have more abnormal corneal topographic patterns than non VKC controls. No correlation between severity, duration, and type of VKC and the corneal topographic patterns and numerical indices. 11.25% demonstrated clinical signs.
Dantas [25]	Brazil	Videokeratography	Holladay Diagnostic Summary	71	10.61 ± 3.96 (N/A)	22.5	100	9.77 ± 3.15 (N/A)	0	Of the KC patients, 97.18% had the palpebral form of VKC and only 2.81% had the limbal form of VKC. KC was associated with longer VKC duration and gender (predominance in males). Only 9.5% showed clinical signs of KC.
Barreto [26]	Brazil	Slit-scanning topographic	Orbscan IIz (Bausch & Lomb, Rochester, New York, USA)	50	16.41 ± 7.8 (N/A)	20.0	54	18.10 ± 6.3 (N/A)	0	Of VKC, 14% had subclinical KC; 5.5% of controls had subclinical KC.
Gautam [27]	Nepal	Videokeratography	Nidek Advanced Vision Information System (NAVIS) ophthalmic operating system (Nidek Magellan Mapper SN MM 2062 2004/5)	115	10.9 ± 4.9 (N/A)	11.3	102	11.8 ± 2.7 (N/A)	0	N/A
Caputo [28]	Italy	Scheimpflug camera combined with Placido corneal topographer	Sirius (software version 2.6; CSO, Florence, Italy)	651	11.54 ± 3.87 (7–23)	0.77	500	11.68 ± 6.10 (6–21)	Corneal indices of patients in the VKC group were extremely similar to those in the control group. ($P > .05$)	All KC eyes in VKC associated with bulbar form. VKC group: 0.61% KC suspect.
Umale [29]	India	Placido disc-based videokeratography	N/A	76	15.92 ± 4.38 (10 - 27)	11.2	N/A	N/A	N/A	The OR of having KC increased significantly in severe disease and duration more than 6 months

KC, keratoconus; N/A, nonavailable information; Ref., reference; SD, standard deviation; VKC, vernal keratoconjunctivitis.

Totan *et al.* [23] found a KC prevalence of 26.8% among VKC patients in Turkey. Computerized videokeratography was used, and the criteria used for diagnosis were a central corneal power greater than 47.2 D and/or an inferosuperior asymmetry (I-S) value greater than 1.4 D. KC is suspected when there is an increase in the cornea curvature (corneal steepening) and in the asymmetry between the inferior and superior average dioptric (D) values. When only slit-lamp biomicroscopy or keratometry were used, the prevalence was of 8.5% and 18.3%, respectively. The authors observed an increased incidence of KC with male gender, long-standing disease, mixed and palpebral forms of VKC and advanced corneal lesions

In a comparative study in Israel, Lapid-Gortzak *et al.* [24] found that patterns of corneal topography were abnormal in nearly 71% of the VKC group versus 40% of the control group. An asymmetric bow-tie (a pattern marking the shape and direction of the steep axis of the cornea) with inferior steepening was found in 31.25% of children with VKC compared with only 8.2% in healthy children. This study revealed a trend of superior corneal steepening among VKC patients: 36.25% versus 22.2% in controls. Overall, the prevalence of KC in VKC patients was 15% compared to no cases among the control group.

In Brazil, Dantas [25] reported KC prevalence in VKC patients of 9.85% when analyzing clinical signs, and 22.53% when videokeratography was used. No KC signs or topographic features were found in the control group. KC was associated with longer VKC duration and predominance in males. Another comparative study conducted in Brazil [26] found among patients with VKC a prevalence of 20% of KC and 14% of forme fruste KC (stable KC), whereas only 5.5% of controls had FFKC patterns. No subject from the control group had KC patterns.

In another study from Nepal [27], KC was found in 11.3% of VKC patients while no control had KC.

A recent noncomparative study from India [29] showed a KC prevalence of 11.2% among VKC patients. Mean keratometric value of more than 47.2 D was present in 26.3% and an abnormal I-S value over 1.4 D was seen in 21.7% of the eyes. The odds of having KC increased with severe VKC and disease duration of more than 6 months.

In contradiction with the above studies, Caputo *et al.* [28] reported a low prevalence of 0.77% of KC among VKC patients in Italy, whereas another 0.61% patients were classified as KC suspects. In their study, the corneal indices of patients in the VKC group were statistically similar to those in the control group.

To our knowledge, only Caputo [28] and Barreto [26] used devices that address information on the posterior corneal surface, strengthening the sensitivity of the KC diagnostic criteria. Both studies were comparative with healthy controls. However, the difference in KC prevalence in VKC might be explained by (i) mean age was higher in the Brazilian study; (ii) VKC appears to be the most common presentation of ocular allergy in Brazil (e.g. 53.2% of all the patients seen in the Outpatient Clinic of Ocular Allergy at a single Tertiary Center [25]), whereas in Italy, VKC represents only 8% of all cases of allergic conjunctivitis [30] and (iii) the number of patients analyzed was higher in the Italian study.

CLINICAL COURSE OF KERATOCONUS AMONG VERNAL KERATOCONJUNCTIVITIS PATIENTS

Onset of KC occurs between the first decade of life and puberty [31]. In younger patients, disease presentation is often more advanced and severe than adults, with a rapidly progressive course and significant asymmetry [32–34]. VKC affects the same age population [1,2▪▪].

Previous studies had demonstrated higher severity of KC in patients who also have VKC. Cameron [35] in 1989 described a series of patients with VKC and corneal ectasia. Among the 53 patients with VKC and KC, 29 (54.7%) had the palpebral form of VKC, whereas 14 had the limbal form and 18 had the mixed form. Sixteen patients (30.2%) had signs of previous hydrops; 8 of them had it bilaterally. Two patients presented to the emergency room with bilateral acute hydrops. Khan [36] described a year earlier, in a series of 530 VKC patients, 7% incidence of KC. This group had long-standing VKC symptoms, of 6–10 years duration. Of the 89 eyes affected with KC, 38 were legally blind, whereas 20 eyes had marked visual debilitation requiring keratoplasty. Six patients (12.5%) developed acute hydrops (1 bilaterally). More recently [37], corneal hydrops in children has been pointed as a presenting sign of VKC associated with KC.

Naderan *et al.* [13] reported that VKC was the most prevalent allergic disease (21.4%) among 885 KC patients. KC patients with VKC had significantly more severe disease than KC patients without a history of allergic disease ($P < 0.05$). Atopic keratoconjunctivitis (AC) was also associated with a more severe KC. Cingu *et al.* [38] studied 315 KC eyes of 171 patients at the southeast region of Turkey. VKC was present in 21.6% of KC eyes. VKC patients with KC were younger ($P < 0.001$), had significant thinner and steeper corneas and significant worse vision at presentation as compared to patients with KC and

AC and patients with KC alone. Grade 4 of Amsler–Krumeich classification was found in 58.5% of KC patients with VKC, much higher than in the KC and AC group (28.4%) and KC alone group (22%). Although not statistically significant, KC patients with VKC presented with more (11.8%) acute hydrops or central corneal scarring that mimic previous hydrops history than the other groups (KC alone: 4.2% and KC and AC: 4.9%).

VKC patients can show rapid KC progression [39,40] and eventually have an increased risk for keratoplasty [41]. In a prospective observational study [41] with 120 KC patients, VKC was a significant risk factor for corneal transplantation ($P = 0.04$). Eye rubbing, corneal scars, lower vision, steeper and thinner corneas were also significant risk factors. Moreover, in a group of 22 eyes of 11 VKC patients in India, Taneja [40] found a KC progression in 36.4% (8 eyes) of the eyes in 1 year.

TREATMENT OPTIONS OF KERATOCONUS AMONG VERNAL KERATOCONJUNCTIVITIS PATIENTS

Corneal collagen cross-linking

The continuous increase in corneal curvature and decrease in corneal thickness induce gradual deterioration of visual function in KC. Spectacles and contact lenses (CL) are used in KC to improve vision. KC patients with VKC however, are less tolerant to CL [35] and therefore, in those patients, there is an urge to halt KC in an earlier stage, before spectacles are less relevant.

Corneal collagen cross-linking (CXL) is the only available treatment that is able to halt KC progression. CXL induce photochemically triggered cross-links within the corneal collagen network by using a combination of vitamin B_2 (riboflavin) and 370 nm-wavelength ultraviolet A radiation [42], increasing the strength of corneal tissue.

In a study comparing CXL in KC pediatric patients with and without VKC, there were no differences in outcome and complications between the two groups. In addition, post-CXL progression of ectasia was not significantly different between both groups although it was slightly increased in the VKC group: 18.5% versus 16.7% in the non-VKC group. The authors concluded that CXL appears to be as safe and effective in pediatric patients with VKC as in those without [43]. In a study comparing trans-epithelial CXL (TE-CXL) with Keraring implantation versus TE-CXL alone for pediatric patients with VKC, Abozaid *et al.* observed significant improvement of outcome indices in the group which had Keraring implants. The TE-CXL group alone did not show progressive cases. Both treatments were found to be safe and effective for KC patients with VKC [44].

However, in other studies, VKC has been associated with post-CXL complications. A significant relationship was detected between VKC and delayed epithelial healing in a large series of CXL [45]. VKC can cause limbal stem cell loss leading to epithelialization problems. In addition, hypertrophic tarsal papillae have been shown to adversely affect the corneal epithelium via a traumatic effect [45]. Shetty *et al.* described 4 cases (0.0017%) of Staphylococcus aureus bacterial keratitis in a series of 2350 CXL procedures. Two of those patients had long-standing VKC and had previously used topical steroids for many years. The authors believed that the chronic use of topical steroids in KC with VKC could induce changes in the ocular flora, leading to an increased risk of postoperative keratitis [46]. In another series [47], of 532 eyes that underwent CXL, 7 (1.3%) cases developed microbial keratitis. Association with VKC was noted in 57.1% of cases ($n = 4/7$). The higher incidence of infection was attributed to poor compliance and prolonged topical steroid therapy [47].

In our experience, CXL can also trigger shield ulcer formation (unpublished case). A 14-year-old VKC male who had surgical scraping of a shield ulcer (Fig. 1A–C) in his left eye 3 years earlier, underwent uneventful CXL for a progressing KC in his right eye (Fig. 1D). Two weeks post-CXL, he developed epithelial irregularities that progressed to a persistent epithelial defect with an opaque stromal bed. Despite intensive topical and systemic steroid treatment healing was impaired for 5 weeks (Fig. 1E, F), until the ulcer was surgically scraped. After surgery, the epithelium healed within one week and 5 years later, both eyes were stable under topical tacrolimus ointment.

Corneal transplantation

In the setting of severe KC with significant visual deterioration, CL intolerance or visually significant corneal scars, corneal transplantation may have the potential for restoring vision. KC more frequently presents with advanced disease in young patients than in adults, as a result of the rapidly progressive course, disease asymmetry and lower awareness of unilateral visual loss in this age group [32–34]. Patients with VKC and KC are usually young patients and show not only earlier and more severe signs of KC at presentation [13,35,36,38] but also faster rate of progression [39–41] than those without VKC. Hence, KC patients with VKC are more likely to need keratoplasty. It is hypothesized that the constant ocular surface inflammation, the

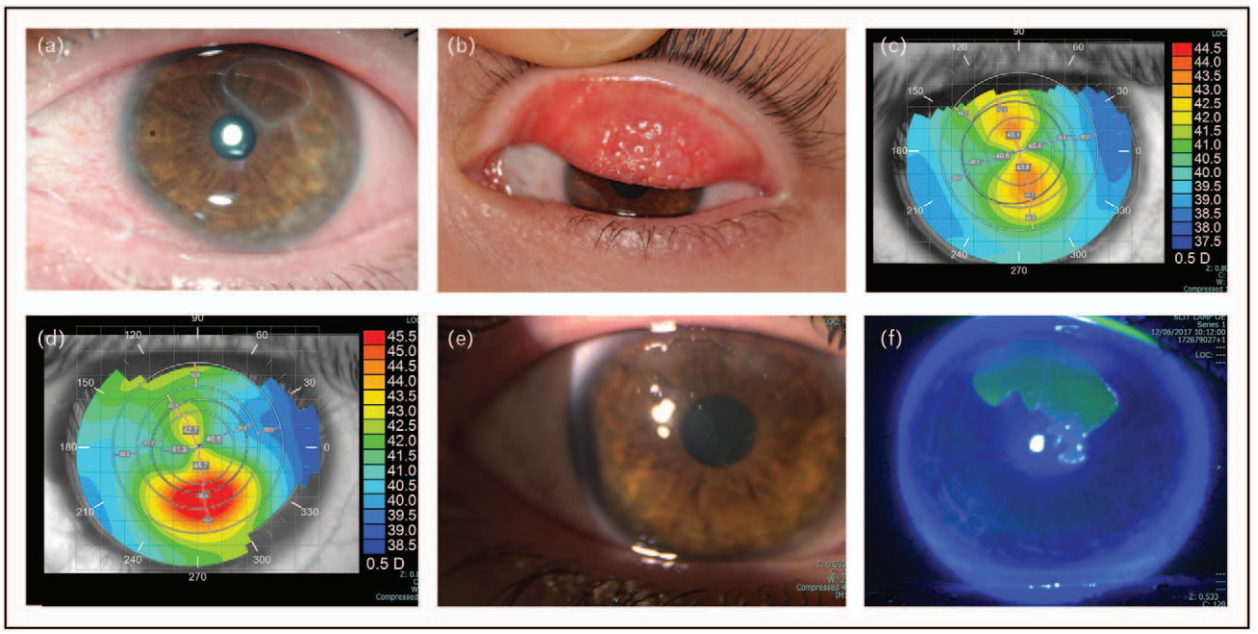

FIGURE 1. A. Refractory shield ulcer in the left eye of an 11-years old boy with severe vernal keratoconjunctivitis (VKC). B. Superior tarsal conjunctival papillae of the same eye. C. Normal topographic pattern of right eye of the patient. D. Progression to keratoconus 3 years later, despite topical 0.03% tacrolimus ointment with no VKC flare ups. Uneventful cross-linking treatment was done in the right eye with full epithelialization followed by shield ulcer formation 2 weeks later. E. Epithelialization was impaired for 5 weeks although intensive topical and systemic steroids were used. F. Shield ulcer with fluorescein staining. Complete healing was achieved only after surgical scraping of the stromal bed. Both eyes are stable 5 years later under topical 0.03% tacrolimus once a day.

secondary vascularization and the tendency toward trophic epithelial defects in VKC can increase the risk of graft failure after keratoplasty [9▪]. In a large retrospective study [48] comparing keratoplasty for KC in young patients (up to 17 years old, $n = 159$) and adults (17 years old and older, $n = 6677$) in the United Kingdom with a 2 year follow-up, Wajnsztajn *et al.* found that a higher proportion of pretransplant corneal vascularization and ocular surface disease was found in children compared to adults. That was most likely the reflection of the high prevalence of atopic allergic eye disease associated with KC. Corneal vascularization in children reduced transplant survival rates of corneal grafts.

A few studies explored the outcomes of keratoplasty for KC in VKC patients. In a series of 61 VKC patients, Cameron *et al.* [35] performed 15 penetrating keratoplasties (PK) in 14 KC eyes (12 patients) with medically controlled or inactive VKC. Clear grafts were obtained in 12 (80%) of the cases with a follow-up of 4–60 months. Three grafts failed due to bacterial keratitis. This group was compared to 94 KC eyes alone who underwent PKs. In the KC with no VKC group, 98.8% of the grafts were clear after a follow-up of 3–85 months, with 1 graft failing due to bacterial keratitis. VKC was a significant risk factor for graft failure ($P < 0.005$). Despite the difference in failure rates, KC and VKC eyes had a higher proportion of eyes with visual acuity of 20/40 or better (57.1%) when compared to KC with no VKC eyes (48.9%).

In another comparative study, Egrilmez and colleagues [49] showed that the clinical outcome of PK in eyes with KC and VKC was comparable to eyes with KC alone, with no differences in the final best-corrected visual acuity. However, the KC and VKC group had more episodes of loosened sutures ($P = 0.016$) and more steroid-induced cataract ($P = 0.038$) than the KC group alone. There was no difference between both groups in rejection and failure rates.

More recently, Wagoner *et al.* [50] compared the outcomes of PK for KC in patients with ($n = 80$ eyes) and without ($n = 384$ eyes) VKC. Like in previous studies [35,49], a higher proportion of patients were younger at time of PK at the VKC and KC group than in the KC alone group. Both groups had a median best-corrected visual acuity of 20/30. Five-year graft survival was 97.3% and 95.5% in eyes with or without VKC, respectively. Eyes with VKC were significantly more likely to experience late-onset persistent epithelial defects (6.3% versus 1.8%; $P = 0.04$).

Deep anterior lamellar keratoplasty (DALK) is a technique of corneal transplantation replacing the abnormal stroma, whereas preserving the host

healthy endothelium, thus avoiding endothelial graft rejection and graft failure. Feizi [51] compared DALK outcomes for KC between 28 eyes with VKC and 262 eyes without VKC. Best-corrected visual acuity was similar between both groups and there was no difference in failure rates and rejection episodes. However, vascularization of suture tracts and stitch abscesses were encountered more frequently in VKC.

Overall, keratoplasty (PK or DALK) for KC in VKC patients shows comparable results to patients with KC without VKC. However, because complications such as bacterial keratitis [35], prematurely loosened sutures, steroid-induced cataract [49], persistent epithelial defects [50], vascularization of suture tracts and stich abscesses [51] are apparently more common in VKC, closer monitoring is necessary in these cases. In his report, Cameron suggested an expectant conduct until the VKC becomes finally inactive, rather than just medically controlled, in order to perform keratoplasty. That would probably offer the best chance for maintaining a clear corneal graft [35].

Topical immunomodulators

An important adjunct to the success of CXL or keratoplasty relies on careful management of the inflammation and the modifiable risk factors such as eye rubbing that would impact KC prognosis and treatment outcomes. Both the discontinuation of eye rubbing [52] and the inflammation control [53] could possibly halt or slow down the KC progression and avoid corneal graft complications.

Currently, there are several topical treatment options for VKC inflammation control. Mast cell stabilizers act by inhibiting mast cell degranulation and cytokine release. They are safe and have minimal side effects. However, they are less effective than topical corticosteroids and immunomodulators [2▪▪]. Topical steroids are the most potent anti-inflammatory agents that act by inhibiting gene transcription and activation of proinflammatory factors. Nonetheless, topical steroids should not be used as the first line of treatment or in long term due to the severe side effects such as increase in intra-ocular pressure, cataract formation, increased susceptibility to infection and wound healing delay [2▪▪].

Calcineurin inhibitors such as cyclosporine A and tacrolimus are potent immunomodulators. They act by blocking Th2 lymphocyte proliferation and interleukin-2 production. In addition, they inhibit histamine release from mast cells and basophils through reduction in IL-5 production and reduce recruitment of eosinophils [2▪▪,9▪]. Several studies reported decrease in signs and symptoms of VKC after cyclosporine A use [54–56] and its efficacy in steroid-resistant VKC [57]. However, cyclosporine A effects start only after a few weeks of therapy and short-duration of steroid cycles are still needed for acute VKC exacerbation control [2▪▪,9▪]. Tacrolimus has a similar mechanism of action as cyclosporine A, and many studies have shown its efficacy in severe VKC resistant to cyclosporine A and steroids [58,59]. Both drugs are considered safe to use with minimal side effects such as burning sensation. However, their use for VKC is still off-label.

CONCLUSION

VKC is a primary allergic inflammatory disease of the conjunctiva that significantly affects the cornea. The persistent inflammatory environment and the secondary eye rubbing habit may induce corneal changes leading to KC. Both VKC and KC affect young patients, and KC appears to be more severe and progress faster in the setting of VKC, with remarkable visual deterioration and with increased need for keratoplasty. CXL and corneal transplantation appear to be as effective for KC patients with VKC as for patients without VKC. However, postoperative complications are higher and demand close monitoring, tight control of local inflammation and serious awareness with consequent restrain of eye rubbing. Patients with VKC should be monitored and screened for KC. Topical treatment with tacrolimus can significantly reduce the allergic inflammatory response in VKC, reducing the chances of developing KC.

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Conflicts of interest

There are no conflicts of interest.

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