Allergen-specific exposure associated with high immunoglobulin E and eye rubbing predisposes to progression of keratoconus

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We report two male children with persistent allergic eye disease (AED) and keratoconus (KC). Both presented with symptoms of vernal keratoconjunctivitis and decreased vision. In view of unrelenting AED, serum immunoglobulin E (IgE) quantification and identification of specific allergens were advised. Increased serum IgE levels were observed in both cases. Sunflower and sheep wool were identified as specific allergens for the first and second patient respectively by skin patch test. There was complete resolution of symptoms of AED in both patients following avoidance of causative allergens. However, the progression of KC in both eyes of the first patient and one eye of the second patient was observed. They were advised collagen cross-linking. Elevated serum IgE indicates the presence of systemic allergy. Avoiding implicated allergens help alleviate ocular symptoms. Using serum IgE and identifying specific allergen can guide in the treatment of AED and thus prevent progressive KC due to eye rubbing and resulting inflammation.

Key words: Allergy, eye rubbing, immunoglobulin E, keratoconus, vernal keratoconjunctivitis

Allergic eye disease (AED), eye rubbing and inflammation are implicated in pathogenesis and progression of keratoconus (KC).[1] Patients with AED and KC tend to present with higher grade of KC[2] and even progression after collagen crosslinking (CXL).[3] Rubbing-induced mechanical damage exacerbates tissue weakness and increases tissue proteases such as matrix metalloproteinase-9.[4] Elevated serum immunoglobulin E (IgE) indicates an ongoing systemic allergy. IgE triggers release of mediators such as histamine and interleukin-13 (IL-13) which activate transient receptor potential channels on sensory nerve endings to trigger an itch response.[5] Resulting symptoms are managed by antihistaminics and avoiding exposure to causative allergens. Hence, serum IgE measurements and identification of specific allergens can help manage AED. This case report emphasizes the relevance of serum IgE measurements and identification of specific allergens in the management of AED and prognosis of KC.

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Case Report

An 11-year-old male, presented with a history of bilateral eye itching and blurred vision since 2 years. His best-corrected visual acuity (BCVA) was 20/32 in both the eyes (right eye [RE] −2.0DC ×40), (left eye [LE] −2.5DC ×145) which had worsened over the past 6 months. On examination, he had bilateral tarsal conjunctival congestion with papillae indicating moderate tarsal vernal keratoconjunctivitis (VKC). Corneal tomography suggested bilateral grade 3 KC as per Amsler-Krumeich classification.[6,7] The patient had failed to respond to topical steroids, and cyclosporine treatment in the past, hence, CXL for KC was deferred until allergy was controlled. In view of unrelenting allergy, serum IgE levels were determined which were high, 706 IU/ml (normal: <200 IU/ml). There was no history or evidence of skin, respiratory or gastrointestinal manifestations of allergy or raised IgE levels. Serum Vitamin D level was < 10 ng/ml (normal: 30–100 ng/ml). Immunology reference and skin patch test revealed allergy to sunflower. History suggested that he ate food cooked in sunflower oil, which he was then advised to avoid. After 2 months of dietary alteration, eye rubbing ceased completely. However, pentacam reports suggested KC progression. Keratometry in the RE increased by 2.3 Dioptres (D), and thinnest pachymetry remained same, while the left cornea showed 1.6 D of steepening and thinning by 19 µ. Since ocular allergic symptoms had subsided, but KC had progressed, CXL was advised for both eyes.

A 15-year-old male, presented with bilateral eye itching, which worsened on tapering topical steroids, and decreased vision since 1 year. BCVA in both eyes was 20/20 with (RE − 1.0DC ×55), (LE − 1.0DS/−1.75DC ×140). Examination revealed bilateral upper tarsal conjunctival papillae and prominent corneal nerves. Corneal tomography revealed grade 2 KC in the RE [Figs. 1 and 2] and forme fruste KC (FFKC) in the LE [Figs. 3 and 4]. The patient

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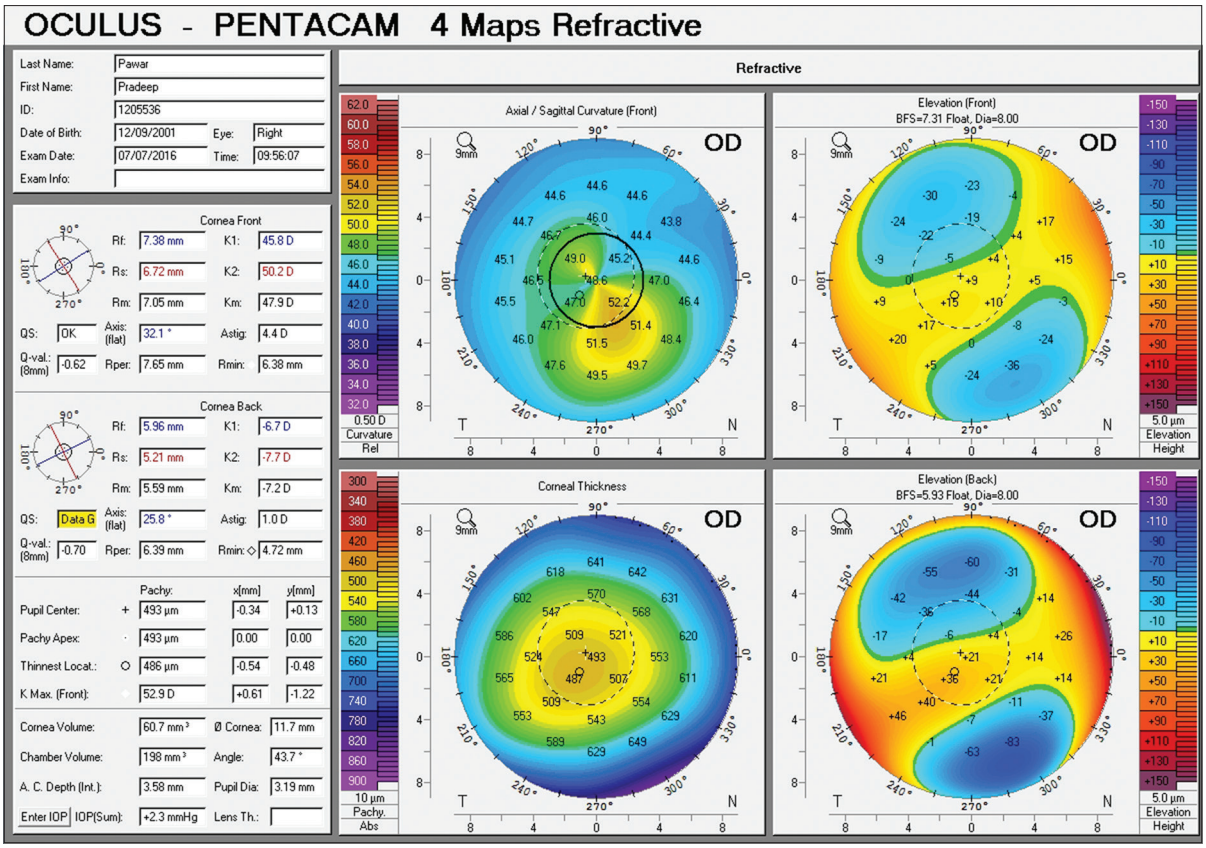

Figure 1: Right eye corneal topography of patient number 2

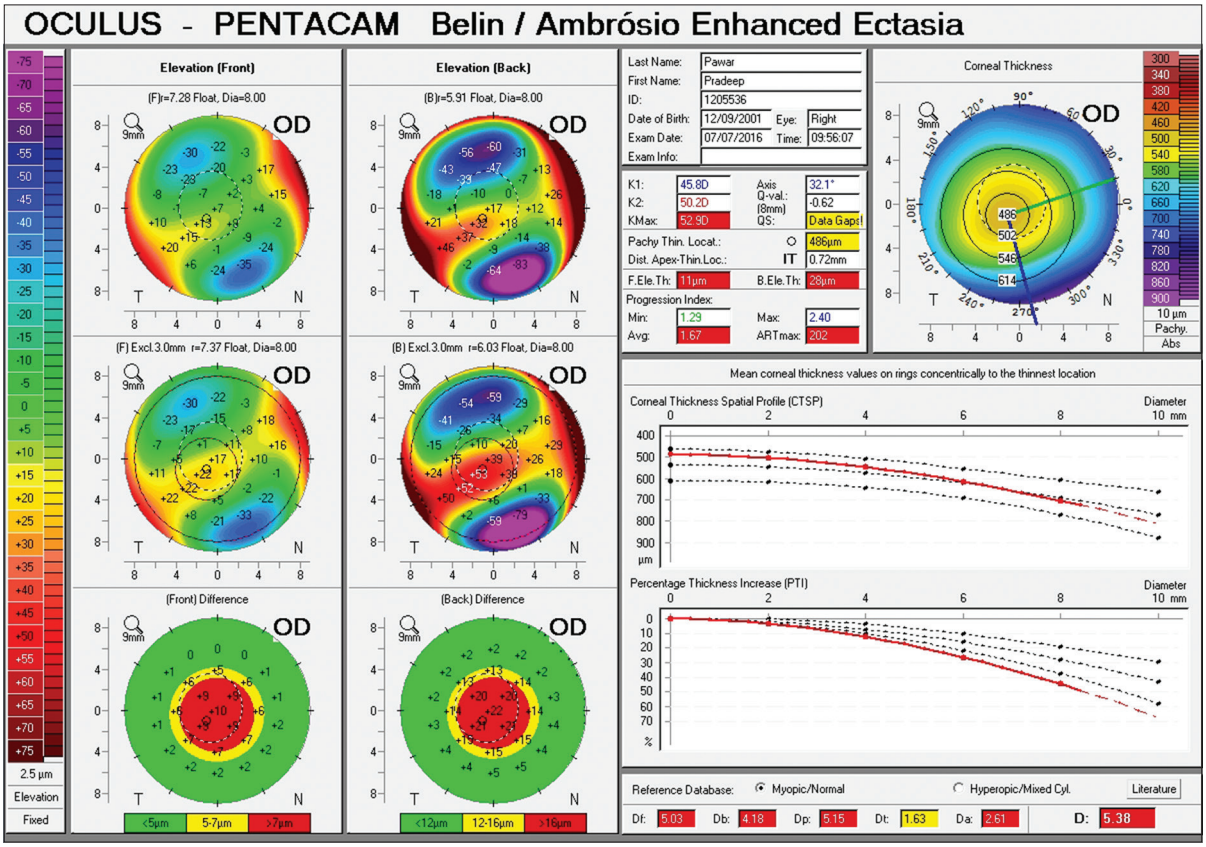

Figure 2: Right eye Belin Ambrosio Display of patient number 2

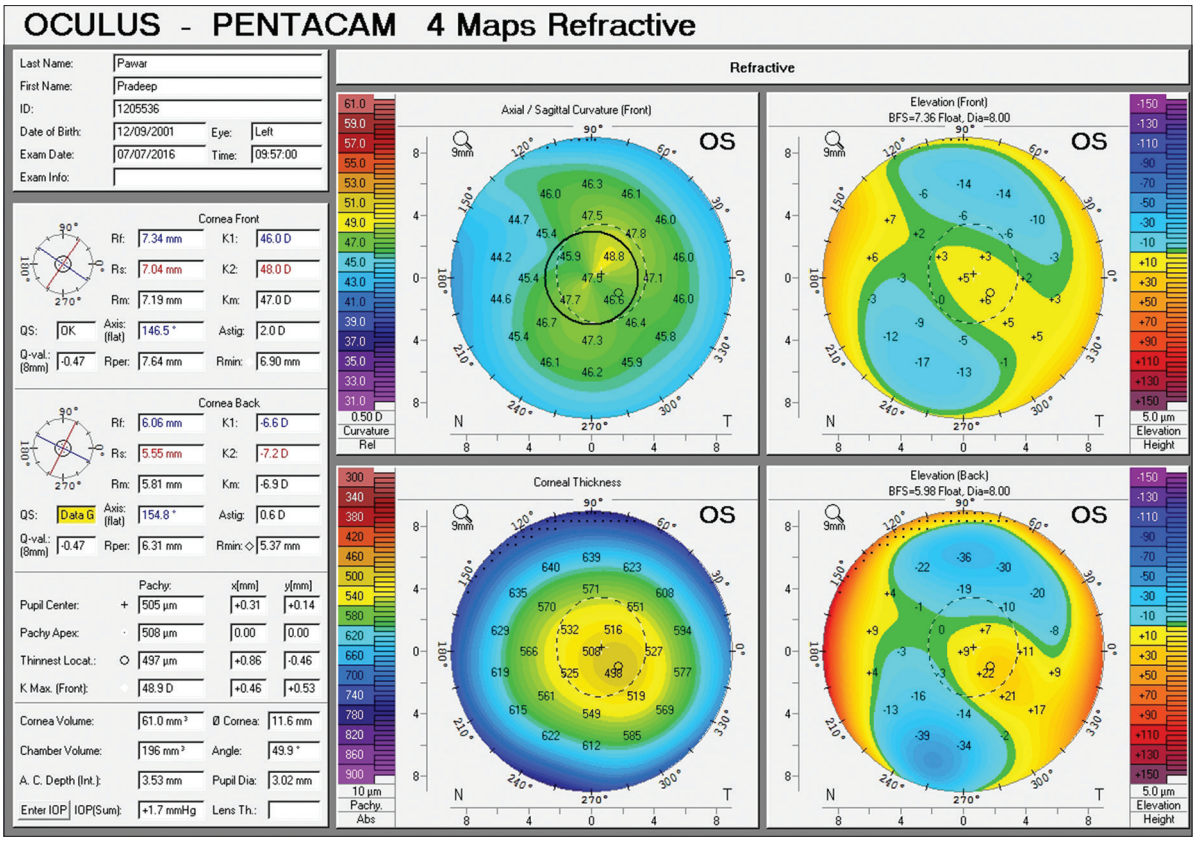

Figure 3: Left eye corneal topography of patient number 2

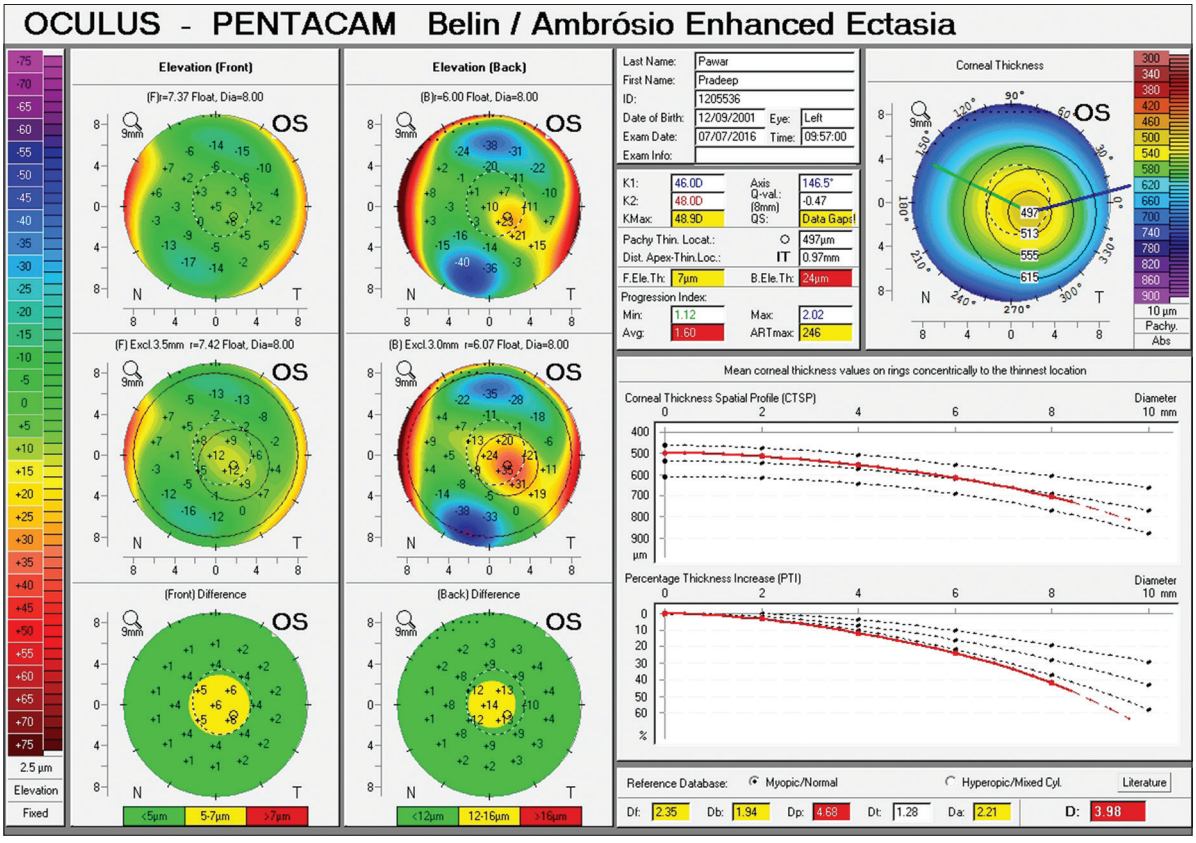

Figure 4: Left eye Belin Ambrosio Display of patient number 2

was given topical fluorometholone in tapering doses and tacrolimus (0.03%) eye ointment. Serum IgE level was high, 845 IU/ml (normal: <200 IU/ml), serum Vitamin D was 6.14 ng/ml (normal: 30–100 ng/ml). There was no history or evidence of skin, respiratory or gastrointestinal manifestations of allergy or raised IgE levels. Patch test revealed allergy to sheep wool, house mite, and chicken feathers. He had a history of wearing woolen clothes. He was advised to avoid the same and given a short course of antihistaminics. After 6 months, the patient remained asymptomatic despite stopping all topical medications by 3rd month, but KC had progressed in the RE with keratometric steepening of 1.4 D. There was no progression in the LE, hence, CXL was advised only for RE.

Discussion

The association between KC and allergy suggests an immune-mediated pathogenesis.[1,8,9] Patients with VKC and family history of AED are at increased risk of KC incidence, severity, and progression.[10,11] VKC is a chronic allergic disease affecting tarsal conjunctiva and limbus.[12,13] It is an IgE-mediated hypersensitivity reaction where binding of allergen-specific IgE to high-affinity IgE receptors on mast cells releases histamines and other cytokines causing inflammation.[12] Histamine is a mediator of itch response,[5] which triggers eye rubbing leading to KC progression by increasing protease activity.[4] The inflammation in VKC damages corneal epithelium and stroma that may cause KC progression.[12] Patients with VKC and KC are more prone to develop hydrops and undergo corneal transplants. Early control of allergy may decrease eye rubbing-related inflammation and corneal complications. We found increased levels of serum IgE and causative allergens in both patients. Avoiding allergen reduced symptoms and eye rubbing. However, KC progressed despite control of AED possibly due to molecular effects of eye rubbing over a long time before our management. In these patients, failure to control AED and eye rubbing with standard topical medications prompted investigation for serum IgE. High serum IgE indicates systemic sensitization and warrants investigation with a panel of common allergens. We correlated identified potential allergens from skin test with patient's history to derive causative allergens. Both patients had dramatic improvement of AED after avoidance of allergen. The eye with FFKC remained stable; however, there was progression in eyes with frank KC because we may have been unable to halt progression in advanced KC despite removing triggering factors. CXL was deferred until alleviation of symptoms because its failure has been linked to eye rubbing, VKC, and uncontrolled neurodermatitis. Thus, in patients with unrelenting allergy, evaluating serum IgE and subsequently identifying allergens could guide specific management. This would decrease inflammation and mechanical stress thus retarding KC progression and preventing CXL failure. A limitation of this report is unavailability and cost constraints of serum specific IgE test. In conclusion, if we routinely identify raised levels of IgE and specific allergens, we may be able to decrease overuse of topical medications, facilitate faster resolution of allergic symptoms, and prevent progression of KC.

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Conflicts of interest

There are no conflicts of interest.

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