Epithelial remodelling masquerading as keratoconus progression: An interesting case report

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A 25-year-old male patient presented with chief complaints of itching in both eyes (OU) for the past one month. Detailed ophthalmic examination showed best-corrected visual acuity of 6/6 OU. On slit-lamp examination of the left eye, Vogt’s striae were documented and rest of the anterior segment was normal OU. Pentacam-HR and ASOCT confirmed the diagnosis of keratoconus. The patient was started on Trehalose containing preparation for both eyes. On follow-up visit at 8 months, progression was documented on Pentacam-HR. MS-39 showed epithelial remodeling, but no stromal or posterior elevation, indicative of a pseudo-progression. Corneal epithelial remodeling post topical trehalose containing eye drops application has been very sparsely reported in literature. It is an important differential to consider when faced with a situation of a likely progression of keratoconus, especially to differentiate true from pseudo-progression.

Key words: Epithelial remodeling, keratoconus, progression, trehalose

Keratoconus (KC) is a progressive bilateral corneal ectatic disease which is typically first seen in the early adolescence. Corneal steepening and thinning in the central or paracentral regions lead to an irregular astigmatism affecting quality and quantity of vision. These clinical features worsen as the disease progresses to advanced stages.[¹]

In recent years, it has been shown that the corneal epithelium overlying the cone apex in keratoconus is thinned out in a localized zone with a ring of thickening in the periphery. This epithelial thickness alteration could create a masking effect over the underlying stromal irregularity. Thus, the epithelial and stromal thickness profiles in a keratoconic cornea could behave differently when compared to a healthy cornea.[²]

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Case Report

A 25-year-old male presented to us with chief complaints of itching in both eyes (OU) for the past one month. He had no past history of eye rubbing, ocular or systemic allergies. Family history of KC was absent. His unaided visual acuity was 6/12 OU. His best-corrected visual acuity (BCVA) with spectacles was 6/6 OU with Plano/-2DC at 65° OD and Plano/-3.25DC at 120° OS. Intraocular pressure measured by non-contact tonometer was 12 mm of Hg OU. On slit-lamp biomicroscopic
examination, OU few papillae on upper palpebral conjunctiva, Vogt’s striae OS were documented. Rest of the anterior segment examination and dilated fundus examination were normal OU.

Figure 3: Pentacam-HR comparative scan of OU at 8 month follow-up showing and increase in the keratometric value, with a difference of more than 0.5 D in both eyes along with 3 points of steepening in the cone region indicative of progression.

Figure 4: OU MS-39 comparative maps of the epithelial thickness, stromal elevation and posterior elevation suggestive of epithelial remodelling with no evidence of stromal or posterior elevation, 8 months apart from baseline (a). Right Eye: Comparative maps of the epithelial thickness, stromal elevation and posterior elevation at baseline (on left column) and at 8 months follow-up (on right column) (b). Left Eye: Comparative maps of the epithelial thickness, stromal elevation and posterior elevation at baseline (on left column) and at 8 months follow-up (on right column).
Corneal Topography was performed on Pentacam-HR (Oculus Optikgeraete GmbH, Wetzlar, Germany) and Epithelial mapping was done on MS-39 (ASOCT CSO Italia) [Figs. 1 and 2]; 3 scans each to ensure the repeatability of the scans. Based on the corneal topography, a diagnosis of stage 2 KC OU was established according to the Amsler Krumeich classification and the ABCD grading was A2B3C0D0 OU.[3,4]

As the patient had a BCVA of 6/6 and a low risk of progression according to our previously published nomogram, no surgical intervention was planned.[3] He was prescribed a combination of Trehalose and sodium hyaluronate 1% eye drops (Trehalube eye drop, Micro Labs, Bengaluru, India) OU four times a day for 6 months along with Loteprednol Etabonate 0.5% OU (Lotepred eye drops, Sun Pharmaceuticals, Mumbai, India) in tapering dose for 20 days.

At 8 months follow-up, there was no change in refraction OU. The patient was not using contact lenses, or had any complains of eye rubbing in interim period between the two visits. Pentacam-HR (3 scans) comparative maps revealed increase in keratometric values, with a difference of more than 0.5 Dioptre (D) along with 3 points of steepening in the cone region indicative of progression OU.[1] [Fig. 3] On MS-39 (3 scans), there was enhanced concentric epithelial thickening around the area of the cone with an increase in the minimum epithelial thickness from the baseline scans. However, there were no changes in the stromal elevation or posterior elevation [Fig. 4a and b]. Thus, the signs of steepening on pentacam comparative map may be attributed solely to the remodeling of epithelium around the cone region. The epithelial remodeling is masquerading as progression, hence a diagnosis of pseudoprosesssion was made.

Discussion

KC is a progressive disease with several known and unknown risk factors.[1] We defined progression as either a 0.5 diopter (D) or more of increase in two or more keratometry values in the cone area, or a decrease in corneal thickness of 10% or more at the thinnest point between 2 visits, minimum 6 months apart, based on our previous work.[3] When there is a low risk for progression along with a normal unaided vision, cross-linking is usually deferred. In such situations, patients are usually advised to avoid eye rubbing and additionally, certain medications that can lower the risk of progression can be used.

In KC, there is an increased oxidative stress and generation of reactive oxygen species leading to thinning of epithelium and stroma as evidenced by disintegration of the basal cell layers which are concentrated more at the cone region histologically and topographically.[2,6] Oxidative stress causes impairment in autophagy regulation, particularly in KC, playing a crucial role in the pathogenesis and progression of the disease. Trehalose is a disaccharide that has bioprotective mechanisms towards oxidative stress and inflammation.[7] In-vitro studies have revealed that Trehalose containing eye drops show good efficiency in maintaining normal cellular morphology and cell membrane function.[8] Trehalose is also known to regulate inflammation.[9] Loteprednol Etabonate 0.5% in tapering dose suppressed the inflammation in a short burst followed by longer term suppression of inflammation by the mild immunomodulation of trehalose.

On follow-up at 8 months, there was an increase in keratometry values in the steep meridian; 0.8D OD and 0.9D OS respectively from baseline suggestive of progression, based on Pentacam-HR. However, on a closer look at the comparison maps on MS-39, we were able to identify a significant epithelial remodeling and absence of any changes in the stromal or posterior elevations; this is typically indicative of a pseudo-progression of KC.

In cases of irregular astigmatism that is seen in KC, the epithelium has known to exhibit a compensatory mechanism.[9] Epithelial thickness changes have a masking effect on the true curvature of the irregular stromal surface. Previous studies have reported that it is possible to calculate the stromal surface shape by subtracting the epithelial thickness from the corneal front surface elevation data.[9] However, with the advent of the MS-39 topographer the stromal elevation can be mapped directly and compared over subsequent visits. Identifying the true cause of the increase in the keratometry values is essential. With an obvious epithelial thickening and no corresponding change in stromal and posterior elevation, the change in the keratometry can be attributed to epithelial remodelling, MS-39 comparative epithelial and stromal elevation maps play an important role in thus differentiating differentiating pseudo progression from true progression.

Conclusion

To the best of our knowledge, this is the first report differentiating pseudo from true progression. By delineating the epithelial change from the true change at the stromal surface, presence or absence of true progression could be defined.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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