Guest Editorial

Altered tear inflammatory profile in Indian keratoconus patients

Keratoconus is a progressive disorder characterized by thinning and ectasia of the central and paracentral cornea with a consequent increase in corneal curvature, irregular astigmatism, and loss of uncorrected and best-corrected visual acuity. The etiopathogenesis of the disease is poorly understood, and investigators have put forth several theories for explaining progressive stromal weakness and ectasia and included heredity, abnormality of corneal collagen, the role of keratocytes, corneal innervation, and inflammation.

Although the disease is classically described as a noninflammatory disorder investigators have evaluated inflammatory markers in keratoconus subjects.[1] Several aspects of the condition cannot be explained without considering inflammation as the basis of the disease and include:

- Why the disease occurs in late childhood or adolescence and young adults?
- What is the basis of the association between keratoconus and allergic eye diseases?
- How rubbing promotes progression of keratoconus?
- Why do we see stromal scarring even in patients not wearing contact lenses?

On the other hand, there are arguments against the inflammatory theory as well. We find it difficult to explain following questions based entirely on inflammation theory:

- Why thinning and ectasia are seen only in central or paracentral cornea? How peripheral cornea is spared despite being closer to the limbus and near vascular arcades?
- Why the rate of progression of the disease is slowed down with advancing age? Are there changes in or modulation of the inflammatory phenomenon with age?
- Is this derangement in the inflammatory control a local phenomenon or are these patients vulnerable to inflammatory diseases elsewhere in the body? What are triggers of this local inflammation?
- If it is generalized derangement, is collagen in other parts of the body also affected?

Despite these contradictions, inflammatory theory has been widely investigated. In a paper published in this issue,[2] investigators from Narayana Nethralaya evaluated levels of different inflammatory markers in tear film in patients with keratoconus and compared these with those in otherwise healthy individuals with no evidence of keratoconus or other inflammatory diseases. The authors hypothesized that altered collagen structure and consequent biomechanical weakening as well as deregulated epithelial and stromal proteins demonstrated in KC could be because of inflammation. The authors included levels of a variety of cytokines and chemokines including Interleukin-1 alpha (IL-1α), IL-1 β, IL-2, IL-4, IL-5, IL-6, IL-8, IL-9, IL-10, IL-12p70, IL-23p40, IL-13, IL-17A, IL-17F, IL-21, Interferon alpha (IFNα), IFNγ, CCL2/MCP-1, CCL4/MIP-1 β, MIP-1α, CCL5/RANTES, CXCL10/IP10, sICAM1, sCD62E/sE-selectin, vascular endothelial growth factor and transforming growth factor beta (TGFβ). The measurements were performed using cytometric bead array. The authors found significantly higher levels of inflammation-associated cytokines, chemokines, growth factors, and soluble cell adhesion molecules in tears of patients with keratoconus when compared with healthy control subjects. Earlier the same group as well as other investigators evaluated the role of the lysyl oxidase enzyme (LOX) and found reduced levels in patients with keratoconus.[3-6] LOX and other lysyl oxidase-like enzymes mediate formation of covalent bonds between collagen and elastin fibrils, which maintain the biomechanical properties of the cornea. Reduced activity of LOX enzymes might be potential reasons for the inadequate collagen cross-linking in keratoconus with consequent weakening and ectasia. It is also known that LOX enzymes (cyclooxygenase and lipoxygenase) also mediate biosynthesis of arachidonic acid-derived lipid mediators that are intimately involved in inflammation.

Based on these observations, it seems that inflammation plays an important if not the sole role in the pathogenesis of keratoconus.

This knowledge if substantiated by other investigators can be of great value. Some of these cytokines and chemokines can be developed as biomarkers for predicting the susceptibility of an individual to keratoconus thereby facilitating intervention much before the disease deteriorates the quality of vision or progresses to levels where only keratoplasty will be the treatment option.

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In conclusion, the work published by the authors is an important addition to our understanding of the pathogenesis of keratoconus. This knowledge has a potential for developing a biomarker for keratoconus and possibly a therapeutic strategy for preventing loss of vision in children and young adults.

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