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Editorial

Keratoconus: is it a Non-inflammatory Disease?

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Keratoconus has been recognized and investigated for more than 150 years (1). Historically, ophthalmologists have described keratoconus as a bilateral, progressive, non-inflammatory disorder of the cornea that is associated with corneal steepening and thinning (1,2). The Global Panel on Keratoconus and Ectatic Diseases recently stated that 'abnormal posterior ectasia, abnormal corneal thickness distribution and clinical non-inflammatory corneal thinning are mandatory findings to diagnose keratoconus (3).' Nevertheless, it is well established that keratoconus is characterized by a marked degradation of the corneal extracellular matrix involving inflammatory features such as increased levels of matrix metallopeptidase 9 (MMP-9), interleukin 6 (IL-6), and tumor necrosis factor alpha (TNF-αa), as well as increased oxidative stress (4,5). Moreover, patients with keratoconus have increased levels of inflammatory mediators in their tears, as shown in numerous studies (4-7).

The role of inflammation induced by eye rubbing, wearing contact lenses, and ultraviolet irradiation, is another aspect of the inflammatory nature of keratoconus (4). Eye rubbing is a proven risk factor for the development and progression of keratoconus, and it involves several pathways, including the stimulation of inflammation (8-9). The complex interactions between genetic predisposition and environmental trigger factors, (such as eye rubbing and wearing contact lenses) in the development of keratoconus probably represents the key to understanding the role of inflammation in the pathophysiology of keratoconus (10).

However, there are several enigmatic discrepancies impeding our understanding of the proposed 'inflammatory model' of keratoconus. Despite the evidence of inflammation accumulated from translational and laboratory studies, keratoconic corneas are strikingly lacking in the histological and clinical features of inflammation, such as cell infiltration and neovascularization. Moreover, the coexistence of ocular

allergic disease, which is very frequent among patients with keratoconus (to different extents in each individual patient) (2), potentially masks the true inflammatory effect underlying keratoconus, and differentiates its phenotype.

Whether or not the mere presence of inflammatory markers in keratoconic corneas is sufficient proof of inflammation remains controversial. Could these biochemical findings of inflammation represent epiphenomena, not primary pathophysiological events? Lastly, is it justifiable to classify keratoconus as a quasi-inflammatory or inflammatory-related condition, as suggested by McMonnies? Ongoing research may provide tools for further investigation of keratoconus-related inflammation and future studies may identify specific biomarkers that will enhance our understanding of the inflammatory condition involved in keratoconus, which will elucidate the etiopathological mysteries of keratoconus.

DISCLOSURE

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