Suggested Reference


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INTRODUCTION

Keratoconus is a debilitating corneal ectasia that principally affects young people in the second or third decade of their lives.

In recent years, there has been a large amount of literature published on keratoconus. However, most of this concerns the surgical management of patients with the disease, rather than exploring the mechanism of the disease process itself (for a review see Rabinowitz, 1998).

In a previous study (Sherwin et al., 2002), our group developed a novel approach to studying keratoconus, based on our observation that there is a gradient of damage between the central (most damage/heaviest) and peripheral (least damaged) regions of the keratoconic cone. We hypothesised that the peripheral parts of the cone exhibited the earliest morphological and biochemical signs of keratoconic pathogenesis.

In this current study we aim to use immunohistochemical techniques to dissect the cellular and molecular pathogenesis of keratoconus, and in particular explore how these observations fit the mechanisms of wound healing and matrix remodeling known from studies of other connective tissues.

METHODS

In this study, we examined keratoconic buttons removed at transplantation, together with normal human corneas obtained via the New Zealand National Eye Bank that could not be used for transplantation. A central limbal transection was taken from the normal cornea, followed by a limbus from the keratoconic button, along with the keratoconic button. Corneal pieces were labelled and fixed with the fluorescent viability probe S-chloroethylmyruthonium diacetate (CellTracker-Green), then cryosectioned anterior-posteriorly. Sections were immunohistochemically labelled with a panel of antibodies, including: - Antibodies: - Collagen Type VI (R & D), - Collagen Type IV (Abcam), - Fibronectin (Abcam), - Vimentin (Abcam), - Desmin (Abcam), - Ki67 (Abcam), - Phospho-Histone H3 (Abcam), - Ki67 (Abcam), - Phospho-Histone H3 (Abcam).

RESULTS

Cross-sections of the keratoconic corneas showed a gradient of increasing damage, from normal at the periphery to scarred at the apex. There were discrete disruptions of the cellular processes from the anterior keratocytes in association with localised indentation of the basal epithelium, and increased levels of Collagen Type VI and Collagen Type IV in keratoconic keratocytes compared to normal keratocytes. Bowman’s layer, and also deeper in the stroma. Keratocytes were often seen between the stroma and epithelium at sites of early degenerative change. Anterior keratocyte nuclei were seen edging around the nerves, as they pass through Bowman’s layer, and in more compromised tissues keratocytes existed higher levels of Collagen Type IV and Collagen Type VI, and were displaced anteriorly into the epithelium. In the most damaged parts of the cone, nerves that pertain to the area seen within the epithelium, which expressed very high levels of Collagen Type VI, and appeared to be very destructive to the cornea.

CONCLUSIONS

These observations of keratoconic disease pathogenesis and progression correlate well with the processes of scar healing and extracellular matrix remodeling known from studies of a range of connective tissues including the cornea. Future studies are required to determine how well the processes of keratoconic pathogenesis and progression fit the details of this model.

REFERENCES


