THE ROLE OF ANTI-VEGF IN MANAGMENT OF PTERYGIUM

Essay

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List of Abbreviations

AMP: Adenosine monophosphate
ARMD: Age related macular degeneration
ATP: Adenosine triphosphate
CAG: Conjunctival autograft
CLAG: Conjunctival limbal autograft
DNA: Deoxyribonucleic acid
FDA: Food and drug administration
FGF-2: Fibroblast growth factor- 2
GAC: Glycosaminoglycan
HMP: Hexose monophosphate
HPV: Human papiloma virus
IL: Interleukin
MMC: Mitomycin C
MMPs: Matrix metalloproteinases
PDGF: platelet derived growth factor
RNA: Ribonucleic acid
TCA: Tricarboxylic acid
TGF- β: Transforming growth factor beta
TNF-a: Tumor necrosis factor alpha
TSP-1: Thrombospondin-1
USA: United States of America
UVR: Ultraviolet radiation
VEGF: Vascular endothelial growth factor

Introduction

A pterygium is an elevated, superficial, external ocular lesion that is formed over the perilimbal conjunctiva and extends onto the corneal surface.[1] It is a common disorder of the ocular surface, with a prevalence of 2% in temperate areas and up to 20% in tropical regions.[2]

The pathogenesis behind its formation is not fully understood. Various studies have implicated environmental factors, such as ultraviolet light, chronic irritation, and inflammation. Recent studies have also provided evidence implicating genetic components, antiapoptotic mechanisms, cytokines, growth factors, extracellular matrix remodeling, immunological mechanisms, and viral infections in the pathogenesis of the disease.[3]

Immunohistochemistry studies show that immunostaining of VEGF is more intensive in pterygial sections than in normal conjunctival sections. Decreased angiogenic inhibitors, together increased stimulators, have been hypothesized as playing roles in the formation and progression of pterygia.[4]

Surgical excision of pterygium is generally essential when the visual axis is threatened and/or the pterygium causes severe irritation or cosmetic problems.[5]

The primary aim is to excise the pterygium and prevent its recurrence. As bare sclera excision is associated with a high recurrence rate, pterygium excision is often combined with conjunctival autograft, mitomycin C, beta-irradiation, or other adjunctive therapies to reduce recurrence rates.[6]

Anti-VEGF treatment has shown great promise in other ocular neovascular diseases and potentially has a significant role in inhibiting fibroblastic and neovascular proliferation that promotes pterygium growth and recurrence.[7]

Aim of the Study

The aim of this study is to highlight the role of anti-VEGF drugs in the management of pterygium.

Anatomy Of The Cornea

Gross Anatomy:

A healthy cornea, together with the overlying tear film, is necessary to provide a proper anterior refractive surface and to protect the eye against infection and structural damage. In the adult, the average horizontal diameter is 11.5-12 mm and about 1.0 mm larger than the vertical diameter. The shape of the cornea is prolate, being flatter in the periphery and steeper centrally, which creates an aspheric optical system.[8]

Microscopic Anatomy

The cornea consists of five layers, the epithelium, Bowman's layer, the substantia propria, Descemet's membrane and the endothelium.[9] (Fig.1)

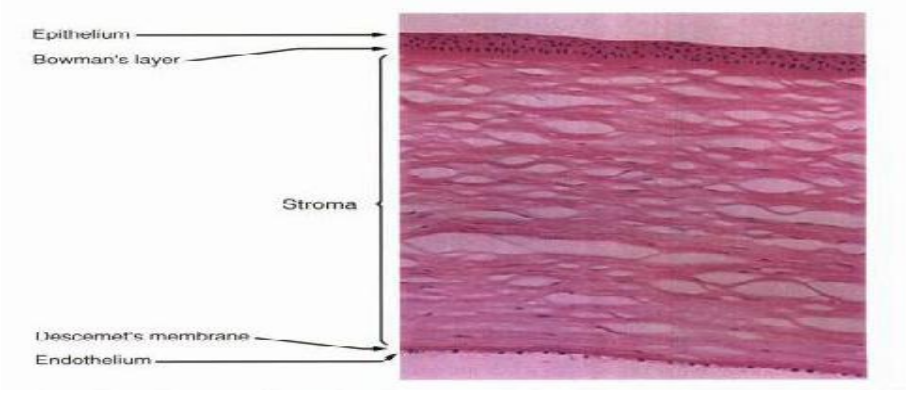

Fig. 1: Microscopic Anatomy of the cornea.[8]

Epithelium: It is composed of nonkeratinized, nonsecretory stratified squamous epithelium.[8]

It is typically several cell layers thick, consisting of the apical squamous cell layer, the multilayered, polygonal-shaped wing cells beneath the apical layer, and the posterior-most layer basal cells (Fig.2).

Apical surface cells appear broad and flattened, freshly emerged surface cells appear bright during specular microscopy and have relatively small numbers of microvilli covering their apical membrane. The margins of the apical cell membrane possess the important tight junctions surrounding the cell circumference near the apical margin. The lateral and basal membranes of the apical cells have gap junctions, numerous desmosomal junctions, and numerous membrane-bound vesicles.

Wing cells are distinguished by a variety of polygonal shapes and by their large ovoid nuclei. The cells are roughly 12 to 15µm in diameter, and their cytoplasm contains few rough endoplasmic reticulum, mitochondria, or Golgi's complexes.[10]

Basal cells appear as elongated polygonal cells approximately 10µm in width and 15 to 20µm in height, with prominent ovoid nuclei. [11] They possess lateral intercellular junctions characterized by being gap junctions and zonulae

adherens,[8] the basal membrane is notable for the presence of hemidesmosomes.[10]

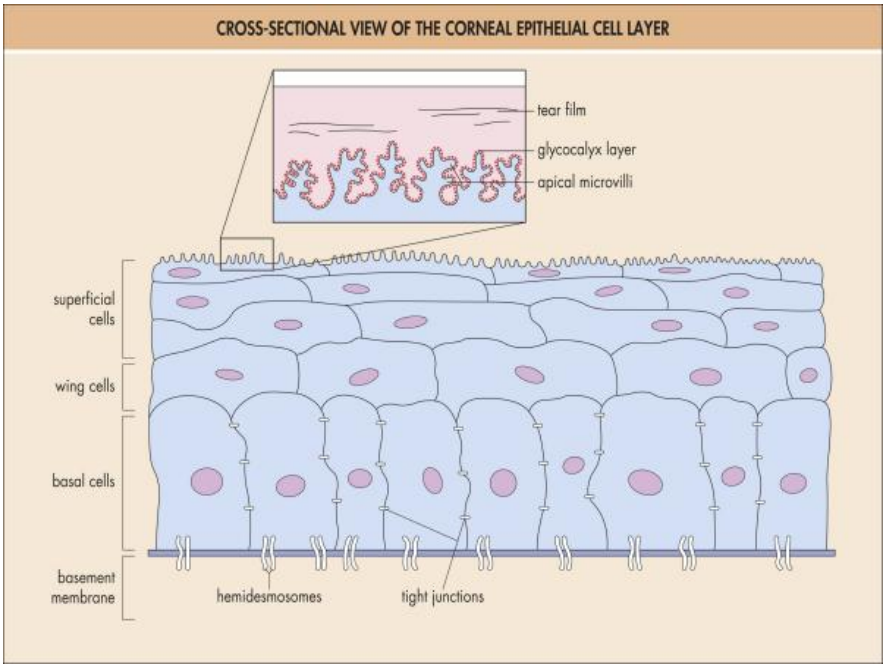

Fig. 2: Cross-sectional view of the corneal epithelial cell layer.[8]

Bowman's Layer: Bowman's layer lies immediately beneath the basement membrane of the corneal epithelium. It measures about 8 to 12 µm in thickness. It is acellular and consists of interwoven collagen fibrils embedded in intercellular substances. Electron microscopy reveals its collagen to be finer and more randomly arranged than that in the substantia propria. Bowman's membrane ends abruptly at the limbus. Its deep surface merges into the substantia propria.[9]

Stroma: The stroma is composed predominantly of type I collagen with types III, V, and VI also in evidence.[10]

It is estimated that there are about 200 to 250 flattened lamellae, each of which is 2 µm thick. The direction of the collagen fibrils in any given lamella is the same, but they run at right angles to those of adjacent lamellae. The collagen fibrils measure between 21 and 65 nm in diameter.[9]

After collagen, proteoglycans are the second most abundant biological constituents of the cornea, constituting approximately 10% of the dry weight of the cornea. Proteoglycans are glycosylated proteins with at least 1 glycosaminoglycan (GAG) chain bound to the protein core. GAGs are composed of repeating disaccharides, The GAGs found in corneal stroma include Keratan sulfate, Chondroitin sulfate and Dermatan sulfate.

Matrix metalloproteinases (MMPs), a family of Zn^{2+} - dependent enzymes, are responsible for degradation of the components of the extracellular matrix (including proteoglycans and various types of collagen) during normal development as well as in disease processes. Of more than a dozen known metalloproteinases, only MMP2 proenzyme has been found in the healthy cornea.[12]

Keratocytes: The lamellar stroma is secreted and maintained by the stromal fibroblasts, commonly termed

Keratocytes. Keratocytes are flat, with many long attenuated processes, extending from a central cell body in all directions, the tips of the processes touch processes of adjacent cells forming gap junctions (Fig.3). Thus, cells of the stroma form a network of coupled cells. The cytoplasm of the stromal fibroblast is rich in rough endoplasmic reticulum and golgi apparatus, in keeping with its function as the synthesizer and maintenance cell of the stromal lamellae. Recent data suggest that the stroma also houses a relatively high number of bone marrow derived cells.[13]

Descemet's membrane: Descemet's membrane is a 10-µm-thick specialized basement membrane present between the endothelium and posterior stroma. It is secreted by endothelium and is constituted of an anterior banded portion and a posterior nonbanded portion (Fig.4). Type IV collagen is the most abundant collagen in Descemet's membrane.[12]

Endothelium: The human corneal endothelium is a single layer of 400,000 to 500,000 cells. Cells are 4 to 6 µm in height and 20 µm in width, and their posterior surfaces are predominantly hexagonal when viewed under specular microscopy.[10]

A group of tight junctions forms the junctional complex that occludes the lateral extracellular spaces from the aqueous humor. [12]