NEW VIEWS ON THE PATHOPHYSIOLOGY OF PTERIGIUM

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https://doi.org/10.5281/zenodo.10690913
Keywords: pathophysiology, pterygium, surgical removal.
Abstract: Pterygium is a relatively common disease of the eye surface. Its clinical aspects and treatment methods have been studied for many years, but there are still many uncertainties, as in other diseases. The main pathological mechanisms in the development of pterygium remain interesting to researchers. In addition to the refractive properties of pterygium removal, the role of pterygium in corneal disorders is increasingly recognized in many studies. The association between pterygium and ocular surface neoplasia challenges traditional notions of the safe profile of this disease. The need for a comprehensive clinical classification system has helped to homogenize studies and predict the frequency of recurrence of pterygium after surgical removal. The development of surgical techniques is associated with some complications, the diagnosis and treatment of which are essential for ophthalmic surgeons. According to the review, ultraviolet radiation remains the main risk factor for the development of pterygium. A key part of the clinical evaluation should be to distinguish between typical and atypical pterygium, the latter of which may be associated with increased risk of ocular surface neoplasia. The effect of the pterygium on astigmatism and corneal aberration may require early removal to reduce secondary refractive errors.

Pterygium (also known as surfer's eye) is a disease of the ocular surface characterized by wing-like growths of the limbal and conjunctival tissues, mainly on the cornea. As a result of changes in the local homeostasis of the ocular surface, the main components of the pterygium include the proliferative accumulation of limbal stem cells (LO'H), epithelial metaplasia, active fibrovascular tissue, inflammation of Bowman's layer and the formation of the pterygium apex. includes invasive disorder.[1]Because experimental models do not cause pterygium formation in animals, pterygium is an eye disease that only occurs in humans.[2]Although this eye disease has been known for many years, many studies on the pathophysiology and treatment of pterygium have not resolved the main doubts about this common ocular surface disease.

Epidemiology

The prevalence of pterygium ranges from 1% to more than 30%, depending on the population studied.[3-7]According to a meta-analysis of 20 studies published in 2015, the overall prevalence of pterygium is approximately 10%.[8]The highest prevalence of pterygium was reported in a study of Chinese rural population, where it was 33%.[9]

Risk factors for pterygium include age,[3,4]male gender,[10,11]outdoor experience,[3,12]low education level,[5]living in the countryside[11]low income[5]skin color[3 of them]and smoking were recorded.[5]In a North American study, the prevalence of pterygium was reported to be 2.5 to 3 times higher in blacks than in whites.[3]Despite its worldwide distribution, pterygium is most commonly found around the equator at 40° latitude.[13]It turned out that the prevalence of

pterygium in this area is 10 times higher than outside it,[this]strongly supports the role of ultraviolet (UV) exposure in the pathogenesis of pterygium.

Histopathology

Epithelial cells of the pterygium

The main histological findings in the pterygium specimen include the growth of pterygium epithelial cells with proliferative properties, squamous metaplasia, goblet cell hyperplasia, collapsed Bowman's layer, stromal fibroblasts and vessels, altered cellular extratricular cells (multilayered cells). fibers and inflammatory infiltration.

The discovery of pterygium cells and their migratory and proliferative abilities revolutionized the traditional understanding of pterygium pathogenesis. For a long time, the development of pterygium was thought to be the result of two consecutive events in the limbal region: (1) primary disruption of the limbal barrier due to chronic exposure to ultraviolet radiation and (2) and subsequent proliferation of conjunctival tissue and blood vessels; and inflammatory cells on the adjacent cornea as a result of an active process called conjunctivalization.[19]It is believed that the process of conjunctivalization occurs along the entire length of the grown tissue of the pterygium, from the head to the body. However, the results of subsequent studies did not agree with the previous impressions. Bai and colleagues[20] demonstrated the spatial presence of proliferating stem cells over the pterygium tissue. Epithelial cells with proliferative markers such as p63 and CK15 were found to be located over the head of the pterygium, while these factors were absent over the limbus. In addition, PAX6 predominates in the head region, while matrix metalloproteinases (MMPs) 2 and 9 are located just above the edge of the head.[20]These topographical data indicated the migratory front and proliferative capacity of LSCs located at the head of the pterygium, acting as a proliferative battery for progressive growth and acting as a migratory force through MMP-induced degradation of the ECM. In accordance with this spatial divergence, the head of the pterygium, with its altered LBFs, is now believed to be responsible for the pathogenesis of pterygium, and the pathological events cannot be justified solely by limbal barrier defects and conjunctivalization.[20]The decisive factor for the initiation of pterygium is not simple limbal deficiency, but limbal reorganization through the formation of pterygium cells. This rearrangement is thought to be due to damage caused by UV radiation or genetic predisposition. In addition to pterygium cells, cytology of the surface cell population in the pterygium specimen revealed a characteristic feature of the pterygium surface: squamous metaplasia associated with an increased goblet cell population.[23]

Squamous metaplasia results from a wide range of ocular surface disorders, including dry eye syndrome and vitamin A deficiency.24 It is abnormal[keratinization]characterized by stratified epithelial cells associated with At the cellular level, squamous metaplasia is manifested by flattening and enlargement of surface epithelial cells and pyknotic changes in cell nuclei.[24]Squamous metaplasia has been reported in more than 70% of pterygium cases,[23]and this has led some authors to suggest a link between pterygium and dry eye syndrome.[25,26]Another sign observed in about 50% of cases is pigmentation of the epithelium.[22]The presence of pigment deposits can be confirmed by exposure to ultraviolet radiation.

Etiology and risk factors

Previous studies have shown that many risk factors are associated with pterygium, including UV exposure,[30,31]environmental irritants such as dust and wind,[13]viral agents,[32,33]family and genetic factors,[34]as well as immunological and inflammatory factors.[35,36]

Other risk factors suggested in recent studies include transcription factors, cAMP response element-binding protein,[37]phospholipase D,[38]cytochrome P450 protein 1A1,[39]and possibly aquaporin-1 and aquaporin-3.[40]Despite the recent increase in our knowledge about the role of various factors in the pathogenesis of pterygium, exposure to sunlight remains the most important risk factor for the occurrence and development of pterygium.

Ultraviolet radiation

The relationship between the development of pterygium and UV exposure can be determined on the basis of many epidemiological studies.[41]The "Pterygium Zone" has been described as an area from 40° north to south of the equator where high intensity UV radiation affects the population of the region.[42]The similarity between the histopathological findings of UV-induced skin damage and pterygium supports this idea.[43]In addition, the susceptibility of the nose to pterygium is known to be associated with a 20-fold increase in exposure of the nasal limbus, making this area more vulnerable to UV damage and pterygium development.[13,44]

UVA and UVB are the main subtypes of the sun's UV rays that reach the surface of the eye. Although early studies focused on the role of UV-B in DNA damage and changes in intracellular signaling in ocular surface diseases, epidemiological studies have shown that both UV-B and UV-A are associated with the development of pterygium. By inducing reactive oxygen species, UVA indirectly causes DNA damage and activation of transcription factors that regulate the expression of several genes involved in ECM changes.[45,46]

[16,47]altering stromal fibroblast function,[17]or can lead to the development of pterygium by provoking inflammatory reactions.[48]Among them, inflammatory reactions may be the least important.[49,50]A two-step hypothesis has been proposed for the role of UV in pterygium development; the initiation of the process depends on LSC damage and the formation of pterygium cells, and the progression occurs due to the disruption of the limbal barrier, the increase in the level of inflammatory cytokines and the production of growth factors and MMPs.[42]

UV exposure is also responsible for the abnormal behavior of pterygium fibroblasts. These fibroblasts were found to be more proliferative than normal conjunctival stromal cells.[17]They can colonize in culture media, require less exogenous growth factor for activation, and are characterized by elongated nuclei and irregular nuclear pores in electron microscopy.[56,57]Three different pathways have been proposed for the activation of pterygium fibroblasts by UV exposure: (1) they can be directly damaged by UV radiation through multiple DNA alterations; (2) UV-modified LSCs can activate primary fibroblasts through a mechanism dependent on transforming growth factor-β (TGF-β) and fibroblast growth factor (β-FGF);[52]or (3) injury to conjunctival endothelial cells may alter stromal fibroblast metabolism, manifested by changes in the expression of collagen and elastin fibers.[58]Although it is believed that ultraviolet radiation plays a major role in the formation of pterygium fibroblasts, there are conflicting opinions on this matter.[59,60]These hypotheses may question the role of UV in pterygium fibroblast changes.

Finally, UV-induced inflammation and tissue remodeling are involved in the pathogenesis of pterygium. Many studies report elevated levels of inflammatory cytokines, growth factors, and

MMPs in the pterygium.[43,61] In vitro experiments showed that the proliferation of these factors in pterygium cells was induced by ultraviolet radiation.[42] UV-induced changes in limbal stem cells induce the production of numerous inflammatory factors and MMPs, which promote inflammation, angiogenesis, and pterygium invasion. Similarly, UV-activated pterygium fibroblasts produce high levels of growth factors and extracellular enzymes that facilitate pterygium invasion by remodeling the ECM and dissolving Bowman's layer.[42]

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