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Research Article

Is Injury an Important Risk Factor for the Development of Black Cornea? (Corneal Malignant Melanoma)

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Abstract

Primary Malignant melanoma of the cornea is extremely rare tumor. Cornea is avascular structure and lacks melanocytes. The presence of melanocytes in the cornea is always pathological. Corneal injury has significant role of this pathological melanocytes presence in the corneal tissue.

We reviewed the literature to find out the role of ocular injury in patients with primary malignant melanoma of the cornea.

Our finding of this case reports and literature review was highly supportive that history of previous ocular injury with corneal epithelium breach and melanocytes implantation at the time of injury, could be the only identifiable risk factor for the development of primary malignant melanoma of the cornea.

We recommend that any patient with the history of corneal injury with corneal pigmentation should be regularly followed up with the high index of suspicion of malignant change.

Keywords: *Malignant Corneal Melanoma; Corneal Injury; Black Cornea*

Introduction

Cornea is an avascular structure and has three functionally distinct layers, the two limiting membranes (epithelium and endothelium) and a tough dense, avascular and relatively acellular collagenous connective tissue, the stroma. Stroma is sandwiched between Bowman`s layer under the epithelium and Descemet`s membrane above the endothelial layer [1,2].

Cornea gets its nourishment from nutrients diffused through the tear film and from the aqueous humour and additionally from the neurophins supplied by the nerve fibers innervating the cornea. Most of the oxygen supply is through the oxygen dissolved in the tears that diffuses throughout the cornea to keep it healthy and partly from the aqueous humour.

Corneal tissue has a unique characteristic that makes it less prone to primary malignancies and lack of vascularity makes it less prone to secondary malignancies.

Melanocytes are derived embryologically from neural crest cells located predominantly in the skin, but can also be found in the eyes, ears, gastrointestinal tract and leptomeninges, oral and genital mucosa.

The corneal tissue is not rich in melanocytes therefore primary melanoma of the cornea is extremely rare. Presence of melanocytes in the cornea is always pathological. Very few cases of Primary Malignant Melanoma of the cornea have been reported in the literature and the history of ocular injury was the single most common reported finding. The likelihood of melanocytes presence in the cornea after ocular injury is either due to direct implantation of melanocytes at the time of ocular injury or encroachment from the surrounding structure like conjunctiva and sclera or on exposure to chemicals or sunlight [3-9].

Melanoma is malignancy of melanocytes (pigment producing cells). Most reported cases of primary corneal melanoma had history of corneal epithelium breach after the ocular injury [4,6-8,10,11].

Methodology

We reported the case of Malignant Melanoma after industrial injury [4]. Our patient like other reported cases in the literature with Primary Malignant Melanoma of the Cornea had a history of corneal injury. We thought the corneal injury has a very strong relationship with the development of primary Malignant Melanoma of the cornea.

We did the systematic review of the literature to confirm the importance of corneal injury as a risk factor for development of Primary Corneal Malignant Melanoma and also to ascertain the mechanism involved by which Melanocytes migrate into corneal tissue abnormally and how they develop this malignant change as corneal tissue is not the usual structure for the melanocytes to be present.

Results

There are scattered cases of Primary Malignant Melanoma of cornea reported in the literature. Almost all the reported cases had previous history of injury to the cornea before they developed malignant change in their cornea. The important thing to note is that all the patients with history of corneal injury had corneal epithelial breach suggestive of possible deposition of melanocytes into the corneal tissue at the time of injury. These melanocytes were abnormally deposited in the cornea at the time of injury and subsequently develops malignant change over time due to possible exposure to chemicals at the time of injury and sun rays [4,6-8,10,11].

However, it is difficult to ascertain how these melanocytes reach the corneal tissue after ocular injury and how they develop mutations that leads to malignant change in these melanocytes. There are certain theoretical risks of presence of abnormal melanocytes in the corneal tissue after ocular injury.

One of the theories is that Melanocytes deposition in the corneal tissue mostly occurred due the direct implantation of melanocyte into the cornea tissue from the surrounding ocular tissue or remotely from the skin, at the time of injury. It is prudent for this melanocytes deposition, that the breach in corneal epithelium should be present which is only possible with injury involving the corneal tissue [4,6-8,10,11].

The possibility of origin of primary melanoma from the melanocytes migrating at the time of initial injury from the surrounding structures of the cornea into the inflammatory pannus post injury cannot be ruled out [4,10].

Although the importance of corneal injury involving the epithelial breach as the only known contributing risk factor for the corneal malignant melanoma due to abnormal deposition of melanocytes cannot be ignored but the possibility of primary conjunctival melanoma spreading to the cornea and primary malignant conjunctival melanoma without initial conjunctival involvement and growing onto the cornea i.e. corneally displaced malignant conjunctival melanoma, cannot be excluded as a risk factor for these tumours [7,9,12].

The major contradictory factor to this possible pagetoid spread from the conjunctiva is that, mostly reported had a strong history of corneal injury and histological findings suggest that main factor involved is corneal injury.

Pathophysiology and cell histology

Corneal epithelium and sub epithelial tissue lacks melanocytes but Higa., *et al*. found in their study that Melanocytes can exits in the normal human corneal epithelium as sporadic cells with dendritic processes that extend to surrounding epithelial cells from the limbus of the human cornea [13].

Most of the reported cases had histological evidence of sub epithelial and intraepithelial spread of the Malignant Melanoma of the cornea suggestive of confinement of malignant corneal melanoma to the area of initial deposition of melanocytes from external structures at the time of epithelial breach. These abnormal melanocytes later spread into the corneal structures if left untreated by forming extensions. This important finding excludes the possibility of this melanocyte origin from the cornea itself [4,6,11,14,15].

The amount of melanin pigment in the tumour cells, macrophages and extracellular matrix has a direct relation with the degree of pigmentation in melanomas [16].

A corneal malignant melanoma may vary in its appearance from nodular to flat and from amelanotic to pigmented. There could be a possibility to isolate the origin of these abnormal melanocytes in future by comparing the structural characteristics of these cells with surrounding melanocytes [4,6,17-19].

Epithelioid type melanoma cells are most common cell type seen in the histological sections of Corneal Melanomas and are found singly or in clusters, scattered throughout the epithelium. The other common cell type is a spindle type melanoma cell [4,15,19-21].

Discussion

The cornea is a transparent tissue. Cornea contributes significantly towards Refraction of the eye and has important barrier function. The corneal epithelium serves as the principal barrier to fluid and pathogens, and this function of cornea is through production of tight junctions between the epithelial cells and constant repopulation through differentiation and maturation of dividing cells in epithelium basal cell layer [22].

After detailed review of the literature we found that history of previous ocular injury with breach in corneal epithelium, as the only identifiable risk factor contributing towards extremely rare primary malignant melanoma of the cornea [4,6-8,10,11].

The most likely explanation for these melanocytes to be present abnormally within the corneal tissue is either direct implantation or migration of melanocytes within the inflammatory pannus from the surrounding melanocyte source such as limbal conjunctiva or conjunctiva itself.

It is possible that these abnormal melanocytes develop mutation over period of time after initial implantation and convert to malignant melanoma, possibly due to slow chronic and recurrent inflammation after ocular trauma [8].

Interestingly most of the histological sections of corneal melanoma showed, tumour confinement and spread to sub epithelium and intraepithelial region of the cornea. The cornea is devoid of melanocytes and for the implantation of these abnormally located melanocytes into the corneal intraepithelial or sub epithelial region breach in epithelium is required as its impossible for melanocytes to penetrate the intact corneal epithelium.

Although chronic inflammation seems to have a significant role but the likelihood of this malignant change in these abnormally located melanocytes can be multifactorial and may involve exposure to chemicals, sunshine or indoor tanning [4,5,8,10,11,23,24].

Conclusion

From this intensive but limited literature review due to rarity of Malignant Melanoma of cornea, we conclude that corneal injury involving breach in the corneal epithelium is important risk factor for melanocytes deposition in the corneal tissue and later mutation into primary malignant melanoma of the cornea but further research is warranted.

We recommend that any patient with pigmentation of cornea after ocular injury should have regular follow up with high index of suspicion of malignant change especially in patient with any change in the characteristics of these corneal pigmented lesion keeping in mind previous history of ocular trauma if present.

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