Pigmented epithelial tumours of the conjunctiva

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Abstract
Two out of 60 conjunctival epithelial tumours reviewed between 1973 and 1989 were found to be pigmented. One tumour was a pigmented papilloma and the other a pigmented squamous cell carcinoma. The melanin pigment was found in epithelial tumour cells as well as in macrophages, dendritic melanocytes, and Langerhans cells. The distinction between the latter two types of cells was possible in one of the tumours only. Both tumours were found in dark-skinned white patients without any evidence of conjunctival acquired melanosis.

Both benign and malignant tumours of the cutaneous surface of the eyelid (for example, basal cell carcinoma, seborrhoeic keratosis, etc), at times become pigmented as a result of melanin ingestion.1,4 However pigmented epithelial tumours of the conjunctiva, especially in white patients, are rarely encountered.5,6 This finding is attributed mainly to the paucity of melanocytes in the epibulbar conjunctiva.

We present two cases of pigmented conjunctival tumours found in dark-skinned white patients. These tumours represent 3-33% of all conjunctival tumours examined histologically in the past 16 years in the Pathology Department of the Beilinson Medical Center.

Materials and methods
All the conjunctival tumour biopsies performed in the Eye Department at the Beilinson Medical Center between the years 1973 and 1989 were reviewed by two pathologists and their haematoxylin-eosin stained slides were re-examined. These epithelial tumours included those excised from the bulbar, limbal, caruncular, fornix, and palpebral conjunctiva and were either benign or malignant. When melanin pigment was found in the tumour bleached sections were examined in order to confirm the true nature of the pigment. Additionally immunohistochemically stained slides for S-100 protein were reviewed. Electron microscopic specimens were examined in one case only.

Results
The breakdown of the total series of 60 conjunctival epithelial tumours is presented in Table 1. Among these epithelial tumours only two (3-33%) were found to be pigmented. One tumour was a pigmented squamous papilloma and the other a pigmented squamous cell carcinoma (SCC). The two cases are presented.

CASE 1
A 65-year-old dark-skinned white male presented with a pigmented conjunctival tumour in his right eye increasing in size over a period of 8 months. His visual acuity was 6/6 in both eyes and the intraocular pressure was normal. Slit-lamp examination revealed a dark-brown coloured, cauliflower-like, exophytic conjunctival tumour abutting the right limbus (Fig 1). There was no evidence of melanosis in the whole conjunctival surface. The skin of both eyelids was completely normal. The tumour was excised and light microscopy revealed an exophytic conjunctival tumour consisting of epithelial cells with marked atypia, pleomorphism, large prominent nucleoli, and melanin-filled dendritic cells (Fig 2). Many atypical keratinocytes contained large amounts of cytoplasmic melanin (Fig 3). According to the electron microscopic examination melanin was also found in macrophages as well as in Langerhans cells and dendritic melanocytes. The Langerhans cells were identified by electron microscopy by the finding of 'Birbeck' granules in their cytoplasm; they were also found to be S-100 positive as were the melanocytes.

Additionally many dyskeratotic cells, mitotic figures, and areas of marked acantholysis were noted in light microscopy. In several areas tumour cells were seen beyond the epithelial basement membrane. The diagnosis of completely excised conjunctival pigmented SCC was made. A 4-year follow-up showed no evidence of metastasis.

Table 1 Conjunctival epithelial tumours (1973–89)

<table>
<thead>
<tr>
<th>Tumour Type</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>Papilloma</td>
<td>42 (70%)</td>
</tr>
<tr>
<td>In situ SCC</td>
<td>3 (5%)</td>
</tr>
<tr>
<td>Epithelial dysplasia</td>
<td>8 (13.3%)</td>
</tr>
<tr>
<td>SCC</td>
<td>5 (8.33%)</td>
</tr>
<tr>
<td>Pigmented</td>
<td>2 (3.33%)</td>
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</tbody>
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Figure 1 A brown coloured cauliflower-like conjunctival tumour abutting the limbus.
Pigmented epithelial tumours of the conjunctiva

Figure 2. An epithelial tumour consisting of pleomorphic atypical cells with large nuclei and prominent nucleoli; several melanin-filled dendritic cells are noted (arrows) (haematoxylin and eosin, magnification ×270).

Figure 3. Melanin pigment is noted within keratinocytes (arrow), macrophages, and dendritic cells (arrowhead), present among the epithelial tumour cells (haematoxylin and eosin, magnification ×270).

Figure 4. A dark-brown coloured cauliflower-like pedunculated conjunctival tumour protruding from the inferior fornix.

Figure 5. Giant dendritic cells filled with melanin pigment (arrow) are seen among the tumour epithelial cells in which no melanin is found (haematoxylin and eosin, magnification ×270).

CASE 2
A 22-year-old dark-skinned white male noticed a dark-coloured mass in the inferior fornix of his right eye increasing rapidly in size over the past 4 months.

In addition his visual acuity was 6/6 and the intraocular pressure was normal in both eyes. The slit-lamp examination of the right eye revealed a cauliflower-like, darkly pigmented, pedunculated tumour protruding from the conjunctiva of the inferior fornix (Fig 4). There was no evidence of melanosis in the whole conjunctival surface. The skin of both eyelids was completely normal. The anterior and posterior segments of both eyes were found to be normal.

The tumour’s pedicle was excised and light microscopy revealed a conjunctival papilloma consisting of basaloid non-keratinised squamous epithelial cells. Many melanin-filled dendritic cells, some of them being very large, were noted lying in between the tumour cells (Fig 5). These dendritic cells were found to be S-100 positive following immunohistochemical staining (Fig 6). However we could not differentiate between melanocytes and Langerhans cells, either by electron microscopy or by immunohistochemical staining for HLA–DR, as the whole tumoural tissue was primarily fixed in formalin.

It should be noted that there were no tumour cells containing melanin pigment. The diagnosis of completely excised pigmented squamous papilloma of the conjunctiva was made.

Discussion
Pigmented tumours of the conjunctival epithelium are generally a rare finding. In blacks they are usually associated with racial conjunctival melanosis. SCC arising from the ocular mucous membrane are well known in man and cattle. There are considerable geographical variations in the incidence of SCC of the conjunctiva. This tumour appears to be more common in African countries than in other parts of the world. Most SCC of the conjunctiva and cornea are non-pigmented. Duke-Elder states that surface ulceration of SCC may lead to haemorrhages which colour the tumour almost black. This should be differentiated from pig-
melanocytes. In contrast we could hardly find any tumour cells containing melanin pigment in our papilloma case; melanin was mainly found in either dendritic melanocytes or Langerhans cells, which unfortunately could not be distinguished from each other. The conclusion drawn from our study is that pigmented tumours of the conjunctiva rarely develop in whites, but they are found in dark-skinned patients but are not associated with conjunctival melanosis. These tumours may cause clinical diagnostic problems as they can be confused with the more common pigmented conjunctival lesions such as malignant melanoma, naevoid naevus, or primary acquired melanosis undergoing malignant change.

We wonder about the association between the melanocytes, melanin-filled Langerhans cells, and these pigmented epithelial tumours as clinical evidence of melanosis surrounding the tumours was not found. We have no other explanation for this association other than the pre-existence of these two types of cells among the epithelial cells which are the progenitors of the tumour cells. The embryonal origin of these cells is totally different; Langerhans cells are thought to be of bone marrow origin and melanocytes of neural crest origin, while conjunctival epithelial cells are of ectodermal origin. The relationship between these two types of dendritic cells and the epithelial tumour cells is yet to be studied.


Figure 6  S-100 positive dendritic cells (arrows) are noted between the epithelial tumour cells (immunoperoxidase staining for S-100 protein; magnification ×270).