

# Primary Conjunctival Pigmented Basal Cell Carcinoma with Increased Numbers of Intra-Tumour Melanocytes, Mimicking Melanoma: A Case Report and Review of the Literature

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## Established Facts

- Basal cell carcinoma (BCC) is a common eyelid skin tumour that can arise very rarely from the conjunctiva.
- The pigmented variant of BCC accounts for 6% of skin BCCs but has never been reported in the conjunctiva.

## Novel Insights

- This is the first report of a pigmented BCC of the conjunctiva, mimicking a conjunctival melanoma.
- The pigmented BCC showed prominent melanocyte hyperplasia, melanophages and tumour cell cytoplasmic melanin.
- Pigmented BCC should be considered in the differential diagnosis of pigmented, non-melanocytic tumours of the conjunctiva.

## Keywords

Pigmented basal cell carcinoma · Conjunctival melanoma · Conjunctival non-melanocytic pigmented tumours · Basal cell carcinoma

## Abstract

A 60-year-old, South-Asian male patient presented with a dark brown lesion on his left conjunctiva surface near the

limbus for 2 years. Examination showed a globular, dark brown-coloured mass near the temporal limbus at 4 to 5 o'clock position, measuring 3 × 3 × 2 mm. There were a few scattered flat pigmented lesions near the mass and also a few prominent vessels. The mass underwent wide local excision, with a clear margin, followed by double freeze cryotherapy of the conjunctival margins along with the application of Mitomycin C. The bare sclera was covered by amniotic membrane. Histology surprisingly revealed a nodular

basal cell carcinoma (BCC) containing melanin. The melanin was present in the tumour cell cytoplasm, within melanophages and within dendritic, Melan A-positive melanocytes. The BCC was immunohistochemically positive for BerEP4 and negative for EMA. The clinically observed smaller nodules flanking the main pigmented BCC corresponded histologically to pigmented superficial growth pattern BCC connected to the under surface of the conjunctival epithelium. This is the first report of a pigmented BCC of the conjunctiva, mimicking a conjunctival melanoma. Pigmented BCC should be considered in the differential diagnosis of pigmented tumours of the conjunctiva.

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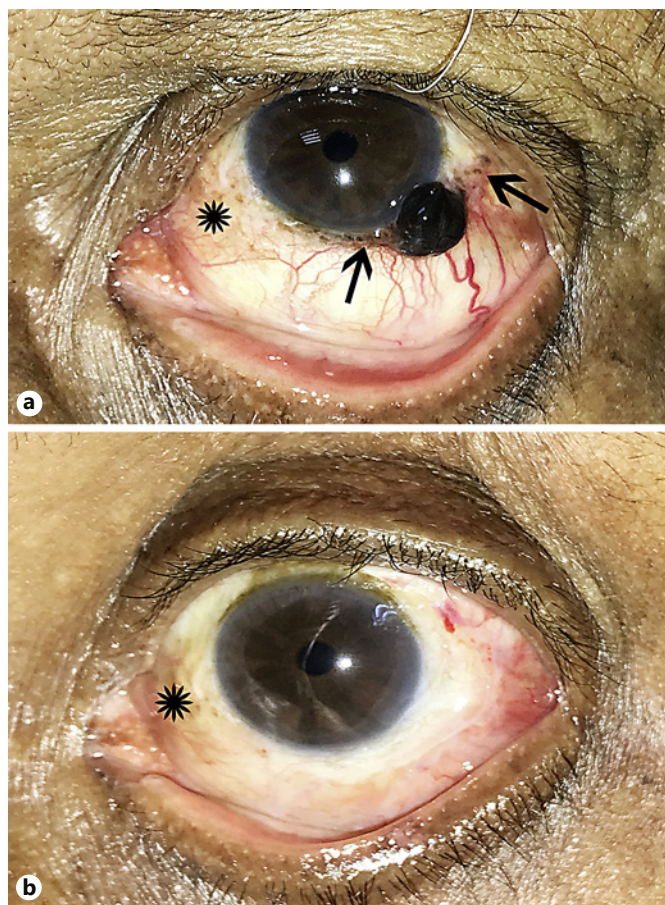
## Introduction

Pigmented conjunctival neoplasms can be divided into melanocytic and non-melanocytic. Common pigmented melanocytic neoplasms include naevi and melanoma. An example of a well-described pigmented non-melanocytic tumour is squamous carcinoma, occurring in patients with brown or black skin [1]. Basal cell carcinoma (BCC) has been very rarely reported to arise as a primary tumour of the conjunctiva [2–5]. Pigmented BCC is well documented in the dermatopathology literature and accounts for around 6% of all cutaneous BCCs [6]. We describe the clinical and histopathological features of a dark brown mass at the left inferotemporal limbal area of a South-Asian male, thought to be a melanoma, but which histologically was a pigmented BCC and represents the first description of this rare subtype in the conjunctiva.

## Case Report

A 60-year-old, South-Asian, Bangladeshi male patient attended the Orbit and Oculoplastic Department of the Chittagong Eye Infirmary and Training Complex (CEITC) in Bangladesh, with a dark brown lesion on his left conjunctiva surface near the limbus for 2 years, gradually increasing in size for 1 year. There was no history of trauma and no other systemic complaints.

On ocular examination, his best-corrected visual acuity was 20/30 in both eyes, and intraocular pressure was within normal limits. The biomicroscopic examination of the left eye showed a raised, globular, irregular, dark brown-coloured pigmented mass near the temporal limbus at 4 to 5 o'clock position, measuring about  $3 \times 3 \times 2$  mm (Fig. 1a). There were a few scattered flat pigmented lesions near the mass, and also a few prominent vessels were seen around the growth. The cornea was clear without any pigmentation. The posterior segment examination in both eyes revealed no abnormality. There was no evidence of preauricular or submandibular lymphadenopathy. There was no evidence of sys-



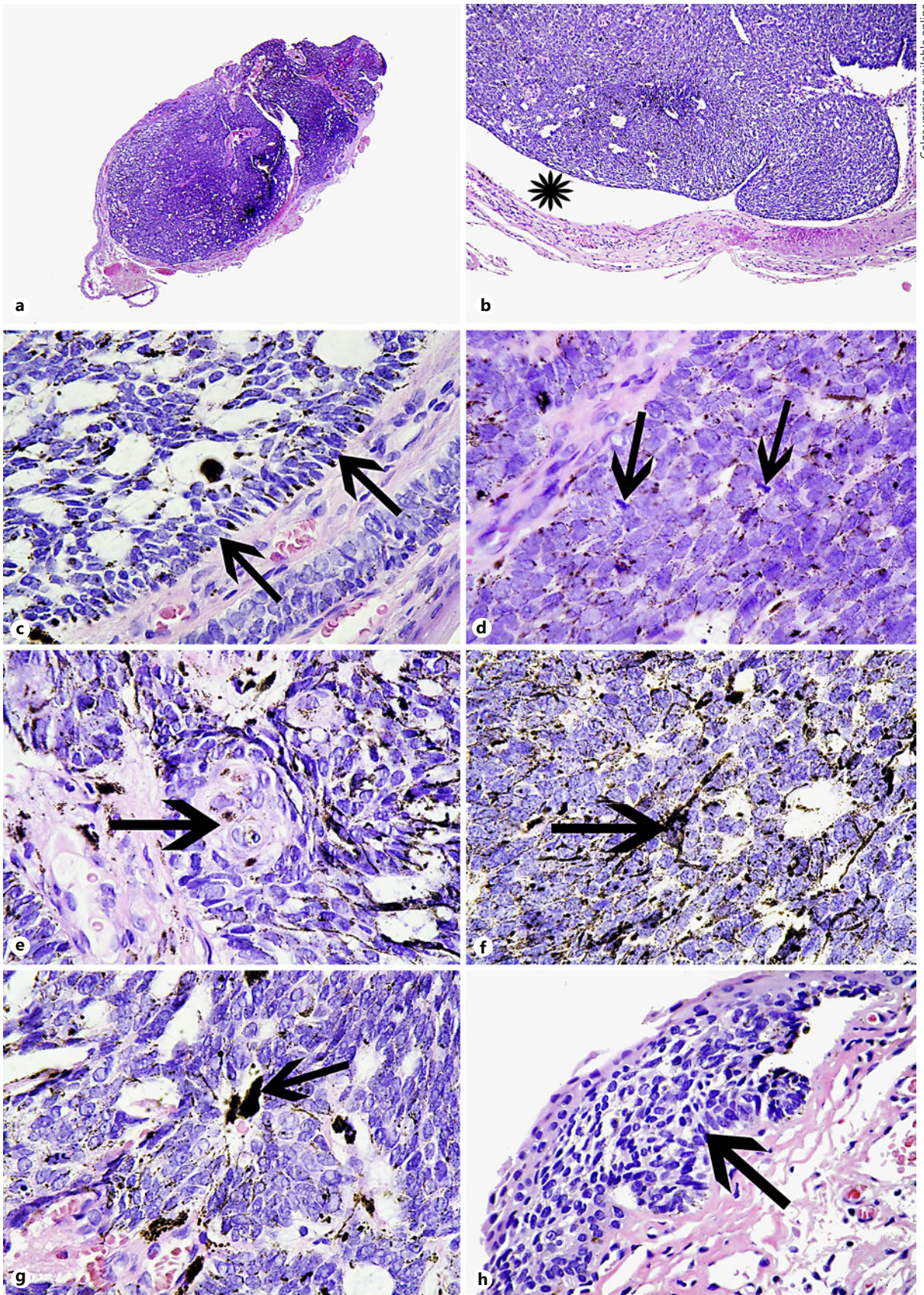
**Fig. 1.** **a** Clinical photograph of the left ocular surface showing the black dome-shaped pigmented BCC. The asterisk indicates racial/complexion-associated benign melanosis. The arrow points to smaller black lesions either side of the main tumour mass. These are areas of pigmented superficial growth pattern BCC. **b** The post-surgical appearance of the left ocular surface. The asterisk indicates racial/complexion-associated benign melanosis.

temic endocrinopathy and no documented history of medication that could increase pigmentation (e.g., tetracyclines). The working clinical diagnosis was invasive conjunctival melanoma.

The mass was removed by wide local excision of the tumour, with a clear margin of 4 mm, followed by double freeze cryotherapy of the conjunctival margins along with the application of Mitomycin C. The bare sclera was covered by amniotic membrane (Fig. 1b). The lesion was sent for histopathology. Postoperative recovery was uneventful. He was prescribed topical Mitomycin C (MMC) 0.04% as a surgical adjunct. The patient has been followed up for 2 months with no evidence of recurrence.

Histology showed a well-defined, mitotically active basaloid tumour, focally connected to the overlying epithelium (Fig. 2a). Between the tumour and surrounding stroma, artefactual clefts were present (Fig. 2b). The tumour cells were basaloid with a peripheral palisade (Fig. 2c), and the requisite cells were mitotically active (Fig. 2d) and some contained brown pigment in minimal cyto-





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(For legend see next page.)



plasm (Fig. 2d). Focal squamous differentiation was identified (Fig. 2e). Pigmented dendritic melanocytes were diffusely present in the tumour (Fig. 2f) along with melanophages (Fig. 2g). Separate superficial tumour deposits were seen flanking the main lesion, connected to the under surface of the conjunctival epithelium (Fig. 2h).

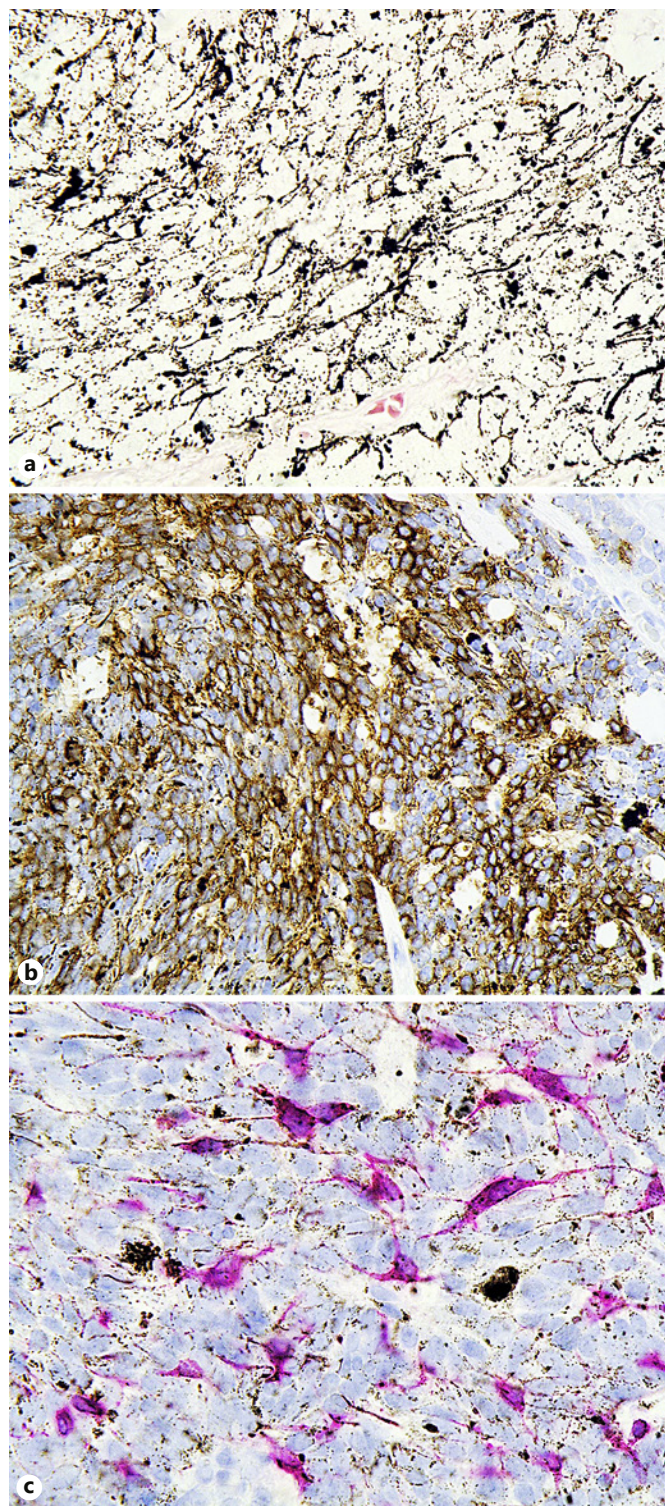
A Masson-Fontana stain confirmed the dense network of melanin granules present in the tumour (Fig. 3a). Immunohistochemistry showed that the basaloid cells were positive for BerEP4 (Fig. 3b) and BCL2 (not shown) and negative for EMA, CK20 and TTF1 (not shown). Melan A showed an evenly distributed population of spindle to dendritic, pigmented and non-pigmented melanocytes through the tumour (Fig. 3c) with the background epithelial cells not unstained. No lymphatic, blood vessel or perineural invasion was identified. There was no evidence of a primary melanocytic malignancy. The features were those of a conjunctival primary pigmented BCC of nodular type with a smaller superficial component. One peripheral margin was contaminated by tumour.

## Discussion

We report a primary pigmented BCC of the left infero-temporal conjunctiva in a South-Asian male, which mimicked conjunctival melanoma clinically. It is far more common to observe BCC of the eyelid with secondary conjunctival involvement [7]. Rarer still are examples of primary caruncle BCC with secondary conjunctival involvement [8]. Primary BCC of the conjunctiva has only been reported on 4 previous occasions and none of these were of the pigmented variety [2–5]. Table 1 summarises the features of these previously reported cases compared with the present case.

Regarding skin BCC, the pigmented variant accounts for 6% of all cases and presents in all BCC growth patterns. Melanin pigment can be present in melanocytes, melanophages and tumour cells [6]. There have been rare reports of colonisation of BCC by in situ melanoma [9],

**Fig. 2.** **a** Haematoxylin and eosin (HE)-stained section at scanning power of the BCC. **b** Artefactual processing cleft between the BCC and background conjunctival stroma. **c** HE. A peripheral palisade where the cells are lined up parallel to one another (arrows). **d** HE of the tumour cells showing mitotically active (arrows) tightly packed basaloid cells. Many tumour cells contain brown pigment in their minimal cytoplasm. **e** HE showing focal squamous differentiation (arrow). **f** HE. Arrow points to a dendritic pigmented melanocyte within the tumour. **g** HE. Arrow points to a melanophage in the tumour. **h** HE. The arrow points to a superficial pattern BCC connected to the under surface of the conjunctival epithelium. This corresponds to the smaller pigmented nodules flanking the main tumour (see Fig. 1a).



**Fig. 3.** **a** Masson-Fontana stain indicating the extensive presence of melanin pigment in dendritic melanocytes in the BCC. **b** BerEP4 immunohistochemistry showing that the BCC stains positively (brown = positive staining). **c** Melan A immunohistochemistry showing cytoplasmic staining in intra-tumoral dendritic melanocytes (red = positive staining).

**Table 1.** Details of the previous cases of primary conjunctival basal cell carcinoma of the conjunctiva, in relation to the present case

Studies	Sex and age, Race years	Eye, L/R	Location on conjunctiva	Appearance	Histological diagnosis	Follow up data
Aftab and Percival [2], 1973	M, 82	Unspecified	Nasally in the palpebral aperture between the limbus and the plica	Pedunculated, fleshy, mobile, 4 mm	BCC (type unspecified) with focal squamous differentiation	No recurrence for 2 months
Apte et al. [3], 1975	F, 69	R	Nasally in the palpebral aperture between the limbus and the plica	Fleshy, pedunculated, 2 × 1.5 inches, mobile, and lobulated surface with irregular margin	BCC (type unspecified)	No recurrence, but period not specified
Husain et al. [4], 1993	M, 66	L	Nasal limbus	Nodular, fleshy, vascular	BCC (type unspecified) with focal squamous differentiation	No recurrence for 12 months
Cable et al. [5], 2000	M, 69	L	Temporal limbus	6 × 6 mm, elevated nodule at the 3-o'clock position with overlying conjunctival hyperemia	BCC-morphoeic type	Intraocular invasion by BCC, no further follow-up data
Present case, 2019	M, 60	L	Temporal limbus 4 to 5 o'clock	Sessile, non-mobile, black hemispherical nodule with feeder vessels	Nodular and superficial BCC, focal squamous differentiation	No recurrence for 2 months

M, male; F, female; L, left; R, right; BCC, basal cell carcinoma.

cutaneous melanoma metastasizing to BCC [10] and skin collision tumours of BCC and melanoma [11]. Brankov et al. [12] investigated pigmented skin BCC using immunohistochemistry with the melanocytic markers MART-1 and Melan A and established that “the mean melanocyte count per high powered field in pigmented BCCs from sun-exposed skin was 101.9 and from intermittently sun-exposed skin was 122.5, as compared to the controls (nodular non-pigmented BCC) of 27.4 ( $p = 0.002$ ) and 34.9 ( $p = 0.002$ ), respectively.” Therefore, they concluded that the pigmentation was attributable to increased melanin and to increased melanocytes [12]. In our case, melanin pigment was present in tumour cell cytoplasm, in dendritic melanocytes and in melanophages in the main nodular tumour and within the peripheral superficial component, identical to that reported in the skin. The melanocyte count per ×40 objective on an Olympus BX51 microscope was 98 melanocytes (counted over 3 × 40 fields), comparable to the melanocyte counts in pigmented skin BCC quoted above [12].

A key question relates to the pathogenesis of BCC in the conjunctiva. Possible mechanisms include (a) metaplasia of the conjunctival epithelium to epidermis or hair follicular type tissue with ultraviolet damage and induction of BCC; (b) BCC development within a dermoid choristoma; and (c) metastatic BCC from skin (eyelid and non-eyelid). The patient had no skin tumours, ruling out metastasis. This leaves the first two possibilities, with the first example more plausible because of the absence of a choristoma from the histopathology. Other conjunctival neoplasms that are known to mimic conjunctival melanoma are pigmented squamous cell carcinomas, which occurs in patients with brown or black skin [1]. Like our case of pigmented BCC, the pigment is found in some tumour cells but is mainly concentrated within dendritic intra-tumour melanocytes [1].

In summary, we report a unique case of pigmented primary conjunctival BCC, manifesting as a dark brown conjunctival tumour, resembling melanoma. We suggest that pigmented BCC be considered in the differential diagnosis of pigmented neoplasms of the conjunctiva.

### Statement of Ethics

The study was conducted ethically in accordance with the World Medical Association’s Declaration of Helsinki. The subject has given his written informed consent to publish his case (including publication of images).



## Disclosure Statement

The authors have no conflicts of interest to declare.

## Funding Sources

This study attracted no funding.

## Author Contributions

H.S.M. wrote the paper and contributed the pathology figures. S.R.R. and F.H. were the surgeons and documented the case. M.N. wrote and edited the paper.

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