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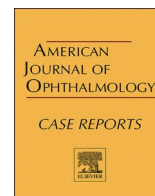
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# Primary bulbar conjunctival basal cell carcinoma: A clinical-pathologic report and literature review

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## ARTICLE INFO

### Keywords:

Basal cell carcinoma  
Conjunctival tumor  
Bulbar conjunctiva  
Histopathology  
Immunohistochemistry  
Oncology

## ABSTRACT

**Purpose:** To enhance the characterization of primary bulbar conjunctival basal cell carcinoma (BCC) clinically and histologically, via report of a case and review of the relevant medical literature.

**Observations:** We report the case of a 73-year-old man with no history of skin cancer who presented with a bulbar conjunctival nodule without connection to the eyelid or caruncle, originally thought to represent a pyogenic granuloma. After one month without improvement on topical prednisolone, excisional biopsy was performed, with routine histopathology and immunohistochemistry. The tumor was found histologically to be primary conjunctival BCC. Immunostaining exhibited negative Ber-EP4 and S100, mostly negative CK7 and EMA, and positive p63. Margins were negative, and the patient had no recurrence six months after excision.

**Conclusions and Importance:** Primary conjunctival BCC must be considered in the differential diagnosis of a conjunctival lesion which may initially appear benign but does not behave as expected clinically. The location of the tumor in the case presented here refutes a prior postulate that primary conjunctival BCC arises from basal adnexal epithelium in the caruncle. Of the immunohistochemical findings, only the Ber-EP4 result differed from the typical immunostaining profile of cutaneous BCC. Further study is needed to determine the frequency of Ber-EP4 positivity in primary conjunctival BCC.

## 1. Introduction

Basal cell carcinoma (BCC) is a malignant epithelial neoplasm typically arising in areas of long-term sun exposure, such as the eyelid skin. Primary conjunctival BCC is exceedingly rare, with few cases reported in the literature.<sup>1–6</sup> Notably, primary conjunctival carcinomas are far more likely to be squamous cell carcinoma (SCC) than BCC.<sup>5</sup> To our knowledge, of the few existing reports of primary conjunctival BCC, only one included immunohistochemistry.<sup>6</sup> We describe a case of primary bulbar conjunctival BCC to gain insight into the clinical manifestations and histopathologic characterization of this tumor.

## 2. Case report

A 73-year-old Caucasian man presented for evaluation of an asymptomatic nodule in the temporal interpalpebral conjunctiva of the right eye. Although first documented two months before presentation, the patient noted it may have been present for “several years” and

worsened after a cataract procedure eight months prior. Medical history included hypertension, hyperlipidemia, type 2 diabetes mellitus, and prostate cancer, but no skin cancer. Ocular history included bilateral cataract surgery and glaucoma. Examination revealed a well-circumscribed, semi-translucent, mobile nodule with “feeder” vessels measuring 4 mm vertically by 2.3 mm horizontally in basal dimensions, with an area of leukoplakia (Fig. 1A). Topical prednisolone was initiated for presumed pyogenic granuloma. After one month without improvement, excisional biopsy was performed with wide margins. Histopathology revealed primary conjunctival BCC with visible connections to the basal epithelium (Fig. 2A). Immunostaining exhibited negative Ber-EP4 and mostly negative cytokeratin 7 (CK7) and epithelial membrane antigen (EMA, Fig. 2B–D), with only patchy positivity of the latter two in a few foci of squamoid differentiation. Additional markers tested included diffusely positive p63 and negative S100 (not shown). Margins were negative, and the patient had no recurrence six months after excision (Fig. 1B).

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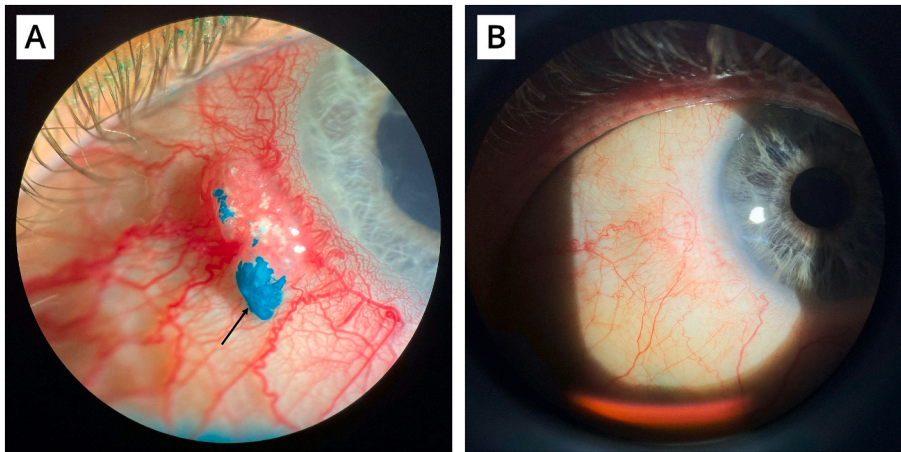
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<https://doi.org/10.1016/j.ajoc.2023.101906>

Received 14 March 2023; Received in revised form 26 May 2023; Accepted 20 July 2023

Available online 27 July 2023

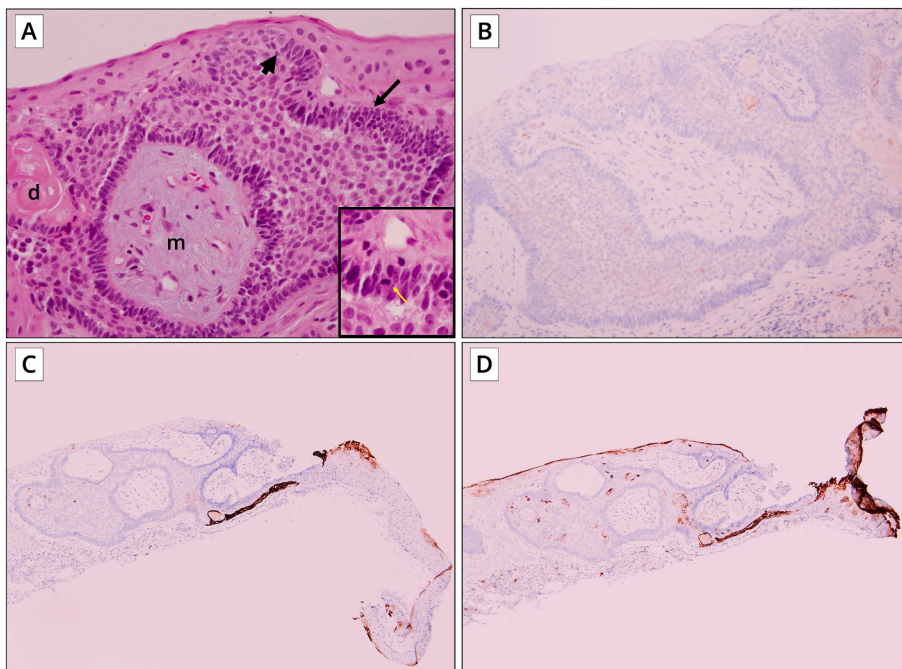
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**Fig. 1.** Right Eye with Bulbar Conjunctival Lesion in a 73-Year-Old Man

A, Slit-lamp image of the right eye at presentation showing a well-circumscribed, semi-translucent, mobile nodule with “feeder” vessels measuring  $4 \times 2.3$  mm, with lissamine green staining in a few areas of leukoplakia (arrow).

B, Slit-lamp image of the same eye six months after excisional biopsy showing clinical resolution of the lesion.



**Fig. 2.** Histopathology of Bulbar Conjunctival Lesion

A, Histology demonstrates basal cell carcinoma with visible connection to the basal epithelium (block arrow), peripheral palisading (arrow), stromal mucinous change (m), focal dyskeratosis (d), and mitotic figure (yellow arrow, inset) (hematoxylin & eosin stain, original magnification,  $\times 400$ ).

B, C, D, Immunohistochemical staining showing negative Ber-EP4 (B, original magnification,  $\times 100$ ) and mostly negative CK7 (C, original magnification,  $\times 100$ ) and EMA (D, original magnification,  $\times 100$ ), with only patchy positivity of the latter two in a few foci of squamoid differentiation.

### 3. Discussion and conclusions

There have been only five previously well-described cases of primary conjunctival BCC, to our knowledge (Table 1).<sup>2-6</sup> While its pathogenesis remains uncertain, it has been postulated to arise from pluripotent basal epithelial germ cells,<sup>5</sup> with ultraviolet light-induced metaplasia to adnexal-type and/or epidermal-type epithelium ultimately leading to primary conjunctival BCC.<sup>6</sup> Another hypothesis, based upon the papillary appearance of some cases, is that primary conjunctival BCC may arise from pre-existing squamous papillomas.<sup>4</sup> Alternatively, some have asserted that it arises from caruncular adnexal epithelium, because previously, all reported cases were located in the nasal conjunctiva between the limbus and plica.<sup>4</sup> However, even those cases were not definitively continuous with the caruncle. Furthermore, several recent cases, including the case presented here, demonstrate primary conjunctival BCC arising from the temporal bulbar conjunctiva adjacent to the limbus, unquestionably far separated from the caruncle.<sup>5,6</sup> Of particular interest, one primary conjunctival BCC in a 60-year-old Bangladeshi male patient clinically simulated melanoma based on the frequency of intra-tumoral dendritic melanocytes and melanophages.<sup>6</sup>

This is reminiscent of primary conjunctival SCC sometimes mimicking melanoma in darkly-pigmented individuals. In another report, in a 69-year-old male construction worker with no history of ocular surgery or trauma, the temporal bulbar tumor invaded intraocularly into the trabecular meshwork and ciliary body,<sup>5</sup> as is occasionally seen in conjunctival SCC. Of note, advent or growth of cutaneous basal cell carcinoma has been previously reported in some cases following ionizing radiation or trauma.<sup>7,8</sup> In our case, the minor trauma of cataract surgery performed eight months prior to presentation may have prompted growth of the lesion. Alternatively, cataract surgery may have been incidental to growth of the lesion that occurred with the passage of time. While exceedingly rare, this report demonstrates that besides SCC, BCC must be considered in the differential diagnosis of a conjunctival lesion which may initially appear benign but does not behave as expected clinically.

Regarding immunohistochemistry in this case, only the Ber-EP4 result differed from what is typically seen in cutaneous BCC. Although Ber-EP4 has been reportedly positive in almost all cases of cutaneous BCC<sup>9</sup> including of the eyelids,<sup>10</sup> areas with squamoid features may not express Ber-EP4.<sup>11</sup> As only one prior case of primary conjunctival BCC

**Table 1**  
Clinical summary of well-described cases of primary conjunctival basal cell carcinoma.

Authors (year)	Age (y)	Sex	Laterality (Location)	IHC	Treatment	Outcome
Aftab & Percival <sup>2</sup> (1973)	82	Male	Not specified (between nasal limbus and plica)	No	Excisional biopsy	No recurrence after 2 months
Apte et al. <sup>3</sup> (1975)	69	Female	Right (between nasal limbus and plica)	No	Excisional biopsy, pedicle graft [sic] <sup>c</sup>	No recurrence after > 3 weeks
Husain et al. <sup>4</sup> (1993)	66	Male	Left (nasal limbus)	No	Excisional biopsy	No recurrence after 1 year
Cable et al. <sup>5</sup> (2000)	69	Male	Left (temporal limbus at 3-o'clock), intraocular invasion	No	Enucleation	No recurrence after 8 years
Mudhar et al. <sup>6</sup> (2020)	60	Male	Left (temporal limbus at 4 to 5-o'clock)	Yes <sup>a</sup>	Excisional biopsy, double-freeze cryotherapy, mitomycin C	No recurrence after 2 months
Lin et al. (2023 present study)	73	Male	Right (temporal limbus at 8 to 9-o'clock)	Yes <sup>b</sup>	Excisional biopsy	No recurrence after 6 months

IHC = immunohistochemistry, y = years.

<sup>a</sup> IHC exhibited + BerEP4, +BCL2, -CK20, -EMA, -TTF1.

<sup>b</sup> IHC exhibited -BerEP4, -CK7, -EMA, -S100, +p63.

<sup>c</sup> This report states that the lesion “was excised along full thickness of upper lid, and gap was repaired by a full-thickness pedicle graft from lower lid,” implying that the lesion had been located on the upper eyelid skin, contradicting the information elsewhere in the report that the lesion was located on the bulbar conjunctiva, and that the “extreme rarity” of this location was the finding prompting the case report. One may conclude that an incorrect procedure description was entered into the report.

included Ber-EP4 immunostaining (which was positive),<sup>6</sup> the frequency of Ber-EP4 positivity in conjunctival BCC has not yet been definitively established. This report provides clinicopathologic evidence of primary bulbar conjunctival BCC, with no connection to the eyelid or caruncle. Further study is needed to determine the frequency of Ber-EP4 positivity in primary conjunctival BCC.

#### 4. Patient consent

The patient consented to publication of the case in writing. (However, this report does not contain any personal information that could lead to the identification of the patient.)

#### Funding

This work was supported in part by an unrestricted grant from Research to Prevent Blindness.

#### Authorship

All authors attest that they meet the current ICMJE criteria for authorship.

#### Declaration of competing interest

The authors have no conflict of interest.

#### Acknowledgements

None.

#### References

- Ash JE, Wilder HC. Epithelial tumors of the limbus. *Am J Ophthalmol.* 1942;25: 926–932. [https://doi.org/10.1016/S0002-9394\(42\)90592-0](https://doi.org/10.1016/S0002-9394(42)90592-0).
- Aftab M, Percival SP. Basal cell carcinoma of the conjunctiva. *Br J Ophthalmol.* 1973; 57(11):836–837. <https://doi.org/10.1136/bjo.57.11.836>.
- Apte PV, Talib VH, Patil SD. Basal cell carcinoma of conjunctiva. *Indian J Ophthalmol.* 1975;23(3):33.
- Husain SE, Patrinely JR, Zimmerman LE, Font RL. Primary basal cell carcinoma of the limbal conjunctiva. *Ophthalmology.* 1993;100(11):1720–1722. [https://doi.org/10.1016/S0161-6420\(93\)31411-9](https://doi.org/10.1016/S0161-6420(93)31411-9).
- Cable MM, Lyon DB, Rupani M, Matta CS, Hidayat AA. Primary basal cell carcinoma of the conjunctiva with intraocular invasion. *Arch Ophthalmol.* 2000;118(9): 1296–1298.
- Mudhar HS, Roy SR, Nuruddin M, Hoque F. Primary conjunctival pigmented basal cell carcinoma with increased numbers of intra-tumour melanocytes, mimicking melanoma: a case report and review of the literature. *Ocul Oncol Pathol.* 2020;6(3): 168–173.
- Li C, Athar M. Ionizing radiation exposure and basal cell carcinoma pathogenesis. *Radiat Res.* 2016;185(3):217–228. <https://doi.org/10.1667/RR4284.S1>.
- Chlebicka I, Jastrzab B, Stefaniak A, Szepietowski J. Basal cell carcinoma secondary to trauma: a 3-year experience of the single center. *Adv Clin Exp Med.* 2021;30(1): 83–86. <https://doi.org/10.17219/acem/130593>.
- Tellechea O, Reis JP, Domingues JC, Baptista AP. Monoclonal antibody Ber EP4 distinguishes basal-cell carcinoma from squamous-cell carcinoma of the skin. *Am J Dermatopathol.* 1993;15(5):452–455. <https://doi.org/10.1097/00000372-199310000-00007>.
- Sramek B, Lisle A, Loy T. Immunohistochemistry in ocular carcinomas. *J Cutan Pathol.* 2008;35(7):641–646. <https://doi.org/10.1111/j.1600-0560.2007.00871.x>.
- Yu L, Galan A, McNiff JM. Caveats in BerEP4 staining to differentiate basal and squamous cell carcinoma. *J Cutan Pathol.* 2009;36(10):1074–1176. <https://doi.org/10.1111/j.1600-0560.2008.01223.x>.