American Journal of Ophthalmology Case Reports 38 (2025) 102300

Contents lists available at ScienceDirect

American Journal of Ophthalmology Case Reports

journal homepage: www.ajocasereports.com/

Basal cell carcinoma and squamous cell carcinoma of the conjunctiva in a single lesion

Melissa A. Trudrung *, Cole Bacig, Brandon Vander Zee, Heather Potter

Department of Ophthalmology and Visual Sciences, University of Wisconsin School of Medicine and Public Health, Madison, WI, USA

ARTICLE INFO

Keywords:
Basal cell carcinoma
Conjunctiva
Squamous cell carcinoma
Collision tumor

ABSTRACT

Introduction: Basal cell carcinoma (BCC) occurrences in the conjunctiva are exceptionally rare. These lesions become exceedingly rarer next to an adjacent area of squamous cell carcinoma. A collision tumor of both basal cell and squamous cell carcinoma is infrequently encountered in the literature.

Case presentation: An elderly male patient was evaluated for concern of ocular surface squamous neoplasia on his left conjunctiva. The lesion appeared as a tan-white elevated lesion with atypical vessels in papillary fronds. The patient underwent surgical excision of the lesion, and the tissue was sent to ocular pathology for histopathologic evaluation. The final diagnosis was basal cell carcinoma and squamous cell carcinoma. The two tumors of both basal cell carcinoma and squamous cell carcinoma were juxtaposed with an abrupt transition zone with no fluidity of differentiation. The lesion had typical features for BCC with positive stain for Bcl-2, P63, P53, CD10, and BerEP4. Additionally, the SCC region stained positive for EMA, P63, and P53.

Conclusion: We report a single lesion of the conjunctiva with features of both basal cell carcinoma and squamous cell carcinoma. This case report describes a unique case of two independent neoplasms of the conjunctiva. This further adds to the literature of collision tumors to characterize the lesion with appropriate immunohistochemical analysis.

1. Introduction

Primary basal cell carcinoma (BCC) of the conjunctiva is rarely documented in the literature.[1–8] Eyelid BCC comprises about 20% of all BCC and is most commonly found on the lower lid followed by the medial canthus, upper lid, and lateral canthus.[9] The location of BCC in sun-exposed areas reflects the risk factor of ultraviolet light exposure.[9] Other factors associated with BCC are toxic substance exposure, radiotherapy, immunosuppressed status, and a history of skin cancers in family members.[9] Previous reports of a BCC tumor originating from the conjunctiva are exceedingly rare, but have been described, usually presenting as an elevated nodule with vessels.[1–4,7]

Squamous cell carcinoma (SCC) of the conjunctiva has a much higher incidence of conjunctival involvement.[10] Invasive SCC of the conjunctiva is the end stage of a spectrum of ocular surface disorders called ocular surface squamous neoplasia (OSSN).[11] Risk factors include UV light, allergic conjunctivitis, HIV/AIDS, and human papilloma virus.[10,11] SCC can present commonly with conjunctival injection, irritation of the eye, and photophobia.[11,12] Most often a white lesion appears on the ocular surface with dilated "feeder" vessels.[11]

The co-existence of both BCC and SCC is rarely reported in the literature.[13–15] The co-existence of two distinct carcinomas in one biopsy specimen has been referred to as a collision tumor.[16] We describe a unique case of BCC and SCC of the conjunctiva and further characterize the lesion with appropriate immunohistochemical analysis.

2. Case Presentation

An elderly male patient with a past medical history of conjunctival intraepithelial neoplasia of the right eye five years prior, cutaneous actinic keratosis, and basal cell carcinoma was evaluated for concern of OSSN on his left conjunctiva. Clinical examination revealed a prominent lesion at 2 o'clock with elevation and atypical vessels in papillary fronds (Fig. 1). The left eye limbal and conjunctiva lesion measured 13 × 5 × 1 mm and was tan-white in color (Fig. 1). The patient underwent surgical excision of the lesion. The tumor extended from the limbus with two-thirds of the lesion extending onto the corneal surface. The conjunctiva was incised to bare sclera extending posterior several millimeters

* Corresponding author.
E-mail address: trudrung@wisc.edu (M.A. Trudrung).

https://doi.org/10.1016/j.ajoc.2025.102300
Received 5 October 2024; Received in revised form 22 January 2025; Accepted 3 March 2025
Available online 5 March 2025

into conjunctiva that grossly appeared normal. The conjunctiva was undermined with Wescott scissors anteriorly to the limbus. A 69 Beaver blade was used to debride the corneal epithelium centrally and then extend peripherally under the growth, which did not violate Bowman's layer. Once the conjunctival extent and the corneal extent were undermined to the limbus, a combination of sharp and blunt dissection allowed removal from the limbal base. Erasure cautery was used to control surface bleeding from the sclera. A double-freeze thaw cryotherapy to the edges of the conjunctiva resection was done. A piece of amniotic membrane, 1.0 cm by 1.5 cm was used to cover the exposed sclera areas. The membrane was secured with Tisseel fibrin glue. A soft contact lens was placed over the cornea as a bandage due to the underlying corneal epithelial defect. The tissue was sent to ocular pathology for histopathologic analysis. The final diagnosis confirmed the presence of both BCC and SCC with the deep margins positive for residual BCC. No topical chemotherapeutic was utilized, and due to the patient's age, he elected to undergo observation. To date, there has been no evidence of recurrence of the lesion.

Histopathologically, the BCC and SCC components were juxtaposed with an abrupt transition zone, lacking any evidence of gradual differentiation between the two tumor types (Fig. 2). Transitioning epithelium from conjunctiva to cornea could be seen indicating that the specimen may be involving the limbus. Furthermore, genetic sequencing was not performed on the tissue which could have provided additional insights into the molecular characteristics and behavior of the tumors.

For definitive tissue diagnosis of this rare combination of lesions, three hematoxylin and eosin (H&E)-stained sections were examined. EMA, p53, p63, CD10, cytokeratin (CK) 7, and BerEP4 immunohistochemistry as well as a PAS stain were also performed. The slides showed conjunctival epithelium with stratified squamous epithelium, mild keratinization, and rare goblet cells. The epithelium was acanthotic, with one area containing multiple clusters of atypical basaloid cells that proliferated into the substantia propria with prominent nuclear palisading and peritumoral artifactual retraction. A fibrous desmoplastic stromal reaction can also be appreciated adjacent to the basaloid cells. These features were most consistent with a nodular basal cell carcinoma, and there was a lack of concerning histopathologic features that would indicate a more aggressive basal cell tumor, including micronodular, morpheaform, or infiltrative basaloid lesions. In the adjacent epithelium, there was a marked change from atypical basaloid cells to atypical squamous cells with eosinophilic cytoplasm with loss of normal epithelial maturation. These cells displayed cellular pleomorphism with prominent nuclei as well.

EMA stain revealed membranous and diffuse cytoplasmic staining in the area of squamous cell atypia and negative staining in the nests of basaloid cells. P53 staining showed intense nuclear staining in the conjunctival basal layer and in some peripheral palisading cells of the basaloid islands. Additionally, some atypical squamous cells showed positive nuclear staining which appeared to be lost superficially. Bcl-2 staining demonstrated diffuse cytoplasmic staining the basaloid cells only. P63 showed diffuse and intense nuclear staining, especially in the nests of basaloid cells and the basal third of the conjunctiva in the areas of atypical squamous cells in a similar manner to the p53. CD10 revealed intense clumpy irregular staining of basaloid cell areas. CK7 was largely negative throughout. BerEP4 staining highlighted the basal cell area and spared the squamous areas. The case was reviewed with dermatopathology who concurred with the diagnosis.

3. Discussion

In summary, we report a unique case of BCC and SCC of the conjunctiva. BCC is rarely found on the conjunctiva with only eight reported instances in the literature,[1–8] and it is even more rarely found directly adjacent to SCC[13–15] suggestive of a collision tumor. Three previous cases of collision tumors have been reported in the literature but not prior on the conjunctiva (Table 1). The reason for the low occurrence of BCC on the conjunctiva as compared to the skin is uncertain but several theories have been posited. Perhaps the conjunctival epithelium underwent metaplasia from ultraviolet damage, a dermoid choristoma developed into BCC, or a skin cancer from another area metastasized into the conjunctiva.[1]

A collision tumor is histologically distinct from metatypical basal cell carcinoma (MBCC) and basosquamous carcinoma (BSC). MBCC is defined as aggregations of metatypical cells with loss of peripheral palisading and no SCC, while BSC has features of BCC or MBCC that blend into areas of SCC.[17] Metatypical cells are found within the transition zones of BSC and are described as intermediate cells that are larger and paler than the basaloid cells found in BCC, yet smaller and less eosinophilic than the spinous cells seen in SCC. A collision tumor lacks metatypical cells or a blending of BCC to SCC.[17] Some consider MBCC, BSC, and collision tumor the same entity and use the terms interchangeably while others believe these to be separate entities.[18] We appreciate the potential subjectivity to defining metatypical cells and relied on immunohistochemical staining to further characterize the transition zone.

The lesion we report exhibits classic histologic features of both BCC and SCC. In the region consistent with BCC, staining for Bcl-2, P63, P53, CD10, and BerEP4 was positive. In contrast, the area containing atypical squamoid cells with intercellular bridging, characteristic of SCC, showed positive staining for EMA, P63, and P53 (and negative for BerEP4 and CD10), corroborating the diagnosis. The two tumors were adjacent but differentiated showing the unique, definitive histological characteristics of each tumor. The clear demarcation between the two tumor types, without any blending or transitional zone, is emblematic of a collision tumor.[16] Furthermore, the immunohistochemical characteristics of lesions are often closely linked to their molecular composition. Although genetic sequencing was not performed on our lesion, there is a growing body of evidence exploring the molecular differences between various malignancies, including SCC and BCC. These findings are likely to play an increasingly significant role in guiding future treatment strategies. SCC commonly harbors mutations in genes that regulate cell growth and DNA repair, including TP53 mutations, CDKN2A inactivation, NOTCH pathway mutations, and EGFR alterations.[19] In contrast, BCC is strongly associated with aberrations in the hedgehog signaling pathway,

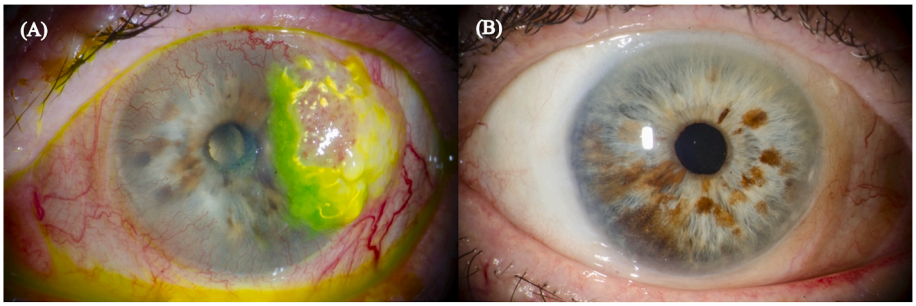

Fig. 1. Slit lamp images of patient with left eye conjunctiva lesion. (A) Lesion with fluorescein staining. (B) Clinical appearance post-excision.

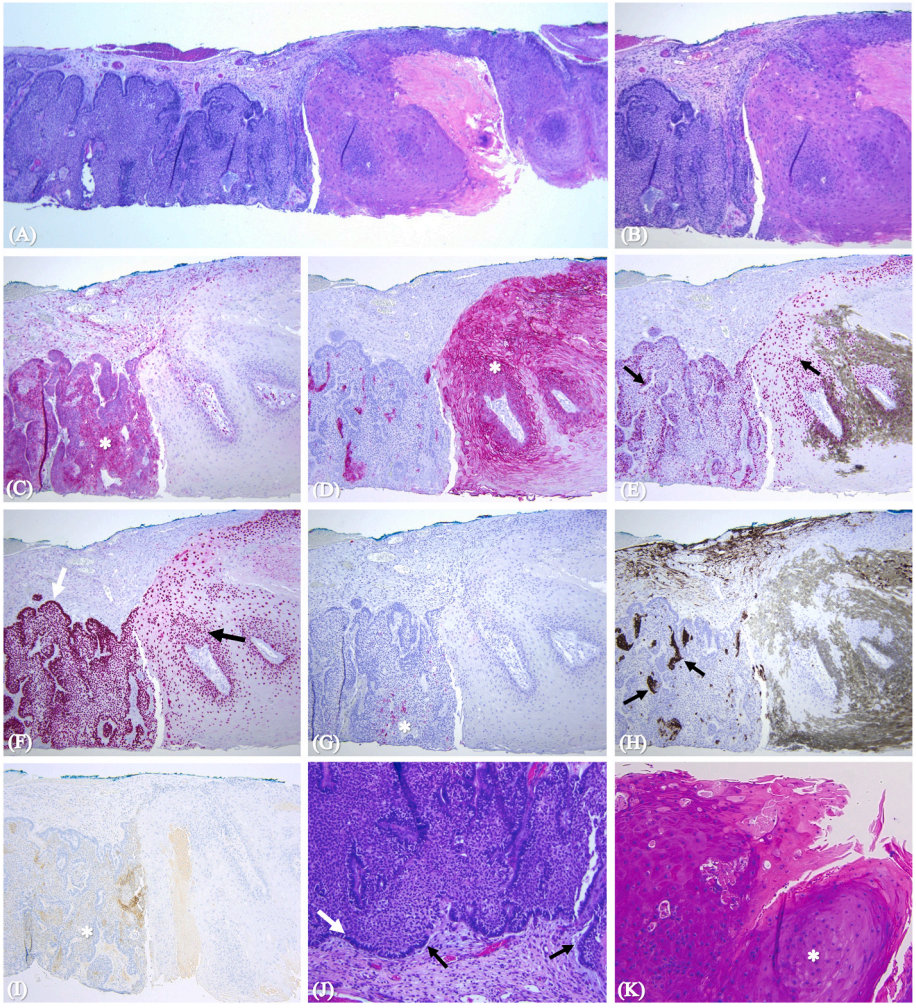

Fig. 2. (A) Hematoxylin and eosin (HE)-stained section at 40x showing both areas of BCC and SCC juxtaposed. Surrounding the basaloid cells, a fibrous desmoplastic stromal reaction can be appreciated, in addition to prominent nuclear palisading. (B) HE-stained section at 100x. (C) BCL2-stained section at 100x showing a diffuse stain pattern of the BCC (asterisk) and negative staining of the SCC. (D) EMA-stained section at 100x exhibiting a cytoplasmic staining of the SCC tumor (asterisk). (E) Nuclear p53 staining is interpreted as increased in neoplastic cells (black arrows). The light brown staining is a result of air-drying artifact. (F) Positive p63-stained section at 100x showing strong nuclear expression in the basal layer of the BCC (white arrow) and diffusely positive staining of the SCC (black arrow), highlighting squamous epithelial cells. (G) CK7-stained section at 100x showing weak focal cytoplasmic staining of the BCC (asterisk) and negative staining of the SCC. (H) Patchy strong staining in a subset of BCC tumor cells (black arrows) and negative staining in SCC areas. Again, the light brown staining is a result of air-drying artifact. (I) BCC cells show blush staining for BerEP4 (asterisk). SCC areas are negative. (J) HE-stain of the BCC tumor exhibiting peripheral palisading (white arrow) and retraction artifact (black arrows). (K) HE-stain of the SCC tumor exhibiting infiltrating nests (asterisk) of neoplastic squamous cells with eosinophilic cytoplasm. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Table 1
Summarizes details of previous cases of BCC and SCC collision tumors.

Studies	Age and Sex	Location	Appearance	Histologic Diagnosis	Treatment
Braunstein et al. (2018)[13]	65 F	Right lower eyelid	Pigmented papillomatous, hyperkeratotic tumor with telangiectasias	Collision tumor consisting of highly differentiated grade 1 SCC and fibrosing BCC	Wedge excision
Lam et al. (2019)[15]	71 F	Left palm	Well-demarcated, erythematous, ulcerated plaque	Collision tumor of a SCC in situ and a BCC	Mohs micrographic surgery
Lee et al. (2020)[14]	70 F	Anterior auricular area	Reddish, ulcerated lesion with irregular boundaries	BCC and SCC	Wide excision of the tumor

typically resulting from mutations in PTCH1, SMO, and TP53.[20]

To the best of our knowledge, this is an exceptionally rare report of a collision tumor involving BCC and SCC in the conjunctiva. The patient was treated with excisional biopsy followed by double-freeze thaw cryotherapy. This case not only expands the current understanding of collision tumors but also underscores the importance of thorough histopathologic analysis in accurately identifying such complex and rare neoplasms. Additionally, understanding these tumors will only enhance our understanding of tumor behavior but also open avenues for targeted therapeutic approaches. The recognition of these unique cases can guide clinicians in optimizing diagnostic and therapeutic approaches, ultimately contributing to improved patient outcomes in ocular surface neoplasms.

CRediT authorship contribution statement

Melissa A. Trudrung: Writing – review & editing, Writing – original draft, Visualization, Investigation, Conceptualization. **Cole Bacig:** Writing – review & editing, Writing – original draft, Visualization, Investigation, Conceptualization. **Brandon Vander Zee:** Writing – review & editing, Writing – original draft, Visualization, Investigation, Conceptualization. **Heather Potter:** Writing – review & editing, Visualization, Supervision, Investigation, Conceptualization.

Patient consent

Written consent to publish this case has not been obtained. This report does not contain any personal identifying information.

Funding

This work was supported by the Research to Prevent Blindness, Inc. under an unrestricted grant to the UW-Madison Department of Ophthalmology and Visual Sciences.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

The authors would like to express our sincere gratitude to Christopher Croasdale, MD for his invaluable contributions to this case report and the excellent surgical outcome of this case.

References

1. Low KL, Lai YP, Alias R, Che Hamzah J. Primary basal cell carcinoma of the conjunctiva. *Cureus*. 2022;14(11), e31516. https://doi.org/10.7759/cureus.31516.
2. 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.
3. Cable MM, Lyon DB, Rupani M, Matta CS, Hidayat AA. Case reports and small case series: primary basal cell carcinoma of the conjunctiva with intraocular invasion. *Arch Ophthalmol*. 2000;118(9):1296–1298. https://doi.org/10.1001/archopht.118.9.1296.
4. 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. https://doi.org/10.1159/000504413.
5. 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.
6. Apte PV, Talib VH, Patil SD. Basal cell carcinoma of conjunctiva. *Indian J Ophthalmol*. 1975;23(3):33–34.
7. Lin RZ, Hong AR, Harocopos GJ. Primary bulbar conjunctival basal cell carcinoma: a clinical-pathologic report and literature review. *Am J Ophthalmol Case Rep*. 2023;32, 101906. https://doi.org/10.1016/j.ajoc.2023.101906.
8. Nag A, Krema H, Saeed Kamil Z, Akbar BA, Laperriere N. Primary conjunctival basal cell carcinoma treated with plaque brachytherapy: a rare case report. *Orbit*. August 7, 2024:1–3. https://doi.org/10.1080/01676830.2024.2387094. Published online.
9. Shi Y, Jia R, Fan X. Ocular basal cell carcinoma: a brief literature review of clinical diagnosis and treatment. *OncoTargets Ther*. 2017;10:2483–2489. https://doi.org/10.2147/OTT.S130371.
10. Emmanuel B, Ruder E, Lin SW, Abnet C, Hollenbeck A, Mbulaiteye S. Incidence of squamous-cell carcinoma of the conjunctiva and other eye cancers in the NIH-AARP Diet and Health Study. *Ecancermedicalscience*. 2012;6:254. https://doi.org/10.3332/ecancer.2012.254.
11. Gichuhi S, Sagoo MS. Squamous cell carcinoma of the conjunctiva. *Community Eye Health*. 2016;29(95):52–53.
12. Tunc M, Char DH, Crawford B, Miller T. Intraepithelial and invasive squamous cell carcinoma of the conjunctiva: analysis of 60 cases. *Br J Ophthalmol*. 1999;83(1):98–103. https://doi.org/10.1136/bjo.83.1.98.
13. Braunstein J, Holz FG, Löffler KU. *Kollisionstumor Der Ophthalmologe*. 2018;115(1):71–73. https://doi.org/10.1007/s00347-017-0447-5.
14. Lee IS, Hong IP, Lee HK. Basal cell carcinoma and squamous cell carcinoma in a single tumor in the anterior auricular area. *Arch Craniofac Surg*. 2020;21(4):257–260. https://doi.org/10.7181/acfs.2020.00262.
15. Lam C, Fuller C, Flamm A, Billingsley EM. Collision tumor of basal and squamous cell carcinoma of the palm. *J Clin Aesthet Dermatol*. 2019;12(4):28–30.
16. Boyd AS, Rapini RP. Cutaneous collision tumors. An analysis of 69 cases and review of the literature. *Am J Dermatopathol*. 1994;16(3):253–257.
17. Allen KJ, Cappel MA, Killian JM, Brewer JD. Basosquamous carcinoma and metatypical basal cell carcinoma: a review of treatment with Mohs micrographic surgery. *Int J Dermatol*. 2014;53(11):1395–1403. https://doi.org/10.1111/ijd.12587.
18. Shukla S, Khachemoune A. Reappraising basosquamous carcinoma: a summary of histologic features, diagnosis, and treatment. *Arch Dermatol Res*. 2020;312(9):605–609. https://doi.org/10.1007/s00403-020-02058-1.
19. Ashford BG, Clark J, Gupta R, Iyer NG, Yu B, Ranson M. Reviewing the genetic alterations in high-risk cutaneous squamous cell carcinoma: a search for prognostic markers and therapeutic targets. *Head Neck*. 2017;39(7):1462–1469. https://doi.org/10.1002/hed.24765.
20. Bonilla X, Parmentier L, King B, et al. Genomic analysis identifies new drivers and progression pathways in skin basal cell carcinoma. *Nat Genet*. 2016;48(4):398–406. https://doi.org/10.1038/ng.3525.