

CASE REPORT

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A case of poorly differentiated carcinoma of the palpebral conjunctiva and its pathological dilemma

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ABSTRACT

Introduction: The differential diagnosis of advanced eyelid carcinoma includes squamous cell carcinoma and sebaceous gland carcinoma. Both carcinomas predominantly affect older adults, and they have the potential for aggressive local invasion and recurrence. We report a case of a 79-year-old woman who presented with a poorly differentiated eyelid mass diagnosed as a carcinoma, which staining could not distinguish definitively, and reconstructed with amniotic membrane graft AMNIOGARD.

Case Report: A 79-year-old woman reported a 6-week history of a rapidly enlarging right lower eyelid mass of the conjunctiva that was previously diagnosed as a poorly differentiated carcinoma, incompletely excised. The patient later complained of enlarged lymph nodes of her right preauricular region for which she underwent biopsy, and these nodes were identical in morphology to her conjunctiva and eyelid lesion. Given the aggressive nature of this lesion, the patient decided on further resection with margin evaluation. We proceeded with right lower lid lesion excisional biopsy and fornix reconstruction. Pathologic examination showed an ulcerated polypoid tumor arising in the conjunctiva with

numerous infiltrative nests embedded in desmoplastic stroma, with prominent lymphocytic infiltrate. The overall immunoprofile was not entirely specific and does not reliably differentiate between squamous cell carcinoma (SCC) and sebaceous gland carcinoma (SGC).

Conclusion: Both carcinomas in the differential diagnosis commonly affect older adult patients and have the potential for aggressive local invasion and metastasis. Distinguishing between these two diagnoses can be accomplished with immunostaining for androgen receptor (AR) and adipophilin if the neoplasm is well-differentiated. In this case of poorly differentiated carcinoma, however, these staining techniques are not reliable enough to make a definitive diagnosis.

Keywords: Eyelid carcinoma, Poorly differentiated carcinoma, Sebaceous gland carcinoma, Squamous cell carcinoma

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INTRODUCTION

The differential diagnosis of advanced eyelid carcinoma includes squamous cell carcinoma (SCC) and sebaceous gland carcinoma (SGC). Orbital SCC most commonly involves the lower lid margin and the medial canthus, and it originates from the squamous cell layer of the skin epithelium [1, 2]. In SGC, the upper eyelid is more likely to be involved because meibomian glands, a type of sebaceous cell, are denser in this region [3]. Both SCC and

SGC predominantly affect older adults, and each of them is capable of invading local structures with aggressive pathologic features and high likelihood of recurrence after resection [1–3]. Here we present the case of such a carcinoma, its surgical resection, and reconstruction with AMNIOGARD (Biotissue, Miami, Florida, USA), and its diagnostic dilemma.

CASE REPORT

A 79-year-old woman was referred to the oculoplastic clinic at the University of Louisville for evaluation of a lesion on her right lower eyelid and conjunctiva. She reported a 6-week history of a rapidly enlarging mass that was tender to touch. Comprehensive ophthalmology in her hometown performed an excisional biopsy of the lesion. The pathology records from this biopsy reported that the lesion was a poorly differentiated carcinoma, incompletely excised, with a differential diagnosis of squamous cell carcinoma (SCC) and sebaceous gland carcinoma (SGC). The margins of the biopsy were positive for tumor involvement, prompting further resection. All final margins were negative for carcinoma. The patient later complained of enlarged lymph nodes of her right preauricular region for which she underwent biopsy with her local ear, nose, and throat surgeon. The pathology report for these enlarged lymph nodes demonstrated that three intraparotid lymph nodes were positive for metastatic poorly differentiated carcinoma, and these nodes were identical in morphology to her conjunctiva and eyelid lesion. At our initial appointment, she had symptoms of blurry vision in the right eye (OD) with epiphora. Pertinent medical history and family history were noncontributory. Review of systems was negative for diplopia.

Measured visual acuity was 20/160 OD improving to 20/40 with pinhole, and 20/20 left eye (OS). Intraocular pressure via applanation was 17 mmHg OD and 20 mmHg OS. Her exam showed a right lower palpebral conjunctival neoplasm measuring 1.4 cm, firm to palpation, extending from the inferior fornix to involve a broad base of palpebral conjunctiva medially and laterally (Figure 1). Hertel measurements were symmetric. Anterior segment exam was notable for conjunctival injection OD and nuclear sclerotic cataracts bilaterally (OU). Dilated fundus exam was unremarkable OU. Head and neck exam demonstrated a preauricular scar on the right side. Examination of other organ systems was unremarkable.

Given the aggressive nature of this lesion, the patient decided on further resection with margin evaluation. We proceeded with right lower lid lesion excisional biopsy and fornix reconstruction. The circular marginal rim of the lesion was outlined via clock face technique. Because of tumor invasion, lamellar tarsectomy was performed as follows: pretarsal orbicularis muscle fibers and anterior fibers of the muscle of Riolan were divided until the external surface of the tarsus was visualized. Two lines

were marked 2–3 mm apart, and deep incisions were made to excise a small wedge of superficial lamella of tarsus. This interlamellar pocket was deepened, and then the posterior lamella epithelium of conjunctival was removed to promote tissue adhesion. Sutures were then used to suture the mucous graft, AMNIOGARD, into position on the posterior lamella [4]. Figure 2 shows fornix reconstruction using AMNIOGARD.

Pathologic examination showed an ulcerated polypoid tumor arising in the conjunctiva with numerous infiltrative nests embedded in desmoplastic stroma, with prominent lymphocytic infiltrate. The tumor had a solid epithelial growth pattern, brisk mitotic activity, and abundant apoptoses (Figure 3A–C). These features are consistent with a poorly differentiated tumor with a differential diagnosis of SCC and SGC. An immunohistochemical workup was performed. The tumor cells were positive for cytokeratin (CK) AE1/AE3 (patchy), CAM5.2 (patchy; Figure 3D), CK5/6 (patchy), p63, p40 (patchy), GATA3, and CD117 (patchy). The tumor was negative for CK7, CK20, S100, and androgen receptor (AR). Ki-67 proliferation index was greater than 90%. Expression for mismatch repair proteins (MLH1, PMS2, MSH2, and MSH6) was retained. The overall immunoprofile is not entirely specific and does not reliably differentiate between SCC and SGC; however, the CAM5.2 immunoreactivity favored SGC.

On postoperative exam week 1, the patient had stable visual acuity with mild lateral canthal tendon laxity. The graft was stable and showed no evidence of tumor recurrence. Her inferior cul-de-sac was formed and functional. Given the high-grade nature of the tumor as well as lymph node involvement, radiation therapy started



Figure 1: Pre-operative physical exam. Right lower palpebral conjunctival neoplasm measuring 1.4 cm, firm to palpation, extending from the inferior fornix to involve a broad base of palpebral conjunctiva medially and laterally.

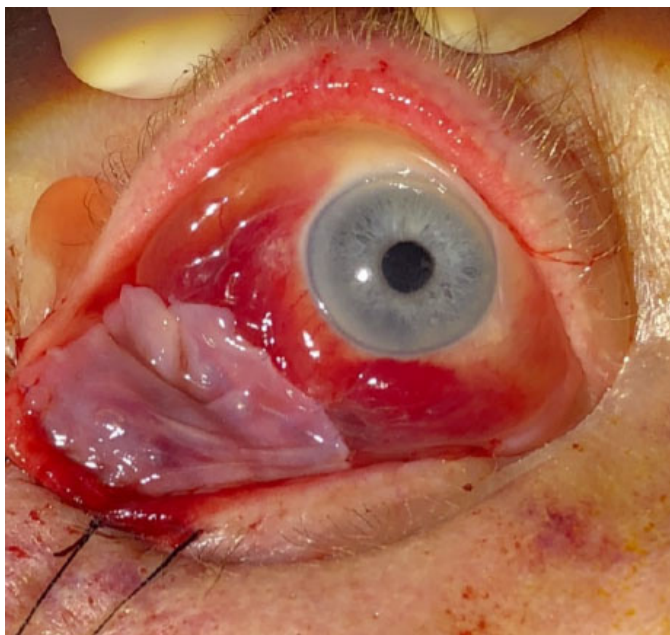


Figure 2: Intraoperative fornix reconstruction with cryopreserved umbilical cord substrate. The lesion was marked for large excisional biopsy. Next, the circular marginal rim was outlined via clock face technique. The fornix was then reconstructed using cryopreserved umbilical cord substrate, AMNIOGARD.

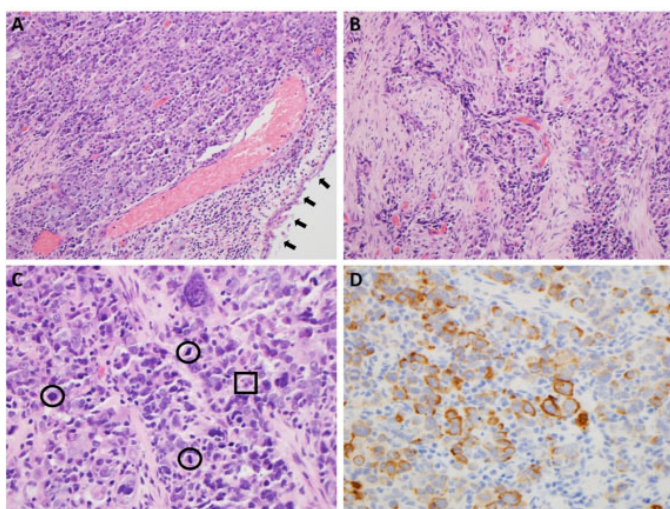


Figure 3: Surgical pathology of poorly differentiated carcinoma. The conjunctival tumor shows a solid infiltrating pattern. Note the conjunctival lining in the right lower corner (arrows) (A). The stroma are desmoplastic and variably infiltrated by lymphocytes (B). On high power, the tumor cells are highly pleomorphic and show abundant mitoses (circles) and apoptoses (square) (C). The tumor cells are immunoreactive for CAM5.2 (D) but negative for androgen receptor (not shown).

two weeks after surgery per her radiation oncologist. The patient was subsequently lost to follow-up.

DISCUSSION

Advanced eyelid carcinoma can have a differential diagnosis that includes SCC and SGC. Squamous cell carcinoma mainly affects fair-skinned, older adults, and the most common risk factor is ultraviolet light exposure [1, 2]. In orbital lesions, it most commonly involves the lower lid margin and the medial canthus [1, 2]. Squamous cell carcinoma originates from the squamous cell layer of the skin epithelium, and it may arise de novo or from actinic keratosis, xeroderma pigmentosum, carcinoma in situ, or after radiotherapy [1]. On examination, it is an elevated painless indurated plaque or nodule, often with central ulceration and irregular rolled borders. Advanced cases may recur locally, spread to adjacent structures, and metastasize to lymph nodes and distant organs in up to 21% of cases [1, 2]. Mortality rates, especially in metastasis, are as high as 40% [2]. Sebaceous gland carcinoma of the eyelid is more common in older adult and women patients [1, 3]. The upper eyelid is more likely to be involved due to the increased presence of sebaceous cells in the form of meibomian glands [3]. It can present in one of two ways: either as a solitary nodule that is firm and painless and may mimic recurrent chalazion or intractable blepharitis, or as a diffuse thickening of the eyelid that may involve the forniceal or bulbar conjunctiva [1, 5]. This tumor is also highly malignant with the potential for aggressive local invasion and metastasis [1].

Fornix reconstruction is accomplished with either the older techniques of conjunctival or tarsal autografting, mucous membrane grafting, or the newer technique of amniotic membrane grafting [6]. Amniotic membrane grafting has risen in favorability due to good results in reconstruction and being easily available without sacrificing the patient's tissue [7, 8]. These grafts act as a basement membrane for the growth of conjunctival epithelial tissue, and this property makes it resistant to contraction and confers a short healing period [7, 9]. As a result, it has been used successfully in fornix reconstruction after symblepharon lysis in cicatricial pemphigoid, Stevens–Johnson syndrome, chemical burns, recurrent pterygium excision, contracted sockets, and post-enucleation for prosthesis optimization [7].

When well-differentiated, distinction between SCC and SGC is straightforward. It is when the tumor is poorly differentiated that separating the two can be problematic even with the aid of immunohistochemical stains. Several immunohistochemistry stains have been proposed to differentiate between the two entities, including AR and adipophilin, but the sensitivity and reliability of these markers are not foolproof, leaving some cases without definitive diagnosis [10–14].

CONCLUSION

Both SCC and SGC commonly affect older adult patients and have the potential for aggressive local invasion and

metastasis. Distinguishing between these two diagnoses can be accomplished with immunostaining for AR and adipophilin if the neoplasm is well-differentiated. In this case of poorly differentiated carcinoma, however, these staining techniques are not reliable enough to make a definitive diagnosis. For palpebral conjunctival neoplasms, amniotic membrane grafting is a useful technique in reconstruction of the fornix.

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Author Contributions

S Elizabeth Dugan – Design of the work, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Eyas M Hattab – Analysis of data, Interpretation of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Jeremy D Clark – Conception of the work, Acquisition of data, Analysis of data, Interpretation of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Guarantor of Submission

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Written informed consent was obtained from the patient for publication of this article.

Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.

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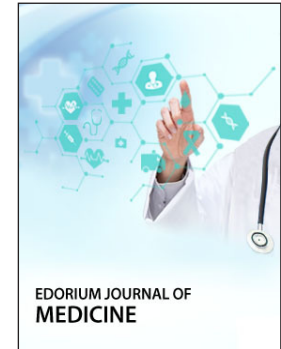
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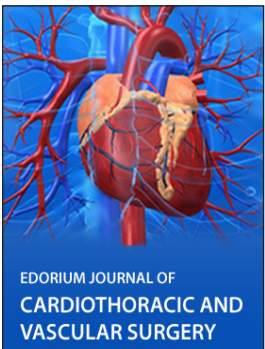
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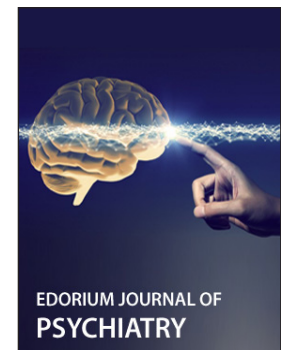
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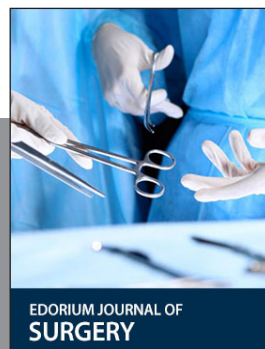
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