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Journal
Dermatology Online Journal, 25(5)

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Publication Date
2019

DOI
10.5070/D3255044069

Apocrine adenocarcinoma of the eyelid: case report and literature review on management

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Abstract

Apocrine adenocarcinoma of the eyelid is a rare sweat gland cancer. It is predominant in older adults and has increased prevalence in males. Management is based on recommendations from reported cases and their outcomes. Surgical excision is considered effective in apocrine adenocarcinoma of the eyelid. We report the case of a 58-year-old woman with apocrine adenocarcinoma located on her left upper eyelid. Excisional biopsy demonstrated focal apocrine secretion in a basaloid nest proliferation. The patient had no recurrence at four months. Our case provides insight into the workup and management of eyelid apocrine adenocarcinoma. Furthermore, we discuss key management recommendations according to previous authors' experiences with eyelid apocrine adenocarcinoma.

Keywords: apocrine adenocarcinoma, Moll's gland, eyelid, sweat gland

Introduction

Apocrine adenocarcinoma of the eyelid is a rare sweat gland cancer that was first reported by Stout and Cooley in 1951 [1]. It presents in older adults with a greater male to female prevalence. Owing to its rare occurrence there are few studies in the literature regarding management for this tumor with variable behavior. Herein, we report a patient with apocrine adenocarcinoma on her left upper eyelid.

Case Synopsis

A 58-year-old woman presented for evaluation of a pruritic nodule located on the left upper eyelid increasing in size for the past year. She reported intermittent burning and leaking sensation at the lesion site. Additionally, she experienced intermittent left eye lacrimation. She had no significant co-morbidities or history of cancer. There was no personal or family history of eye-related medical or surgical history. Review of systems was negative for fever, fatigue, lymphadenopathy, or chills. Physical examination revealed a hypervascular, semicystic, red nodule located on the medial left upper eyelid overlying the eyelashes (**Figure 1**). Eye examination showed no significant findings. V1 and V2 dermatome sensation was intact. There was no lymphadenopathy. A full thickness, stepped lesion excision was done on the lesion. Histopathology from the excisional biopsy demonstrated a dermis with proliferation of basaloid nests with mild cytologic atypia and infrequent mitoses (**Figure 2A, B)**. Focal apocrine secretion was seen with the apocrine glands present at the periphery of the tumor (**Figure 2C**, **D)**. All margins were clear on histopathology examination. Immunohistochemistry stains were positive for

Figure 1. *Hypervascular, semicystic, red nodule located on the medial left upper eyelid overlying the eyelashes.*

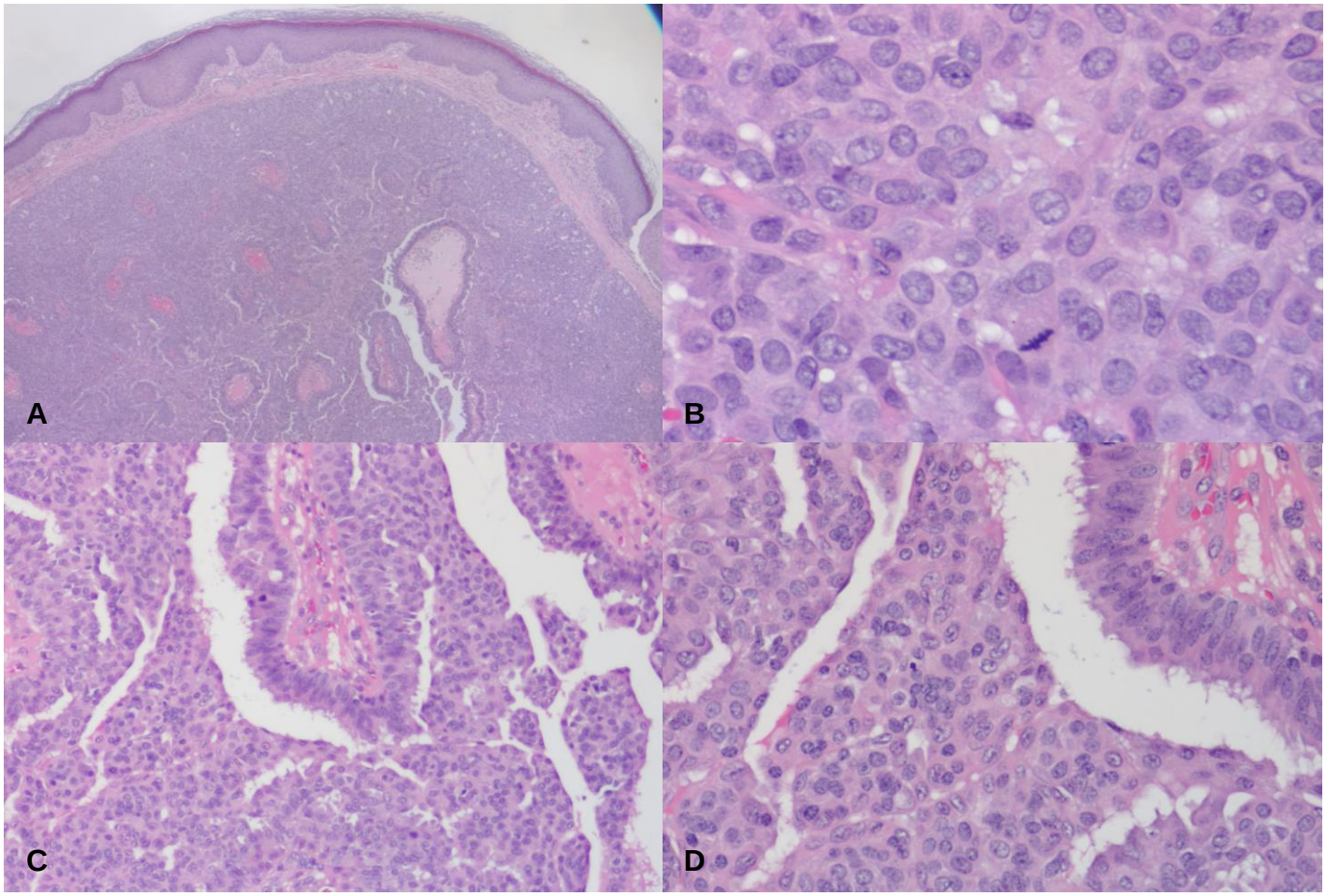

Figure 2. ***A)*** *Cellular tumor with intratumoral papillary proliferations forming clefts. Fibrovascular cores lined by tumor epithelium are seen. H&E, 40×.* ***B)*** *Cellular areas with mild cytologic atypia and mitosis. H&E 400×.* ***C)*** *Solid tumor areas with papillary proliferations showing fibrovascular cores covered by epithelial cells with apocrine cytoplasmic features. H&E, 200×.* ***D)*** *Higher magnification of solid areas with apocrine cytoplasmic projections in tumor clefs and the epithelial lining of papillary fronds. H&E, 400×.*

GCDFP-15, CK7, mammaglobin, and CEA (**Figure 3**). Adipophilin stained a few tumor cells. These findings confirmed apocrine adenocarcinoma of the eyelid. The patient had no recurrence at 4-month follow-up.

Case Discussion

Apocrine adenocarcinoma is a rare sweat gland cancer that typically arises in areas populated by apocrine glands, most commonly the axilla. The eyelid is less commonly affected by this tumor, which arises from the glands of Moll. The first apocrine adenocarcinoma of the eyelid case was reported by Stout and Cooley in 1951 [1]. A recent literature search showed 26 cases of apocrine adenocarcinoma of the eyelid, not including our current report (**Table 1**). There is a male to female predominance with increased prevalence in the older population (**Table 1**). These cases, including ours, provide insight into the importance of follow-up and early detection to lower the risk of regional and metastatic spread.

Eyelid apocrine adenocarcinoma may appear clinically similar to a chalazion. There were six cases that were initially diagnosed as a chalazion [3-5, 9,17, 19]. Three of the six cases were recurrent

lesions initially excised with no histopathological evaluation performed. Initial biopsy with histopathological analysis of the presumed chalazion could have prevented delay in adequate treatment [4]. For instance, one of the six cases underwent orbit exenteration after recurrence owing to intraorbital invasion [3]. The patient initially had no visual defects, such as diplopia [3].

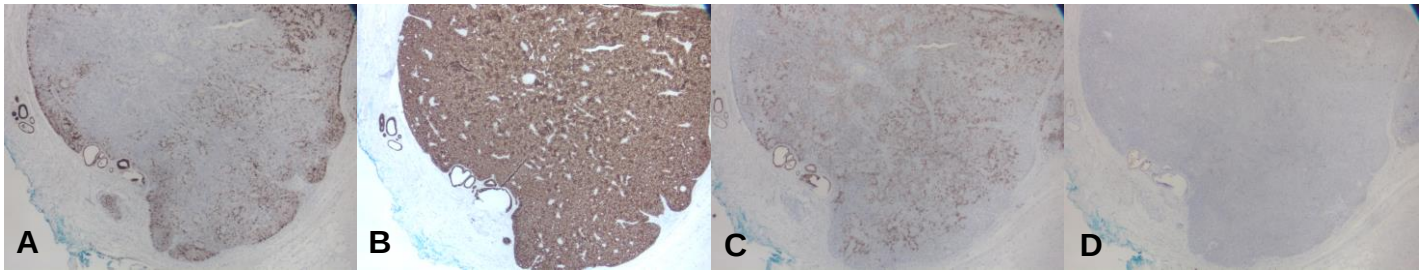

Figure 3. ***A)*** *Positive GCDFP-15 stain of excised lesion supporting apocrine tumor diagnosis. H&E, 40×.* ***B)*** *Positive CK7 stain of excised lesion supporting primary apocrine adenocarcinoma origin. H&E, 40×.* ***C)*** *Positive mammaglobin stain of excised lesion supporting primary apocrine adenocarcinoma origin. H&E, 40×.* ***D)*** *Positive CEA stain of excised lesion indicating apocrine or eccrine origin of the patient's excised nodule from left upper eyelid. H&E, 40×.*

Other diagnoses in the differential diagnosis for eyelid apocrine adenocarcinoma include apocrine hidrocystoma, apocrine cystadenoma, primary cutaneous mucinous carcinoma, and endocrine mucin-producing sweat gland carcinoma. Apocrine hidrocystomas are unilocular or multilocular c ysts that may appear dark blue on clinical presentation [22]. They are lined by a single or double cuboidal-columnar epithelium located above an outer myoepithelial cell layer. Apocrine hidrocystomas contain periodic acid Schiff (PAS)-positive granules and exhibit decapitation of secretory cells [22]. Apocrine cystadenomas are cysts demonstrating papillary growth of columnar cells with a fibrovascular stroma, are cytokeratin positive, and are human milk fat globulin 1 positive [23]. Primary cutaneous mucinous carcinoma (PCMC) of the eyelid, such as endocrine mucin-producing sweat gland carcinoma, is a pink-to-flesh-colored, slow-growing, mucinous sweat gland tumor typically located on the eyelid [24]. PCMC may have apocrine differentiation [25]. It is PAS-positive, estrogen receptor positive, progesterone receptor positive, cytokeratin 7 (CK7)-positive, and cytokeratin 20 (CK20)-negative [25]. Recurrence following wide-local excision is common [26]. Endocrine mucin-producing sweat gland carcinoma is a low-grade, skin-colored, sweat gland cancer commonly located on the eyelid with neuroendocrine differentiation that has papillary, solid, and cystic components. Excision is recommended owing to its association with invasive mucinous adenocarcinoma. In our case, the positive GCDFP-15, CK7, and mammaglobin stains favored apocrine origin [**Figures 3A-C**]. Additionally, there was no mucin present on histopathology.

The histologic diagnostic criteria include: strongly eosinophilic cytoplasm, PAS positivity, tumor located where apocrine glands are typically found, decapitation secretion, and the presence of iron-positive intracellular pigment [27]. However, some apocrine adenocarcinoma cases do not meet all the criteria since the tumor may be poorly differentiated [9]. PAS stain was not performed in our case. On histopathological examination, the tumor has small acini with a cuboidal epithelium. The epithelium may have large-nucleated cells with granular chromatin [9]. Within the lesion, there are scattered glands of Moll. The interstitium may contain hemosiderin deposits with scarring [9]. The tumor may demonstrate rapid local growth [5, 9, 19]. Immunohistochemical stains are another important diagnostic step for distinguishing primary cutaneous apocrine adenocarcinoma from other metastatic tumors, such as breast apocrine adenocarcinoma. In our case, we performed immunohistochemistry stains for GCDFP-15, CK7, mammaglobin, CEA, and adipophilin. GCDFP-15 is a helpful marker for staining apocrine tumors whereas CK7, mammaglobin, and adipophilin are good for distinguishing primary from metastatic apocrine adenocarcinoma [28-30]. Our patient had no history of cancer prior to presentation. CEA positivity supports apocrine or eccrine origin [31].

Imaging and lymph node staging were performed in some reported cases (**Table 1**). In our case, the patient did not have positive lymph nodes on

examination and no signs or symptoms suggestive of tumor invasion; therefore, imaging was not performed. In the reported cases, CT and MRI imaging was performed on cases with visual impairment, signs of malignancy such as ulceration, or signs of tumor invasion (**Table 1**). Lymph node staging has been suggested owing to potential metastasis in apocrine adenocarcinoma [3]. In the study by Hollowell et al. analyzing apocrine adenocarcinoma cases, patients without lymph node metastasis had a greater median survival of 55 months, compared to 33 months in patients with lymph node metastasis [32].

Surgical excision was an effective treatment for most of the reported cases, whereas radiotherapy and orbital exenteration were additional treatments in patients with extensive tumor characteristics (**Table 1**). In the review by Figueira et al., the authors recommended 4mm surgical margins based on the reported eyelid apocrine adenocarcinoma cases [2]. Chamberlain et al. suggested having 1-2cm surgical margins in apocrine adenocarcinoma of the axillae based on what is recommended for other dermatologic neoplasms [33]. Successful chemotherapy treatment has been reported in cases with lymph node metastasis [12, 19]. Chemotherapy regimens include cyclophosphamide, cisplatinum, and adriamycin. Close follow-up in the reported cases was recommended to monitor for tumor recurrence (**Table 1**).

Conclusion

Apocrine adenocarcinoma of the eyelid is a rare tumor present in the older patient population with male predominance. It can appear similar to a chalazion, leading to misdiagnosis and delay in treatment. Histopathological analysis of persistent presumed chalazion lesions is recommended. Immunohistochemical studies help confirm apocrine adenocarcinoma. Lymph node staging is useful for determining prognosis. Although surgical excision is the most common treatment, management depends on tumor extent and patient preference. Follow-up is recommended to monitor for recurrence.

Potential conflicts of interest

The authors declare no conflicts of interests.

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Table 1. *A summary of the published cases of apocrine adenocarcinoma of the eyelid.*

Case	Age (years.)/Sex	Associated Signs/Sx	Location	Imaging	Management	Follow-up	Author, Year, Reference
1	87/M	Right ptosis, decreased vision and extra-ocular movements	Mass in right upper and lower eyelids w/ soft tissue infiltration.	CT, MRI, PET-CT	Rt. subbrow incisional biopsy; 3 wk 45-Gy radiation therapy	10 months; improved vision, reduced size	Figueira, 2013, [2]
2	56/F	Intermittent bleeding at site	5×4mm hemorrhagic cystic mass on left lower eyelid.	None	Incisional biopsy; 4-mm wide margin resection with primary closure	12 months; no recurrence	Figueira, 2013, [2]
3	78/M	Diplopia	35mm recurrent mass on right lower eyelid with intraorbital extension; submandibular node involvement	CT; full body CT/PET	Rt. eye complete exenteration; 70 Gy radiotherapy to right parotid and neck, 66 Gy radiotherapy to exenterated orbit, 54 Gy radiotherapy to skin and right neck lymph nodes	2 ½ years; no recurrence	Valenzuela, 2012, [3]
4	59/F	Loss of eyelashes	Recurrent mass on left lower eyelid with vascular and skeletal muscle infiltration	None	Surgical excision	6 months; no recurrence	Aldrees, 2016, [4]
5	81/M	Not reported	Nodular mass on left upper eyelid	NR	NR	NR	Aldrees, 2016, [4]
6	57/M	Lacrimation and discomfort at site	2.5cm subcutaneous mass on left upper eyelid with subconjunctival, EOM, cervical lymph nodes, and bone invasion.	CT/ MRI	Left orbital complete exenteration and left radical neck dissection	6 months; no recurrence	Shintaku, 2002, [5]
7	57/M	None	50×35mm subcutaneous mass on right lower eyelid extending to upper eyelid through the medial canthus	CT/MRI	Partial excision with radiotherapy	16 months; no increase in mass size	Akcay, 2008, [6]
8	63/M	None	8.5×8.5×5.5mm^3 pigmented nodular mass on left lower eyelid	None	Wedge resection	3 years.; no recurrence	Hunold, 2012, [7]
9	47/F	NA	Mass located on the lower eyelid	NA	Not available	Not available	Simionescu, 1990, [8]
10	66/M	Poor right eye vision	Round mass located on right lower eyelid	CT	Right orbit radical exenteration	15 months; no recurrence	Thomson, 1989, [9]
11	85/F	Not reported	Bluish mass on medial left upper eyelid	None	Full-thickness left eyelid excision	1 year; no recurrence	Seregard, 1993, [10]
12	NA	NA	Not available	NA	Not available	Not available	Pornpanich, 2005, [11]
13	62/M	Excess lacrimation, left eye swelling	Left lower eyelid; lymph node & bone involvement	CT head & neck	Cisplatinum, Adriamycin, and cyclophosphamide	Metastasis with poor prognosis	Kumar, 2011, [12]
14	91/M	Bleeding, ulceration	Blue-brown mass on left temporal upper eyelid	Full body CT/PET	Simple primary closure	12 months; no recurrence	Pagano Boza 2018, [13]

Case	Age (yrs.) /Sex	Associated Signs/Sx	Location	Imaging	Management	Follow-up	Author, Year, Reference
15	NA	NA	Not available	NA	Not available	Not available	Whorton, 1955, [14]
16	80/M	Eyelash loss	6×4mm blue-brown mass located on right medial upper eyelid	NA	Full-thickness, wide block excision	2 years.; no recurrence	Paridaens, 2001, [15]
17	58/M	Serosanguinous drainage	7x6x6mm red mass on left upper eyelid	NA	Surgical excision with 5mm margins, full-thickness block excision of left upper eyelid	4 months; no recurrence	Aurora, 1970, [16]
18	44/F	None	1.5×1cm blue cystic mass on right lower eyelid; ethmoid, nasal cavity, and lung metastasis	NA	Three excisions, radiotherapy, orbit exenteration	Patient died 2 years since onset due to lung metastasis	Stout and Cooley 1951, [1]
19	66/M	Ulceration, eyelash loss, bleeding at site	5×6mm recurrent bluish mass on left lower eyelid	NR	Surgical excision	9-15 years; no recurrence	Barker-Griffith 2006, [17]
20	53/M	None	Dome-shaped mass with telengiectasias on right lower eyelid	NR	Surgical excision	9-15 years; no recurrence	Barker-Griffith 2006, [17]
21	71/M	None	2×2mm recurrent polycystic, gray mass with telengiectasias on left lower eyelid.	NR	Wedge resection	9-15 years; no recurrence	Barker-Griffith 2006, [17]
22	NA	NA	Not available	NA	Not available	Not available	Paties, 1993, [18]
23	66/M	None	Mass on left lower eyelid; preauricular and submandibular node involvement on recurrent mass	NA	Full-thickness lid resection, orbital exenteration, lymph node dissection	Patient died 1 year after intracranial tumor involvement	Ni, 1984, [19]
24	50/M	Left eye proptosis with edema, impaired EOM of left eye	Firm mass on left lower eyelid; preauricular and submandibular nodes involvement.	IV pyelogram; skull & chest x-ray	Radiotherapy, left orbital exenteration w/ partial maxillectomy; neck dissection w/ chemotherapy.	Lost to follow-up.	Ni, 1984, [19]
25	59/F	None	1×1cm nontender nodule on right upper eyelid; parotid gland involvement	None	Wide excision, superficial right parotidectomy, radical neck dissection	7 years; no recurrence	Futrell, 1971, [20]
26	74/M	Congestion and swelling at site	Indurated mass on right lower eyelid with lacrimal sac and nasolacrimal duct invasion	CT, gallium scintigraphy	Wide excision w/ 3cm margins, total orbital exenteration; postoperative right orbit radiotherapy (50Gy of X-ray, 46 days)	22 months; no recurrence	Kanazawa, 2008, [21]
27	58/F	Pruritus, lacrimation, poor vision at site	Mass located on left upper eyelid	None	Surgical excision	4-month follow-up: No recurrence	Our case

NA: not available; NR: not Reported.