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CASE REPORT

Clear cell hidradenocarcinoma of the eyelid: a case report with a review of the literature

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Abstract Clear cell hidradenocarcinomas are extremely rare neoplasms, with very few well-documented cases reported in the literature. The most common sites are the head and neck regions. These tumors are histologically malignant but are not always aggressive. They are known for recurrence and may metastasize widely. Treatment is wide local resection. We report on a case of clear cell hidradenocarcinoma occurring over the eyelid together with a review of the literature.

Keywords Hidradenocarcinoma · Clear cell · Eyelid · Malignant

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Introduction

Clear cell hidradenocarcinoma is a rare tumor of eccrine sweat gland origin that has a predilection for the head and neck. It has an indolent growth pattern and higher incidence of regional and distant metastases [1]. Pathological characteristics may mimic its benign counterparts causing diagnostic confusion. Therefore, such tumors should not be neglected as they have the propensity to metastasize or recur [2]. Most cases reported in pathology literature have limited clinical information. We report a case of clear cell hidradenocarcinoma occurring over the upper eyelid. Our article reviews the literature of this rare entity with differential diagnosis and discussion of its treatment strategies.

Case report

A 65-year-old lady presented with a 3-month history of a solitary mass on the right upper eyelid. It was insidious in onset and gradually increased in size, and was associated with watering of the eyes. Examination revealed a hard non-tender solitary mass measuring 2.5 × 1.5 cm with a pink shiny epidermal surface on the right upper eyelid (Fig. 1a). Mechanical ptosis, ectropion of the lateral half of the eyelid and conjunctival congestion was noted. The right-sided preauricular lymph node was palpable. A clinical diagnosis of meibomian gland carcinoma was offered.

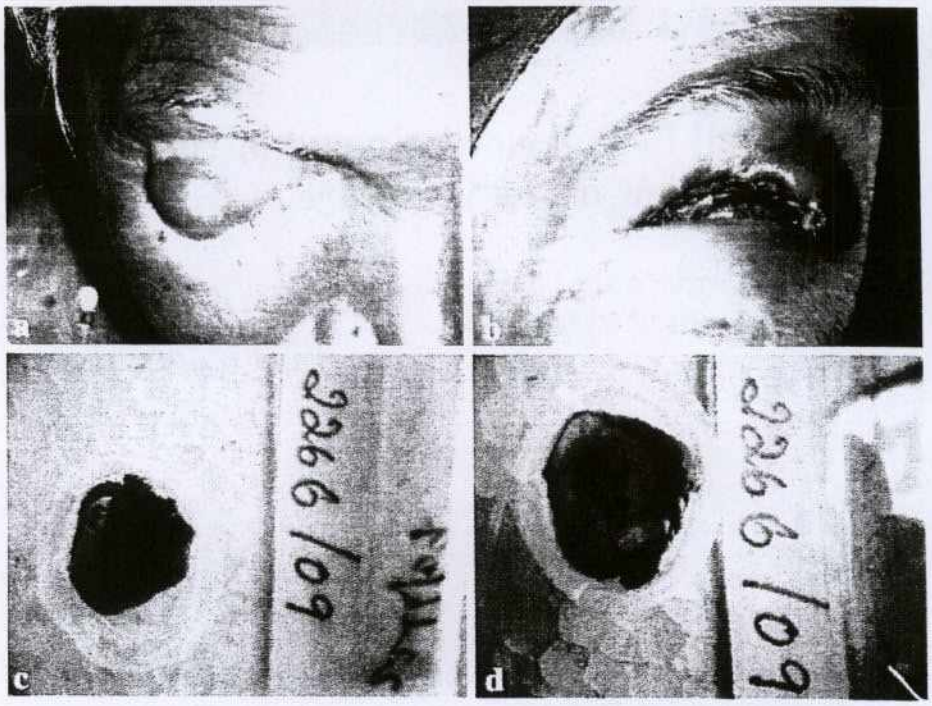

Fig. 1 **a** Photograph showing a hard solitary mass with a *pink shiny* epidermal surface, and **b** a curvilinear incision made on the mass. **c** Gross photograph showing a skin-covered soft tissue mass measuring 2.5 × 2 × 1.5 cm. **d** Cut surface showed a poorly demarcated, lobulated tumor with *gray white* areas

Surgical procedure

A 5-mm curvilinear excision (Fig. 1b) of the tumor along with excision of the right preauricular lymph node and reconstruction of the eyelid was performed under general anesthesia. The resected specimen was sent for histopathology.

Histopathology findings

Gross: A skin-covered soft tissue mass measuring 2.5 × 2 × 1.5 cm (Fig. 1c). The cut surface showed a poorly demarcated, lobulated tumor with gray white areas (Fig. 1d).

Microscopy: This showed poorly circumscribed tumor tissue arranged in lobules infiltrating the subcutaneous tissue (Fig. 2a). The tumor cells were pleomorphic round to oval with vesicular nucleus, 1–2 prominent nucleoli and clear cytoplasm. Mitotic activity was 3–4/high-power fields (Fig. 2b). Tubular lumina of varying sizes and cystic spaces filled with eosinophilic secretion were present within the lobules. Stroma showed mild to moderate infiltrate of lymphocytes and eosinophils (Fig. 2c, d). A diagnosis of clear cell hidradenocarcinoma was offered.

The preauricular lymph node showed reactive hyperplasia. No tumor deposits were seen.

Discussion

Clear cell hidradenocarcinoma (malignant acrospiroma, malignant nodular hidradenoma, malignant clear cell hidradenoma) is an extremely rare eccrine neoplasm. Less than 70 cases are documented in the literature [3]. Tumors with eccrine differentiation are among a large variety of cutaneous tumors that present in the head and neck. The common tumors of the head and neck include basal cell and squamous cell carcinomas. Malignant clear cell hidradenoma, a variant of the more common benign clear cell hidradenoma, is one such type of tumor with eccrine differentiation [4]. These tumors have insidious growth patterns [2].

They present as intradermal nodular tumors said to have predilection for the face and extremities. [5] We report a case of clear cell hidradenocarcinoma occurring over the eyelid.

Recent literature has described the tumor occurring at a diverse range of sites including the scalp, lip, neck, chest wall, breast, back, leg, toe [3] and vulva. Mezzabotta et al. [6] recently reported clear cell hidradenocarcinoma of the breast in a 77-year-old women who presented with a palpable inflammatory nodule in the right breast. Messing et al. [7]. reported metastatic clear cell hidradenocarcinoma in the vulva of a young women and Lee et al. [8] reported the first

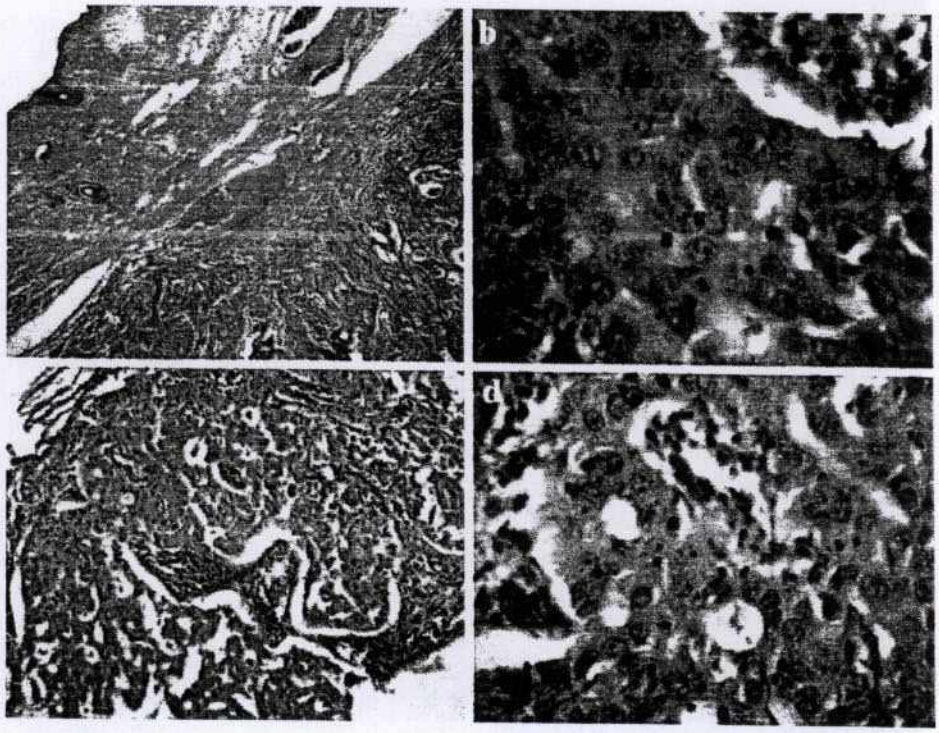

Fig. 2 Microphotograph showing **a** tumor tissue arranged in lobules infiltrating the subcutaneous tissue (H&E, ×100), **b** pleomorphic round to oval tumor cells with vesicular nucleus, 1–2 prominent nucleoli and clear cytoplasm (H&E, ×400), **c** tubular lumina of various sizes and cystic spaces filled with eosinophilic secretion with stroma showing lymphocytic infiltrates (H&E, ×100), and **d** tubular lumina (H&E, ×400)

case of dural-based hidradenocarcinoma with local brain invasion. In their report there was no scalp or skull bone involvement and hence they speculated that the tumor may have arisen from ectopic sweat gland cells entrapped in the dural mater.

The age range is wide, extending from childhood through to the elderly [9].

The etiopathogenesis is unknown. Occasionally tumors have arisen within a pre-existing benign clear cell hidradenoma [10].

Histopathologically the tumor may be arranged in lobules or anastomosing cords, occasionally with a diffuse growth pattern. Epithelial cells are polygonal to slightly fusiform showing bland ovoid nuclei with slightly eosinophilic to clear cytoplasm. The epithelial cells show varying degrees of mitotic activity and nuclear pleomorphism, have vacuolated cytoplasm due to the presence of abundant glycogen and a tendency toward squamous differentiation with many of the neoplastic cells demonstrating individual cell keratinization [10, 11]. A cystic variant has been encountered. A characteristic finding is the presence of intracytoplasmic ductal differentiation, sometimes showing a well-formed cuticular border. Central necrosis may be variable giving comedo carcinoma-like features [10].

Diastase–periodic acid Schiff reaction and epithelial membrane antigen or carcinoembryonic antigen (CEA) immunohistochemistry are of value in highlighting these structures [10]. Exceptionally, in situ carcinoma has been described in the adjacent sweat glands [12].

Wong et al. [13] reported three cases of clear cell hidradenocarcinoma which developed metastases. The lymph nodes, lungs and bones are the sites most commonly affected [3, 9]. Both lung and myocardial metastases from hidradenocarcinoma of the dorsum of the hand was reported by Lopez et al. [14]. Engel et al. [15] observed hidradenocarcinoma developing in the flank and showing metastatic deposits in right axillary and inguinal lymph nodes causing multi-organ failure and death.

The literature showed clear cell hidradenocarcinoma developing at unusual sites presented with certain complications. Khalil et al. [16] reported a case which presented as a medical emergency with symptoms of severe anemia and acute heart failure secondary to intermittent bleeding from a huge ulcerative neck lesion, which was subsequently diagnosed as eccrine hidradenocarcinoma.

Associations

Caccialanza et al. [17] reported a case of clear cell malignant hidradenoma associated with intra-epidermal epitheliomas of the Bowen type following repeated fluoroscopic examinations. Kazakis et al.

[18] observed metastatic malignant clear cell hidradenoma associated with bullous pemphigoid.

Differential diagnosis

Clear cell hidradenoma may occasionally show mild focal cytological atypia and increased mitotic activity (atypical hidradenoma). Hence any tumor with brisk mitotic activity and infiltrating growth should be reported with caution and a wide excision is recommended [10].

It must be distinguished from tumors showing conspicuous cytoplasmic vacuolations such as clear cell squamous carcinoma, clear cell melanoma, trichilemmal carcinoma, and metastatic clear cell carcinoma from kidney, bronchus, liver and female genital tract. Sometimes the tumor is composed predominantly of basaloid cells with no vacuolations and in such cases a differential of basal cell carcinoma should be considered [10].

Immunohistochemical analysis showed that hidradenocarcinoma revealed reactivity for high molecular weight cytokeratins, cytokeratin (CK5 and CK7), p53, p63, CEA (focal), androgen receptor, epidermal growth factor receptor, estrogen receptor, MUC5AC, and strong/diffuse membranous staining for Her-2/neu. Negative stains included villin, TTF-1, CDX2, S-100 protein, vimentin, gross cystic disease fluid protein 15, mammoglobulin, and MUC2 [19].

Treatment strategies

A wide local excision or complete surgical excision and block dissection of involved nodes followed by radiotheraphy and chemotheraphy if there is distant metastasis [14–16]. Nash et al. [19] were the first to demonstrate Her-2/neu amplification in a malignant skin adnexal tumor and suggested application of trastuzumab for patients with metastatic adnexal carcinomas.

Conclusion

Clear cell hidradenocarcinoma occurring over the eyelid is very rare. They may present as low-grade, well-differentiated to highly aggressive, high-grade tumors with a definite potential for uncontrollable local recurrence and metastasis. Hence, though it is a rare disease, the aggressive behavior and the poor prognosis warrant alertness to this neoplasm [20].

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Conflict of interest None declared

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