Case Report

Clear Cell Variant of Squamous Cell Carcinoma of Eyelid, Mimicking Sebaceous Carcinoma: A Rare Case Report

Sonali Dixit, Priyanka Gogoi, Preeti Diwaker

Department of Pathology, University College of Medical Sciences and Guru Teg Bahadur Hospital, Delhi, India

Abstract

Clear cell variant of squamous cell carcinoma (SCC) is an extremely rare neoplasm. Here, we report a case of clear cell variant of SCC which presented as an eyelid nodule. A 56-year-old male presented with a painless, small, pedunculated nodule in the left upper eyelid. On microscopic evaluation, tumor cells were arranged in nests and lobules with few foci of necrosis. Tumor cells were polygonal in shape, having abundant clear and vacuolated cytoplasm with peripherally pushed hyperchromatic nuclei. Two main differential diagnoses considered were sebaceous carcinoma and clear cell variant of SCC. On immunohistochemistry, tumors cells were negative for androgen receptor. A final diagnosis of clear cell variant of SCC was made. In a malignant eyelid tumor with clear cell morphology, a differential diagnosis of clear cell variant of SCC should be kept in mind before making a diagnosis of sebaceous carcinoma because sebaceous carcinoma possesses a poorer prognosis.

Keywords: Clear cells, eyelid, sebaceous carcinoma, squamous cell carcinoma

Introduction

The most common malignant tumor of eyelid is basal cell carcinoma followed by sebaceous carcinoma and squamous cell carcinoma (SCC).[1] Clear cell variant of SCC is an extremely rare neoplasm.[2] Histomorphologically, clear cell variant of SCC mimics sebaceous carcinoma, however, making a correct diagnosis is of great importance as sebaceous carcinoma has a poorer prognosis.[2]

Case Report

A 56-year-old male presented with a painless, small, pedunculated nodule in the left upper eyelid. The lesion was excised and sent for the histopathological examination. Gross examination revealed a skin covered nodular mass measuring 2.0 cm × 1.5 cm × 1.0 cm. Cut surface was solid, gray-white, and homogeneous.

On microscopy, tumor cells were arranged in nests and lobules with few foci of necrosis. Tumor cells were polygonal in shape and displayed moderate-to-marked pleomorphism. Many of the tumor cells had abundant clear and vacuolated cytoplasm with peripherally pushed hyperchromatic nuclei and inconspicuous to conspicuous nucleoli. Mitotic count was 6 mitoses per 10 high-power field. In between the tumor cells lobules, dense lymphoplasmacytic infiltrate and congested blood vessels were also seen [Figure 1a and b].

The differentials included clear cell variant of SCC and sebaceous carcinoma. On special stains, Periodic acid-Schif (PAS) stain was done to assess the glycogen content in the cytoplasm of tumor cells; however, all the tumor cells turned out to be negative for PAS [Figure 1c].

On immunohistochemistry, tumors cells were positive for cytokeratin (CK) [Figure 1d] and epithelial membrane antigen (EMA) [Figure 1e] and negative for androgen receptor (AR) [Figure 1f]. On the basis of the above findings, a final diagnosis of clear cell variant of SCC was made. The patient was followed up for 6 months. No

Received: 03-07-2020 **Revised:** 09-09-2020
Accepted: 16-09-2020 **Published:** 09-01-2021

Access this article online

Quick Response Code:

Website: http://www.jmau.org/

DOI: 10.4103/JMAU.JMAU_70_20

Address for correspondence: Dr. Priyanka Gogoi, Department of Pathology, University College of Medical Sciences and Guru Teg Bahadur Hospital, Delhi - 110 095, India.
E-mail: drpriyankagogoi@gmail.com

How to cite this article: Dixit S, Gogoi P, Diwaker P. Clear cell variant of squamous cell carcinoma of eyelid, mimicking sebaceous carcinoma: A rare case report. J Microsc Ultrastruct 2022;10:30-2.

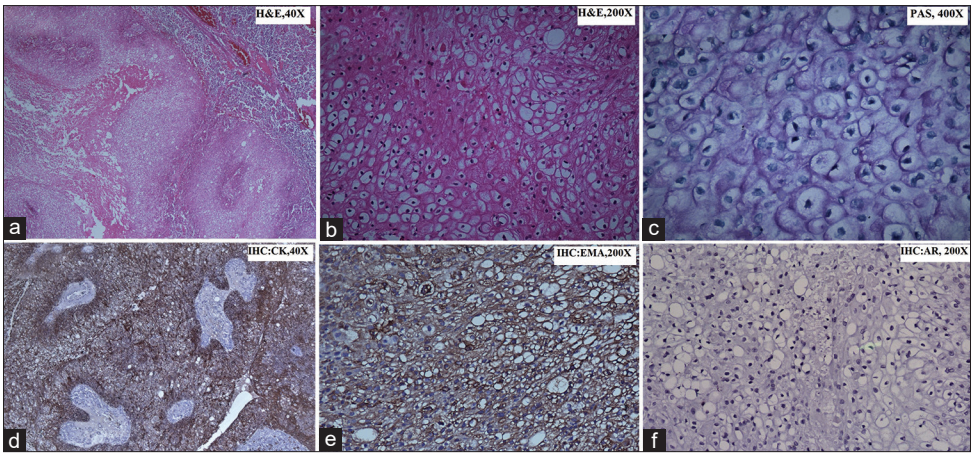

Figure 1: (a) (H and E, ×40) Islands and lobules of tumor cells, along with foci of necrosis and inflammation. (b) (H and E, ×200) Tumor cells are showing moderate-to-marked pleomorphism; cells are polygonal in shape having abundant clear and vacuolated cytoplasm and peripherally pushed hyperchromatic nuclei. (c) (Periodic acid-Schif, ×400) Clear cells are negative for periodic acidSchiff stain. (d) (Immunohistochemistry: Cytokeratin, ×40) Tumor cells are showing immunopositivity for cytokeratin. (e) (Immunohistochemistry: Epithelial membrane antigen, ×200) Tumor cells are showing strong membranous expression of epithelial membrane antigen. (f) (Immunohistochemistry: Androgen receptor, ×200) No nuclear expression of androgen receptor was identified in tumor cells

evidence of recurrence or metastasis was observed during that period.

Discussion

Basal cell carcinoma is the most common malignant tumor of eyelid followed by sebaceous carcinoma and SCC.[1] SCC has a wide histopathologic diversity. The different variants of SCC are associated with markedly different clinical behavior which can range from indolent tumors with very low metastatic potential to aggressive tumors with high metastatic potential.[3,4] Therefore, in view of treatment and prognosis, a correct microscopic diagnosis of these variants is very important. It is easy to differentiate conventional SCC from sebaceous carcinoma histomorphologically, but SCC with clear cell features can mimic sebaceous carcinoma leading to diagnostic dilemma.[1]

Clear cell variant of SCC is an extremely rare variant of SCC with minimally understood etiopathology. Kuo in 1980 first described it as a variant of SCC with extensive hydropic changes.[5] Hence, it is also known as hydropic SCC. Excessive sun exposure is a predisposing factor for this carcinoma. Very few cases are reported in the literature and most of these being described in the head-and-neck region. Mandible is the most common site for this carcinoma.[6] Most of the cases have been reported in elderly white men. The lesions mostly present as nodule or ulcerated masses and can be confused with sebaceous carcinoma, pilar tumors, or trichilemmal carcinomas clinically.[7]

Histomorphologically, clear cell variant of SCC is a close mimicker of sebaceous carcinoma. The reported metastatic potential of clear cell SCC is low compared to sebaceous carcinoma, but due to paucity of literature, it is not well established.[2]

The tumor cells of clear cell variant of SCC are polygonal in shape and have clear vacuolated cytoplasm, resembling sebaceous carcinoma. Occasional keratin pearl and evidence of cellular keratinization may be seen in clear cell variant of SCC, but its absence causes difficulty in differentiating with sebaceous carcinoma. The cytoplasmic clearing in the clear cell variant of SCC occurs due to hydropic changes, which causes the nuclei to be pushed eccentrically. However, in sebaceous carcinoma, the tumor cells show scalloped, centrally placed nuclei and microvacuolated cytoplasm due to lipid deposition.

Fat stain (Oil Red O) on fresh tissue sample can be used to differentiate between these two entities, as sebaceous carcinomas show positive staining.[7] Classical SCC shows PAS positivity due to the presence of glycogen in the cytoplasm. However, clear cell variant of SCC shows negative staining for PAS, indicating that cytoplasmic clearing occurs because of hydropic changes and not due to the presence of glycogen. Therefore, in a tumor with clear cell morphology, PAS and fat stain should be done to identify the cause of cytoplasmic clearing and also to rule out adnexal tumors. In the present case, PAS was negative in tumor cells and fat stain could not be done because formalin-fixed tissue was received for histopathological examination.

On immunohistochemistry, positivity for CK and EMA can be seen in both sebaceous carcinoma and clear cell variant of SCC. AR is known to be a highly sensitive and specific marker for diagnosing sebaceous carcinoma and is always negative in SCC.[8] Adipophilin is another valuable immune marker for the identification of sebaceous carcinoma.[9] In the present case, AR was done and found negative in the tumor cells, confirming the diagnosis of clear cell variant of SCC.

In conclusion, clear cell variant of SCC is an extremely rare entity. A differential diagnosis of clear cell variant of SCC should be

kept in mind before making a diagnosis of sebaceous carcinomas, especially in eyelid tumors. Making a correct diagnosis is of prognostic significance as clear cell variant of SCC has a better outcome. Accurate early diagnosis in light of clinical, histopathological, and immunohistochemical investigations could improve clinical management and outcome of these disparate conditions. For better understanding of this rare variant of SCC, more reports on such cases should be documented.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Pe'er J. Pathology of eyelid tumors. Indian J Ophthalmol 2016;64:177-90.
2. Rashid A, Jakobiec FA, Mandeville JT. Squamous cell carcinoma with clear-cell features of the palpebral conjunctiva. JAMA Ophthalmol 2014;132:1019-21.
3. Lohmann CM, Solomon AR. Clinicopathologic variants of cutaneous squamous cell carcinoma. Adv Anat Pathol 2001;8:27-36.
4. Cassarino DS, Derienzo DP, Barr RJ. Cutaneous squamous cell carcinoma: A comprehensive clinicopathologic classification–part two. J Cutan Pathol 2006;33:261-79.
5. Kuo T. Clear cell carcinoma of the skin. A variant of the squamous cell carcinoma that simulates sebaceous carcinoma. Am J Surg Pathol 1980;4:573-83.
6. Rinker MH, Fenske NA, Scalf LA, Glass LF. Histologic variants of squamous cell carcinoma of the skin. Cancer Control 2001;8:354-63.
7. Yanofsky VR, Mercer SE, Phelps RG. Histopathological variants of cutaneous squamous cell carcinoma: A review. J Skin Cancer 2011;2011:210813.
8. Jakobiec FA, Werdich X. Androgen receptor identification in the diagnosis of eyelid sebaceous carcinomas. Am J Ophthalmol 2014;157:687-96.
9. Jakobiec FA, Mendoza PR. Eyelid sebaceous carcinoma: Clinicopathologic and multiparametric immunohistochemical analysis that includes adipophilin. Am J Ophthalmol 2014;157:186-208.