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Case Report

Pathology Section

Orbital Adnexal Malignant Tumours: A Report of Two Cases

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ABSTRACT

Sebaceous carcinoma of the eyelid is a very rare malignant tumour, accounting for 1-1.5% of total eyelid malignancies. It typically arises from the meibomian glands, making it more common in the upper eyelids. It predominantly affects individuals in their sixth to eighth decade, with a higher incidence in females. Histologically, the tumour cells are arranged in well-defined lobules with circumscribed borders. These cells exhibit pleomorphism, eccentric hyperchromatic nuclei, inconspicuous nucleoli, and multivacuolated cytoplasm. The clinical course of sebaceous carcinoma is aggressive, often characterised by recurrences and metastasis to regional lymph nodes. Unfortunately, it is not commonly considered in the differential diagnosis of eyelid tumours, leading to delayed treatment. Thus, it is crucial to raise awareness about this uncommon neoplasm occurring at unusual sites in order to improve patient survival. In the present case report, the authors present two cases: a 54-year-old male patient with intraocular sebaceous carcinoma, which recurred, and an 83-year-old male patient with extraocular sebaceous carcinoma. In both the cases, imaging and other investigations were performed, followed by excision of the mass and confirmation of the diagnosis through histopathological reporting. Subsequent follow-up was conducted for both cases and the postoperative recovery was uneventful.

Keywords: Eyelid, Extraocular, Immunohistochemistry, Intraocular, Sebaceous gland carcinoma

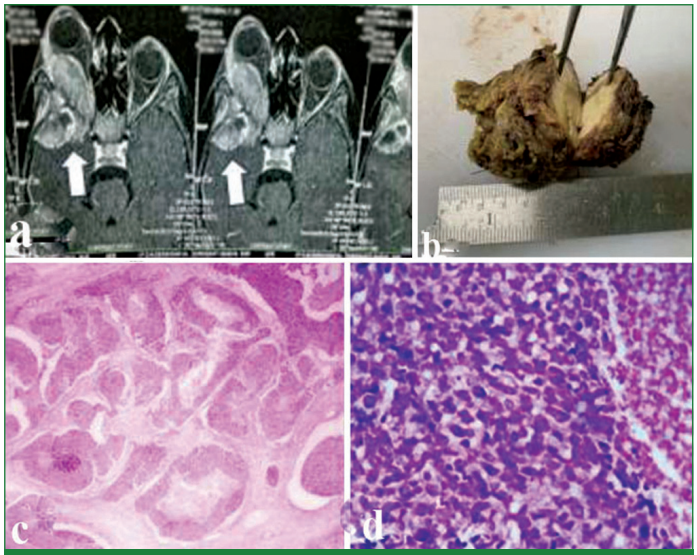
CASE REPORT

Case 1

A 54-year-old male patient presented to the eye Outpatient Department (OPD) three years ago with a complaint of a lump over the medial canthus of the right upper eyelid. The lump was operated on as a sebaceous cyst in 2019. Cutler Beard stage I and stage II surgery was performed. The postoperative period was uneventful. However, the histopathological report revealed sebaceous carcinoma.

Again in 2022, the patient returned to the eye OPD with a recurrence in the previously operated area due to positive surgical margins. An MRI (T1 weighted) showed a heterogeneous lesion involving the medial portion of the right orbit, the right peri-orbital region, the right eyelid, and affecting the extraocular muscles and right lacrimal gland [Table/Fig-1a]. The features were suggestive of a neoplastic mass, with squamous cell carcinoma with hydropic changes and basal cell carcinoma with sebaceous differentiation considered as differential diagnoses. There was also pressure effect observed on the right ocular bulb with involvement of the extraocular muscles. Patient was also examined for any enlargement of sentinel lymph nodes.

He underwent reoperation and the specimen was sent to the Pathology department for histopathology. Grossly, the size of the specimen was 7.5×4.5×3 cm, with the optic nerve measuring 0.8 cm. On grossing, a greyish-white growth measuring 4.5×3.5×3 cm was noted [Table/Fig-1b]. Microscopically, the tumour mass was arranged in a lobular pattern, composed of pleomorphic cells with eccentric hyperchromatic nucleus, inconspicuous nucleolus [Table/Fig-1c, 1d]. Extensive areas of comedo necrosis were observed, along with lymphovascular invasion. The adjacent inferior orbital bone margin showed invasion by the growth. The histomorphological features were suggestive of sebaceous carcinoma with stage pT3bNxMx. Immunohistochemical expression of HER2/neu was negative. The patient had an uneventful postoperative recovery and is doing well after six months of follow-up.



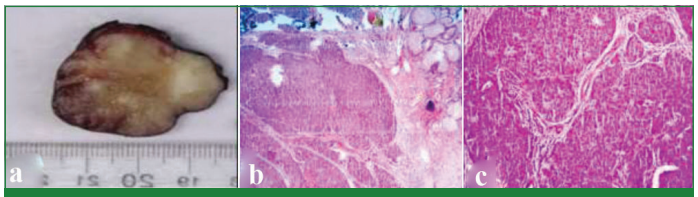
[Table/Fig-1]: (a) MRI (T1 weighted) shows heterogenous lesion involving medial portion of right orbit; (b) Gross specimen shows white mass; (c) Section shows tumour mass arranged in lobular pattern (x100, H&E); (d) Section shows pleomorphic cells having eccentric hyperchromatic nucleus with inconspicuous nucleolus and multivacuolated clear cytoplasm (x400, H&E).

Case 2

An 83-year-old male patient presented to the eye OPD with pain, swelling, and a foreign body sensation in the left lower eyelid for the last six months. On examination, his visual acuity was 6/18 in both eyes, with senile immature cataracts in both eyes and a normal fundus. During the local examination of the left lower lid, a vascular mass measuring 5×10 mm and located near the lateral lid margin was discovered. Due to suspicion of a pre-malignant lesion, he was examined for any enlargement of sentinel lymph nodes. An ultrasound revealed a heterogeneous lesion on the left lower eyelid, which raised concerns of a malignant lesion. No bone involvement was observed. Fine needle aspiration cytology was performed using a standard technique, followed by staining with Papanicolaou and May Grunwald Giemsa (MGG). The smear showed irregular clusters of tumour cells with pleomorphic centrally located nuclei and coarse

chromatin. The patient underwent surgery, and the specimen was sent for histopathology.

Macroscopically, the specimen was a globular skin-covered tissue piece measuring 2×1×1 cm [Table/Fig-2a]. Microscopically, the section revealed the histology of a neoplastic lesion composed of pleomorphic, hyperchromatic cells with centrally placed vesicular nuclei, prominent nucleoli, and granular eosinophilic cytoplasm. These cells were arranged in lobules, sheets, and glands separated by fibrocollagenous tissue [Table/Fig-2b,c]. Mitosis, necrosis, and haemorrhage were present. The histomorphological features were suggestive of sebaceous carcinoma with pT3bNxMx. Immunohistochemical expression of HER2/neu was negative. The patient's postoperative recovery was uneventful, but he was lost to follow-up after two months.



[Table/Fig-2]: (a) Gross specimen; (b) Section shows tumour mass arranged in lobular pattern separated by fibrocollagenous tissue (x100, H&E); (c) Section shows pleomorphic, hyperchromatic cells, centrally placed vesicular nucleus, prominent nucleoli, granular prominent eosinophilic cytoplasm (x400, H&E).

DISCUSSION

Sebaceous carcinoma of the eyelid is a very rare malignant tumour, accounting for 1-1.5% of all eyelid malignancies [1]. It is more commonly observed in the sixth to eighth decade of life, with a higher incidence in females. Typically, it originates from the meibomian glands, making it more prevalent in the upper eyelids. This aggressive tumour has a tendency to metastasise to regional lymph nodes and distant organs, resulting in a poor prognosis [2]. Extraocular sebaceous carcinoma constitutes approximately 25% of sebaceous neoplasms and primarily affects the head and neck regions, followed by the trunk, salivary glands, genitalia, breast, ear canal, and intra-oral cavity [3].

Clinically, sebaceous carcinoma on the eyelid can be mistaken for persistent conjunctivitis, chronic blepharophlebitis, or chalazion. If conjunctivitis or chalazion does not improve after three months of observation, a biopsy should be performed. It predominantly occurs in elderly Caucasian individuals. Ocular sebaceous carcinoma often exhibits regional metastasis and affects both sexes equally, whereas extraocular sebaceous carcinoma is more common in men. In this case, both patients were elderly males, consistent with previous studies [4-7].

The clinical presentation of sebaceous carcinoma varies, presenting as a small, erythematous, or yellow slowly enlarging firm papule or nodule on the skin. Diagnosis is often delayed, requiring pathological confirmation of neoplastic cells with sebaceous differentiation. Histologically, the tumour cells are arranged in well-defined lobules with circumscribed borders. The cells display pleomorphism with eccentric hyperchromatic nuclei, inconspicuous nucleoli, and multivacuolated cytoplasm. Lymphovascular invasion is observed, and common findings include mitosis, marked nuclear atypia, hemorrhage, and necrosis. Microscopically, sebaceous carcinoma often resembles molluscum contagiosum, pyogenic granuloma, keratoacanthoma, and squamous cell carcinoma with hydropic changes, as well as basal cell carcinoma with sebaceous differentiation. Squamous cell carcinoma is ruled out due to the absence of evidence of keratinization in the form of dyskeratotic cells and keratin pearls. Additionally, the absence of basaloid differentiation and peripheral palisading excludes basal cell carcinoma as a diagnosis. Sebaceous carcinoma has poorly differentiated and anaplastic types. The poorly differentiated variant exhibits marked pleomorphism, prominent nucleoli, and a high mitotic count, while the anaplastic variant displays scanty basophilic cytoplasm and extensive necrosis. Poorly differentiated squamous cell carcinoma and anaplastic basal cell carcinoma can be differentiated from these variants using oil red O stain and Sudan black stain, which show positive results [8].

The clinical course of sebaceous carcinoma is aggressive, with frequent recurrences and metastasis to regional lymph nodes. The recurrence rates for ocular sebaceous carcinoma range from 11% to 30%, and distant metastases occur in 3% to 25% of cases [9]. Poor prognostic indicators include large size, multicentricity, poor differentiation, infiltrative pattern, vascular invasion, and orbital infiltration. Immunohistochemical markers such as cytokeratin, Epithelial Membrane Antigen (EMA), Cam 5.2, and anti-breast carcinoma-associated antigen-225 antibody are expressed by sebaceous carcinoma cells. HER2/neu, the human epidermal growth factor receptor 2, is often evaluated through Immunohistochemistry (IHC) to identify molecular alterations that could be potential therapeutic targets. In both cases mentioned, the expression of HER2/neu was negative. Adipophilin, an IHC test, is useful in differentiating sebaceous carcinoma from other dermatological malignancies, like squamous cell carcinoma and basal cell carcinoma, with a sensitivity and specificity of 100% [2,10,11]. Unfortunately, adipophilin was not available in the department, so the authors were unable to perform the test. Recent studies are investigating the molecular mechanisms underlying tumour development and progression, suggesting that the loss of p53 and disruption of genomic integrity may play a critical role in sebaceous carcinoma progression [12].

When considering a diagnosis of sebaceous carcinoma, a detailed history and physical examination should be conducted. Colonoscopy and barium enema are essential for ruling out internal malignancies associated with Muir-Torre syndrome, an autosomal dominant genetic condition caused by germline mutations in DNA mismatch repair genes. Muir-Torre syndrome is a variant of Lynch syndrome and is characterised by a predisposition to skin malignancies and visceral malignancy, particularly colorectal cancer [13]. In cases of extraocular sebaceous carcinoma, IHC for microsatellite instability (MLH1, MSH2, MSH6, PMS2) should be performed to exclude Muir-Torre syndrome.

Although extraocular sebaceous carcinoma is generally less aggressive than ocular carcinomas, there have been reports of regional and distant metastasis [14]. In one of the cases, the tumour recurred at the local site after treatment, which was also observed in another study [4]. Mohs Micrographic Surgery (MMS) is an ideal treatment option, while subtotal or complete exenteration may be required if the tumour is large, recurrent, or has spread to the bulbar conjunctiva, other eyelids, or orbital tissue. Radical neck dissection, along with partial parotidectomy, is performed if there is spread to regional lymph nodes. Due to its fastgrowing nature, postoperative patients should be followed-up at three-month intervals during the first year, six-month intervals during the second year, and then annually for life [15]. Metastatic disease, if present, may be treated with a combination of excision, radiation, and chemotherapy. The mortality rates for both ocular and extraocular sebaceous carcinoma range from 9% to 50% [16].

CONCLUSION(S)

Sebaceous cell carcinoma is a rare condition with an unfavorable prognosis and a tendency to metastasise. It is generally not considered as a differential diagnosis for tumours arising from the eyelids, resulting in delayed treatment. Hence, we emphasise the need to raise awareness about this uncommon neoplasm occurring in unusual sites to expedite patients' survival.

REFERENCES

[1] Schmitz EJ, Herwig-Carl MC, Holz FG, Loeffler KU. Sebaceous gland carcinoma of the ocular adnexa-variability in clinical and histological appearance with analysis of immunohistochemical staining patterns. Graefes Arch Clin Exp Ophthalmol. 2017;255(11):2277-85.

[2] Lee MJ, Kim N, Choung HK, Choe JY, Khwarg SI, Kim JE. Increased gene copy number of HER2 and concordant protein overexpression found in a subset of eyelid sebaceous gland carcinoma indicate HER2 as a potential therapeutic target. J Cancer Res Clin Oncol. 2016;142(1):125-33.

[3] Lazar AJ, Lyle S, Calonje E. Sebaceous neoplasia and Torre-Muir syndrome. Curr Diagn Pathol. 2007;13(4):301-19.

[4] Bhardwaj S, Mukutawat P, Kaushal V. Recurrent sebaceous gland carcinoma of upper eyelid-a case report. Int J Inn Sci Res Tech. 2020;5(7):30-31.

[5] Pandey AN, Raina A, Hatwal D, Chaudhary S. A rare case of sebaceous cell carcinoma of lower lid. Ophthalmol Res Rep. 2017:ORRT-123.

[6] Singh S, Kaur S, Mohan A, Goyal S. Sebaceous carcinoma of right upper eyelid: Case report and literature review. Int J Can The Onc. 2013;1(2):01-03.

[7] Joshi R, Jangir MK, Kochar A. Sebaceous gland carcinoma: A case report. Int J Ocul Oncol Oculoplasty. 2016;2(3):208-10.

[8] Laxenaire A, Saihi E, Huault M, Levy J. Eyelid sebaceous carcinoma. A case report with literature review. Ann Chir Plast Esthet. 2000;45(1):48-57.

[9] Muqit MM, Roberts F, Lee WR, Kemp E. Improved survival rates in Sebaceous Carcinoma of the eyelid. Eye. 2004;18(1):49-53.

[10] Cabral ES, Auerbach A, Killian JK, Barrett TL, Cassarino DS. Distinction of benign sebaceous proliferations from sebaceous carcinomas by immunohistochemistry. Am J Dermatopathol. 2006;28(6):465-71.

[11] Kwon MJ, Shin HS, Nam ES, Cho SJ, Lee MJ, Lee S, et al. Comparison of HER2 gene amplification and KRAS alteration in eyelid sebaceous carcinomas with that in other eyelid tumours. Pathol Res Pract. 2015;211(5):349-55.

[12] Gonzalez-Fernandez F, Kaltreider SA, Patnaik BD, Retief JD, Bao Y, Newman S, et al. Sebaceous carcinoma. Tumour progression through mutational inactivation of p53.Ophthalmology. 1998;105(3):497-506.

[13] Shields JA, Demirci H, Marr BP, Eagle RC, Shields CL. Sebaceous carcinoma of the eyelids: Personal experience with 60 cases. Ophthalmology. 2004;111(12):2151-57.

[14] Kaliki S, Ayyar A, Dave TH, Ali MJ, Mishra DK, Naik MN. Sebaceous gland carcinoma of the eyelid: Clinicopathological features and outcome in Asian Indians. Eye. 2015;29(7):958-63.

[15] Gardetto A, Rainer C, Ensinger C, Baldissera I, Piza-Katzer H. Sebaceous carcinoma of the eyelid: A rarity worth considering. Br J Ophthalmol. 2002;86(2):243-44.

[16] Doxanas MT, Green WR. Sebaceous gland carcinoma. Review of 40 cases. Arch Ophthalmol. 1984;102(2):245-49.

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