

Sebaceous carcinoma of right upper eyelid: case report and literature review

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Case Report

Abstract

Sebaceous gland carcinoma is a rare fast growing cutaneous cancer. It is derived from the adnexal epithelium of sebaceous glands. Sebaceous carcinomas are generally divided into those occurring in periocular or extraocular locations. Ocular sebaceous carcinomas occur most commonly in upper eye lid, in the elderly with a predilection for females and Asian populations. Due to its clinical resemblance with chalazion or other chronic inflammatory conditions, there is a delay in diagnosis. Due to its rarity, we present a case of sebaceous carcinoma of right upper eyelid in a 65-year-old female.

Keywords: Upper eyelid; ocular sebaceous carcinoma; chalazion

Introduction

Sebaceous carcinoma was first reported by Allaire in 1891. Its incidence is less than 1% of all skin malignancies. Sebaceous carcinoma is the fourth most common neoplasms of the eyelid and arises mainly from the meibomian or less commonly from Zeis glands. It is a rare but fast growing malignant neoplasm with a tendency for both local recurrence and distant metastases. Sebaceous carcinoma can either be ocular or extraocular, and extraocular type is rare.¹ Advanced age, Asian or South Asian race, women, previous irradiation to the head and neck, a genetic predisposition for Muir-Torre syndrome or possibly familial retinoblastoma are various predisposing factors for sebaceous carcinoma. It mostly spread to regional lymph nodes. It may invade orbit, and 22% of patients die due to visceral metastases.²

Case History

A 65-year-old female patient presented with a mass over right upper eyelid (Figure 1). Patient complained of decreased vision & foreign body sensation in the right eye for 6

months prior to reporting the case. Fine needle aspiration cytology (FNAC) was performed using standard technique. Staining was done with papanicolaou stain & May Grunwald Giemsa (MGG) stain. Smears demonstrated tumor cells arranged in irregular clusters and as single cells. The cells contain moderate amount of finely reticular cytoplasm with various degrees of vacuolization. Pleomorphic centrally located nuclei containing coarse chromatin & prominent nucleoli were seen (Figure 2).

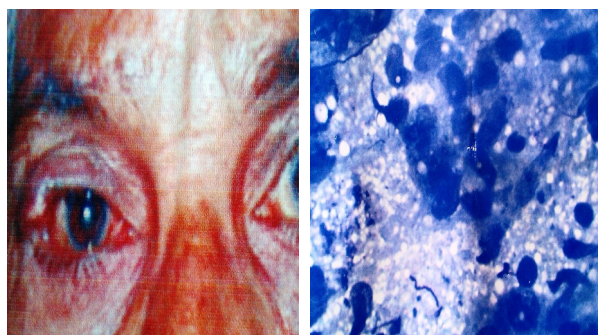


FIG. 1 (left): Patient Photo showing swelling right upper eyelid.

FIG. 2 (right): Cytological smear showing sebaceous carcinoma MGG (high power).

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Tumor was excised and Oil red O staining of fresh frozen tissue was done for confirmation of sebaceous carcinoma. Histopathology revealed irregular epithelial lobules with atypical dark pleomorphic cells with abundant foamy, finely vacuolated cytoplasm & well defined borders. The tumor

cells manifested marked pleomorphism, prominent nucleoli & numerous mitotic figures (Figures 3 and 4). CAM 5.2 staining was done to differentiate between the normal & malignant sebaceous lesions. CAM 5.2 staining was strongly positive for sebaceous carcinoma.

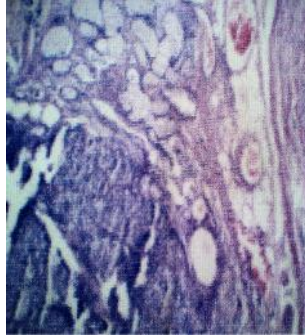


FIG. 3: Histopathology slide showing sebaceous carcinoma H&E under low power.

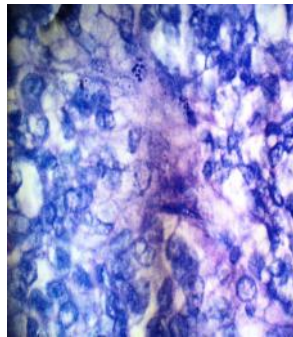


FIG. 4: Histopathology slide showing sebaceous carcinoma H&E under high power.

Discussion

Sebaceous carcinoma is a rare and destructive malignant neoplasm. It frequently occurs in adults with a female predominance.³ This malignancy can occur as periocular and extraocular regions and the former type is about 75% of sebaceous neoplasms. Upper eyelid is affected two to three times more often than the lower eyelid due to high number of meibomian glands.⁴ According to literature, ocular sebaceous carcinoma arose from the meibomian glands in 51 to 70% of cases; multicentric in origin in 12 to 24 %; and 4 to 10% arose from the glands of Zeiss; the few originated from the caruncle or orbit. Incidence of extraocular sebaceous carcinoma is about 25% of the sebaceous neoplasms and mostly effects the head and neck areas followed by trunk, salivary glands, genitalia, breast, ear canal, and the intra-oral cavity.³

The clinical presentation of ocular sebaceous carcinoma is varied and an accurate diagnosis is delayed for months to years. The mean delay from onset of disease to diagnosis is about 1 to 2.9 years. The most common clinical presentation is a small, erythematous or possibly yellowish, slowly en-

larging, firm, deep seated papule or nodule on the upper eyelid. It may resemble with a chalazion, keratoconjunctivitis or blepharoconjunctivitis. Numerous other inflammatory conditions, autoimmune diseases, infectious processes, and basal cell carcinoma may clinically imitate sebaceous carcinoma of the eyelid. Due to variable clinical presentations of ocular sebaceous carcinoma, a high degree of suspicion and ultimate biopsy of non-healing lesions is critical in making the final diagnosis. Sometime diagnosis is made only after metastases to the regional lymph node or parotid gland.⁵

TABLE 1: Classification of sebaceous carcinoma based on degree of differentiation by Font⁶ (top) and Wolfe *et al.*⁷ (bottom)

Classification by Font.⁶

Well Differentiated	Contains many neoplastic cells exhibiting sebaceous differentiation with abundant finely vacuolated cytoplasm. Areas of sebaceous differentiation are often toward the center of tumor lobules
Moderately Differentiated	Only a few areas of highly differentiated sebaceous cell are seen. The majority of the tumor is composed of neoplastic cells with hyperchromatic nuclei and prominent nucleoli and abundant basophilic cytoplasm
Poorly Differentiated	The majority of cells exhibit pleomorphic nuclei with prominent nucleoli and scant cytoplasm. A moderate increase in mitotic activity is present.

Classification by Wolfe *et al.*⁷

Grade I	Well differentiated; foamy cytoplasm present in all cells.
Grade II	Large vacuolated nuclei and foamy cytoplasm seen in most cells
Grade III	Small hyperchromatic nuclei and little cytoplasm present in most cells
Grade IV	Undifferentiated; small hyperchromatic nuclei and little cytoplasm; diagnosis requires positive fat stain, ultrastructural study or areas of better differentiation.

Histologically, sebaceous carcinoma has to be differentiated from basal cell carcinoma, squamous cell carcinoma, trichilemmal keratinisation, sebaceous adenoma and sebaceous epithelioma. Special stains such as oil red O may be helpful in confirming the presence of fat, but requires frozen section. Immunohistochemical studies may also be employed to confirm the diagnosis. Sebaceous carcinoma cells express immunohistochemical markers such as cytokeratin, epithelial membrane antigen (EMA), Cam5.2 and anti-breast carcinoma associated antigen-225 antibody. The cause of sporadic sebaceous carcinomas is still unclear. Previous radiation to the area is a well-documented risk factor, especially in children.⁸ Sebaceous carcinoma may be associated with use of oral diuretic like thiazide. The diuretic causes production of carcinogenic nitrosamines which may play a role in the carcinogenesis of the sebaceous carcinomas in these patients.⁹ However, there is no firm etiologic link between diuretic use and the development of sebaceous carcinoma.

The molecular mechanisms for tumor development and progression are recently being studied. It has been assumed that the loss of p53 and the consequent disruption of genomic integrity might play a critical role in the progression of sebaceous carcinoma.¹⁰ Ocular sebaceous carcinoma may metastasize via the lymphatics, the blood vessels, by the lacrimal secretory system, and the lacrimal excretory system. Metastases occur in approximately 8 to 25% of patients, and metastasize to regional lymph nodes, followed by involvement of the liver, lungs, brain, and bones. Lymphatic metastases involve preauricular, submandibular, or cervical lymph nodes, with or without secondary parotid masses. Distant metastases and recurrence rates are more common in the ocular type of sebaceous carcinoma.¹¹ Recurrence rates of ocular sebaceous carcinoma ranges from 11% to 30% with distant metastases occurring in 3% to 25%.¹¹ In sebaceous carcinoma of eye lid, there is local loss of the eyelashes due to tumour infiltration of the follicle. If tumor is one sided and every therapy is ineffective then there are more chances of sebaceous carcinoma. A full thickness eyelid biopsy combined with conjunctival map biopsies is necessary for the diagnosis.¹² Once a diagnosis of sebaceous carcinoma is considered, a detailed history and physical examination should be done. Colonoscopy and barium enema are essential to rule out internal malignancies associated with the Muir-Torre syndrome.

The primary treatment of sebaceous carcinoma is complete surgical excision. Mohs micrographic surgery is most commonly done.¹³ Excision of tumor with frozen section is mandatory for proper management. Conjunctival map biopsies should be done at the time of surgery to assess for potential pagetoid spread. Microscopically it tends to extend far beyond its assessed clinical margins as it may spread by direct extension, be multifocal in advanced cases, and may develop "skip areas" after injury. Despite its ability to develop "skip areas", Mohs micrographic surgery (MMS) is a ideal mode of treatment.¹⁴ Subtotal or complete exenteration is required if the tumour is very large or recurrent with spread to bulbar conjunctiva, to the other eyelid, or to orbital tissue. Radical neck dissection along with partial parotidectomy is performed if it spread to regional lymph nodes.¹²

The missing tarsoconjunctival structures and skin should be reconstructed properly to protect the eye globe and should give a natural appearance with only minor deficiency. Ideally it should be one stage procedure. The vascularised temporal island flap can be used as one stage procedure. As it is fast growing cancer, postoperative patient should be followed up at 3 monthly interval during the first year, 6 monthly during the second year, and then on a yearly basis for life.¹² Cryotherapy can be utilized as adjunctive therapy to treat patients with residual conjunctival intraepithelial disease or in those patients in whom definitive surgical excision is not possible. Topical mitomycin C has also been used as an adjunctive therapy in patients with intraepithelial involvement.¹⁵ Sebaceous carcinoma is relatively radio resistant, so, radiotherapy may be used as palliative therapy for

inoperable patients.¹³ Total dose of radiation is about >50 Gy. If radiation alone is used then tumor may reoccur within 3 years.

Finally, metastatic disease may be treated with a combination of excision, radiation, and chemotherapy. A schedule of intralesional 5-fluorouracil in combination with intravenous 5-fluorouracil, doxorubicin, cisplatin, and vinblastine has been used.¹⁶ Mortality rates irrespective of ocular or extraocular type ranges from 9% to 50%.¹⁷

Conclusion

Sebaceous carcinoma is a fast growing tumor and it is mostly seen on the eyelid. Since it clinically resembles other diseases, it presents challenge in diagnosis. Early, precise and prompt diagnosis is vital as it spreads out regionally as well to other distant organs. It may be associated with Muir-Torre syndrome. The inconsistent appearance mostly causes delay in diagnosis, improper treatment, increased morbidity, and mortality.

Conflict of interest

The authors declare that they have no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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