SEBACEOUS CARCINOMA OF THE EYELID : REPORT OF 3 CASES

Puripakorn Pakdirat*

Wipada Ladapornvittaya**

**Ratchaburi Hospital*

***Photharam Hospital*

ABSTRACT :

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*Department of Anatomical Pathology, Ratchaburi Hospital, Ratchaburi, Thailand.
** Department of Ophthalmology, Photharam Hospital, Ratchaburi, Thailand.

Sebaceous carcinoma is an unusual tumour of the eyelid. It constitutes 1-5.5% of eyelid malignancies in the western world. Some reports have suggested a higher incidence in the far east. This tumour is deceptively benign in its early stage. Lesions are often recognised late, resulting in poorer prognosis. Biopsy is encouraged in all doubtful cases. Frozen section should be applied on fresh or formaldehyde fixed tissue for demonstration of fat whenever hematoxylin & eosin sections yield inconclusive results.

Three cases of sebaceous carcinoma of the eyelid are reported. One of them presented with an initial diagnosis of pyogenic granuloma. Histopatholgic diagnosis was confirmed with oil-red-O technique in all cases. Clinicopathological findings are described. A brief review of the literature is presented.

Introduction

Sebaceous carcinoma of the eyelid is rare, found in 1-5.5% of all eyelid malignancies. Incidence in the east is higher. It is the most lethal ocular adnexal cancer.[1,2] Clinically it appears as benign and less invasive conditions, leading to delayed diagnosis and treatment.[1,3]

Three cases of sebaceous carcinoma of the eyelid, diagnosed clinically at Photharam hospital and histologically at Ratchaburi hospital in a five-month period (June to October 1993), are here reported. Clinicopathological findings are described. Histology including differential diagnosis is also discussed. A concise review of the disease is presented.

Anatomy. The sebaceous gland is a holocrine gland ; its secretion is produced by fatty degeneration of the central cells, which are discharged and then replaced by proliferation of marginal cells.[4] Fat, free fatty acids and cholesterol in the secretion form the lipid layer of the tear film.[2] If the ducts open into hair follicles of the eyelashes, the glands are called glands of Zeis ; whereas glands with ducts that open into the lid margins are known as meibomian glands.[5] Sebaceous glands of the eyelid are large, contain more acini, and are not related to hair follicles. The intermarginal sulcus runs between the eyelashes and the openings of ducts of the meibomian glands, therefore meibomian glands are on the conjunctival part of the eyelid.[4]

Clinical presentation. Sebaceous carcinoma often mimics benign inflammatory conditions. It presents as a slowly enlarging, firm, painless mass.[2] Carcinoma of the meibomian gland involves deep structures and ulceration appears late. The upper eyelid is more often affected. It can masquerade as a chalazion, severe conjunctivitis, or other inflammatory conditions. Many cases of sebaceous carcinoma used to be treated with repeated curettage for suspected chalazia, or as persistent, atypical inflammations.

Material and methods

Three patients with eyelid mass were diagnosed by histologic examination from June 1993 to October 1993. Specimens were submitted by one ophthalmologist in Photharam hospital to the Department of Anatomical Pathology, Ratchaburi hospital. Histologic diagnosis was given by one surgical pathologist through light microscopy with hematoxylin & eosin stained sections.

The histologic findings and diagnosis were documented. Oil-red-O technique was applied afterwards to demonstrate adipose component. Clinicopathological correlation was made.

Results

Clinical details. The tumours presented as a growing mass in the eyelid. They were painless and one was bleeding. Duration of lesion ranged from 3 weeks to 12 months. The lesion was found in the upper eyelid in two cases. No tumour was bilateral or involved both the upper and lower lids. Average age of patients at presentation was 73 years ; all were female. The initial diagnosis was meibomian gland carcinoma in 2 cases, and pyogenic granuloma in 1 case. Clinical details are outlined in table 1.

Gross pathology. The size of specimens received were 1.2 x 1.0 x 1.0 cm, 1.5 x 1.3 x 1.0 cm, and 2.0 x 1.6 x 1.2 cm. The colours were brown and grayish black, yellow white, or gray. The consistency was soft to firm.

Histological findings. Sebaceous carcinoma is graded according to histologic criteria,[6] as outlined in table. 5 Sebaceous origin is evident by cell morphology. The tumour consists of irregular lobules, the cells show foamy or vacuolar cytoplasm. Such cells are found in all 3 cases. They are interspersed with less differentiated cells with indistinct vacuoles, vesicular nuclei, variably prominent nucleoli, round to oval or irregular nuclear outline and basophilic cytoplasm. Nuclear shape and size are irregular, with increased nuclear/cytoplasmic ratio. Presence of fat in the better differentiated cells was confirmed by the oil-red-O technique employed on frozen sections of the Formalin fixed tissue.

Tumour differentiation in the 3 cases varies from well to poor. No tumour was intraepithelial. The tumour patterns were all organoid, with extensive necrosis in one case. All tumours infiltrated deeply, probably corresponding to late clinical presentation. Transition from normal meibomian glands of the tarsal plate was seen in one case.

Inflammatory response varies from heavy to minimal. Infiltrates are mostly plasma cells and small lymphocytes.

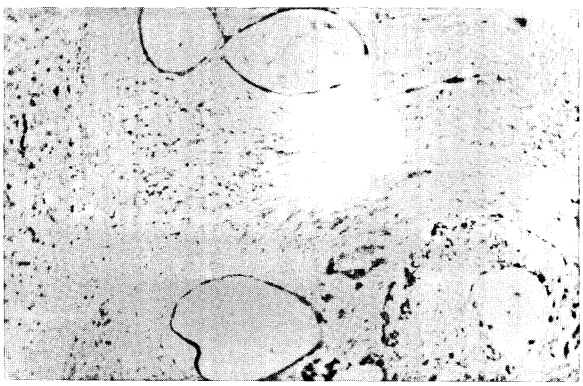

Fig. 1 Sebaceous carcinoma arising in meibomian gland of the eyelid.

Follow up of patients. Progress of cases were available 3-21 months after diagnosis. Recurrence

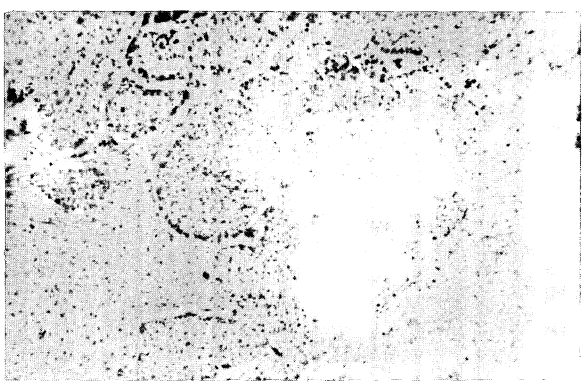

Fig. 2 Sebaceous gland carcinoma. Tumour cells are moderately to poorly differentiated. Note necrotic cells in the lower right corner.

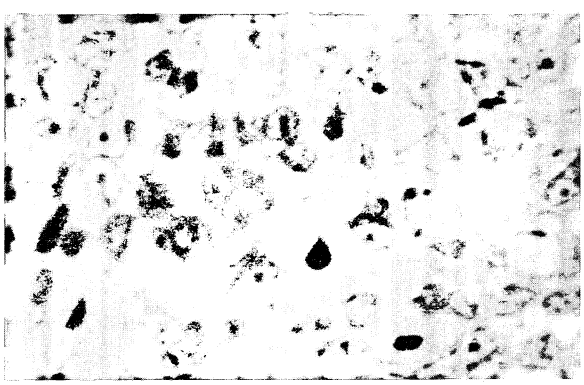

Fig. 3 Tumour cells with cytoplasmic vacuoles, hematoxylin-eosin stain. Fat is demonstrable by oil-red-O technique. (not shown here).

Table 1 Clinical details of patients

Patient	Age (years)	Sex	Duration	Site	Presentation
Case 1	88	F	2 months	left upper	growing, bleeding mass
Case 2	57	F	12 months	left lower	painless mass
Case 3	74	F	3 weeks	left upper	growing mass
Average	73	-	4.9 months	-	-

Table 2 Gross pathologic findings

Patient	Gross pathologic findings		Clinical diagnosis
	Size (cm)	Gross appearance	
Case 1	2.0 x 1.6 x 1.2	brown and grayish black tissue piece	meibomian gland CA
Case 2	1.5 x 1.3 x 1.0	yellow white mass	pyogenic granuloma (15 months before first biopsy)
Case 3	1.2 x 1.0 x 1.0	gray tissue piece	meibomian gland CA

Table 3 Histologic findings

Patient	Diagnosis	Differentiation	Epithelial involvement	Transition from normal glands
Case 1	Sebaceous carcinoma	poor	none	present
Case 2	Sebaceous carcinoma	well	none	absent
Case 3	Sebaceous carcinoma	moderate to poor	none	absent

Table 4 Follow up of patients

Patient	Period after first histologic diagnosis	Results
Case 1	12 months	Recurrence in the 12th month
Case 2	21 months	No recurrence for 9 months after 2nd excision*
Case 3	3 months	No recurrence (Lost to follow up after 3 months)

* No tissue of 2nd excision was obtainable.

Table 5 Criteria for grading of sebaceous carcinomas, according to Wolfe et al. (6)

Grade	Criteria
1	Well differentiated ; foamy cytoplasm in all cells
2	Large vacuolated nuclei and foamy cytoplasm in most cells
3	Small hyperchromatic nuclei and little cytoplasm in most cells
4	Undifferentiated ; small hyperchromatic nuclei and little cytoplasm ; diagnosis requires positive fat stain, ultrastructural study, or areas of better differentiation

was found in 2 cases, 12 to 21 months after first excision. The case with no reported recurrence was lost to follow up after 3 months.

Discussion

Allaire described the first case of adenocarcinoma of the meibomian gland in 1891. Earlier reports by Thiersch and Baldauf were not well documented. Hagerdoorn recommended a separate classification for malignancies of the meibomian glands.[2]

Sebaceous carcinoma is the third most common eyelid malignancy after basal cell and squamous cell carcinomas. Its incidence is 1% - 5.5% of all eyelid malignancies in the western world. A study from Shanghai, however, reported an incidence of 33%, with larger, more aggressive tumours.[2] The possibility of higher incidence in the east suggests an influence of genetic, racial and environmental factors. The 3 cases reported here were found in a chronological period of 5 months. In a series collected

at the Mayo Clinic, 43 cases were found in a period of 76 years. Greater awareness, on the parts of the clinician, the ophthalmologist, and the pathologist, may lead to better identification of cases, lower rates of morbidity and mortality, and better insight into the nature of this cancer. The findings in our study shows similarity in patients' age, sex, and tumour location to other studies (see table 1).

Sebaceous carcinoma may arise in the meibomian glands, the glands of Zeis, or the sebaceous glands underneath the eyebrow, the eyelid, or a caruncle. The site of origin usually cannot be determined. No biologic difference between tumours of different gland types has been demonstrated.

Inflammatory conditions are often cited as initial diagnoses of sebaceous carcinoma, especially recurrent chalazion. This is probably due to rarity of the tumour.[1] One of our cases was first diagnosed as pyogenic granuloma. Sebaceous carcinoma can mimic cutaneous horn, ocular pemphigoid, blepharoconjunctivitis, leukoplakia, carcinoma in situ, squamous cell carcinoma or basal cell carcinoma.

Sebaceous carcinoma is more often found in the upper eyelid, corresponding to normal distribution of meibomian glands. Multicentricity is not uncommon ; it may involve both eyelids or occur bilaterally. Whether the tumour is found in the upper or lower lid has no correlation with metastatic spread. Conjunctival tumours are likely to remain undetected until lymphatic involvement occurs, thus the impression that they are more aggressive. Tumour location is not always helpful in differential diagnosis, but usually sebaceous carcinoma is on the conjunctival side ; inverted follicular keratosis more commonly involves the eyelid margin ; keratoacanthoma has a predilection for the lower eyelid, basal cell carcinoma for the lower eyelid and inner canthus, and squamous cell carcinoma for the exposed skin.

Histologic sections stained with hematoxylin and eosin is often sufficient for diagnosis of sebaceous carcinoma. Variations in the histologic patterns sometimes make diagnosis difficult. Unusual cross sections of pilosebaceous units may look like squamous pearls. Peripheral palisading may mimic basal cell carcinoma. Accompanying pagetoid change may be misinterpreted as junctional melanosis.[3] In general, no tumour is composed entirely of a single pattern. Mixtures of basaloid and squamoid features are seen. Fat stain helps confirm the diagnosis of sebaceous carcinoma.

Intraepithelial component of tumour, also known as extramammary Paget's disease, an analog of Paget's disease in mammary carcinoma, was not seen in the 3 cases reported here. Wolfe III et al. observed no prognostic difference between tumours with and without Pagetoid component. However, as pagetoid change of the overlying conjunctival epithelium is frequently adjacent to invasive sebaceous carcinomas, it is suggested that sebaceous carcicoma may occur as a field effect of some carcinogenic stimuli. Full thickness eyelid biopsy is recommended in cases in which pagetoid change is observed.[3]

The most prominent ultrastructural feature in sebaceous carcinoma is the presence of intracytoplasmic lipid vacuoles without a limiting membrane.

Clinical and histologic characteristics are associated with prognosis. Tumour size, orbital invasion, and metastasis can be determined clinically,

whereas multicentric origin, sebaceous differentiation, infiltrative pattern, and lymphatic or vascular invasion are described by histologic examination.[2] Close follow up of all patients with sebaceous carcinoma is mandatory for detecting tumour recurrence and metastasis. In this study, the tendency to recur cannot be overemphasised; relapse was found in two cases within 12 months after excision. In the case without recorded recurrence, follow up was possible for only 3 months.

Treatment is by surgery, followed by radiation in case of incomplete removal, recurrence, or metastasis.[1] The French literature has suggested radiotherapy to be of curative value since as early as 1936.[7] Five-year tumour-related death rate has been estimated at around 30%. However, a recent study suggests that increased awareness and early definitive treatment have markedly improved prognosis.[2]

Summary

Sebaceous carcinoma of the eyelid is often overlooked, both by clinicians and pathologists. Cases are usually diagnosed only in the later stages, and a few are probably missed altogether. Thorough history taking, physical examination, and biopsy, even in apparently benign but recurrent lesions, are encouraged. Demonstration of fat on frozen section is helpful in supporting the diagnosis. The proposition that incidence may be higher in the far east should substantiate the need to be aware of this cancer. Better surveillance and early diagnosis of this disease should lead to better clinical outcome and decrease in health impairment, organ damage, and number of deaths.

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