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Research Article

HISTOMORPHOLOGICAL STUDY OF SEBACEOUS CARCINOMA OF THE EYELIDS

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ABSTRACT

Scope of the study: Sebaceous carcinoma is a rare neoplasm, arising commonly in the periocular region. They present clinically with a varied masquerade of benign lesions, thus posing diagnostic challenges to both pathologists and clinicians. This study aims to assess the histomorphological characteristics of sebaceous carcinoma.

Procedure: A single centre retrospective study of a consecutive series of patients with sebaceous carcinoma of the eyelid (6 cases) diagnosed over a period of one year from November 2015 to November 2016.

Results: The median age was 57 years with an equal sex incidence, but two cases occurred in young males. Initial clinical diagnoses were sebaceous carcinoma (16.7%), blepharoconjunctivitis (16.7%), chalazion (33.3%) basal cell carcinoma (16.7%) and squamous cell carcinoma (16.7%). Most of the tumours were in left eye (66.7%), poorly differentiated (50%), in upper eyelid (66.7%) with varied patterns including lobular (50%), comedo (33.3%), mixed pattern (16.7%) and were between 11 to 20mms in size (50%). A very rare case of squamoid variant was seen. Intraepithelial pagetoid spread (16.7%), recurrence (16.7%) and fatal outcome (16.7%) were seen in one case each. Tumours with poor differentiation, comedo pattern and pagetoid spread had a poor outcome.

Conclusion: Our study not only corroborates previous reports of high incidence in upper eyelid, mean age at presentation and morphological features indicating poor outcome, But also emphasizes the fact that diagnosis of sebaceous carcinoma should always be considered even in young patients, without any syndromic associations, since early diagnosis and prompt surgery will lead to a better outcome.

INTRODUCTION

Sebaceous carcinoma (SC) of the eyelid is a rare neoplasm that originates in various sebaceous glands like meibomian glands, Zeis glands or the glands of the caruncle and is included in the adnexal tumors of the skin.[1] It has a poor prognosis and is usually a tumor seen in elderly patients with a mean age of 73 years.[2] In most cases the etiology is unknown, but is more common in Asians,[3] and may be associated with Muir-Torre syndrome,[4] *p53* mutations[5] and Human papilloma virus infection.[6] The peculiar features of SC include its multifocal origin and intraepithelial pagetoid spread.

MATERIALS AND METHODS

A single centre retrospective study of six consecutive cases of sebaceous carcinoma of the eyelid, diagnosed histopathologically over a period of one year from November 2015 to November 2016 in our laboratory. Patient's clinical presentation and diagnosis data were collected from the laboratory information system (LIS). The histological slides of all these cases were reviewed and different morphological details were evaluated by the authors. The age of the patient, sex, site of the tumor, clinical diagnosis and associated syndromes if any, were reviewed and correlated with the morphological features and the histopathological diagnosis.

RESULTS

The characteristics of our study population are given in the table 1, various clinical features and diagnosis of the patient is given in table 2 and the histopathological features in table 3.

Histologically, most tumors showed lobular pattern, had well delineated lobules of varying size (Figure 1) and composed of basaloid cells. The 'comedo' pattern characterised by large lobules with areas of conspicuous central necrosis (Figure 2), was seen in three cases. Mixed pattern with combination of any of the above patterns (Figure 3) were noted. Based on the percentage of tumor cells which had abundant foamy or vacuolated cytoplasm, resembling normal sebaceous tissue, the tumors were classified as well differentiated in two cases, moderately differentiated in three cases and poorly differentiated in one case.

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Table 1 Characteristics of study population

Study factor	Number	Percentage
Sex		
Male	3	50 %
Female	3	50 %
Size of tumour (mm)		
5 – 10	2	33.3 %
11 – 20	3	50 %
21 – 30	1	16.7 %
Eye affected		
Right	2	33.3 %
Left	4	66.7 %
Site		
Upper eyelid	4	66.7%
Lower eyelid	2	33.3 %
Age		
Mean	56.7	
Range	30 – 83	

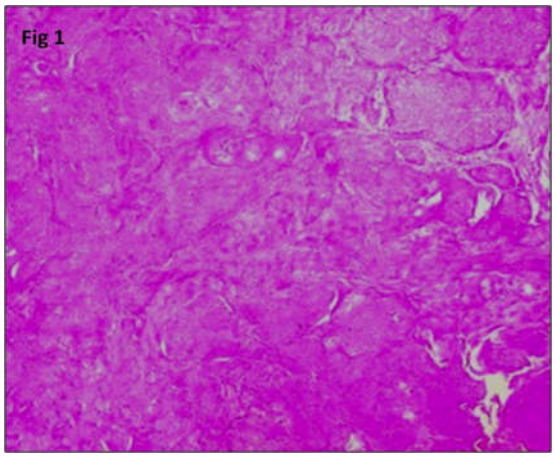

Fig 1 Lobular pattern of sebaceous carcinoma. Well delineated lobules of varying sizes composed of variable admixture of vacuolated cells and basaloid cells (Haematoxylin & Eosin, 40X).

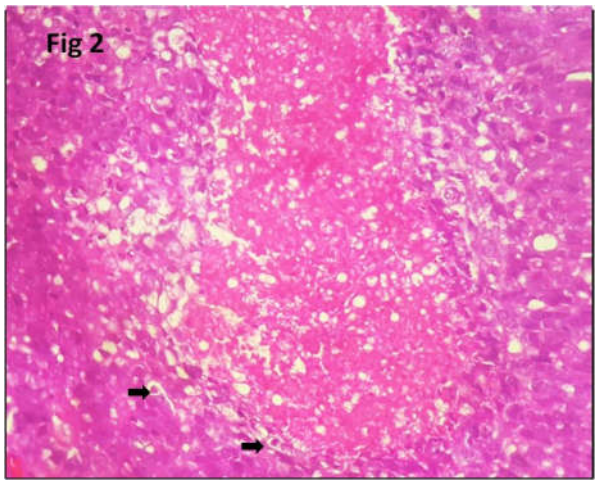

Fig 2 Comedo pattern of sebaceous carcinoma. Poorly differentiated tumour, with central zone of necrosis and apoptotic bodies (Arrow) (Haematoxylin & Eosin, 100X).

The well differentiated lesions exhibited a high degree of sebaceous differentiation especially in the centre of the lesion (Figure 4), while moderately differentiated tumours showed a few patches of sebaceous differentiation and the poorly differentiated variants had cells with scant cytoplasm, highly pleomorphic nuclei and numerous mitotic figures, including atypical mitoses (Figure 5). One case of squamoid variant characterised by areas of keratinisation (Figure 6) and keratin pearls were noted (Figure 7). Epithelial involvement either in the form of intra epithelial pagetoid spread or tumour cells infiltrating directly into the overlying epithelium was assessed.

Table 2 Clinical diagnosis of study population

Case Number	Age (years)	Sex	Tumour Size (mm)	Clinical Diagnosis
1	83	Male	10 X 8	Recurrent Chalazion
2	65	Female	15 X 15 X 5	? Basal cell Carcinoma
3	37	Male	12 X 5 X 4	Chalazion
4	30	Male	14 X 10 X 5	? Sebaceous Carcinoma
5	54	Female	21 X 15 X 5	? Squamous cell carcinoma
6	71	Female	9 X 7	Bhlepharoconjunctivitis

Table 3 Histopathological characteristics of tumour

Morphological feature	Cases	Percentage
Pattern		
Lobular	3	50%
Papillary	-	-
Comedo	2	33.3%
Mixed	1	16.7%
Differentiation		
Well differentiated	2	33.3%
Moderately differentiated	1	16.7%
Poorly differentiated	3	50 %
Variant		
Classical	5	83.3%
Squamoid	1	16.7%
Intra epidermal Pagetoid spread		
Present	1	16.7%
Absent	5	83.3%

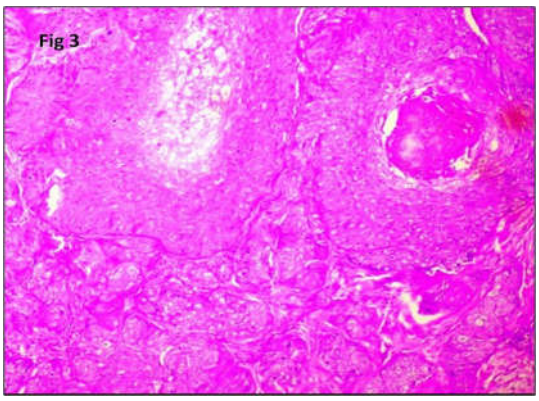

Fig 3 Mixed pattern of sebaceous carcinoma. Both lobules and comedo areas are seen (Haematoxylin & Eosin, 40X).

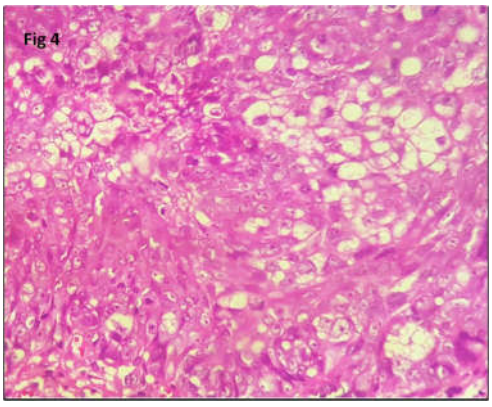

Fig 4 Well differentiated sebaceous carcinoma. Cells with abundant vacuolated cytoplasm, showing sebaceous differentiation (Haematoxylin & Eosin, 400X).

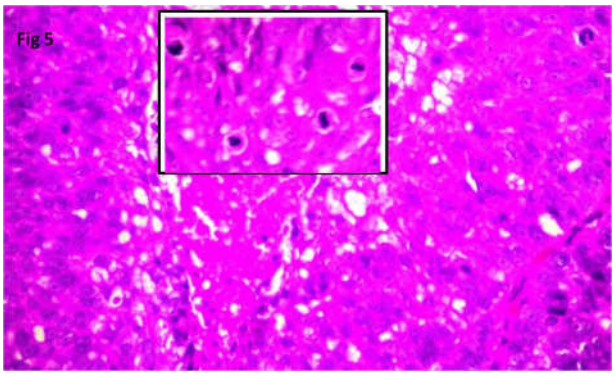

Fig 5 Poorly differentiated sebaceous carcinoma. Basaloid Cells with scant cytoplasm, comedo necrosis and numerous mitotic figures(Inset) (Haematoxylin & Eosin, 100X).

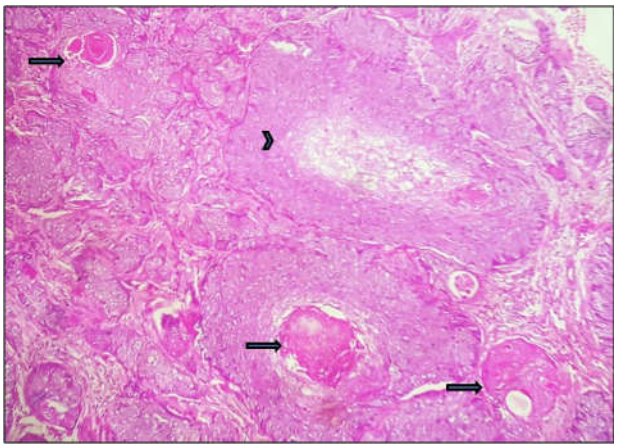

Fig 6 Squamoid variant of sebaceous carcinoma. Low power view showing areas of squamoid differentiation (arrows) admixed with areas of sebaceous differentiation (Arrow head). (Haematoxylin & Eosin, 40X).

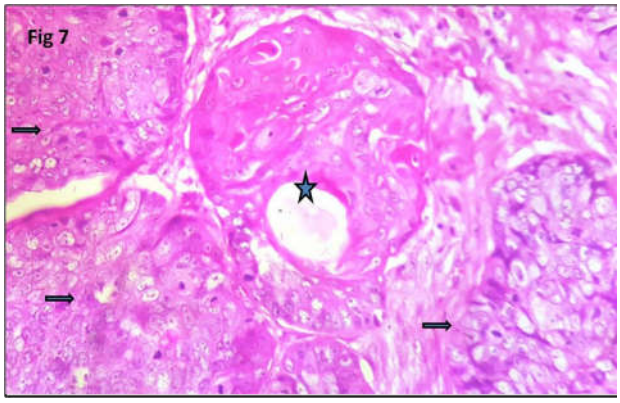

Fig 7 Squamoid variant of sebaceous carcinoma . High power view showing of area of squamoid differentiation (Star), surrounded by areas of sebaceous differentiation (Arrows). (Haematoxylin & Eosin, 400X).

DISCUSSION

Even though sebaceous glands are present in many parts of the body, sebaceous carcinomas occur most commonly in the ocular adnexa.[3]

A higher incidence for females is suggested in literature with a female to male ratio of 1.5 to 1.0, [7] But our study showed no sex distinction with an equal incidence in males and females, which was also observed in some other studies. [8]

We found a wide range in age of incidence from 30 to 83 years with a mean age of 57 years, similar to many studies which have reported mean age ranging from 57 to 68 years.[9] Various risk factors reported to be associated with SC include: Asian origin [10] Muir-Torre syndrome, [11] prior history of irradiation to the head and neck region [12] and familial retinoblastoma. [13] Sc is very rare in young age, nevertheless we had two cases occurring in young males 30 and 37 years, without any known risk factors.

SC poses diagnostic difficulty because of its diverse clinical presentation and has a tendency to masquerade as simple inflammatory lesions like blepharoconjunctivitis, recurrent chalazion or superior limbic keratoconjunctivitis and can mimic as other malignant tumours such as squamous cell carcinoma or basal cell carcinoma as well[14]. Hence the diagnosis is often made at a later stage with metastasis. So it is essential to consider SC in the differential diagnosis of recurrent inflammatory conditions and benign appearing eyelid mass lesions. In our study too, recurrent chalazion was the most common clinical diagnosis, followed by other malignancies.

Due to the presence of numerous meibomian glands in the upper eyelid, SC is more prevalent there which is in contrast to the occurrence of squamous cell carcinomas and basal cell carcinomas.[15] Few cases can have concurrent involvement of both the eyelids either due to the pagetoid intraepithelial spread or because of simultaneous development of multiple primary neoplasms.[15] Our study also showed propensity for the tumor to occur in upper eyelid.

Various prognostic factors based on morphological examination are described in literature. The tumor size greater than 10 millimeter is associated with a poor outcome. [14] Most of our cases were greater than 10 millimeter. Upper lid SC has been reported to have poor outcome and majority of our cases were in upper eyelid. Morphological features like differentiation of the tumour and presence of intraepithelial pagetoid spread have been associated with prognosis.[16] Three of our cases were poorly differentiated and one was moderately differentiated. One case had a pagetoid spread. One of our cases with a poor differentiated morphology and large tumor size had a fatal outcome. Our study findings, though numerically inadequate to be conclusive about the prognostic factors, shows comparable findings to support the described prognostic factors. One case showed squamoid differentiation (squamoid variant), and had outcome similar to classical variant, with no significant effect of squamoid differentiation on prognosis.

SC has a high recurrence and the recurrence rate is reported to be 6% to 29%.[17,18] One of our case with pagetoid spread and poor differentiation had recurrence in the eyelid. Due to the small sample size of our study, comment on risk factors for local recurrence based on morphological evaluation cannot be made, but can be stated that well differentiated SC had a better course than those with moderate differentiation and pagetoid spread.

Distant metastasis is reported in 14 to 25 % of SC. The metastasis can be to a lymphnode or hematogenous spread to liver, lungs, bones or brain. [19]

Literature review states that appropriate treatment, when instituted early results in better outcome with good prognosis to the patient.[20]

CONCLUSION

To conclude our study corroborates previous reports of higher incidence in upper eyelid, mean age at presentation and morphological features indicating poor outcome (large tumour size, poor differentiation, intraepithelial pagetoid spread), But also emphasizes the fact that diagnosis of SC should be considered in young patients, without any syndromic associations, as well. It also highlights the fact that although clinical features of SC are widely described, timely clinical suspicion, **e**arly diagnosis and prompt surgery will lead to a better outcome and good prognosis. Further large studies will be required to estimate other predisposing and prognostic factors.

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