

Eyelid Sebaceous Gland Carcinoma – Devastating Masquerader Revisited

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Abstract

Introduction: Diagnosis of sebaceous gland carcinoma is often delayed because of its ability to masquerade as other periocular lesions.

Materials and Methods: A retrospective consecutive case record analysis of 94 patients, clinico-pathologically diagnosed as sebaceous gland carcinoma was performed. The patients whose first consultation for the eyelid lesion at our centre were grouped as 'Primary visitors'. All the other patients, who had received medical treatment elsewhere before coming to our centre, were grouped as 'secondary visitors'. Statistical analysis was done using SPSS software, version 20.0 employing 'Chi square test' and 'unpaired t-test'.

Results: Statistically significant difference ($P < 0.05$) was found in the following variables- 'Residence', 'Size of lesion', 'Multi-centric spread', 'time lag between the symptoms and correct diagnosis' and 'treatment'. A statistically significant positive correlation between the 'time lag between the symptoms and correct diagnosis' and 'risk of multi-centric spread' (odds ratio) [Pearson's correlation coefficient (r) = 0.85 at 95 % CI & $P < 0.05$] was found leading to orbital exenteration as the primary surgery for treatment.

Discussion: High index of suspicion not just by the practicing ophthalmologists and the training residents, but also primary health provider with whom the rural patients first come in contact, is vital.

Conclusion: Any clinically malignant lesion of the upper lid should be considered SGC until proven otherwise and should be referred to an ocular oncologist soon. Early diagnosis may result in good surgical prognosis not just in terms of morbidity and survival but also in terms of vision and cosmesis.

Keywords: Eyelid; Sebaceous; Gland; Carcinoma; Delay; Diagnosis

Introduction

Eyelid sebaceous gland carcinoma, a rare eyelid malignancy, accounting for 75% of all Sebaceous gland carcinoma (SGC), has a high potential for morbidity and mortality [1]. Higher rate of occurrence has been reported from China and India compared to the west due to unknown factors [2]. It arises from tarsal meibomian glands, glands of Zeis of cilia, pilosebaceous glands of caruncle and from conjunctival epithelium [3,4]. Diagnosis is often delayed because of its ability to masquerade as other periocular lesions, both clinically (recurrent chalazion and chronic blepharconjunctivitis) and histologically [basal cell carcinoma (BCC) and squamous cell carcinoma (SCC)] [5]. Localized SGC is treated by excision and eyelid reconstruction. However, delay in diagnosis leads to mutilating surgical treatment involving removal of eyelids along with an eyeball (exenteration) that has vision. Added to this is the increased risk of recurrence and metastasis [6].

The hospital record analysis of 94 patients diagnosed as eyelid sebaceous gland carcinoma, seen over the period of five years was undertaken to report the demographic details, clinical features, histopathology, treatment and outcome with an aim to highlight

the effect of time delay due to misdiagnosis, on the management. Survival analysis is not the scope of this study.

Material and Methods

The clearance was obtained from the institutional ethical committee for conducting this analysis. A retrospective consecutive case record analysis of 94 patients, clinico-pathologically diagnosed as sebaceous gland carcinoma at a single tertiary care centre in North India, during the period from January 2006 to December 2010 was performed. This time was chosen as all the histopathological slides were available for the review in doubtful cases. For the purpose of study, the patients whose first consultation for the eyelid lesion was at our centre were grouped as 'Primary visitors'. All the other patients, who had received medical treatment elsewhere before coming to our centre, were grouped as 'secondary visitors'. Information of cases in both the groups, regarding demographic details, clinical features, histopathology, treatment and outcome, was computed on separate Microsoft excel sheet for the purpose of statistical analysis. Histopathological examination was done to evaluate pattern, differentiation, epithelial involvement and margins of specimen for tumor cells. The final diagnosis was based on clinico-pathological correlation. In case of a discrepancy, the pathological diagnosis was considered as the mainstay. Surgical procedure was decided on the basis of histopathological evidence of the lesion, extent and presence of metastasis. Surgical excision of tumour with confirmation of tumour free margin or orbital exenteration was performed by a single surgeon. Statistical analysis was done using commercially available SPSS software, version 20.0 (SPSS Inc., IBM Corp., New York, NY, USA) employing 'Chi square test' for testing the non parametric variables and 'unpaired t-test' for the parametric variables between both the groups. P value < 0.05 was taken as statistically significant.

Results

Ninety four patients with unilateral eyelid sebaceous gland carcinoma comprised the study group, 42 of these patients had their first consultation at the study centre (primary visitors). The rest 52 patients reported with history of previous one/multiple consultations elsewhere (secondary visitors). Table 1 summarizes the information of the 'Primary visitors' and 'secondary visitors' respectively. On comparing both the groups (Table 2), statistically significant difference ($P < 0.05$) was found in the following variables- 'Residence', 'Size of lesion', 'Multi-centric spread', 'time lag between the symptoms and correct diagnosis' and 'treatment'. Most of the patients in the 'primary visitors' had urban residence. In contrast to this, maximum 'secondary visitors' had rural residence. Upper lid was the most common site of involvement in both the groups with recurrent chalazion being the most common presentation. In the 'primary visitors' maximum patients had lesion size ≤ 5 mm in contrast to the secondary visitors with most having the size >10 mm in maximum dimension (difference was statistically significant,

Parameter	Primary visitors	Secondary visitors
Number	42	52
Age (mean with SD)(range)	65.4 ±12.52 (52-80)	67.2 ±10.32(55-79)
Gender		
Male	19(45.2%)	25 (48.07%)
Female	23(54.76%)	27(51.92%)
Residence		
Urban	33(78.57%)	15(28.79%)
Rural	9(21.43%)	37(71.12%)
Site of involvement		
Upper lid	30 (71.4%)	37(71.12%)
Lower lid	9(21.42%)	10(19.23%)
Canthus	3(7.14%)	5(9.61%)
Presentation		
Nodule	12 (28.57%)	3(57.69%)
Recurrent chalazion	15(35.71%)	24(46.15%)
Plaque like thickening of tarsal plate	3(7.14%)	2(3.84%)
Chronic blepharoconjunctivitis	12(28.57%)	23(44.23%)
Size of lesion (in maximum dimension)		
≤5mm	36(85.71%)	5(9.61%)
5-10mm	2(4.76%)	16(30.76%)
>10mm	4(9.52%)	31(59.61%)
Multicentric spread	6(14.28%)	29(55.76%)
Conjunctiva	6(14.28%)	16 (30.77%)
Cornea	-	-
Orbit	-	13 (25%)
Associated Lymphadenopathy	-	3 (5.07%)
Distant metastasis	-	-
BCVA of the involved eye at the time of presentation(mean with SD) (LogMAR)	0.66 ±0.20	0.68 ±0.18
Time lag between symptom and correct diagnosis(mean with SD)	12.3 ±6.5 month	24.1 ± 9.5 months
Treatment		
Wide excision with tumor free margin with eyelid reconstruction	36(85.71%)	23(44.23%)
Orbital exenteration	6(14.28%)	29(55.76%)
Radical neck dissection	-	3(5.07%)
Radiotherapy(adjunct to surgery)	-	-
Histopathological pattern		
Moderately differentiated	37(88.1%)	47(90.38%)
Poorly differentiated	4(11.9%)	5(9.62%)
Duration of followup(mean with SD)	24.3 ± 8.2 months	23.2 ± 6.1months
Course and outcome		
Recurrence	-	1
Site of recurrence	-	Orbit
Histopathology	-	-
Management	-	radiotherapy

Table 1: Summary of demographic details, clinical features, histopathology, treatment and outcome of 'primary visitors' and 'secondary visitors'.

$P < 0.05$). Only 14.28% patients among the 'primary visitors' had multi-centric spread to the palpebral conjunctiva. In contrast the patients among 'secondary visitors' showed multi-centric spread with involvement of conjunctiva in 16 patients (30.77%), orbit in 13(25%) and associated lymphadenopathy in 3(5.07%) (difference was statistically significant, $P < 0.05$). These patients required exenteration as primary management. The mean time lag between symptom and correct diagnosis in 'primary visitors' was 12 ± 6 months whereas, in 'secondary visitors' was 24 ± 9 month (difference was statistically significant, $P < 0.05$). Exactly 85.71%

patients in the 'primary visitors' group underwent excision of the tumor with eyelid reconstruction in contrast to the patients in the 'secondary visitors' group who underwent mutilating surgery in most of the cases (difference was statistically significant at $P < 0.05$). The histopathology showed moderate differentiation in 37(88.1%) patients in the 'primary visitors' and 47(90.38%) in the 'secondary visitors' (no statistical difference). The mean follow up time period was also showed no statistically significant difference. No patient developed recurrence of the tumor in the 'Primary visitors' till last follow up. Only one patient had local recurrence

Parameters	Primary visitors	Secondary visitors	P-value
Age (mean)	65.4 ±12.52 (52-80)	67.2 ±10.32(55-79)	0.86*
Gender			0.82*
Male	19(45.2%)	25 (48.07%)	
Female	23(54.76%)	27(51.92%)	
Residence			0.011 (<i>P</i> < 0.05)*
Urban	33(78.57%)	15(28.79%)	
Rural	9(21.43%)	37(71.12%)	
Site of involvement			0.64*
Upper lid	30 (71.4%)	37(71.12%)	
Lower lid	9(21.42%)	10(19.23%)	
Canthus	3(7.14%)	5(9.61%)	
Presentation			0.42*
Nodule	12 (28.57%)	3(57.69%)	
Recurrent chalazion	15(35.71%)	24(46.15%)	
Plaque like thickening of tarsal plate	3(7.14%)	2(3.84%)	
Chronic blepharoconjunctivitis	12(28.57%)	23(44.23%)	
Size of lesion (in maximum dimension)			0.0013(<i>P</i> < 0.5)**
≤5mm	36(85.71%)	5(9.61%)	
5-10mm	2(4.76%)	16(30.76%)	
>10mm	4(9.52%)	31(59.61%)	
Multicentric spread	6(14.28%)	29(55.76%)	0.0016 (<i>P</i> < 0.05)*
Conjunctiva	6(14.28%)	16 (30.77%)	
Cornea	-	-	
Orbit	-	13 (25%)	
Associated Lymphadenopathy	-	3 (5.07%)	
Distant metastasis	-	-	
BCVA of the involved eye at the time of presentation (LogMAR)	0.66 ±0.20	0.68 ±0.18	0.92**
Time lag between symptom and correct diagnosis	12.3 ±6.5 month	24.1 ± 9.5 months	0.018(P<0.05)**
Treatment			0.023 (P<0.05)*
Wide excision with tumor free margin with eyelid reconstruction	36(85.71%)	23(44.23%)	
Orbital exenteration	6(14.28%)	29(55.76%)	
Radical neck dissection	-	3(5.07%)	
Histopathology			0.86*
Moderately differentiated	37(88.1%)	47(90.38%)	
Poorly differentiated	4(11.9%)	5(9.62%)	
Duration of follow up	24.3 ± 8.2 months	23.2 ± 6.1months	0.84**

Table 2: Summary of the statistical analysis between the 'primary visitors' and 'secondary visitors'.

* Chi Square test ** Unpaired t test

in the exenterated orbit, 11 months following initial surgery in the 'Secondary visitors'. None of the patients had lymph node or distant metastasis following surgical treatment till last follow-up.

A statistically significant positive correlation between the 'time lag between the symptoms and correct diagnosis' and 'risk of multicentric spread' (odds ratio) [Pearson's correlation coefficient (*r*) = 0.85 at 95 % CI & *P* < 0.05] was found (Figure 1) leading to orbital exenteration as the primary surgery for treatment.

Discussion

Sebaceous gland carcinoma is a rare tumor in West with reported incidence of 0.2-1.2 % of all lid lesions and 1.13%-3.2% of all malignant lid tumours [7]. But, in Asian countries far higher

incidences from China and India, between 25-40% of malignant lid tumours, has been reported [8]. Possible role of genetic and racial predisposition may be there for difference in prevalence rate of tumor amongst Asian and Caucasian populations. Difference in infection rates with Human Papilloma virus (HPV) between populations of Asian and Caucasian is responsible for reported difference, as this virus leads to inactivation of a tumor suppressor gene p53, is a factor in development of malignancy [9].

The current study, the first of its kind from north India to the best of our knowledge, analyses the demographic details, clinical features, treatment outcome and histopathological characteristics of SGC with an aim to highlight the grim scenario of morbidity resultant of delayed diagnosis. Sebaceous gland carcinoma is a disease of old

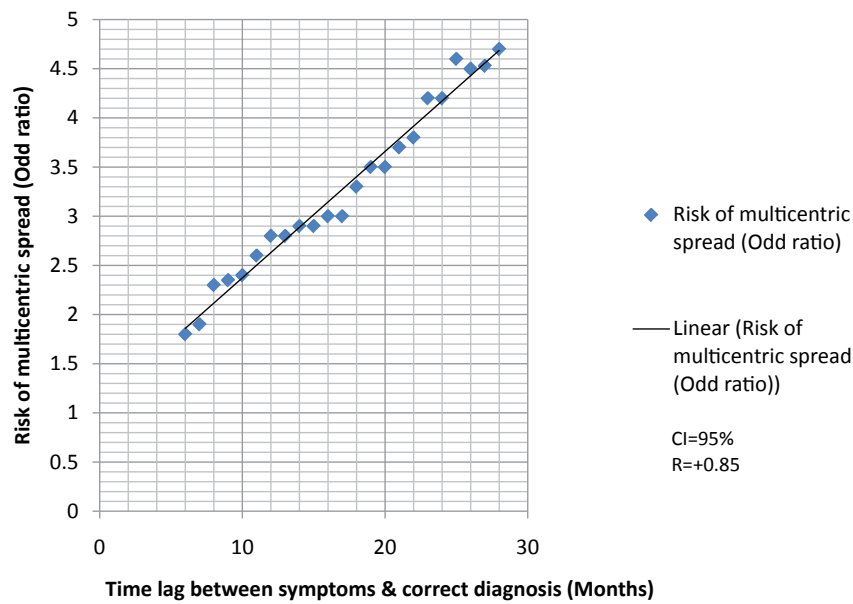


Figure 1: Scatter plot between variable "Time lag between symptoms and correct diagnosis (months)" and "risk of multicentric spread (Odd ratio)"

age. In our study mean age of occurrence in primary and secondary visitors was 65 ± 12 , 67.2 ± 10 years, respectively. These findings are in accordance with previous reports [10]. The clinical presentation is a masquerade, being frequently misdiagnosed as chalazion, inflammatory conditions and other malignancy of eye lids. This masquerade leads to delay in correct diagnosis and subsequent treatment [4]. High incidence of misdiagnosis (79.9% cases of the total) was noted, chalazion being the commonest (42.55%), followed by chronic blepharoconjunctivitis (38.29%). This leads to delay in correct management, compromising the surgical prognosis both in terms of cosmesis and vision. There was a statistically significant difference in the residence, 71.12% patients in the secondary group belonged to rural areas while only 21.43% the primary visitors belonged to similar background. Rural areas have poor accessibility to higher health centres, which are mostly located in the urban areas, thus the delay in the diagnosis and management.

No mortality was recorded during the analysis period. Thus, prognosis on the basis of survival was not ascertained. A statistically significant difference existed in the variables of 'size of lesion', 'time lag between symptoms and correct diagnosis', 'multi-centric spread' and 'treatment'. These findings are consistent with previous reports [11,12]. A statistically significant positive correlation existed between the 'time lag between the symptoms and correct diagnosis' and 'risk of multi-centric spread' (odds ratio) [Pearson's correlation coefficient (r) = +0.85 at 95 % CI & $P < 0.05$]. Thus, it can be inferred that mutilating procedure could have been prevented if they were correctly diagnosed earlier and treated appropriately.

It is interesting to note that there was no statistically significant difference in the histopathology of primary and secondary visitors. Patients with poor differentiation had extensive infiltration involving the conjunctiva in very short duration with rapid growth of sizes. Four out of 6 patients in the primary group and 5 out of 29, who had undergone exenteration showed poor differentiation on histopathology. This emphasizes the importance of preoperative histopathological examination as a guiding factor for the final outcome. The lesser proportions of patients with poor differentiation (10%) in our study as compared to those reported Zurcher et al where poor differentiation was seen in 17%, can be possibly due to histopathological characteristics in Indian

population [10]. Similar trends of these lower proportions have been demonstrated in other studies from Asia [13].

The preoperative best corrected visual acuity (BCVA) in both groups showed no statistically significant difference. A high percentage of orbital exenteration [29(55.76%)] was performed as primary management in secondary visitors because of the multicentric spread due to delayed diagnosis stresses upon the grim scenario of the loss of a seeing eye which is traumatizing for a patient affecting his overall quality of life.

Correct diagnosis of a sebaceous carcinoma of the eyelid is delayed not only as a result of the rarity of this tumor, but also because of its ability to masquerade as a variety of other eye conditions such as chalazion or chronic blepharoconjunctivitis. High index of suspicion not just by the practicing ophthalmologists and the training residents, but also primary health providers with whom the rural patients first come in contact, is vital if this tumor is to be adequately treated as it is an aggressive tumor.

Conclusion

Any clinically malignant lesion of the upper lid should be considered SGC until proven otherwise and should be referred to an ocular oncologist without delay for management. Early diagnosis may result in good surgical prognosis not just in terms of morbidity and survival but also in terms of vision and cosmesis.

References

1. Nelson BR, Hamlet KR, Gillard M, Railan D, Johnson TM. Sebaceous carcinoma. *J Am Acad Dermatol.* 1995;33(1):1-15.
2. Sihota R, Tandon K, Betharia SM, Arora R. Malignant eyelid tumors in an Indian population. *Arch Ophthalmol.* 1996;114(1):108-9.
3. Shields JA, Demirci H, Marr BP, Eagle RC Jr, Shields CL. Sebaceous carcinoma of eyelids: Personal experience with 60 cases. *Ophthalmology.* 2004;111(12):2151-7.
4. Kass LG, Hornblase A. Sebaceous carcinoma of ocular adnexa. *Surv Ophthalmol.* 1989;33(6):477-90.
5. Shields JA, Demirci H, Marr BP, Eagle RC Jr, Shields CL. Sebaceous carcinoma of the eyelids: personal experience with 60 cases. *Ophthalmology.* 2004;111(12):2151-7.

6. Song A, Carter KD, Syed NA, Song J, Nerad JA. Sebaceous cell carcinoma of the ocular adnexa: clinical presentations, histopathology, and outcomes. *Ophthal Plast Reconstr Surg.* 2008;24(3):194-200. doi: 10.1097/IOP.0b013e31816d925f.
7. Welch RB, Duke JR. Lesions of the lids: a statistical note. *Am J Ophthalmol.* 1958;45(3):415-26.
8. Ni C, Searl SS, Kuo PK, Chu FR, Chong CS, Albert DM. Sebaceous cell carcinomas of the ocular adnexa. *Int Ophthalmol Clin.* 1982;22(1):23-61.
9. Gonzalez-Fernandez F, Kaltreider SA, Patnaik BD, Retief JD, Bao Y, Newman S, et al. Sebaceous carcinoma. Tumor progression through mutational inactivation of p53. *Ophthalmology.* 1998;105(3):497-506.
10. Zurcher M, Hintschich CR, Garner A, Bunce C, Collin JR. Sebaceous carcinoma of the eyelid: a clinicopathological study. *Br J Ophthalmol.* 1998;82(9):1049-55.
11. Ginsberg J. Present status of meibomian gland carcinoma. *Arch Ophthalmol.* 1965;73:271-7.
12. Rao NA, Hidayat LCAA, McLean LCIW, Zimmerman LE. Sebaceous carcinomas of the ocular adnexa: a clinicopathologic study of 104 cases, with five-year follow-up data. *Hum Pathol.* 1982;13(2):113-22.
13. Yoon JS, Kim SH, Lee CS, Lew H, Lee SY. Clinicopathological analysis of periocular sebaceous gland carcinoma. *Ophthalmologica.* 2007;221(5):331-9.

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