Malignant Eyelid Tumors in India: A Study of 536 Asian Indian Patients

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Keywords

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Squamous cell carcinoma · Miscellaneous tumors

Abstract

Purpose: To study the proportion of eyelid malignant tumors in an Asian Indian population and to review their clinical features and outcomes. **Methods:** This is a retrospective study of 536 patients. **Results:** The mean age at presentation with eyelid malignancy was 58 years. Histopathology-proven diagnoses of these patients included sebaceous gland carcinoma (SGC) ($n = 285$, 53%), basal cell carcinoma (BCC) ($n = 128$, 24%), squamous cell carcinoma (SCC) ($n = 99$, 18%), and miscellaneous tumors ($n = 24$, 4%). The statistically significant differences between eyelid malignant tumors included age at presentation, tumor location, and tumor extent. The clinicopathological correlation of SGC, BCC, SCC, and miscellaneous tumors was 91, 86, 46, and 38% ($p = 0.001$), respectively. Comparing SGC with BCC, SCC, and miscellaneous tumors, SGC was more commonly associated with tumor recurrence (21 vs. 3, 8, and 13%; $p = 0.001$), sys-

temic metastasis (13 vs. 0, 4, and 13%; $p = 0.001$), and death (9 vs. 0, 4, and 0%; $p = 0.004$). Compared to SGC, BCC, and SCC, locoregional lymph node metastasis was more common with miscellaneous tumors (26 vs. 16, <1, and 8%; $p = 0.001$) over a mean follow-up period of 19 months. **Conclusion:** In Asian Indians, SGC is twice as common as BCC and 3 times more common than SCC. SGC is associated with poorer prognosis compared to other eyelid malignant tumors.

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Introduction

In America and Europe, the most common malignant tumor of the eyelid is basal cell carcinoma (BCC), accounting for 80–95% of all eyelid malignancies [1–5]. Squamous cell carcinoma (SCC) (<5%), sebaceous gland carcinoma (SGC) (1–3%), malignant melanoma (1%), and miscellaneous tumors (<1%) constitute the rest of eyelid malignancies [1]. In a large series of 5,504 cases with eyelid tumors in a European population including 894 malignant eyelid tumors, BCC was seen in 86%, SCC in 7%, SGC in 3%, and miscellaneous tumors in 4% of

Fig. 1. Malignant eyelid tumors in Asian Indian patients. **a** Nodular variant of sebaceous gland carcinoma (SGC) involving the upper eyelid. **b** Nodulo-ulcerative variant of SGC with predominant upper tarsal conjunctival involvement. **c** Large nodular variant of SGC involving lower eyelid. **d, e** Pigmented basal cell carcinoma (BCC) involving lower eyelid. **f** Pigmented BCC involving lateral canthus and extending into the lateral orbit. **g** Diffuse squamous cell carcinoma (SCC) with thickening of lower eyelid. **h** SCC of the lower eyelid with extensive keratin. **i** Nodulo-ulcerative SCC of the upper eyelid with central ulceration. **j** Malignant melanoma of the lower eyelid. **k** Mucoepidermoid/adenosquamous carcinoma of the lower eyelid and medial canthus. **l** Diffuse Merkel cell carcinoma of the upper eyelid with purplish-red discoloration.

cases [2]. Similarly, in studies from the USA, BCC was seen in 82–91%, SCC in 2–9%, SGC in 0–6%, and miscellaneous tumors in <1–9% of cases [3, 5].

The reports from Asia and our personal experience are contrary to this observation. BCC is less common (11–65%) while SCC (5–48%) and SGC (7–56%) occur more frequently than in the West [6–21]. In a large study of 1,086 malignant eyelid tumors from China, BCC accounted for 38%, SCC was seen in 19%, SGC in 32%, and miscellaneous tumors in 7% of cases [6]. However, there are no large case series on malignant eyelid tumors from an Asian Indian population. In this study, we will discuss the proportion of all histopathology-proven eyelid malignancies in an Asian Indian population and compare the clinical presentation, treatment, and outcomes of common eyelid malignancies.

Methods

This is a retrospective study conducted at the Operation Eyesight Universal Institute for Eye Cancer, LV Prasad Eye Institute, Hyderabad, India. Institutional review board approval was obtained. A search was conducted in our medical records and ophthalmic pathology database for the diagnosis of eyelid malignancies. All cases

Table 1. Patients with malignant tumors of the eyelid ($n = 536$)

Feature	<i>n</i> (%)
Histopathology diagnosis	
Sebaceous gland carcinoma	285 (53)
Basal cell carcinoma	128 (24)
Squamous cell carcinoma	99 (18)
Malignant melanoma	12 (2)
Mucoepidermoid carcinoma	7 (1)
Lymphoma	2 (<1)
Merkel cell carcinoma	1 (<1)
Adenoid cystic carcinoma	1 (<1)
Metastasis	1 (<1)

with histopathology-proven eyelid malignancy during the period from January 1995 to December 2016 were included in this analysis. Those patients with a single visit to our institute with a clinical diagnosis of an eyelid malignancy but without a histopathology confirmation of the diagnosis were excluded from the study.

The following data was extracted from the medical records: age (years), gender, tumor location, tumor extent, tumor growth pattern, tumor size, tumor classification based on the 8th edition of the American Joint Committee Classification [22], clinical diagnosis, treatment details, and final histopathology diagnosis. Clinical photographs were reviewed in all cases to confirm the tumor de-

Table 2. Malignant eyelid tumors in Asian Indian population based on age, gender, and diagnosis

Age, years	SGC (<i>n</i> = 285)		BCC (<i>n</i> = 128)		SCC (<i>n</i> = 99)		Miscellaneous tumors (<i>n</i> = 24)	
	male	female	male	female	male	female	male	female
<10	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)	1 (1)	0 (0)	1 (4)
11–20	0 (0)	0 (0)	0 (0)	1 (1)	1 (1)	0 (0)	2 (8)	0 (0)
21–30	3 (1)	5 (3)	1 (1)	3 (2)	3 (3)	1 (1)	2 (8)	0 (0)
31–40	10 (4)	14 (5)	4 (3)	4 (3)	3 (3)	4 (4)	3 (13)	2 (8)
41–50	13 (5)	40 (14)	5 (4)	10 (8)	13 (13)	12 (12)	1 (4)	1 (4)
51–60	30 (11)	51 (18)	13 (10)	23 (18)	8 (8)	18 (18)	1 (4)	0 (0)
61–70	37 (13)	34 (12)	14 (11)	14 (11)	12 (12)	9 (9)	2 (8)	1 (4)
71–80	15 (5)	20 (7)	11 (9)	16 (13)	4 (4)	5 (5)	4 (17)	3 (13)
81–90	5 (3)	6 (2)	4 (3)	5 (4)	1 (1)	3 (3)	1 (4)	0 (0)
>90	2 (<1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Values are *n* (%).

tails. The following data related to outcome were recorded: tumor recurrence, globe salvage, locoregional lymph node metastasis, systemic metastasis, and death. The follow-up duration of each patient was also recorded.

The data were analyzed based on age at presentation and gender. They were further grouped into 4 categories and analyzed based on the diagnosis of SGC, BCC, SCC, and miscellaneous tumors.

For the literature review, a search was conducted with the keywords “malignant,” “tumor,” “eyelid,” and “cancer” in PubMed and Google Scholar, and all related articles were reviewed. Publications from Asian countries were analyzed further.

Statistical Analysis

Statistical analysis was performed using the software Origin v7.0 (OriginLab Corporation, Northampton, MA, USA). Continuous data were analyzed for normality by the Shapiro-Wilk test and described in terms of mean, median, and range. Among the 4 groups, the data were compared using the Kruskal-Wallis test and post hoc analysis was performed using the Mann-Whitney test (multiple comparisons). Categorical data were described in terms of proportions; among the 4 groups, comparisons were made using the χ^2 test and post hoc analysis was performed also using the χ^2 test (multiple comparisons). Kaplan-Meier survival analysis was performed to evaluate the probability of survival over time (events being lymph node involvement, distant metastasis, or death). The log-rank test was performed to test if the survival probabilities differed among the tumor subtypes. A *p* value of less than 0.05 was considered statistically significant.

Results

A total of 536 patients with a histopathology-proven diagnosis of eyelid malignancy were included in this study. The mean age at presentation with eyelid malig-

nancy was 58 years (median, 60 years; range, 4–100 years). The mean age at presentation was 58 years for SGC, 60 years for BCC, 55 years for SCC, and 50 years for miscellaneous tumors. Histopathology-proven diagnoses of these patients (Table 1; Fig. 1) included SGC (*n* = 285, 53%), BCC (*n* = 128, 24%), SCC (*n* = 99, 18%), malignant melanoma (*n* = 12, 2%), mucoepidermoid/adenosquamous carcinoma (*n* = 7, 1%), lymphoma (*n* = 2, <1%), Merkel cell carcinoma (*n* = 1, <1%), adenoid cystic carcinoma (*n* = 1, <1%), and metastases from lung adenocarcinoma (*n* = 1, <1%). There was a female preponderance for all malignant tumors of the eyelid (Table 2). History of prior surgical intervention was present in 189 (35%) cases including SGC (*n* = 118, 41%), BCC (*n* = 23, 18%), SCC (*n* = 42, 42%), and miscellaneous tumors (*n* = 16, 67%). Based on multiple comparisons and statistical analysis, statistically significant differences were noted among various tumors (Table 3). The statistically significant differences among the 4 groups (SGC, BCC, SCC, and miscellaneous tumors) are mentioned below.

SGC versus BCC

The tumor epicenter was most often the upper eyelid in SGC (59%) and the lower eyelid in BCC (59%) (*p* < 0.001). Statistically significant differences between SGC and BCC included higher rates of tumor recurrence (21 vs. 3%; *p* < 0.001), regional lymph node metastasis (16 vs. <1%; *p* < 0.001), systemic metastasis (13 vs. 0%; *p* < 0.001), and death due to metastasis (9 vs. 0%; *p* = 0.001).

Table 3. Details of patients with malignant tumors of the eyelid

Feature	SGC (n = 285)	BCC (n = 128)	SCC (n = 99)	Miscellaneous (n = 24)	All cases (n = 536)	p value
Age at presentation, years	58 (60, 21–100)	60 (61, 20–88)	55 (55, 8–90)	50 (49, 4–81)	58 (60, 4–100)	0.01**, a
Gender						
Male	115 (40)	52 (41)	46 (46)	16 (67)	229 (43)	0.47***
Female	170 (60)	76 (59)	53 (54)	8 (33)	307 (57)	0.53***
Tumor epicenter						
Upper eyelid	168 (59)	22 (17)	40 (40)	11 (46)	241 (45)	<0.001***, b
Lower eyelid	82 (29)	75 (59)	41 (41)	9 (38)	207 (39)	0.003***, c
Medial canthus	9 (3)	13 (10)	5 (5)	3 (13)	30 (6)	0.03***, d
Lateral canthus	7 (2)	10 (8)	5 (5)	0 (0)	22 (4)	0.07***
Diffuse	19 (7)	8 (6)	8 (8)	1 (4)	36 (7)	0.92***
Tumor pattern (n = 519)						
Nodular	155 (56)	52 (42)	51 (52)	13 (54)	271 (51)	0.52***
Nodulo-ulcerative	88 (31)	63 (51)	40 (40)	5 (21)	196 (37)	0.07***
Papillary	7 (2)	0 (0)	3 (3)	2 (8)	12 (2)	0.07***
Cystic	7 (2)	5 (4)	0 (0)	0 (0)	12 (2)	0.22***
Fungating mass	20 (7)	3 (2)	3 (3)	2 (8)	28 (5)	0.17***
Tumor diameter, mm	18 (14, 1–100)	15 (12, 2–50)	18 (15, 2–60)	19 (14, 1–55)	17 (13, 1–100)	0.46**
Tumor thickness, mm	6 (4, 1–44)	5 (4, 1–28)	8 (4, 1–55)	7 (4, 1–36)	6 (4, 1–55)	0.15**
Tumor extent at presentation						
Orbit	35 (12)	8 (6)	16 (16)	7 (29)	66 (12)	0.03***, e
Maxillary sinus	4 (1)	1 (<1)	0 (0)	0 (0)	5 (<1)	0.61***
Frontal sinus	2 (<1)	0 (0)	0 (0)	0 (0)	2 (<1)	0.63***
Ethmoid sinus	2 (<1)	0 (0)	0 (0)	0 (0)	2 (<1)	0.63***
Intracranial extension	3 (1)	0 (0)	0 (0)	0 (0)	3 (<1)	0.45***
T classification based on 8th edition AJCC staging						
T1	104 (37)	49 (38)	26 (26)	8 (33)	187 (35)	0.54***
T2	92 (32)	47 (37)	37 (37)	3 (13)	179 (33)	0.32***
T3	30 (11)	13 (10)	7 (7)	3 (13)	53 (10)	0.80***
T4	59 (21)	19 (15)	29 (29)	10 (42)	117 (22)	0.054***
Primary treatment (n = 518)	275	123	97	23		
Wide excision biopsy	218 (79)	116 (94)	74 (76)	16 (70)	424 (82)	0.62***
Orbital exenteration	38 (14)	6 (5)	18 (19)	6 (26)	68 (13)	0.02***, f
Systemic chemotherapy	17 (6)	0 (0)	4 (4)	1 (4)	22 (4)	0.06***
External beam radiotherapy	2 (<1)	1 (<1)	1 (1)	0 (0)	4 (<1)	0.97***
Clinical diagnosis correlating histo-pathological diagnosis	258 (91)	110 (86)	46 (46)	9 (38)	423 (79)	0.001***, g
Outcome (n = 518)*						
Tumor recurrence	60 (21)	4 (3)	8 (8)	3 (13)	75 (14)	0.001***, h
Locoregional lymph node metastasis	45 (16)	1 (<1)	8 (8)	6 (26)	60 (12)	0.001***, i
Systemic metastasis	35 (13)	0 (0)	4 (4)	3 (13)	42 (8)	0.001***, j
Death due to the disease	24 (9)	0 (0)	4 (4)	0 (0)	28 (5)	0.004***, k
Globe salvage	225 (82)	116 (94)	77 (79)	16 (70)	434 (84)	0.72***
Follow-up period, months	15 (5, <1–185)	29 (11, <1–273)	22 (10, <1–149)	12 (5, <1–83)	19 (7, <1–273)	na

Values are n (%) or mean (median, range), as appropriate. SGC, sebaceous gland carcinoma; BCC, basal cell carcinoma; SCC, squamous cell carcinoma; * 18 patients were lost to follow-up after incision biopsy at presentation; ** Kruskal-Wallis test; *** χ^2 test; na, not applicable. ^a Post hoc analysis with Bonferroni correction showed that only BCC and SCC were significantly different from each other ($p = 0.003$, Mann-Whitney test). ^b Post hoc analysis with Bonferroni correction showed that only BCC was significantly different from SCC ($p = 0.004$, χ^2 test) and SGC ($p < 0.001$, χ^2 test). ^c Post hoc analysis with Bonferroni correction showed that only BCC was significantly different from SGC ($p < 0.001$, χ^2 test). ^d Post hoc analysis with Bonferroni correction showed that only BCC was significantly different from SGC ($p = 0.006$, χ^2 test). ^e Post hoc analysis with Bonferroni correction showed that only BCC was significantly different from miscellaneous tumors ($p = 0.003$, χ^2 test). ^f Post hoc analysis with Bonferroni correction showed that only BCC was significantly different from SCC ($p = 0.004$, χ^2 test) and miscellaneous tumors ($p = 0.003$, χ^2 test). ^g Post hoc analysis with Bonferroni correction showed that only SCC was significantly different from SGC ($p = 0.001$, χ^2 test) and BCC ($p = 0.005$, χ^2 test). ^h Post hoc analysis with Bonferroni correction showed that only SGC was significantly different from BCC ($p < 0.001$, χ^2 test) and SCC ($p = 0.012$, χ^2 test). ⁱ Post hoc analysis with Bonferroni correction showed that only BCC was significantly different from SGC ($p < 0.001$, χ^2 test), SCC ($p = 0.007$, χ^2 test), and miscellaneous tumors ($p < 0.001$, χ^2 test). ^j Post hoc analysis with Bonferroni correction showed that only BCC was significantly different from SGC ($p < 0.001$, χ^2 test) and miscellaneous tumors ($p < 0.001$, χ^2 test). ^k Post hoc analysis with Bonferroni correction showed that only BCC was significantly different from SGC ($p = 0.001$, χ^2 test).

Fig. 2. Kaplan-Meier analysis of lymph node metastasis. Tumor 1, basal cell carcinoma; tumor 2, squamous cell carcinoma; tumor 3, sebaceous gland carcinoma; tumor 4, miscellaneous tumor.

Table 4. Kaplan-Meier estimates of malignant eyelid tumors

Kaplan-Meier estimate	SGC (<i>n</i> = 285)	BCC (<i>n</i> = 128)	SCC (<i>n</i> = 99)	Miscellaneous (<i>n</i> = 24)	All cases (<i>n</i> = 536)	<i>p</i> value
Locoregional lymph node metastasis						
1 year	11.07 (6.74–15.41)	1.43 (0–4.21)	8.08 (1.06–15.09)	22.99 (2.81–43.17)	9.05 (6.03–12.08)	<0.0001
3 years	29.73 (20.18–39.28)	1.43 (0–4.21)	12.91 (1.54–24.29)	33.99 (7.58–60.41)	21.42 (15.08–27.76)	
5 years	42.55 (30.27–54.83)	1.43 (0–4.21)	21.62 (2.47–40.78)	47.19 (15.85–78.53)	31.28 (22.76–39.81)	
10 years	48.93 (32.86–65.01)	1.43 (0–4.21)	41.22 (4.99–77.45)	na	36.93 (26.07–47.78)	
Distant metastasis						
1 year	9.35 (5.28–13.42)	0	5.91 (0–12.42)	17.86 (0–36.71)	7.09 (4.34–9.85)	0.0002
3 years	23.47 (14.54–32.41)	0	10.86 (0–22.14)	17.86 (0–36.71)	16.01 (10.3–21.72)	
5 years	35.74 (23.20–48.29)	0	10.86 (0–22.14)	17.86 (0–36.71)	22.96 (15.05–30.87)	
10 years	35.74 (23.20–48.29)	0	10.86 (0–22.14)	na	22.96 (15.05–30.87)	
Metastasis-related death						
1 year	6.68 (3.15–10.22)	0	6.05 (0–12.69)	0	4.64 (2.39–6.89)	0.003
3 years	16.79 (8.85–24.73)	0	10.99 (0–22.33)	0	11.21 (6.23–16.18)	
5 years	24.88 (13.56–36.2)	0	10.99 (0–22.33)	0	15.66 (0.81–22.5)	
10 years	24.88 (13.56–36.2)	0	10.99 (0–22.33)	na	15.66 (0.81–22.5)	

Values are % (95% confidence interval). na, not applicable.

SGC versus SCC

The clinicopathological correlation was better with SGC compared to SCC (91 vs. 46%; $p = 0.001$). Tumor recurrence was more common with SGC compared to SCC (21 vs. 8%; $p = 0.012$).

BCC versus SCC

The patients with BCC were older than those with SCC (60 vs. 55 years; $p = 0.003$). The following factors were more common and statistically significant with SCC

compared to BCC: tumor epicenter location in the upper eyelid (40 vs. 17%; $p = 0.004$), the need for orbital exenteration (19 vs. 5%; $p = 0.004$), and locoregional lymph node metastasis (8 vs. <1%; $p = 0.007$). The clinicopathological correlation was better with BCC compared to SCC (86 vs. 46%; $p = 0.005$).

BCC versus Miscellaneous Tumors

The following factors were more common with miscellaneous tumors compared to BCC: orbital tumor ex-

Fig. 3. Kaplan-Meier analysis of distant metastasis. Tumor 1, basal cell carcinoma; tumor 2, squamous cell carcinoma; tumor 3, sebaceous gland carcinoma; tumor 4, miscellaneous tumor.

Fig. 4. Kaplan-Meier analysis of metastasis-related death. Tumor 1, basal cell carcinoma; tumor 2, squamous cell carcinoma; tumor 3, sebaceous gland carcinoma; tumor 4, miscellaneous tumor.

tension (29 vs. 6%; $p = 0.003$), need for orbital exenteration (26 vs. 5%; $p = 0.003$), locoregional lymph node metastasis (26 vs. <1%; $p < 0.001$), and systemic metastasis (13 vs. 0%; $p < 0.001$).

Overall, SGC ($n = 38$) and miscellaneous tumors (malignant melanoma [$n = 3$], mucoepidermoid/adenosquamous carcinoma [$n = 2$], lymphoma [$n = 1$], and metastasis [$n = 1$]) were more commonly associated with locoregional tumor invasion into the orbit/paranasal sinuses/brain compared to SCC ($n = 16$) and BCC ($n = 9$). Locoregional lymph node metastasis was more common in patients with miscellaneous tumors ($n = 6$, including malignant melanoma [$n = 2$], Merkel cell carcinoma [$n = 1$], lymphoma [$n = 1$], eyelid metastasis [$n = 1$], and mu-

coepidermoid/adenosquamous carcinoma [$n = 1$]). Over a mean follow-up period of 19 months (median, 7 months; range, 1 week to 273 months), tumor recurrence (21%), systemic metastasis (13%), and death due to metastasis (9%) occurred more commonly in patients with SGC compared to other eyelid malignancies.

The 5-year Kaplan-Meier estimates for locoregional lymph node metastasis for SGC, BCC, SCC, and miscellaneous tumors were 43, 1, 22, and 47% ($p < 0.0001$), respectively (Fig. 2; Table 4), for distant metastasis 36, 0, 11, and 18% ($p = 0.0002$), respectively (Fig. 3; Table 4), and for metastasis-related death 25, 0, 11, and 16% ($p = 0.003$), respectively (Fig. 4; Table 4).

Table 5. Review of the literature on the proportion of eyelid tumors in Asians

Author(s), year	Country	Patients with malignant eyelid tumors, <i>n</i>	BCC, %	SCC, %	SGC, %	Miscellaneous tumors, %	Most common malignant eyelid tumor
Abe et al. [17], 1983	Japan	52	33	48	13	6	SCC
Ni et al. [33], 1983	China	525	47	10	33	10	BCC
Sihota et al. [15], 1996	India	178	30	30	33	7	SGC
Abdi et al. [36], 1996	India	85	39	22	27	12	BCC
Dai et al. [27], 1997	China	960	37	8	31	24	BCC
Lee et al. [29], 2000	Singapore	325	84	3	10	2	BCC
Wang et al. [16], 2003	Taiwan	127	62	9	24	5	BCC
Chang et al. [30], 2003	Taiwan	18	78	6	17	0	BCC
Obata et al. [24], 2005	Japan	24	38	0	38	25	BCC, SGC
Pornpanich et al. [28], 2005	Thailand	32	41	6	38	15	BCC
Takamura et al. [34], 2005	Japan	38	40	11	29	21	BCC
Lin et al. [14], 2006	Taiwan	1,121	65	13	8	14	BCC
Xu et al. [12], 2008	China	363	41	5	39	15	BCC
Kumar [8], 2010	Nepal	37	24	27	41	8	SGC
Mak et al. [35], 2011	China	36	75	6	11	8	BCC
Kale et al. [10], 2012	India	85	48	14	31	7	BCC
Lim et al. [31], 2012	Singapore	333	82	4	11	5	BCC
Wang et al. [7], 2013	China and Korea	75	48	9	29	15	BCC
Hussain et al. [11], 2013	Pakistan	222	59	32	7	3	BCC
Bagheri et al. [32], 2013	Iran	100	83	8	6	3	BCC
Ho et al. [13], 2013	China	28	43	18	7	32	BCC
Ramya et al. [21], 2014	India	24	27	22	41	10	SGC
Krishnamurthy et al. [23], 2014	India	19	26	21	32	21	SGC
Rathod et al. [25], 2015	India	39	41	10	41	8	BCC, SGC
Huang et al. [9], 2015	Taiwan	227	58	10	21	11	BCC
Karan et al. [20], 2016	India	9	33	11	56	0	SGC
Mohan et al. [19], 2017	India	41	15	22	24	39	SGC
Gupta et al. [18], 2017	India	9	22	11	44	22	SGC
Jangir et al. [26], 2017	India	17	29	24	47	0	SGC
Present study, 2018	India	536	18	24	53	4	SGC

BCC, basal cell carcinoma; SCC, squamous cell carcinoma; SGC, sebaceous gland carcinoma.

Discussion

BCC is the most common malignant eyelid tumor in the West [1–5]. In our series, SGC was the most common malignant eyelid tumor and this finding is consistent with some studies from other Asian countries including India, Japan, and Nepal [8, 15, 18–21, 23–26]. In our study, SGC (53%) was twice as common as BCC (24%) and 3 times more common than SCC (18%). Other studies from China, Korea, Singapore, Taiwan, and Thailand have shown BCC as the most common malignant eyelid tumor [7, 9, 11, 14, 16, 24, 27–33]. However, these studies have also shown a lower proportion of BCC and a higher proportion of SGC compared to the West [1–5, 7, 9, 11, 14, 16,

27–33] (Table 5). A study from Japan has shown SCC as the most common malignant eyelid tumor, constituting 48% of all eyelid malignancies [17], while in our study SCC was less common compared to SGC and BCC, constituting only 24% of all eyelid malignancies. Similar to our study, the majority of studies on malignant eyelid tumors in Asian Indians have shown that SGC is the most common eyelid malignancy (32–56%) in the Asian Indian population [15, 18–21, 23, 25, 26]. Referral bias to the tertiary care referral institution may also play a role in this difference of eyelid tumor proportions. The referral of BCC would be much lower compared to other tumors since these tumors may have been more easily managed by referring physicians. In our study, the history of prior

intervention was highest for miscellaneous tumors (67%), SCC (42%), and SGC (41%), suggestive of difficulty in managing these cases compared to BCC (18%).

Malignant eyelid tumors occur more commonly in the elderly [1–21, 23–32, 34–36]. In our series, the mean age at presentation of all malignant eyelid tumors was ≥ 50 years. The patients presenting with miscellaneous tumors (50 years) and SCC (55 years) were younger compared to those with SGC (58 years) and BCC (60 years). Female predominance of malignant eyelid tumors was noted in some studies, while male predominance or no predilection has also been reported [34]. In our study, though there was a slight female predilection, it was not statistically significant. The reason for female preponderance in our study is unknown, though it may be related to increased cosmetic concerns of eyelid disfigurement in females, resulting in a higher rate of doctor consult in females compared to males.

Periocular SGC most commonly arises in the upper eyelid, accounting for half to two thirds of cases due to a predominance of meibomian glands in the upper eyelid [1]. In our study, 59% of tumors arose from the upper eyelid. Female preponderance of SGC has been reported in previous studies [33, 37, 38], while few studies have shown a male preponderance [39]. In our study, there was a female predilection with a male:female ratio of 1:1.5. A Chinese-American collaborative study on malignant eyelid tumors including 525 cases from China and 1,543 cases from the USA revealed a disparity between the frequencies of SGC in both populations, accounting for 33% in China and 2% in the USA [33]. Based on these findings, the authors proposed that the incidence of SGC is higher in the Asian population compared to Caucasians and this could be related to genetics and racial predisposition for SGC in Asians [33]. Subsequent studies from Asian countries have supported this theory. However, this theory of racial predilection may not be true. In a retrospective study of 1,349 cases from a US-based population registry, the incidence of SGC was 2.03 cases per 1,000,000 population in Whites versus 1.07 cases per 1,000,000 population in Asian/Pacific Islanders versus 0.48 per 1,000,000 population in Blacks, suggestive of a lack of racial predilection of SGC [39]. In Asians, SGC accounts for a higher proportion of eyelid malignancies, similar to our study, but this is not due to a higher incidence of SGC but to a relative lack of other malignant eyelid tumors [39]. Asians with malignant eyelid tumors are 6.21 times (range, 3.8–10.1) more likely to have SGC compared to non-Asians [39].

Overall, BCC is the most common malignant eyelid tumor in the world [1, 40], with a male predilection [41].

However, it has been reported that eyelid BCC is more common in young females (<50 years) [39]. In our study, BCC was more common in females across all age groups, with a male:female ratio of 1:1.5. BCC is more common in the lower eyelid (50–66%), followed by medial canthus (13–30%), upper eyelid (15–16%), and lateral canthus (3–5%) [42, 43]. In our study, the most common tumor location was the lower eyelid (59%) and the tumor epicenter location in the medial canthus was less frequent at 10%. Pigmented BCC of the eyelid has been noted in 1–50% patients and was more common in patients with darker skin color [44–46]. Haye and Dufier [45] noted that pigmented BCC of the eyelid was 1% in a Parisian population and increased to 45% in a Mediterranean population, suggestive of increased incidence in a darker-skinned population. In our study, pigmented BCC was noted in 55% of cases.

Eyelid SCC is a disease of the elderly, with a mean age at presentation of 60 years, and has a male predilection [47]. However, in our study, the mean age at presentation of SCC was 55 years and the disease had a slight female preponderance with a male:female ratio of 1:1.1. There was no preference for upper or lower eyelids. The occurrence of malignant melanoma and other eyelid tumors was rare in our series. However, younger patients (<20 years of age) had a preponderance for non-SGC/BCC/SCC eyelid malignancies.

The recommended modality of treatment for all malignant eyelid tumors is wide excision biopsy under frozen section or Moh's micrographic surgery control. In our study, wide excision biopsy under frozen section was performed in all cases when the tumor was limited to the eyelid. Clinical misdiagnosis was more common with SCC and miscellaneous malignant eyelid tumors with a clinicopathological correlation of 46% for SCC and 38% for miscellaneous tumors. Eyelid SCC (85%) was commonly misdiagnosed as SGC, and the most common misdiagnosis of miscellaneous tumors was eyelid metastasis (29%). Locoregional tumor invasion (13%), locoregional lymph node metastasis (16%), tumor recurrence (21%), systemic metastasis (13%), and disease-related death (9%) were more common with SGC compared to SCC and BCC. These findings are comparable with other studies [1, 4, 37–39]. Locoregional lymph node metastasis was also more common with miscellaneous tumors (25%), including malignant melanoma ($n = 2$), Merkel cell carcinoma ($n = 1$), lymphoma ($n = 1$), metastasis ($n = 1$), and mucoepidermoid/adenosquamous carcinoma ($n = 1$).

In summary, the proportion of SGC is higher in Asian Indians compared to other malignant eyelid tumors. This finding differs from the Western population. SGC, malig-

nant melanoma, and Merkel cell carcinoma are associated with poorer prognosis, with higher chances of locoregional lymph node and systemic metastasis compared to BCC and SCC. This finding is similar to studies from the Western population.

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Statement of Ethics

This was a retrospective study conducted at the Operation Eyesight Universal Institute for Eye Cancer, LV Prasad Eye Institute, Hyderabad, India. Institutional review board approval was obtained.

Disclosure Statement

No conflicting relationship exists for any author.

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