Original Article

A clinicopathological study of eyelid malignancies from central India

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Background: Eyelid malignancies are completely treatable if detected early. The treatment depends on the invasiveness of the cancer which in turn depends on the type of malignancy.

Aim: The aim of the study was to characterize the distribution of the types of eyelid malignancies in central India.

Settings and Design: The study was conducted in the Department of Plastic and Maxillofacial Surgery at a tertiary care hospital.

Materials and Methods: We report a series of 27 cases of eyelid malignancies. In the same case series, we also include a case of malignant hemangiopericytoma which is an extremely rare form of eyelid malignancy worldwide.

Statistical Analysis: Depending on the underlying statistical distribution, either analysis of variance (ANOVA) or the Kruskal-Wallis (K-W) test was used to assess the differential distribution of these variables across the types of eyelid malignancies observed in this study.

Results: We observed that sebaceous cell carcinoma (~37%) was almost as prevalent as basal cell carcinoma (~44%) in the study subjects and had an earlier age of occurrence and a more rapid clinical course.

Conclusions: Sebaceous cell carcinoma of the eyelid is almost as common as basal cell carcinoma in a large tertiary care centre in central India.

Key words: Cancer, eyelid, hemangiopericytoma.

Indian J Ophthalmol 2007;55:109-12

Although the incidence of eyelid malignancies is increasing,[1-5] their global distribution is varied and remains under-characterized. It is reported, for example, that 90% of the malignant eyelid tumors are basal cell carcinomas (BCC) while other malignant forms like sebaceous cell carcinoma (SbCC) and squamous cell carcinoma (SqCC) are rare.[3,4,6] However, case series reported from Asian countries have shown a generally higher prevalence of SbCC.[1,2,4,5,7] It is still unclear whether this increased prevalence of SbCC reflects a higher incidence of SbCC, a lower incidence of BCC or differential survival rates associated with these tumors that eventually favor a relative accumulation of SbCC in Asian populations. The aim of the study was to review our experience with a series of 27 eyelid malignancies including one case of an extremely rare form of malignant eyelid neoplasm – hemangiopericytoma (HMP).[8-9]

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Manuscript received: 01.05.06; Revision accepted: 20.07.06

Materials and Methods

The present case series includes all consecutive cases of eyelid malignancies that reported to the Department of Plastic and Maxillofacial Surgery at a tertiary health care facility in central India. We included cases that reported to the study center over a six-year period starting from January 1996. During this study period, a total of 27 cases of eyelid malignancies were identified. In each case, the clinical diagnosis of eyelid malignancy was confirmed by fine needle aspiration biopsy and histopathology. The cases were treated with wide local excision with a 5-10 mm margin of normal tissue and an appropriate combination of split skin grafts (SSG), tarso-conjunctival flaps (TCF) and Mustarde's flaps (MF). Depending on the underlying statistical distribution of the continuous variables, we used analysis of variance (ANOVA) or the Kruskal-Wallis (K-W) test to assess the differential distribution of these variables across the types of eyelid malignancies observed in this study. Statistical significance was tested at an α of 0.05.

Results

In our case series we encountered four types of eyelid malignancies – BCC (12 cases, 44.5%), SbCC (10 cases, 37.0%), SqCC (4 cases, 14.8%) and HMP (1 case, 3.7%). All the tumors

were newly detected without a past history of irradiation. Characteristics of the study subjects are described in detail in Table 1. Using ANOVA we observed that the age of the study subjects at the time of detection of the cancer was statistically significantly different across the type of malignancy ($F = 3.04$, $P = 0.049$) with SqCC cases representing the youngest age group. In all cases, the earliest manifestation was tumor. As the duration of this symptom did not follow normal distribution, we used the K-W test to assess whether it was significantly influenced by the type of malignancy. We observed that it indeed was (K-W $P = 0.003$).

The size of the tumor at the time of diagnosis did not vary by type of malignancy ($F = 0.61$, $P = 0.612$). We thus obtained an estimate of the rate of tumor growth (derived by dividing the size of the tumor at the time of diagnosis by the duration of symptoms). We observed that the rate of tumor growth was strongly associated with the type of malignancy (K-W $P = 0.001$) – BCC being the slowest growing tumor and SqCC the fastest. Figs. 1 and 2 show the representative photomicrographs of the histopathological characteristics of the four types of malignancies observed in our case series. Our case series included 18 (66.67%) females, 15 (55.6%) lower eyelid lesions and 14 (51.9%) right eye lesions.

We make a special mention of the 60-year-old female patient in T3M0N0 stage malignant hemangiopericytoma – an extremely rare form of eyelid malignancy. This patient had a very rapid-growing painful tumor of the left upper eyelid that attained a diameter of 3 cm within two months and developed ulceration. The tumor was associated with a serous discharge and was fixed to the skin but not to deeper structures. There was no itching, restriction of movement, vision problem or eyelash alopecia. This case was treated successfully with wide local excision and split skin graft.

Of the 27 study subjects, one patient refused reconstructive surgery. All 26 operated cases of malignant neoplasms underwent wide local excision. Of these, 11 resulted in partial thickness defects and 15 in full thickness defects. The most common oculoplastic procedure required was SSG alone (nine cases), TCF alone (two cases), SSG followed by TCF (13 cases) and TCF followed by MF (two cases). Postoperatively, it was

Table 1: Clinical and histopathological characteristics of study subjects

Characteristic	Basal cell carcinoma	Sebaceous cell carcinoma	Squamous cell carcinoma
Age (years, mean±SE)	63.5±3.82	55.1±3.15	41.5±9.13
Average duration (years, mean±SE)	2.6±0.81	0.6±0.1	0.4±0.11
Size of tumor (cm, mean±SE)	2.29±0.34	2.85±0.42	2.00±0.71
Rate of tumor growth (cm/year, median)	1.33	3.88	4.64
Sex (n)			
Male	4	4	1
Female	8	6	3
Eyelid involved (n)			
Upper	2	7	2
Lower	10	3	2
Itching (n)	5	0	1
Pain (n)	1	5	1
Movement restriction (n)	0	1	0
Side (n)			
Right	7	7	0
Left	5	3	4
Ulceration (n)	5	5	1
Lid margin involvement (n)	2	9	3
Loss of eyelashes (n)	2	9	2
Fixity (n)			
to skin	10	7	3
to deeper structures	0	1	0
to skin and deeper structures	1	2	1
Discharge (n)	2	3	1
Stage of cancer* (n)			
T2	4	0	1
T3	8	10	3
N0	11	9	3
N1	1	1	1
M0	12	10	4

*Using tumor, nodes, metastasis classification (TNM)

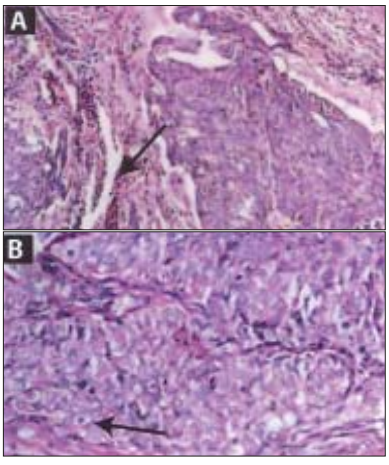

Figure 1: Representative photomicrographs showing hematoxylin and eosin stained histopathological sections (45x) of basal cell carcinoma and sebaceous cell carcinoma observed in the present study. (A) Basal cell carcinoma. The image shows malignant cells with pyknotic nuclei, scanty cytoplasm and adjacent fibrous stromal tissue (arrow). (B) Sebaceous cell carcinoma. In contrast to panel A, this slide shows numerous malignant cells with vacuolated cytoplasm. The arrow points to one such cell

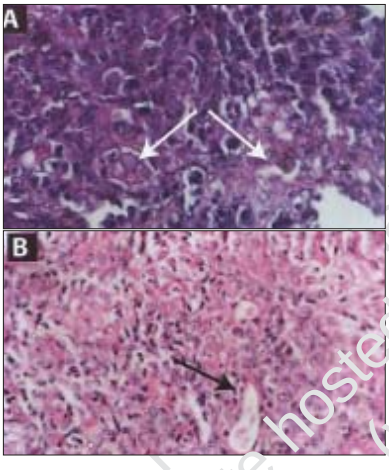

Figure 2: Representative photomicrographs showing hematoxylin and eosin stained histopathological sections (45x) of squamous cell carcinoma and malignant hemangiopericytoma observed in the present study. (A) Squamous cell carcinoma. This view shows pleomorphic malignant cells with areas of keratinization (white arrows). (B) Malignant hemangiopericytoma. The section shows perivascular (arrow), densely packed, small malignant cells with scanty cytoplasm

observed that all the SSGs were taken up successfully. There were only two common postoperative complaints – foreign body sensation and conjunctival congestion. In addition, one subject each developed hematoma and seroma. On follow-up, 10 patients reported itching at the graft site which abated after use of topical Vaseline and oral antihistaminics. Three cases reported epiphora which subsided spontaneously. Closure and blinking of eyes were normal in all patients who completed follow-up.

Discussion

Our results provide further evidence in favor of a higher proportion (30-40%) of SbCC in India. In countries like the USA and Australia, the prevalence of this condition is reported to be 1.5% and 3.8%, respectively. If, as argued,[10] the increased proportion of SbCC in China and India were to merely reflect a decreased incidence of BCC, then one would expect a proportionate increase in both SbCC and SqCC. This expectation can be explained mathematically as follows: Let us assume that a closed population of n subjects had x cases of BCC, y cases of SbCC and z cases of SqCC. Then the proportion of eyelid malignancies with BCC, SbCC and SqCC will be $x/(x+y+z)$, $y/(x+y+z)$ and $z/(x+y+z)$, respectively. If over time the prevalence of only BCC was to decrease (say by a factor r, where $r>1$) and the population size is still n, then the new number of cases of BCC, SbCC and SqCC will be x/r (ensuring that $x/r < x$), y and z. Then, the proportion of eyelid malignances with SbCC and SqCC will be $y/[(x/r)+y+z]$ and $z/[(x/r)+y+z]$, respectively. If we compare the previous proportion of these two types of malignancies with their respective new prevalence, then we can mathematically express the change in the prevalence of SbCC as well as SqCC is a function of the original BCC proportion and the factor by which the prevalence of BCC has fallen [Fig. 3]. Since an assumption of a decreased number of BCC cases is unlikely to alter the values of y and z, it is clear that the inflation in the proportion of both SbCC and SqCC will be quantitatively similar i.e. by a factor of $1/[(x/r)+y+z]$. However, three Indian studies, including the present one, as well as one study each from Japan and Taiwan demonstrate that it is the SbCC that is preferentially enriched in Asian populations.[1,7] Thus, we reemphasize that SbCC should be actively searched for in cases of eyelid malignancies in Asia. We acknowledge a potential limitation in our method of estimation of the rate of tumor growth, which can be strongly influenced by the patient's ability to detect the first appearance of the tumor. However, it seems less likely that this ability will be differential across the type of malignancy. Therefore, given the earlier mean age at occurrence and an estimated faster rate of tumor growth, SbCC and SqCC may deserve a more aggressive treatment protocol.

Conclusion

The present case series points towards the need to realize the different prevalence rates, the age distribution and rate of

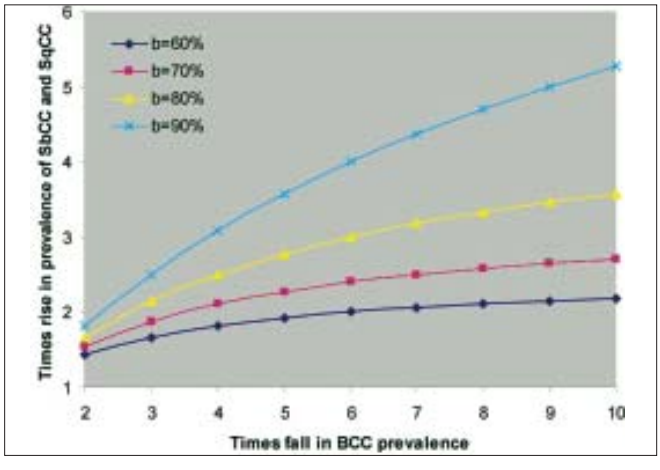

Figure 3: Mathematical model of the projected change in the proportion of SbCC and SqCC as a function of a reduction in the prevalence of BCC. The figure shows the plot of an expected fold change in the prevalence of both SbCC and SqCC as a function of the initial proportion of BCC (b) and a fold reduction (times fall) in the prevalence of BCC

growth of different forms of eyelid malignancies and the attendant need for a careful search for early detection of malignancies such as SbCC and SqCC.

Acknowledgments

We thank Dr. S. K. Bobhate, Professor and Head, Department of Pathology, Government Medical College and Hospital, Nagpur, India for expert histopathological diagnoses and for providing the photomicrographs.

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Source of Support: Nil, **Conflict of Interest:** None declared.