Audit of primary tumors in oculoplastic cases at a tertiary care centre in North India

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Abstract

Introduction: There is geographical variation in pattern of ocular tumors. We aimed to identify and describe the clinicopathologic characteristics of primary tumors of the eye and ocular adnexa in oculoplastic clinics at our tertiary care centre. **Materials and Methods:** In our prospective longitudinal study patients with primary ocular tumors underwent surgical management. Resectable tumors were subjected to excision biopsy. Incision biopsy was taken in advanced malignant tumors. The tissue masses were sent for histopathological examination. Cases were followed up monthly to see recurrences.

Result: Out of 676 oculoplastic cases operated, 68 patients required surgery for tumors with common site being upper eyelid followed by periorbital area & lower eyelid. 75% cases were benign while 25% were malignant. Maximum cases in benign group were in the age group 11-20 year & in malignant group in age group of 41-50 years. Recurrence rate was 17.3%. Sebaceous cell carcinoma (44.4%) was the predominant malignant eyelid tumor.

Conclusion: We observed an interesting geographical variation in malignant eyelid tumor. We have come up with a few recommendations to prevent recurrences.

Keywords: Benign, Malignant, Ocular tumors, Oculoplastic cases.

Introduction

Ocular tumors, both benign and malignant, are encountered frequently by ophthalmologists. 2-3 persons per million of population require orbital surgery for orbital tumors.¹

The eyelids are affected by wide spectrum of lesions. Benign lesion is 3 times more frequent than malignant neoplasm.² Squamous papilloma is the most common benign lesions of the eyelid. Basal Cell Carcinoma (BCC) is the most common malignant tumor of the eyelids and constitutes 85-90% of all malignant epithelial eyelid tumors.3,4 Lacrimal gland lesions represent 5% to 25% of orbital tumors, and range from 23% to 70% of biopsied cases^{5,6} as mentioned in literature.Lesions of adnexal origin arise from the epidermal appendages, which include the sebaceous glands of Zeis, meibomian glands, pilosebaccous units (hair follicles and associated sebaceous glands), eccrine sweat glands, and apocrine sweat glands. Cavernous hemangioma is the most common benign orbital tumor of adults.⁽⁷⁾ The capillary hemangioma is the most common orbital tumor found in children, girls affected more than boys, with 3:2 ratio.

There is geographical variation in pattern of ocular tumors. We attempt to evaluate the profile of primary tumors of eye in oculoplastic clinics in our clinical practice at our tertiary care centre.

Materials and Methods

Ethical Approval: Ethical approval for this study (notice no.52 (A)/ND/2013) was provided by the institutional ethics committee on 15 June 2013. The

study has been conducted as per guidelines of the declaration of Helsinki. We obtained written informed consent from the study participants and their identity has not been disclosed in any form.

Study Design: A longitudinal, observational study was conducted from December 2011 to October 2013. The patients attending out-patient department (OPD) of ophthalmology for various oculoplastic complaints were selected for the study.

Inclusion Criteria: Patients with growths/masses/ tumor of orbit, eye appendages (lid& lacrimal gland and apparatus), conjunctiva, cornea/limbus, medial/lateral canthi, caruncle were included in study.

Exclusion Criteria: All cases of tumors of uveal tissue, posterior chamber, retina, optic nerve or secondaries from other tumors in the body were not included. Also patients of tumor not willing to undergo surgery or participate as study case were excluded.

Methodology: Demographic data of patients qualifying inclusion criteria were recorded. Patients underwent complete ocular examination including visual acuity, slit lamp examination for anterior segment assessment, gonioscopy and fundus evaluation (as per need). All tumors were documented in terms of site, size, consistency, mobility, attachment to underlying overlying structure and skin. Preoperative investigation were done such as complete blood count, random blood sugar, bleeding time, clotting time, HIV & HBs Ag status and X-rays head & orbit/CT scan/ MRI, where ever required.

All patients went under surgical management. Excisable tumors were subjected to excision biopsies. Incision biopsies were taken in advanced malignant tumors (which were rendered inoperable due to their size or depth). The tissue masses were sent for histopathological examination (HPE) and cases were followed up monthly to see for recurrences.

Data collected were analyzed and conclusion drawn at the end of the study.

Results

Pattern of sex distribution: In our study, out of total 52 patients 46.2% were male and 53.8% were females. Female: male ratio was 1:1.16.

Time between onset of symptoms and presentation: Although most patients presented within 3 months of onset of symptom, there was no definite pattern of distribution of time between onset of symptom and presentation. (Table 1)

 Table 1: Time between onset of symptoms and presentation

Duration	Male		Female		
of illness	Number	%	Number	%	
=1 month</td <td>4</td> <td>16.7%</td> <td>1</td> <td>3.6%</td>	4	16.7%	1	3.6%	
>1 month- 3 month	4	16.7%	6	21.4%	
>3 month- 6 month	3	12.5%	5	17.9%	
>6 month- 1 year	3	12.5%	3	10.7%	
>1 year- 2 year	1	4.1%	5	17.9%	
>2 year- 5 year	2	8.3%	3	10.7%	
>5 year - 10 year	5	20.8%	3	10.7%	
>10 year- 20 year	2	8.3%	1	3.6%	
>20 year	0	0%	1	3.6%	
Total	24	100%	28	100%	

Laterality: There was no side predilection.Tumors were equal on right and left.

Distribution of site of involvement: Most common site of involvement of tumor was upper eyelid (28.8%) followed by periorbital area (21.2%) and lower eyelid (19.2%). Upper and lower eyelid together constituted about 48% of total cases in our study. Remaining tumors were found in conjunctiva (13.5%), cornea /limbus (5.8%), medial canthus (5.8%), lacrimal sac area (3.8%) and lateral canthus (1.9%). (Table 2)

	Table 2:	Distribution	of site of	involvement
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Site	Number	%
Periorbital area	11	21.2%
Upper eyelid	15	28.8%
Lower eyelid	10	19.2%
Conjunctiva	7	13.5%
Cornea / Limbus	3	5.8%
Medial canthus	3	5.8%
Lateral canthus	1	1.9%
Lacrimal sac area	2	3.8%
Total	52	100%

Distribution of Frequency of Presenting Symptom: Patients came with growth/cosmetic problem, visual hindrance, pain, watering, bleeding. Some of the complaints overlapped. (Table 3) Most of the patients i.e. 53.2% came to our OPD with a mass or growth. Only 15.3 % had visual problem.

 Table 3: Distribution of frequency of presenting

 symptom

symptom			
Symptom	Frequency	%	
Growth/cosmesis	49	53.2%	
Visual hinderence	14	15.3%	
Pain	11	12%	
Watering	9	9.7%	
Bleeding	9	9.7%	

(Distribution of cases by presenting complaints) n=92

Histopathological Profile of Ocular Tumor: In present study, out of total 52 cases 75% were benign while the remaining 25% were malignant.

Pattern of Age Distribution: Maximum numbers of patients in benign group were in the age group 11-20 year followed by 21-30 years (Table 4). In the malignant group most patients were in age group of 41-50 years followed by 51-60 years. (Table 4)

Table 4: Pattern of age distribution

Age	Benign		Mali	Malignant	
	No.	%	No.	%	
0-10	3	7.7%	0	0%	
11-20	16	41.0%	1	7.7%	
21-30	5	12.8%	1	7.7%	
31-40	3	7.7%	1	7.7%	
41-50	3	7.7%	4	30.7%	
51-60	4	10.3%	3	23.1%	
61-70	3	7.7%	1	7.7%	
>70	2	5.1%	1	7.7%	
Total	39	100%	13	100%	

Histopathological profile among benign ocular tumor: The most common benign tumors which we have come across in our study were naevus (15.4%) and dermoid (15.4%) followed by sebaceous cyst (12.8%). Next in the list in benign cases were cavernous hemangioma (10.3%), squamous papilloma (10.3%), abscess (7.7%), capillary hemangioma (5.2%), dermolipoma (5.2%), epithelial inclusion cyst (5.2%), fibroepithelial cyst (2.6%), plexiformneurofiroma (2.6%), lacrimal cyst (2.6%) and cutaneous lymphoid (2.6%).

Histopathological profile among malignant ocular tumor: In our study most common malignant tumor were squamous cell carcinoma (30.7%) and sebaceous cell carcinoma (30.7%). Other malignant tumors were basal cell carcinoma, adenocarcinoma, orbital melanoma, malignant spindle cell, fibrous cell tumor, refractory neuroblastoma each representing 7.7%. **Rate of recurrences on follow up:** Out of 39 benign cases only 4 cases had recurrences. In malignant group 5 cases had recurrence out of total 13 cases. Thus, out of total 52 cases 9 cases had recurrence.

Overview of time duration of recurrence of tumor: Maximum recurrence in benign group was seen during 3rd month of follow up. Maximum recurrence in malignant group was seen in 1st month. (Table 5)

 Table 5: Overview of time duration of recurrence of tumor

Time	Benign		Malignant	
duration	No.	%	No.	%
Day 1	0	0%	0	0%
Day 7	0	0%	0	0%
1 month	0	0%	3	60 %
3 month	2	50%	1	20%
6 month	1	25%	0	0%
1 year	1	25%	1	20%
1.5 year	0	0%	0	0%
Total	4	100%	5	100%

Histopathological profile among malignant eyelid tumor: In the malignant eyelid lesion group male and female cases were 44.4% and 55.6% respectively. Sebaceous cell carcinoma (44.4%) was the predominant malignant eyelid tumor followed by squamous cell carcinoma (22.2%) and basal cell carcinoma (11.1%). (Table 6)

 Table 6: Histopathological profile among malignant

 eyelid tumors

Histopathological	Number	%
profile		
Sebaceous cell	4	44.4%
carcinoma		
Squamous cell carcinoma	2	22.2%
Basal cell carcinoma	1	11.1%
Orbital melanoma	1	11.1%
Adenocarcinoma	1	11.1%
Total	9	100%

Discussion

Ocular tumors are encountered by all comprehensive ophthalmologists and they are in tough situation to deal with. 676 oculoplastic cases (squint, lid abnormalities, lacrimal passage blockage etc.) were operated during the study interval. Out of these patients 10.06% (68 patients) required surgery for ocular tumors.

Unfortunately out of above mentioned 68 patients 16 patients were lost to follow up. Thus a good motivation and counseling is required to reduce the morbidity and mortality in case of tumors. It should be explained to patient that merely getting operated does not get them rid off the tumor. They should be told about the recurrence chances and symptom to recognize them. Also emphasis on regular follow up with the operating surgeon is essential as recurrence does not necessarily manifest with a definite pattern of sign and symptom as explained during counseling.

Patients of ocular tumors came to our side with complaints of growth/cosmetic problem, visual hindrance, pain, watering, and bleeding (Table 3). Some of the symptoms were overlapping. Maximum number of the patients i.e. 53.2% came to our OPD with complaint of mass or growth. Those who came early were concerned mainly about the cosmetic appearance while those who presented late primarily had a suspicion regarding malignancies. Only 15.3 % cases had visual problem. Thus not much of visual morbidity has been seen due to these tumors in our study. Pain, watering and bleeding was seen in 12%, 9.7% and 9.7% cases respectively.

We all are aware of the fact that malignancies occur in elderly age group. Shields et al published a review of 1,264 patients over a period of 30 years and found that benign were more common than malignant lesions but that malignancy became more likely with advanced age.⁸ Similarly in our study, benign lesions are more common (75%). Maximum numbers of patients in benign group were in the age group 11-20 year followed by 21-30 years. In the malignant group most patients were in age group of 41-50 years followed by 51-60 years. Cases were however registered in all age groups (Table 4).

Ronaldo et al described that benign lesions comprised 61.02% of all tumors, the most common of which were epithelial cysts, dermoids, and nevi.⁹ It was more or less similar to our study. The most common benign tumors which we have come across were naevus (15.4%) and dermoid (15.4%) followed by sebaceous cyst (12.8%).

In one of the study conducted in Netherlands, lymphoma had a relative frequency of 67%, rhabdomyosarcoma 12%, adenocarcinoma 6%, and adenoid cystic carcinoma 5%.¹⁰ This was different from our study. In our study most common malignant tumor were squamous cell carcinoma (30.7%) and sebaceous cell carcinoma (30.7%). Other malignant tumors don the list were basal cell carcinoma, adenocarcinoma, orbital melanoma, malignant spindle cell, fibrous cell tumor, refractory neuroblastoma each representing 7.7% each.

As expected, recurrences are much higher in malignant group as compared to benign group. Thus cases which turn out to be malignant on histopathological examination should be dealt with extra caution. A record of contact information of these cases should be kept by the staff and follow up should be meticulously noted down.

In malignant group, 5 out of 13 cases had recurrence i.e. recurrence rate was 38.5%. Out of these 60% recurred at 1 month, 20 % at 3 month and remaining 20% at 1 year. (Table 5) Two patients refused for chemotherapy after debulking surgery which led to recurrence. These were the cases of refractory neuroblastoma and squamous cell carcinoma. Thus patient counseling is an essential part of treatment of malignancies. Other probability of high rate of recurrence could be due to incomplete removal of tumor mass in spite of best efforts to obtain clear margins. This category included tumor like squamous cell carcinoma, basal cell carcinoma, and sebaceous cell carcinoma. Thus it emphasizes the need of intraoperative frozen section while dealing with malignant tumors. It can give the surgeon a fairly good idea of need of further dissection and management after surgery in form of radiotherapy or chemotherapy. The other option is Moh's Micrographic Surgery, which is the gold standard in dealing with malignancies.¹¹ But the cost of surgery goes up and it requires time during which patient might be lost to follow up. It builds up a situation for second thought in a setup with low infrastructure and less educated patient. Cryotherapy of the tumor bed and margins is also an upcoming recommendation at many centers.¹² Updated cryosurgery provides a low cost option to MMS.¹³ Cryosurgery preserves much healthy ocular structures. Thus, epithelium and endothelium can grow fast resulting in excellent functional and cosmetic outcome. The treatment area can be extended without creating problems of defect coverage. It avoids the need of reconstructive surgery. The risks of dislocation of tumor cell nests or hidden growth beneath grafts are avoided. It is a effective means of treating tumors, achieving cure rates in excess of 90% with 5-year recurrence rates of 0-5% for small BCCs in several larger series.12,13

As per the literature, BCC is the most common malignant tumor of the eyelids in France and other European countries and constitutes 85-90% of all malignant epithelial eyelid tumors.^{3, 4} Sebaceous gland carcinoma is the third most common eyelid malignancy accounting for 1-5.5% of all eyelid cancers.14 Squamous cell carcinoma was found to be the most common tumor (65%) among the elderly persons in Nepal.⁽¹⁵⁾ Recent studies from India and China have shown that sebaceous carcinoma accounts for 33-60% of malignant eyelid tumors. In China the tumor is reported to occur in 28% of the lid cancers.¹⁶ Jahagirdar et al in 2007 observed that sebaceous cell carcinoma (37%) was almost as prevalent as basal cell carcinoma (44%) in the study subjects in a large tertiary care centre in central India.¹⁷ It thus seems that the incidence of sebaceous gland carcinoma has a geographical variation and is more common in Asian population.¹⁸⁻²⁰ This fact has been supported by our study also (table 6). Sebaceous cell carcinoma (44.4%) was the predominant malignant tumor followed by squamous cell carcinoma (22.2%) and basal cell carcinoma (11.1%) among malignant eyelid tumors.More number of sebaceous gland carcinoma can be attributed to oily nature of skin amongst Indians. Decline in basal cell and squamous

cell carcinoma can be due to more melanin in Indian population which provides a protection from sunlight.

Conclusion

Considering the drop out cases and recurrence rate of malignant tumor due to incomplete treatment we emphasize the importance of proper counseling of patients. Considering literature support, cryotherapy of the tumor bed and margins for malignant tumors is a good option to reduce the recurrence rate of tumor especially in developing countries where facility of micrographic surgery or even frozen section is limited due to lack of resources. These are essential recommendations to reduce the morbidity and mortality especially in dealing malignancies.

We observed a geographical variation in trend of malignant eyelid tumor.Sebaceous cell carcinoma outnumbers basal cell carcinoma and squamous cell carcinoma in Asian subcontinent in contrast to the western world.

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Conflict of Interest: None

References

- Coleman DJ, Lizz FL, "Computerized ultrasonic tissue characterization of ocular tumors" Am T Ophthalmo (1983) 196, 165.
- Aurora AL, Blodi FC, "Lesions of the eyelids: a clinicopathological study" Surv Ophthalmol (1970) 15, 94-104.
- 3. Allali J, Hermies FD, Renard G," Basal cell carcinomas of the eyelids" Ophthalmologica (2005) 219, 57-71.
- Margo CE, Waltz K, "Basal cell carcinoma of the eyelid and periocular skin" Surv Ophthalmol (1993) 38, 169-192.
- 5. Kennedy RE, "An evaluation of 820 orbital cases" Trans Am Ophthal Soc (1984) 82, 134-157.
- Shields CL, Shields JA, Eagle RC, Rathmell JP, "Clinicopathologic review of 142 cases of lacrimal gland lesions" Ophthalmology (1989) 96, 431-435.
- Liesegang TJ, Deutsch TA, Grand MG, "Basic and clinical science course" Am Acad Ophthalmol (2002) 6, 341-350.
- Shields JA, Shields CL, Scartozzi R, "Survey of 1,264 patients with orbital tumors and simulating lesions: The 2002 Montgomery Lecture, part 1" Ophthalmology (2004) 111, 997–1008.
- Rolando DDE, Lilibeth ME, Rolando CM, "Tumors of the eye and ocular adnexa at the Philippine Eye Research Institute: a 10-year review" Clin Ophthalmol (2015) 9, 1239–1247.
- Morris DS, Elzaridi E, Clarke L, Dickinson AJ, Lawrence CM, "Periocular basal cell carcinoma: five year outcome following slow Mohs Surgery with formalin-fixed paraffin-embedded sections and delayed closure" Br J Ophthalmol (2009) 93, 474–476.
- 11. Koopman JH, M. van der Heiden-van der Loo, Van Dijk MR, Bijlsma WR, "Incidence of primary malignant

orbital tumours in the Netherland" Eye (Lond) (2011) 25, 461-465.

- 12. Tehrani S, Fraunfelder F, "Cryotherapy in
- Ophthalmology" Open J Ophthal (2013) 3, 103-117. Buschmann W, "A reappraisal of cryosurgery for eyelid 13. basal cell carcinomas" Br J Ophthalmol (2002) 86, 453-457.
- 14. Font RL, "Evelids and lacrimal drainage system, In: Spencer W.H., ed. Ophthalmic pathology: an atlas and textbook, fourth ed., Vol 4. Philadelphia: WB Saunders" (1996) 2218-2433.
- 15. Kumar R, Adhikari RK, Sharma MK, D.R. Pokharel, N. Gautam, Pattern of ocular malignant tumors in Bhairahwa, Nepal,Int J Ophthalmol Vis Sci7 (2009) 1.
- 16. Ni C, Kuo PK, "Meibomian gland carcinoma. A clinicopathological study of 156 cases with long-period follow-up of 100 cases" Jpn J Ophthalmol (1979) 23, 388-401.
- 17. Jahagirdar SS, Thakre TP, Kale SM, Kulkarni H, Mamtani M, "A clinicopathological study of eyelid malignancies from central India" Indian J Ophthalmol (2007) 55, 109-112.
- 18. Maheshwari R, Maheshwari S, Shekde S, "Role of fine needle aspiration cytology in diagnosis of eyelid sebaceous carcinoma" Indian J Ophthalmol (2007) 55, 217-219.
- 19. Shields JA, Demirci H, Marr BP, Eagle RC, Shields CL, "Sebaceous carcinoma of the ocular region: A review" Surv Ophthalmo (2005) 50, 103-122.
- 20. Ni C, Searl SS, Kuo PK, Chu FR, Chong CS, Albert DM, "Sebaceous cell carcinoma of the ocular adenexa" Int Ophthalmol Clin (1982) 22, 23-61.