



RESEARCH ARTICLE

HISTOMORPHOLOGICAL STUDY OF MALIGNANT TUMORS OF EYE & OCULAR ADNEXA

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ABSTRACT

Background: Vision is one of the main special senses of human being. In the visual system eye and its adnexal tissue are affected by variety of lesions. Orbito-ocular malignancies may contribute to visual disturbances, rarely visual loss may take place. The spectrum of malignant tumors of eye and ocular adnexa that can originate, grow, invade and lodge in the relatively small orbital cavity is amazing. Malignant tumors of eyelid, conjunctiva, retina and orbit in both adults and children have been reported. There exists differences in their pattern and frequency on the basis of geographical locations.

Aim: To study the frequency and histopathology of various malignant tumors of eye and ocular adnexa and to correlate pathological findings with clinical data, age and sex distribution in various malignant tumors.

Results: Orbito-ocular malignancies accounted for 1% of malignancies of all organs. Out of 90 tumors of the eye and ocular adnexa 41% were malignant tumors. Malignant tumors are common in males and show bimodal distribution with a peak in first decade and then a plateau in 4th, 5th and 6th decade. The most commonly affected age group was 31-40 years. Eyelid was commonly involved site (45.94%). The most frequently occurring malignant neoplasm was basal cell carcinoma (21.62%). Most of the patients (87.78%) presented with mass in ocular region followed by symptoms like discharge, ulcer, pain, foreign body sensation, loss of eyelashes.

Conclusion: Most of the tumors presented as a mass from eyelid or ocular globe, histopathologically showed malignant ocular or adnexal tumor. Histopathologically negative surgical margins ensure complete removal of the tumor. Tumors of peri-ocular or ocular region, small or large in size should be thoroughly examined by ophthalmologist and pathologist to protect and preserve vision.

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INTRODUCTION

The eye is a highly specialized organ for perception of light, form and color. (Eroschenko, 2012). It is a unique organ made up of three coats, the external fibrous layer comprising of sclera and cornea, the middle vascular layer, the uvea, consisting of choroid, ciliary body and iris and the innermost photosensitive neural layer called the retina. Adnexa of the eye includes the eyelids, lacrimal apparatus, the orbit and its contents like the extraocular muscles, 3rd, 4th, and 6th cranial nerves and the optic nerve. (Henry Gray, 2005). Awareness of the proper techniques for processing eyes is also essential for successful evaluation of ocular specimens by the surgical pathologist. (Deshpande, 1977). Appropriate evaluation of orbital problems draws attention to the number of sight threatening and life threatening disorders that warrant immediate treatment.

Familiarity with the incidence of various aetiologies can be a useful diagnostic tool. (Kim et al., 2010) The present study was undertaken to study the frequency and histopathology of various malignant tumors of eye and ocular adnexa, to correlate pathological findings with clinical data and age, sex distribution in various malignant tumors.

MATERIALS AND METHODS

The present study was carried out in the Department of Pathology in a tertiary care centre. The study was approved by Institutional Ethics committee. The present study included malignant tumors of the eye and ocular adnexa. The present study was retrospective and prospective during the period of 8 years. Data regarding clinical details, histopathology for the retrospective cases was obtained from the record section and departmental records. Data for prospective cases was obtained from clinical records, tissue specimens, tissue blocks and slides. All the biopsies and resected specimens were received in the Department of Pathology. The conjunctival biopsy

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specimens were spread on a filter paper prior to fixation in 10% formalin to prevent rolling up of the tissue. The enucleation specimens were fixed in 10% formalin for 24 hours followed by washing under tap water. The vertical, horizontal and antero-posterior dimensions of the globe, the length of the optic nerve and measurements of the cornea were noted followed by transillumination of the globe to detect presence of sawing motion from back to front, the plane of section beginning in front of the optic nerve and ending at the periphery of the cornea. Remaining biopsy specimens were routinely processed. Multiple sections of the specimen were taken, processed and embedded in paraffin wax. Five microns thick sections were prepared and then stained with Haematoxylin & Eosin. Detailed study of the sections was performed under the light microscope and then the final histopathological diagnosis was done.

Statistical methods applied

- Number and percentage.
- Descriptive statistics

RESULTS AND DISCUSSION

Ocular and adnexal malignant tumors are relatively rare. Most of the malignant tumors present as a mass arising from eyelids or the ocular globe. Clinically this can be detected at early stage with local excision as treatment modality. The present study was a 6 years retrospective and 2 years prospective carried out in the Department of Pathology at tertiary care centre to determine the frequency and to study histomorphology of malignant tumors of eye and adnexal tumors. In the present study the WHO classification of eye and its adnexa was followed. A total of 18,164 specimens were received during the 8 years study period. Out of these 3650 were diagnosed as cancers of various sites in the body with orbito-ocular malignancies accounting for 1% of these malignancies. Out of 18164 specimens, 90 were tumors belonged to the eye and ocular adnexa. Out of 90 neoplasms 41% were malignant tumors.

Table 1. Distribution of malignant ocular and adnexal tumors in various studies with respect to malignancies of other organs

Author	Percentage of Malignant ocular and adnexal tumor
Mohammed A <i>et al.</i> , (2006) n=124	5%
Reddy SC (1996) n=20	1.1%
Malik MOA (1979) n=279	4.3%
Present study n=37	1%

The percentage of malignant ocular and adnexal tumor of the present study was in accordance with the study of Reddy SC (1996). However a higher percentage was observed by Mohammed A *et al.*, (2006) and Malik MOA (1979) which could be due to a large sample size in their studies.

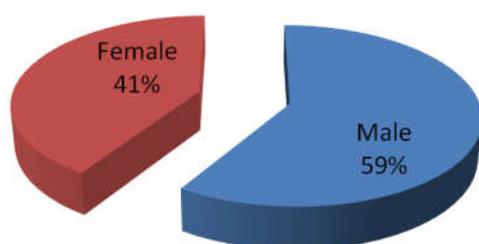


Figure 1. Gender wise distribution of malignant tumors

The malignant tumors were more common in males as compared to females. Male to female ratio was 1.44:1.

Table 2. Age and gender wise distribution of tumor

Age in years	Male	Female	Total	Percentage
0 – 10	2	5	7	18.91
11 – 20	-	-	-	0
21 – 30	-	-	-	0
31 – 40	5	4	9	24.32
41 – 50	6	2	8	21.63
51 – 60	6	2	8	21.63
61 – 70	2	2	4	10.81
71 – 80	-	-	-	0
81 – 90	1	-	1	2.70
TOTAL	22	15	37	100

Tumors were distributed over a wide age range of 2 to 90 years with a mean age of presentation of 38.85 years. The malignant tumors had a bimodal distribution with a peak in the first decade of life and in elderly persons in the age group of 4th to 6th decades. Retinoblastoma being most common tumor of first decade and malignant eyelid neoplasms common in elderly persons lead to bimodal age distribution. These observations were similar to the study by Kumar *et al.*, 2009. Sunder raj P (1991) noted male predominance (54.9%) in malignant orbito-ocular tumor as observed in the present study (59.4%). However Mohammed A *et al.*, (2006) reported equal gender distribution and Kumar R. *et al.*, (2009) observed a female preponderance (54.2%). The anatomical sites harbouring ocular and adnexal malignancies in the present study were in the decreasing order of frequency of eyelids (45.94%), conjunctiva (35.13%) and retina (18.93%). Most of the studies revealed eyelid as the most common location of malignant orbito-ocular tumors. The variation in the number of tumors at other sites like intraocular tumors might be because of difference in the number of cases studied. The most frequently occurring malignant neoplasm in the present study was basal cell carcinoma (21.62%), followed by squamous cell carcinoma of conjunctiva (18.92%), retinoblastoma (18.92%), sebaceous carcinoma (16.21%), conjunctival intraepithelial neoplasia (CIN) (16.22%). However, squamous cell carcinoma of the eyelid was seen in only two cases and one case of Non - Hodgkin lymphoma of eyelid was observed. Kumar R *et al.* (2009) and Sunder raj P *et al.* (1991) found squamous cell carcinoma as a common neoplasm of eyelid however Reddy S C *et al.*, and present study found Basal cell carcinoma as a common neoplasm eyelid. In present study retinoblastoma accounted 18.92% cases as also noted by Sunder raj P *et al.* (1991). The differences in the findings were due to availability of operative and chemotherapy facilities.

MALIGNANT EYELID TUMORS

Basal cell carcinoma

In the present study eight cases (47.06%) of basal cell carcinoma were noted. This was the commonest malignant tumor noted. Kale SM *et al.*, 2012 (48.2%), Paul I 2011 (71.8%), Coroi *et al.* 2010 (72.5%) and Farhat *et al.* 2010 (55.6%) observed basal cell carcinoma as the most common eyelid malignancy in their studies. In the present study the age range of presentation was 39-90 years, majority of the cases occurring in the fifth decade. The male female ratio was 3:1. Kale SM *et al.*, 2012 and Wang *et al.*, 2003 showed female predominance with average mean age 59 years and 62.6 years respectively.

Table 3. Comparative distribution of malignant tumors according to anatomic sites in various studies

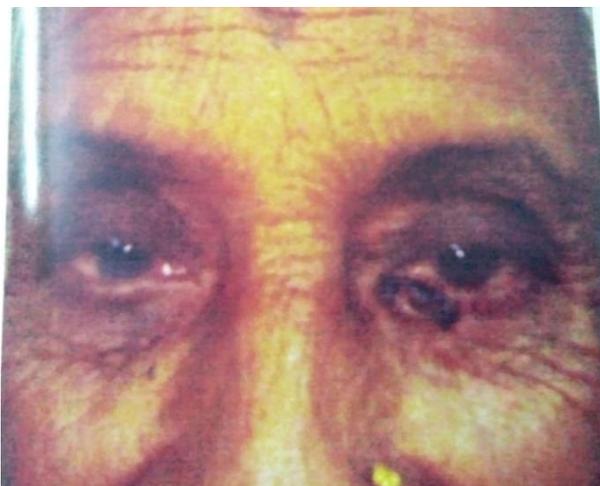
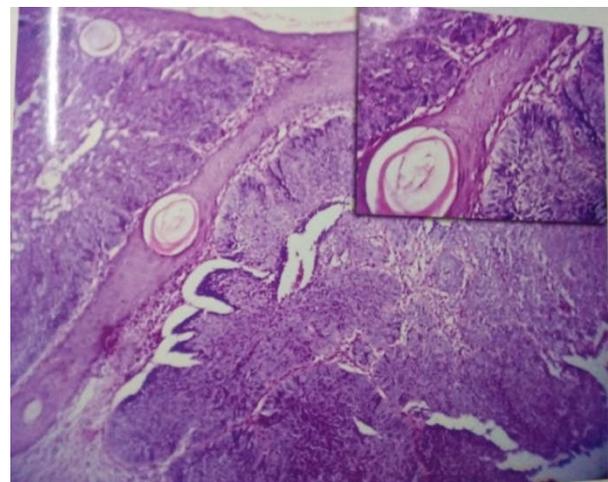
	Eyelid	Conjunctiva and cornea	Lacrimal apparatus	Orbit	Intraocular	Total
Kumar R et al (2009)n=59	35.59	54.25	1.69	-	8.47	100
Reddy SC (1996) n=20	25	10	-	15	50	100
Sunderraj P (1991) n=263	28.9	26.24	2.66	8.36	33.84	100
Reddy SC et al (1982) n=105	50.5	14.3	2.9	5.7	26.6	100
Gogi R et al (1979) n= 198	44.8	8.2	-	13.2	33.8	100
Present study n =37	45.94	35.14	-	-	18.92	100

(n = total number of orbito - ocular malignant tumors)

Table 4. Distribution of malignant tumors according to histologic types

	Histologic Type	Kumar R et al(2009) n= 59	Reddy SC et al(1996) n=20	Sunder raj P (1991)n=263	Present study n=37
Eyelid	BCC	10.17	15	5.7	21.62
	SGC	10.17	-	9.51	16.21
	SCC	13.57	5	10.27	5.41
	NHL	-	-	0.76	2.70
	MM	1.69	5	0.76	-
	OTHERS	-	-	1.9	-
	Total	35.6	25	28.9	45.94
Conjunctiva and cornea	DYSPLASIA	-	-	7.6	16.22
	SCC	49.16	5	14.45	18.92
	SCC(CORNEA)	3.39	-	-	-
	OTHERS	1.69	5	4.18	-
	Total	54.24	10	26.23	35.14
Lacrimal apparatus	ADENOCARCINOMA	1.69	-	1.52	-
	OTHERS	-	-	1.14	-
	Total	1.69	-	2.66	-
Retina	RETINOBLASTOMA	6.78	50	32.32	18.92
	OTHERS	-	-	1.52	-
	Total	6.78	50	33.84	18.92
Others		1.69	15	8.37	-
Total		100	100	100	100

BCC- Basal Cell Carcinoma, SGC- Sebaceous Gland Carcinoma, SCC- Squamous Cell Carcinoma, NHL- Non Hodgkin's Lymphoma, MM- Malignant Melanoma

**Figure 2. Photograph showing noduloulcerative mass of basal cell carcinoma over left lower eyelid in a 70years old female patient****Figure 3. Photomicrograph of nodular basal cell carcinoma of eyelid (H&E X 100). Inset shows nodules of basaloid cells showing mild pleomorphism and peripheral palisading of nuclei (H&E X 400)**

An equal involvement of the right and left side was observed. Patients with BCC presented as ulcerative growth in 4 cases and as an ulcer in 3 cases. In only one case the presentation was in the form of a solitary nodule (Figure 2).

Microscopically the common histological finding in all the basal cell carcinomas was presence of basaloid tumor cells in nests, cords and sheets in the dermis (Figure 3). The most common histologic type in the present study was solid seen in 50% of the cases while there was one case each of infiltrative, superficial, pigmented and cystic type. Our findings correlated with Hussain *et al.*, 2011, Farhat *et al.*, 2010 and Corio *et al.*, 2010.

Sebaceous (Meibomian gland) Carcinoma

Sebaceous (Meibomian gland) carcinoma was the second most common malignant tumor of eyelids in our study. Most of the cases belonged to the sixth decade. We observed an equal frequency in males and females. The right and left sides were involved with equal frequency. Upper lid was involved in 66.67% cases, while lower lid was involved in 33.33% of cases. Microscopically the tumors were composed of well defined lobules and sheets of polygonal cells in the dermis showing sebocytic differentiation.

Some of the lobules showed central comedo necrosis. There was a single case of squamoid sebaceous carcinoma who was a 60 years old female patient. Microscopically the tumor was showing areas of squamous metaplasia and keratin pearl formation in architecture of sebaceous carcinoma. Other malignant tumors were squamous cell carcinoma, lymphoma accounting 5.41% and 2.7% respectively.

Malignant tumors of conjunctiva

Malignant conjunctival tumors (OSSN) are broadly divided histologically into conjunctival intraepithelial neoplasia and invasive squamous cell carcinoma. In the present study squamous cell carcinoma (53.85%) was more common than Conjunctival intraepithelial neoplasia (CIN) (46.15%). Sunder raj P (1991) (55.07%), Ogun GO et al (2009) (80.44%) also found squamous cell carcinoma as the commonest malignant conjunctival tumor in their studies.

Conjunctival intraepithelial neoplasia (CIN) (Dysplasia)

Clinically patients showed conjunctival growth. There was a female preponderance with a male to female ratio 1:2. A 43 years old male patient presented with a conjunctival growth towards the nasal side of the limbus histologically showed moderate dysplasia. Three cases of severe dysplasia were observed. Two patients were observed in the 4th decade and one female patient was in 3rd decade. In two cases the growth was located over limbus in temporal area while one case showed lower eyelid mass. Microscopically, all the three cases showed epithelial dysplasia involving the entire thickness of the epithelium with cells having highly pleomorphic nuclei. However, the basement membrane was intact.

Squamous cell carcinoma

A total of seven cases (53.86%) of Squamous cell carcinoma were observed in the present study. Majority of the patients were in the 5th decade. The male to female ratio was 6:1. Limbus was the most common site of involvement by squamous cell carcinoma followed by temporal area and nasal quadrant. In only one case tumor was seen over upper palpebral conjunctiva. Waddell *et al.*, (1996) observed nasal limbus as a predominant site of involvement (78.95%) by conjunctival squamous cell carcinoma in their study. Bilateral involvement by conjunctival squamous cell carcinoma was seen only in one case. Histologically majority of tumors (five cases) were well differentiated squamous cell carcinoma.

Tumors of the retina

Retinoblastoma

In the present study, all the tumors arising from the retina were malignant. All the seven cases were of retinoblastoma. Retinoblastoma is the third most common malignancy in the present study. All children with retinoblastoma in the present study were below 5 years of age. In the present study the mean age of presentation for retinoblastoma was 3.86 years however mean age of presentation was reported between 2 years to 2.8 years by Nabie *et al.*, 2012 (2 years), Reddy *et al.*, 1996 (2.5 years) and Deshpande 1977 (2.8 years). The higher age of presentation (3.85 years) in the present study might be due to lack of awareness among parents regarding the nature of the disease. Some of the patients were diagnosed at periphery and

for the fear of enucleation parents try other forms of treatment and present to the tertiary care centre when the disease was already advanced. There was a female predominance with male female ratio of 1:2.5. Four patients showed involvement of the left eye, two involved the right eye and only one patient had bilateral involvement.

Table 5. Clinical presentation of retinoblastoma

Symptoms	No. Of cases (n=7)	Percentage (%)
Leukocoria	6	85.71
Proptosis	4	57.14
Strabismus	2	28.57
Mass	1	14.29

Leukocoria was the most common presentation (85.71% cases) of retinoblastoma, followed by proptosis, strabismus and a fungating mass. Similar observations were noted by Nabie *et al.*, 2012 (97.5%), Bakshi *et al.*, 2010 (74.5%), Reddy *et al.*, 1996 (80%). There was only 1 case of differentiated retinoblastoma while remaining 6 cases were undifferentiated (85.7%) (Figure 3). Similar observations were noted by Owocyte 2005 (82.6%) and Biswas *et al.*, 2003 (58%).

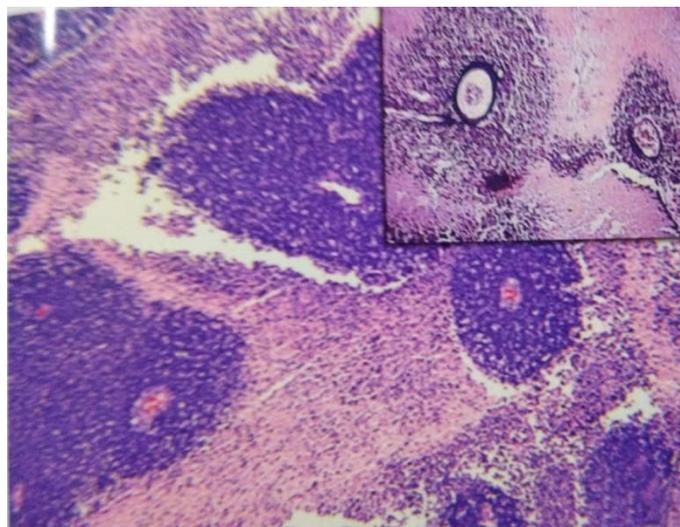


Figure 4. Photomicrograph of undifferentiated retinoblastoma (H&E X100). Inset shows round to oval cells with oval hyperchromatic nuclei and scanty basophilic cytoplasm arranged around blood vessels surrounded by large areas of necrosis (H&E X400)

Optic nerve infiltration was seen in 2 cases (28.5%). Similar findings were noted by de Souza *et al.*, 2005 (29.6%) and Reddy *et al.*, 1996 (30%). One of the patient was a 3 years old female having bilateral involvement with metastasis to the suprasellar region of the brain.

Conclusion

The present study concludes that various histologic types of malignant tumors are noted in the periorcular region affecting the persons from early childhood to late childhood. Most of the tumors presented as a mass arising from the eyelids or the ocular globe. Clinically these can be detected at an early stage with local excision as the treatment modality. But all the lesions should be subjected to histopathological examination owing to the clinical resemblance of malignant lesions to benign lesions or inflammatory conditions. Histopathologically negative surgical margins also ensure complete removal of the

tumors. Proptosis as a presentation in childhood needs prompt and complete evaluation including a biopsy from a tumor. In the present era early diagnosis of retinoblastoma yield 100% cure with current chemotherapy and radiotherapy. Tumors in the periocular region no matter how small or large should be thoroughly evaluated by ophthalmologist and pathologist to protect and preserve vision, one of the most important special senses possessed by human beings.

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