Original Article

Ocular Tumors in Iran: A 10-Year Histopathological Study on 384 Cases of Enucleation

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ABSTRACT

***Background and Objective*: The frequency and pattern of eye neoplasms differ in various geographic areas. Our aim was to determine the distribution of patient age, gender, ocular tumor origin, location and histological type in our region.**

***Materials and Methods*: In this cross-sectional study, all of the 384 eye globe enucleation cases carried out during a 10-year period in Farabi Medical Center in Tehran were selected and reviewed. The inflammatory and non-tumoral conditions were excluded.**

***Results*: Out of 350 primary tumors, 344 (98.6%) were malignant including 248 cases of retinoblastomas (70.9%), 76 cases of (21.7%) melanomas and 14 cases of (4%) squamous cell carcinomas. Mean ages for these tumors were 3.2, 51 and 64.8 years respectively. Overall the tumors were 1.15 times more frequent in left eye and 1.53 times more common in males. Out of 248 cases of retinoblastomas, only 12 (4.8%) cases were bilateral (mean age 3.46 years; male to female ratio 1.4:1). Some rare cases in our series included a primary non-Hodgkin lymphoma of choroid, two choroidal leiomyomas and an adenocarcinoma of the retinal pigment epithelium.**

***Conclusion*: The overall frequency of the three most common primary malignancies in our series was similar to the reported Asian countries but slightly differed with western countries in terms of lower incidence of melanoma here. Also bilateral retinoblastoma was less frequent here and occurred in a slightly older age. The actual frequency of metastatic eye tumors could not be evaluated precisely due to lack of systematic autopsy data.**

Key words: Eye enucleation, Eye neoplasms, Melanoma, Retinoblastoma, Squamous cell carcinoma

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Introduction

The incidence of ocular tumors is relatively low and there are different opinions about the actual frequency of eye globe tumors; however; the intraocular neoplasms pose an important challenge both to the clinician and pathologist in several ways. Some non-tumoral lesions such as retinal detachment may clinically simulate ominous tumors and unnecessary enucleation in these cases may be performed. On the other hand, in contrast to other organs, diagnostic biopsy of intraocular tissues before enucleation is rarely feasible except for rare iridiocyclectomy specimens. The reported incidence of eye globe tumors is different in many countries and there are regional differences in the prevalence of intraocular and orbital tumors (1-5). For example, retinoblastoma is much more common than melanoma in Singapore while the melanoma is the most common tumor in New York and the median age at diagnosis differs in these two regions as well (3). Therefore, any epidemiologic data acquired via enucleation, evisceration, exenteration or autopsy specimens will provide valuable information and help to adopt correct diagnostic and management strategy. Moreover, epidemiologic study of malignant eye tumors is very important in identifying the relationship between various external factors and tumor incidence in order to determine methods of prevention and effective therapy.

To the best of our knowledge, there are no published epidemiological and histopathological studies of ocular tumors in Iran in English literature. In this study, we reviewed 384 cases of ocular tumors referred to the greatest ophthalmology and ophthalmopathology center in Iran during a 10-year period. Our primary goal was to elucidate the distribution of patient age, pathology and tumor origin and location in this center. Some of our cases such as choroidal leiomyoma, retinal adenocarcinoma and primary choroidal lymphoma are quite rare.

Materials and Methods

In a cross-sectional study, the files and routine histologic sections of all of the ocular tumors diagnosed between 1993 and 2003 in ophthalmopathology Department of Farabi Hospital in Tehran (Iran) were reviewed. Patients were from different ages and regions of the country referred to this hospital. All of the enucleation and exenteration cases were included in this study. The inclusion criterion was presence of the entire eye globe that is involved by the tumor. This criterion was also applied to any extraocular tumor secondarily involving the eye globe. We excluded the excisional biopsy specimens that were not accompanied by the entire globe. All of the available epidemiologic data were recorded and all histological sections were blindly reviewed by two pathologists. In equivocal cases, further investigations such as immunohistochemical (IHC) studies performed for definitive diagnosis. The inflammatory and non-tumoral conditions were excluded. In 384 remaining cases, the age, gender, location, laterality and histological types of tumors were recorded.

Results

Out of 384 tumors, 350 (91.15%) were primary ocular while 34 (8.85%) (mostly malignant) were secondary involving the eye globe either by direct invasion or by metastasis. Tumor types, location, relative frequency and patients' age and gender are presented in Table 1. Overall the tumors were slightly more common in males at a ratio of 1.53 to 1. This ratio was 1.57 to 1 for primary neoplasms and 1.12 to 1 for secondary ocular tumors. Laterality of tumors is presented in Table 2. Overall the left eye was afflicted slightly more than the right eye at a ratio of 1.15 to 1 and bilaterality was seen only in 12 retinoblastomas (Table 2). Out of 248 cases of retinoblastomas, 12 cases (4.84%) were bilateral (mean age 3.46; male to female ratio 1.4:1) and 236 cases (95.16%) were unilateral (mean age 3.19; male to female ratio 1.5:1). In addition, 56 out of 76 uveal melanomas (73.7%) were in choroid and 20 (26.3%) in ciliary body. Meanwhile, 14 primary ocular squamous cell carcinomas (SCC) included 1 (7.14%) corneal and 13 (92.86%) conjunctival tumors. Out of 13 cases of conjunctival SCCs, 9 (69.23%) were palpebral and 4 (30.77%) were bulbar in origin. Our most common secondary ocular malignancies included 14 cases of rhabdomyosarcomas originating in orbital soft tissues and 14 cases of basal cell carcinomas (BCC) taking their origin from palpebral and facial skin and directly invading the eye globe. The primary source of the only recorded metastatic tumor (SCC) was from facial skin.

Table 1: Tumor type and location according to the patients' gender and age

TUMOR TYPE	No (%)	Sex		Age (year)				*Primary location*
		Female	Male	Mean	Sd	Min.	Max.	
Primary								
Benign								
- Leiomyoma	2 (0.52)	2		26		16	36	Choroid
- Melanocytic Nevus	1 (0.26)		1	44				Choroid
- Melanocytoma	1 (0.26)		1	1.17				Choroid, Ciliary body
- Adenoma	1 (0.26)		1	19				Ciliary body
- Capillary Hemangioma	1 (0.26)	1		0.25				Retina
Malignant								
- Retinoblastoma	248 (64.58)	99	149	3.2	2.3	0.08	14	Retina
- Melanoma	76 (19.8)	27	49	51	16.3	17	83	Choroid, Ciliary Body
- Squamous Cell Carcinoma	14 (3.65)	4	10	64.8	9.2	51	85	Conjunctiva, Cornea
- Optic Glioma	2 (0.52)	2		4		2	6	Optic Nerve
- Astrocytoma	2 (0.52)		2	48		31	65	Retina
- Adenocarcinoma	1 (0.26)		1	60				Retina
- Lymphoma	1 (0.26)	1		37				Choroid
Total	**350 (91.15)**	**136**	**214**	**29.9**		**0.08**	**85**	
Secondary								
Directly invasive								
- Embryonal Rhabdomyosarcoma	14 (3.65)	9	5	13	14.3	2	60	Orbit
- Basal Cell Carcinoma (BCC)	14 (3.65)	5	9	54.5	12.9	30	73	Eyelid, Face
- Neuroblastoma	2 (0.52)		2	16.7	21.6	1.4	32	Orbit
- Meningioma	2 (0.52)	1	1	27.5	9.2	21	34	Optic Nerve
- Angiosarcoma	1 (0.26)		1	11				Orbit
Metastatic								
- Squamous Cell Carcinoma(SCC)	1 (0.26)	1		65				Face
Total	**34 (8.85)**	**16**	**18**	**31.3**		**1.4**	**73**	

Discussion

Overall the most common cancers in our series included retinoblastoma and melanoma followed by SCC and secondary tumors. This finding is in agreement with the study of Lee et al (3). The distribution of primary eye cancers by age is bimodal with the peaks occurring during early childhood (retinoblastoma) and again during adulthood (melanoma). As in other ethnic groups, retinoblastoma is our most common primary intraocular malignancy in children (3;4) and is more prevalent in males than in females (6) at a ratio of 1.5 to 1; however; in spite of the report of Melamud et al (7), the mean age at diagnosis of bilateral retinoblastoma in our series (3.46 years) was slightly higher than unilateral tumor (3.19 years). This is possibly due to a delay in diagnosis or less probably is the result of clinical presentation at a slightly older age. Although a larger scale study may be necessary, bilateral retinoblastoma in our series (4.8%) is significantly less frequent than the rate of 25% reported by Cerecedo et al (8) and 30.7% by

Table 2: Laterality of tumors

Tumor type	Laterality			Total
	Right eye	Left eye	Bilateral	
Retinoblastoma	109 (44%)	127 (51.2%)	12 (4.8%)	248
Melanoma	36 (47.4%)	40 (52.6%)	-	76
Embryonal Rhabdomyosarcoma	8 (57.1%)	6 (42.9%)	-	14
SCC-Ocular	9 (64.3%)	5 (35.7%)	-	14
BCC	4 (28.6%)	10 (71.4%)	-	14
Leiomyoma of choroid	-	2 (100%)	-	2
Optic Glioma	1 (50%)	1 (50%)	-	2
Neuroblastoma	2 (100%)	-	-	2
Meningioma		2 (100%)	-	2
Astrocytoma of retina	-	2 (100%)	-	2
Adenoma of pigmented epithelium	-	1 (100%)	-	1
Capillary Hemangioma	-	1 (100%)	-	1
Melanocytic Nevus	-	1 (100%)	-	1
Adenocarcinoma	1 (100%)	-	-	1
Angiosarcoma	-	1 (100%)	-	1
Lymphoma	1 (100%)	-	-	1
Melanocytoma of choroid	-	1 (100%)	-	1
SCC-Face	1 (100%)	-	-	1
Total	**172 (44.8%)**	**200 (52.1%)**	**12 (3.1%)**	**384 (100%)**

Gunalp (6). About 60% of retinoblastomas are sporadic and 40% are familial, inherited as an autosomal dominant trait. Bilaterality is more common (>90%) in familial cases as compared to sporadic cases (30%). Although no information was available about the familial incidence of retinoblastoma in our cases, less observed bilaterality may be the result of lower incidence of familial disease in this region. Other possibilities include sampling error and inadequate follow-up of the patients. One of the bilateral retinoblastomas occurring in left eye of a 9 year old boy was accompanied by intraocular astrocytic hamartoma. His right eye had already been enucleated 2 years earlier due to retinoblastoma. Development of a secondary malignancy such as osteosarcoma or rhabdomyosarcoma in familial (including bilateral) retinoblastoma is a well-known entity. The development of an apparently benign astrocytic hamartoma along with bilateral retinoblastoma in this patient may also point toward a predisposing genetic hint. Considering the primary ocular cancers (344 cases), we found retinoblastoma as the most common tumor (72.1%) followed by melanoma (22.1%) irrespective of patients' age. Like other authors (3;9), we found uveal melanoma as the most common ocular malignancy in adults, more prevalent in males (1.8 fold) and the majority of cases (73.7%) arising in choroid. In an epidemiologic study performed in New York State, the prevalence of melanoma (70.4%) clearly outnumbered retinoblastoma (9.8%) and a similar data was also reported from the University of Alabama (3); however; according to studies in Singapore, Nigeria and Madras, just as our study, the most common primary ocular malignancy was retinoblastoma followed by melanoma. The high incidence of melanoma in western countries may be partly explained by higher susceptibility of fair-complexioned people in those countries to ultraviolet exposure in sunlight (3). Melanoma of iris was not recorded in our series, possibly due to treatment modalities other than enucleation performed for these cases but considering the large difference between the frequency of retinoblastoma and melanoma in our series this probably does not play a major role in underestimation of melanoma. We also had a case of intraocular melanocytosis composed of

melanocytoma of the optic nerve head associated with choroidal and ciliary body nevi in left eye of a 14 month old boy. The third most common primary tumor in our study was squamous cell carcinoma (4.1% of primary cancers) that is similar to studies elsewhere (3). The most common site for SCC was conjunctiva and this is similar to other reports (3). Considering the secondary malignancies in our series (34 cases), the great majority consists of 14 cases of orbital rhabdomyosarcomas and 14 cases of cutaneous basal cell carcinomas (41.2% each). These findings correspond to the previous data since the former tumor is well-known as the most common soft tissue sarcoma of the orbit in children and the latter is the most common skin malignancy in adults. We were also encountered some rare primary ocular neoplasms. These include a benign adenoma of the pigmented epithelium of the ciliary body in left eye of a 19 years old man; two cases of low-grade retinal astrocytoma in 2 men aged 31 and 65 years and two cases of choroidal leiomyoma in 2 women aged 16 and 36 years respectively; both appearing in left side, (10) as well as a very rare case of primary large B-cell lymphoma of the choroid in right eye of a 37 years old immunocompetent woman (11).

A rare capillary hemangioma of choroid seen in a 3 months old infant without any nervous system or visceral abnormality also deserves mention (12-14). A very rare instance of adenocarcinoma of retinal pigment epithelium in right eye of a 60 years old man was also in our record (15). The only corneal squamous cell carcinoma in our series was a primary in situ neoplasm without stromal invasion at the time of diagnosis and has already been reported as a rare case (16). We found only one case of metastatic carcinoma to the eye. This makes only less than 0.3% of all of our malignant cases and is very low as compared to the reported frequency of about 2% in Japan (1); however; the frequency of metastatic carcinoma to the eye certainly can not be extrapolated from our study because these patients usually are not candidates for biopsy or enucleation and our study did not include autopsies.

Conclusion

Taken together, it is concluded that this study, although is not an expanded multidisciplinary one, may serve to provide pathologists and ophthalmologists with a foundation to monitor future patients in this country and provide a basis for comparison with other selected populations elsewhere.

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