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Malignant tumors of the eye and ocular adnexa at King Chulalongkorn Memorial Hospital: A twelve year review (1988 - 1999)

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Objectives : *To establish the relative frequencies of malignant tumors of the eye and ocular adnexa regarding to their anatomic location, and to study the gender prevalence and average age of presentation of the diseases*

Setting : *Department of Pathology, Faculty of Medicine, Chulalongkorn University*

Design : *Retrospective descriptive study*

Method : *Data was collected from pathology record files from the department of pathology, King Chulalongkorn Memorial Hospital over a 12-year period from January 1988 to December 1999. All available pathology slides were reviewed. The histopathology results were stratified by the anatomic location: eyelid, conjunctiva, orbit, lacrimal gland, and intraocular. Data regarding the patients' gender and age of presentation were collected.*

Results : *Of all 128 cases, intraocular malignancy was the most common tumor (39.8%). The conjunctiva was the second most common location (34.4%). The eyelid was affected in 9.4% of all cancers, followed by the orbit (8.6%) and the lacrimal gland (7.8%). Retinoblastoma was found in 82.4% of all*

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intraocular malignancies. The mean age of presentation was 22 months. Of all conjunctival cancers, squamous cell carcinoma including carcinoma in situ was found in 79.5 %. Tumors affected both sexes almost equally, with an average age of 56.7 years. Of all eyelid cancers, sebaceous carcinoma was found in 66.7 %. All of the patients were female with an average age of 56.5 years. For orbital malignancies, there were only one to two cases in each tumor category. Adenoid cystic carcinoma contributed to 40 % of all lacrimal gland malignancies, which was similar to malignant mixed tumor. Average ages of presentation were 30 and 37 years, respectively.

Conclusions : *Intraocular malignancy was the most common site of malignancies of the eye and ocular adnexa. Retinoblastoma was the most common intraocular malignancy, mainly affecting young children. Squamous cell carcinoma was the most common malignant tumor of the conjunctiva, affecting middle aged patients of both sexes. Sebaceous carcinoma was the most common malignancy of the eyelid, affecting middle aged females. There were a small number of orbital malignancies. The most common malignancies of the lacrimal gland were adenoid cystic carcinoma and malignant mixed tumor, mainly affecting middle aged patients.*

Key words : *Malignant tumors, Eye, Eyelid, Conjunctiva, Orbit, Lacrimal gland, Intraocular malignancy.*

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วสี ตูลวรรณะ, ธนภัทร ไผสุนทรสุข, สมบูรณ์ ศีลาวัฒน์, ลลนา แสนโสภา, ศยามล พารไสว.
มะเร็งของตาและเนื้อเยื่อรอบตาในช่วงสิบสองปีที่ผ่านมาในโรงพยาบาลจุฬาลงกรณ์ (2531-
2542). จุฬาลงกรณ์เวชสาร 2544 เม.ย; 45(4): 283 - 93

- วัตถุประสงค์** : เพื่อศึกษาถึงการกระจายของโรคมะเร็งของตาและเนื้อเยื่อรอบตาโดยแยกตามตำแหน่งที่เกิดโรค และเพื่อศึกษาถึงเพศและอายุเฉลี่ยของผู้ป่วยที่มารับการรักษาในโรคเหล่านี้
- สถานที่ศึกษา** : ภาควิชาพยาธิวิทยา คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย
- รูปแบบการศึกษา** : การศึกษาเชิงพรรณนาชนิดย้อนกลับ
- วิธีการ** : ทำการรวบรวมข้อมูลจากแฟ้มบันทึกทางพยาธิวิทยาจากภาควิชาพยาธิวิทยา โรงพยาบาลจุฬาลงกรณ์ในช่วงสิบสองปีที่ผ่านมา นับตั้งแต่ มกราคม 2531 ถึง ธันวาคม 2542 โดยนำสไลด์ทั้งหมดเท่าที่จัดหาได้มาศึกษาทบทวนอีกครั้งด้วยกล้องจุลทรรศน์ โดยจัดเก็บข้อมูลผลการอ่านทางพยาธิวิทยาแยกตามตำแหน่งที่เกิดโรคดังนี้คือ กระจกตา เยื่อตา เบ้าตา ต่อมมน้ำตา และในลูกตา พร้อมกับบันทึกข้อมูล เพศ และอายุของผู้ป่วยแต่ละรายมารับการรักษาที่โรงพยาบาล
- ผลการศึกษา** : จากผู้ป่วยทั้งหมด 128 ราย พบว่ามะเร็งในลูกตาเป็นตำแหน่งที่พบมากที่สุดคือพบร้อยละ 39.8 รองลงมาคือ เยื่อตาพบร้อยละ 34.4 กระจกตาพบร้อยละ 9.4 ในเบ้าตาพบร้อยละ 8.6 และต่อมน้ำตา พบร้อยละ 7.8 มะเร็งในลูกตาที่พบมากที่สุดคือ retinoblastoma พบร้อยละ 82.4 อายุเฉลี่ย 22 เดือน ในผู้ป่วยที่เป็นมะเร็งเยื่อตาพบว่ามะเร็งชนิด squamous cell carcinoma พบได้บ่อยที่สุด คือ ร้อยละ 79.5 โดยพบในผู้ป่วยชายและหญิงในจำนวนใกล้เคียงกัน อายุเฉลี่ย 56.7 ปี ในผู้ป่วยมะเร็งกระจกตาพบว่ามะเร็งชนิด sebaceous carcinoma พบได้บ่อยที่สุด คือ ร้อยละ 66.7 โดยผู้ป่วยทุกราย เป็นผู้หญิง อายุเฉลี่ย 56.5 ปี สำหรับมะเร็งที่พบในเบ้าตาแต่ละชนิดนั้นมีจำนวนน้อย เพียงชนิดละ 1 - 2 รายเท่านั้น มะเร็งต่อมน้ำตาที่พบบ่อยที่สุดมี 2 ชนิดคือ adenoid cystic carcinoma และ malignant mixed tumor โดยพบอย่างละร้อยละ 40 อายุเฉลี่ย 30 และ 37 ปี ตามลำดับ

สรุป : มะเร็งในลูกตาเป็นตำแหน่งที่พบบ่อยที่สุดของมะเร็งของตาและเนื้อเยื่อรอบตา ซึ่งพบว่า *retinoblastoma* เป็นมะเร็งในลูกตาที่พบบ่อยที่สุด มักเกิดในเด็กเล็ก *Squamous cell carcinoma* เป็นมะเร็งเยื่อตาที่พบบ่อยที่สุด มักเกิดโรคในผู้ป่วยวัยกลางคนทั้งชายและหญิง *Sebaceous carcinoma* เป็นมะเร็งหนังตาที่พบบ่อยที่สุด มักเกิดโรคในผู้หญิงวัยกลางคน มะเร็งในเบ้าตาพบน้อย มะเร็งต่อมน้ำตาที่พบบ่อยได้แก่ *adenoid cystic carcinoma* และ *malignant mixed tumor* มักเกิดโรคในผู้ป่วยวัยกลางคน

คำสำคัญ : มะเร็ง, ตา, หนังตา, เยื่อตา, เบ้าตา, ต่อมน้ำตา, มะเร็งในลูกตา

During the past decades, the main causes of death of Thai people have changed from communicable diseases to non-communicable diseases such as cardiovascular disease, accidents and neoplasms.⁽¹⁾ Tumorigenesis, oncogenes, cancer incidence reports and the new development of cancer treatments are receiving incremental attention from all practitioners. The highest incidences of malignant tumors in King Chulalongkorn Memorial Hospital are in liver cancers in males and cervical cancers in women.^(2,3) Malignant tumors of the eye and ocular adnexa are not common. However, they are of great interest since tumors in this area may cause severe deformity and loss of visual function.

In Thailand, there is a scarcity of epidemiological reports upon tumors in this particular area. Most studies are from tertiary care centers. A report from Siriraj hospital documented 38 cases of malignant tumors of the eye during 1956-1957, including tumors of the eyelids, conjunctiva, limbus, cornea, and retinoblastoma.⁽⁴⁾ There have been no recent reports on the overall picture of malignant tumors in this location. The following series were reports of selected areas of the eye or ocular adnexal region. Shuangshoti and Panyathanya studied 206 cases of retinoblastoma and uveal melanoma in 1973.⁽⁵⁾ In 1988, Kasantikul et al. reported a series of intraorbital extraocular tumors in 56 patients.⁽⁶⁾ A series from Chiang Mai University Hospital on lacrimal gland tumors was recently published.⁽⁷⁾ Therefore, we conducted this study to establish the relative frequencies of malignant tumors of the eye and ocular adnexa during the past 12 years, and also to study the age range and gender distribution of the diseases.

Methods

The data was collected from pathology record files from the department of pathology, King Chulalongkorn Memorial Hospital from January 1988 to December 1999. All the available histology materials were reviewed by all authors. The pathology results were stratified into different anatomic locations, i.e. eyelid, conjunctiva, orbit, lacrimal gland, and intraocular. Histological diagnosis, the patient's age of presentation and sex were recorded.

Results

As shown in Table 1, of all 128 cases of malignant tumors of the eye and ocular adnexa, the most common site was intraocular (39.8 %). The anatomical locations of the tumor presented as a decreasing frequency were conjunctiva (34.4 %), eyelid (9.4 %), orbit (8.6 %), and lacrimal gland (7.8 %).

Intraocular tumor

Retinoblastoma was the most common intraocular tumor (82.4 %). The male to female ratio was 1.47:1. Mean age of presentation was 22 months.

Table 1. Frequencies of malignant tumors of the eye and ocular adnexa distributed by the anatomic locations.

Location	Frequency (%)
Intraocular	39.8
Conjunctiva	34.4
Eyelid	9.4
Orbit (extraocular)	8.6
Lacrimal gland	7.8

Uveal malignant melanoma was in the second rank (15.7 %), while choroidal metastasis was seen in only one case (1.9 %), as shown in Table 2.

Conjunctiva

The most common malignancy of the conjunctiva was squamous cell carcinoma, including carcinoma in situ. Mean age of presentation was 56.7 years, with a male to female ratio of 1.06:1. Malignant melanoma was in the second rank, showing a female preponderance (the male to female ratio = 1:3). Average age of presentation was 55 years. Lymphoma was found in 6.8 % of all conjunctival malignancies. All cases were male. There was only one case of poorly differentiated adenocarcinoma (male) and one case of basal cell carcinoma (female). The details of tumor histology in relation to age and gender distribution are shown in Table 3.

Eyelid

The most common eyelid malignancy in this series was sebaceous carcinoma (66.7 %). Mean age of presentation was 56.5 years. All of the patients were female. Basal cell carcinoma was the second

most common (16.7 %). Mean age of presentation was 56 years. The male to female ratio was 1:1. We found only a small percentage of squamous cell carcinoma (8.3 %) and malignant melanoma (8.3 %). The percentages of each tumor, age and gender preference are shown in Table 4.

Orbit

There was a diversity of malignancies in the orbit. Squamous cell carcinoma was found in 2 cases. Both of the patients were male. Alveolar soft part sarcoma was reported in 2 cases, both of which were female. There was only one case each of other tumor categories as shown in Table 5.

Lacrimal gland

The two most common malignancies of the lacrimal gland were adenoid cystic carcinoma (40 %) and malignant mixed tumor (40 %). Adenoid cystic carcinoma showed a female sex predilection (male to female ratio = 1:3). Malignant mixed tumor showed no gender difference. Lymphoma, occurring equally in both sexes, was found in 20 % of cases with a mean age of 52.5 years. Details are shown in Table 6.

Table 2. Relative frequencies of intraocular malignancies.

Tumor histology	Frequency (%)	Mean age of presentation (Years)	Gender preference
Retinoblastoma	82.4	1.8	Male
Choroidal malignant melanoma	15.7	49.9	Equal
Choroidal metastasis (endodermal sinus tumor)	1.9	40	Male

Table 3. Relative frequencies of conjunctival malignancies.

Tumor histology	Frequency (%)	Mean age of presentation (Years)	Gender preference
Squamous cell carcinoma and carcinoma in situ	79.5	56.7	Equal
Malignant melanoma	9.1	55	Female
Lymphoma	6.8	77.7	Male
Poorly differentiated adenocarcinoma	2.3	45	Male
Basal cell carcinoma	2.3	68	Female

Table 4. Relative frequencies of eyelid malignancies.

Tumor histology	Frequency (%)	Mean age of presentation (Years)	Gender preference
Sebaceous carcinoma	66.7	56.5	Female
Basal cell carcinoma	16.7	56	Equal
Squamous cell carcinoma	8.3	61	Male
Malignant melanoma	8.3	74	Male

Table 5. Relative frequencies of orbital malignancies.

Tumor histology	Frequency (%)	Mean age of presentation (Years)	Gender preference
Squamous cell carcinoma	18.2	50.5	Male
Alveolar soft part sarcoma	18.2	11.5	Female
Lymphoma	9.1	44	Male
Poorly differentiated carcinoma	9.1	59	Male
Myxoid liposarcoma	9.1	22	Female
Malignant fibrous histiocytoma	9.1	38	Male
Malignant nerve sheath tumor	9.1	52	Male
Metastatic adenocarcinoma	9.1	48	Male
Undifferentiated sarcoma	9.1	48	Male

Table 6. Relative frequencies of lacrimal gland malignancies.

Tumor histology	Frequency (%)	Mean age of presentation (Years)	Gender preference
Adenoid cystic carcinoma	40	30	Female
Malignant mixed tumor	40	37	Equal
Lymphoma	20	52.5	Equal

Discussion

During the past twelve years, the overall number of pathology reports of tumors of the eye and ocular adnexa found in King Chulalongkorn Memorial Hospital was not high. We performed a survey on the malignant tumors registered in the pathology department in our hospital. The pathology reports were used because the definite pathologic diagnosis was required. There may have been a number of cases that were not sent for histopathological diagnosis, and some cases, which were clinically misdiagnosed as benign lesions and were completely excised without submitting the specimens to the pathology department. There may also have been a number of cases that were sent to pathology units elsewhere, for instance, dermatopathology or private pathology services. Nevertheless, we believe that the pathology department has collected the major burden of all tumors in King Chulalongkorn Memorial Hospital.

In this series, malignant tumors of the eye and ocular adnexa were classified into different anatomic locations for easy a reference. This knowledge about the tumor frequencies is based on a tertiary care facility data, where referral bias may have affected the results and incidence rates cannot be truly determined because denominator populations are unknown. Since a national epidemiological survey has not been

constructed, these results may give more or less important information on the overall picture of the country.

Intraocular tumors are the most common tumors found in this area. This observation was not different from two previous studies on overall tumors of the eye.^(4,8) The second most common location in those series was the eyelid. By contrast, we found that the conjunctiva was the second most common site in our series.

Retinoblastoma was far more common than malignant melanoma. As reported earlier by Shuangshoti et al,⁽⁵⁾ the most common intraocular malignancy in Thai people is not uveal melanoma. Our series confirmed their findings. For intraocular malignancy, the ratio of retinoblastoma to uveal malignant melanoma in our series was 5.25:1. The age range of presentation was between 3 months to 7 years and the average age of presentation was 22 months.

Choroidal metastasis may be under-reported since some of those tumors might not be enucleated due to an advanced stage of systemic malignancy or the status of the patients. The estimation of microscopic ocular metastasis in patients with cancer was 12.6 %.⁽⁹⁾ In this series, the case of choroidal metastasis was managed with enucleation to rule out choroidal melanoma because a choroidal mass was

the first manifestation of the disease. The patient was later diagnosed to have endodermal sinus tumor, as previously reported.⁽¹⁰⁾

Conjunctival squamous cell malignancies were the most common conjunctival cancers in our series. The mean age of presentation was 12 years higher than a previous report from Tanzania.⁽¹¹⁾ Since our country is in the tropical area, the incidence of this tumor is expected to be higher than in North American or European countries.^(12,13)

In eyelid malignancies, sebaceous carcinoma was found in more than 50 % of cases. In accordance with our series, recent studies from other Asian countries have found that sebaceous carcinoma of the eyelid was more common than squamous cell carcinoma.⁽¹⁴⁻¹⁶⁾ This observation is different from western countries, where basal cell carcinoma and squamous cell carcinoma are the two most common malignant eyelid tumors, and sebaceous carcinoma is not a common disease.^(17,18) These findings need to be later investigated by studying a larger series of patients or by conducting a national epidemiological survey to establish the real incidence of the tumors. As we have discussed above, the relative frequencies may not be absolutely accurate because small masses could be under-diagnosed and not submitted for pathology.

Malignant orbital tumors were found in 8.6 % of all cases. Since the overall number is low, the tumor distribution may not be used as a good reference. In our series, we found two cases of squamous cell carcinoma and alveolar soft part sarcoma. A study of orbital malignancy in Papua New Guinea over a 21-year-period found that orbital extension of retinoblastoma was most common, and squamous cell carcinoma was

the second most common.⁽¹⁹⁾ Lymphoma was the most common orbital malignancy in one large series.⁽²⁰⁾ In Thailand, Kasantikul et al⁽⁶⁾ reported a series of 56 cases of intraorbital extraocular tumors during a period of ten years. Their series included all intraorbital tumors, benign and malignant, involving intraorbital tissue and lacrimal glands. Lymphoma, found in 12.5 % of all cases, was the most common orbital malignancy excluding lacrimal gland tumors.

There have been several previous reports of lacrimal gland tumors in Thailand.^(6,7,21) The most common epithelial malignancy was adenoid cystic carcinoma. Malignant mixed tumor and lymphoma were also reported. In our series, we found an equal distribution of adenoid cystic carcinoma and malignant mixed tumor. Lymphoma was the third most common malignant lacrimal gland tumor in our study.

Conclusion

We report on the relative frequencies of malignancies of the eye and ocular adnexa. Intraocular malignancy was the most common site. Retinoblastoma was the most common intraocular malignancy, mainly affecting young children, with a mean age of presentation of 22 months. Uveal malignant melanoma was far less common than retinoblastoma in our series. Squamous cell carcinoma was the most common malignant tumor of the conjunctiva, affecting middle aged patients in both sexes. Sebaceous carcinoma was the most common malignancy of the eyelid, affecting middle aged females. For orbital malignancies, there was a diversity of tumor histology, each of which had affected only one to two patients during the past twelve years. The most common lacrimal gland malignancies were adenoid cystic carcinoma

and malignant mixed tumor, affecting middle aged patients.

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