

An Epidemiologic Assessment of Enucleated Eyes for Malignant Melanoma of Choroid

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Abstract

Purpose: Choroidal melanoma is the most common primary ocular malignancy among the adult population. Authors investigated the clinical findings, histopathologic features, types of retinal detachment and the precise anatomic origin of enucleated eyes for primary ocular malignant melanoma in Shiraz University of Medical Sciences (SUMS) hospitals between 1990 and 2005.

Methods: This was a cross sectional study in which medical records of patients with pathologically proven ocular malignant melanoma were reviewed; and then the relevant clinical data were gathered, based on the modified Callender classification for uveal melanomas.

Results: Over the 15-year period of this study, there were 40 patients with microscopically confirmed ocular melanoma at the pathology department of SUMS. Mean age at initial diagnosis was 45.9 years (range, 5-74 years). Women constituted 51.9% of patients. The most common histological type in uveal melanoma was mixed cell type and painless visual loss was the most frequent presenting complaint. Retinal detachment was seen in 88.8% of cases.

Conclusion: In this study we found more epitheloid (malignant) cell type (11.1%) in Iranian population comparing to western countries (3%) and also there was more malignant cell type (epitheloid cells) in male comparing to female (m/f=2) which may be related to sex hormonal differences that should be investigated in future. Histopathologically, the more malignant cell types become more prevalent with advanced age groups.

Keywords: malignant melanoma, epidemiology, histopathology, uvea, choroid, ocular tumors

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Introduction

Melanoma of the uveal tract (iris, ciliary body, and choroid), though rare, is the most common primary intraocular malignancy in adults. The mean age-adjusted incidence of uveal melanoma in the United States is approximately 4.3 new cases per million population.¹

Uveal melanoma is diagnosed mostly at older ages; with a progressively rising age-specific incidence rate that peaks near

the age of 70.¹ Host susceptibility factors associated with the development of this cancer include caucasian race, light eye color and fair skin color.^{1,2} In view of these susceptibility factors, numerous observational studies have attempted to explore the relationship between sunlight exposure and risk of uveal melanoma. To date, these studies have found only weak associations or yielded contradictory results.¹

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Uveal melanomas can arise in the anterior (iris) or the posterior (ciliary body or choroid) uveal tract. Iris melanomas have the best prognosis, whereas melanomas of the ciliary body have the worst. Most uveal tract melanomas originate in the choroid. The ciliary body is less commonly a site of origin, and the iris is the least common.³ Melanomas of the posterior uveal tract are cytologically more malignant, detected later, and metastasize more frequently than iris melanomas. The typical choroidal melanoma is a brown, elevated, dome-shaped subretinal mass. The degree of pigmentation ranges from dark brown to totally amelanotic.

Most uveal melanomas are initially completely asymptomatic. As the tumor enlarges, it may cause distortion of the pupil (iris melanoma), blurred vision (ciliary body melanoma), or markedly decreased visual acuity caused by secondary retinal detachment (choroidal melanoma). Serous detachment of the retina frequently complicates tumor growth. If extensive retinal detachment occurs, secondary angle-closure glaucoma occasionally develops. Clinically, several lesions simulate uveal melanoma, including metastatic carcinoma, posterior scleritis, and benign tumors, such as nevi and hemangiomas.⁴

Careful examination by an experienced clinician remains the most important test to establish the presence of intraocular melanoma. Ancillary diagnostic testing, including fluorescein angiography and ultrasonography, can be extremely valuable in establishing and/or confirming the diagnosis.⁵

A number of factors influence prognosis. The most important are cell type, tumor size, location of the anterior margin of the tumor, the degree of ciliary body involvement, and extraocular extension. Cell type, however, remains the most often used predictor of outcome.⁶ The selection of treatment depends on the site of origin (choroid, ciliary body, or iris), the size and location of the lesion, the age of the patient, and whether extraocular invasion, recurrence, or metastasis has occurred. Extraocular extension, recurrence, and metastasis are associated with an extremely poor prognosis.⁷ The 5-year mortality rate caused by metastasis from ciliary body or choroidal melanoma is approximately 30%, compared with the rate of

2% to 3% for iris melanomas.⁸ In a group of patients with large tumors of the choroid or choroid and ciliary body, the concurrent presence of abnormalities in chromosomes 3 and 8 was also associated with a poor outcome.⁹

In the past, enucleation (eye removal) was the accepted standard treatment for primary choroidal melanoma, and it remains the most commonly used treatment for large tumors.

Because of the effect of enucleation on the appearance of the patient, the diagnostic uncertainty encountered by the ophthalmologist (particularly in the case of smaller tumors), and the potential for tumor spread, alternative treatments, such as radiation therapy (i.e., brachytherapy or external-beam, charged-particle radiation therapy), transpupillary thermotherapy, photocoagulation, and cryotherapy have been developed in an attempt to spare the affected eye and possibly retain useful vision.^{10,11}

Though in most countries the epidemiological assessments about this cancer has been completed many years ago and now working on genetics, immunohistochemistry and the other aspects of this malignancy is being continued, unfortunately there are no acquiescent studies about this malignancy in Iran, even we have no prevalence or incidence rates of this tumor yet. The results of the only investigation in our country which was done by Asadi Amoli et al. at Farabi Hospital¹² (Tehran-Iran) was the same as what western articles had mentioned though some results were different. In this study we investigated the clinical findings, histopathologic features, types of retinal detachment and the precise anatomic origin of enucleated eyes for primary ocular malignant melanoma in Shiraz University of Medical Sciences (SUMS) hospitals between 1990 and 2005, with respect to age distribution, gender, and mitotic index.

Methods

A cross sectional study consisted of patients with uveal melanoma between 1990 and 2005. SUMS cancer registry was searched for the patients with pathologically proven ocular malignant melanoma. Each patient was identified through a unique registration number. Relevant clinical data were gathered regarding features of the patient, clinical

manifestations, mitotic index, stage of cancer, retinal detachment, anatomic origin of the primary tumor, as well as cell type. The data files were double-checked against hospital files and histopathologic slides for each patient. New slides were prepared from the formalin-fixed embedded sections if any slide had not an appropriate quality for study. Callender modified classification was used to classify tumor cell types.

Findings were recorded on a data form based on protocol applies to malignant melanoma of the uvea revised on January 2004 based on AJCC/UICC TNM 6th edition. Repeated cases due to relapse and the cases which their pathologic slides were sent to us from other parts of country for further study were eliminated. Each gender was analyzed separately, and the patients were divided into five age groups, each spanning 15 years. Descriptive statistics were used to describe the basic features of the data in this study.

Results

Over the 15-year period of this study, there were 40 patients with microscopically confirmed ocular melanoma at the pathology department of SUMS. 30 cases had uveal melanoma, 5 cases had melanoma of conjunctiva and 5 cases had melanoma of lids. Among 30 cases of uveal melanoma 27 (90%) cases had Choroidal involvement and 3 (10%) cases had ciliary body involvement.

Painless visual loss was the most frequent presenting complaint (66.7%).

48% of cases were male and 52% were female. Mean age at initial diagnosis was 45.9 years (range, 5-74 years). The age group 45-59 years was included 40.7% of patients. Age

of 3.7% of cases was not reported in their records (Figure 1).

The most prevalent histopathologic type was mixed type (63%). Spindle B type was in second place with 22.2%. Epitheloid type was the third common type with 11.1%. No pure spindle-A type was found in this investigation. 3.7% of cases were necrotized. Sex percent frequency distribution of histopathologic types is showed in figure 2.

In the age group of less than 14 years, the only patient had mixed cell type involvement. In the age group of 15-29 years, the most common type was spindle-B type and mixed type was in the second place. In the age group of 30-44 years, epitheloid and mixed types were the most common types. In the age group of 45-59 years, the most common type was mixed type; spindle B and epitheloid were in second and third places in this age group. Age percent frequency distribution of histopathologic types is completely shown in figure 3.

88.8% of all cases had retinal detachment. Percent distribution frequency of retinal detachment is shown in figure 4. Stage II (48.1%) was the most common stage we had found in our cases at the time of enucleation. Stages III (33.3%), I (11.1%), IV (7.4%) were in next places. Percent frequency distribution of mitotic index in each stage is shown separately in figures 5-8.

Considerable local invasion was seen: 66.7% of cases had retinal invasion. 44% of cases had Ant. chamber invasion. 33.3% of cases had vitreous invasion. 18.5% of cases had invasion to extrasclera and angle and optic nerve invasion was present in 14.8% of cases.

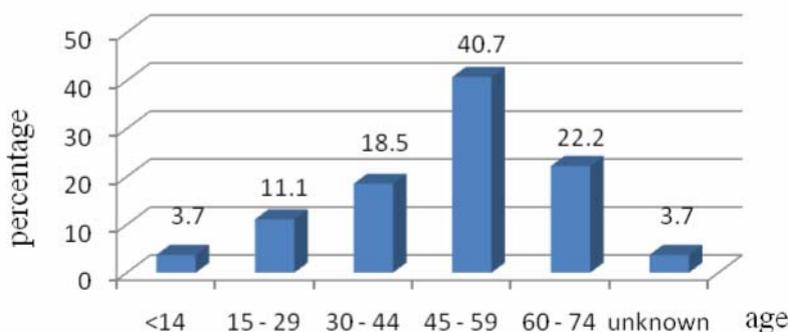


figure 1. Age distribution frequency

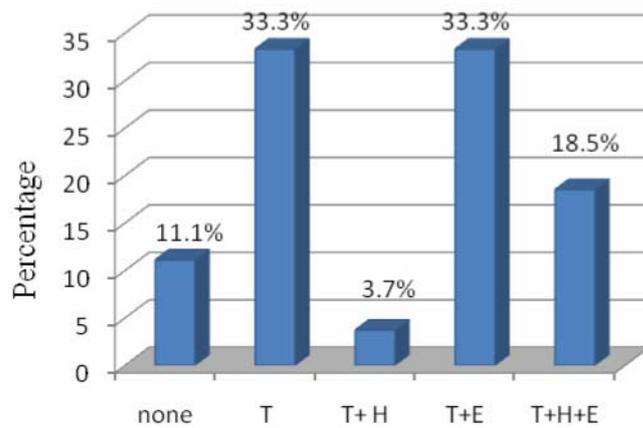
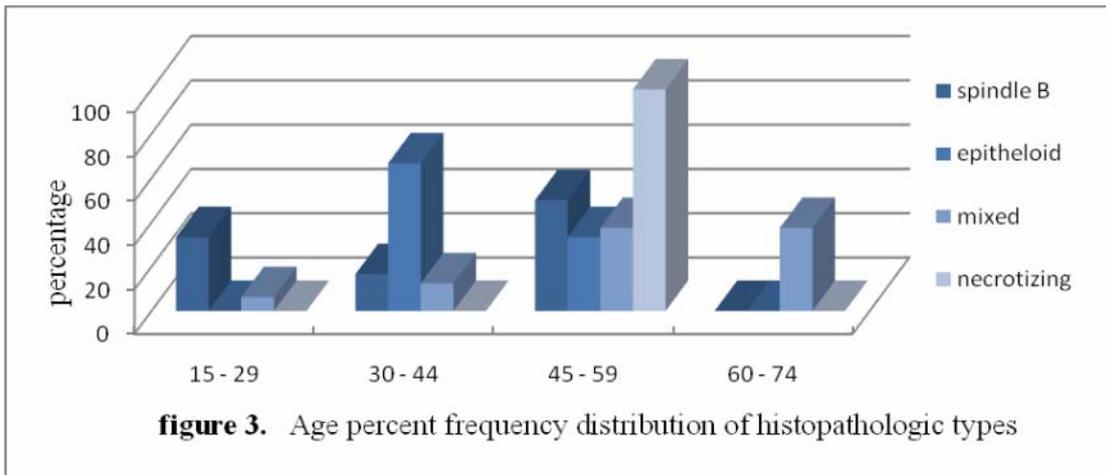
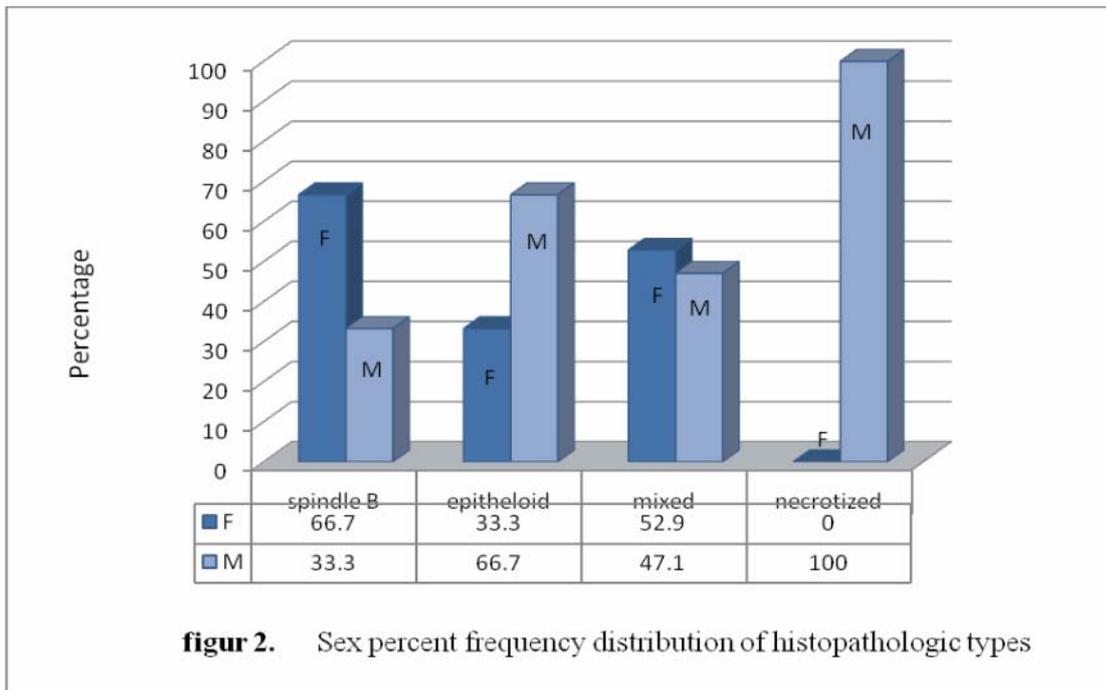


Figure 4. Retinal Detachment

T=Tumoral RD
 E=Exudative RD
 H=Hemorrhagic RD

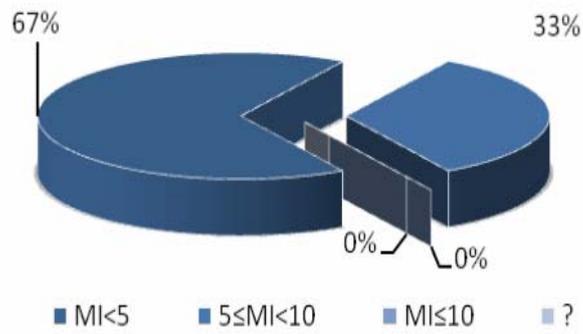


figure 5. Percent frequency distribution of mitotic index in stage I

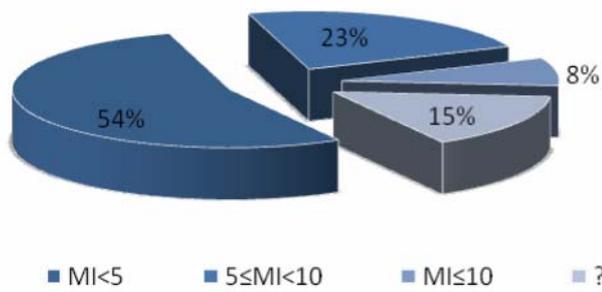


figure 6. Percent frequency distribution of mitotic index in stage II

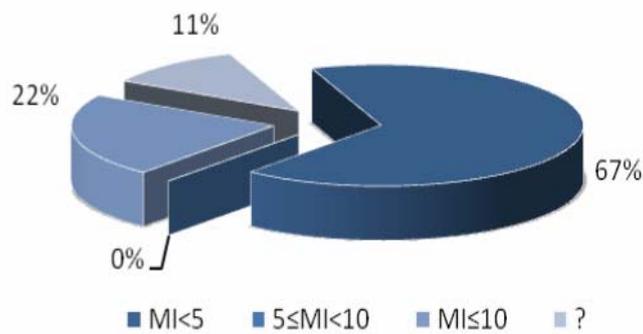


figure 7. Percent frequency distribution of mitotic index in stage III

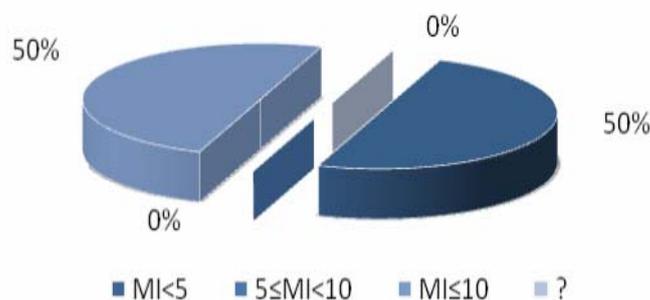


figure 8. Percent frequency distribution of mitotic index in stage IV

Discussion

In this study we found that in our population (like other populations); choroid was the most common site for ocular melanoma.

Sex frequency distribution has not significant difference in both genders, though in our study female were slightly more involved comparing to men. There was no predilection for one or the other eye in either sex. In our study, the most common histopathologic cell type was mixed type and spindle-B was in second place as it was suggested in other studies. We found no pure spindle-A cell type in our study, other studies remark at least 5% of this cell type.¹³

Retinal detachment was found in 89% of our cases which is more than other studies.¹³ This study shows clearly the relationship between mitotic index and the stage of the malignancy.

Two new findings were achieved in this investigation which was not mentioned in previous studies: First, there was more malignant cell type (epitheloid cells) in male comparing to female (M/F=2/1) which may be related to sex hormonal differences and should be investigated in future. Second; histopathologically, the more malignant cell types were more prevalent in advanced age groups.

Totally in this study we found more epitheloid (malignant) cell type (11.1%) in our population comparing to western countries which epitheloid is called the rarest type (3%).

Similar results were considered in the study which was done at Farabi Hospital (Tehran-Iran) in 1992¹² and the study which was done by Khoshniyat at SUMS (Shiraz-Iran) in 1987, (20% and 17% of cases were epitheloid). As this cell type carries the worst prognosis; more care is needed in our population. Mean age at initial diagnosis was 45.9 which is about 10 years lower than western countries.

Conclusion

As other studies in Iran shows similar results,¹² we consider as a possibility that it can be the result of more malignant cell type (and its earlier presentation) or can be due to lower life expectancy in our country.

As parts of our statistics are different from advanced countries, it is essential to have our own studies and programs in Iran to make this cancer under control.

Many patients with melanoma have asymptomatic tumors with higher stages when discovered on routine ophthalmic examination. This fact emphasizes the importance of routine, periodic, dilated fundus examinations and shows the low acquaintance of general population about the cancer.

All the facts above show the importance of more researches on ocular melanomas in our population.

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