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Malignant Melanomas of the Iris

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Abstract: The recognition of iris melanoma is important because a number of benign lesions clinically resemble these tumors. In this article, the epidemiological, clinical and histopathological features, treatment modalities, and prognosis of 41 iris melanoma patients, seen between 1964 and 1996 were evaluated. Of the patients, 20 were men and 21 women. Their mean age was 44.6 years. After determining the size, localization, and extension of the tumor, the management of choice was observation in 9, sector iridectomy in 15, iridocyclectomy in 6 and enucleation in 11 of the patients. During the follow-up, enucleation was also required in 6 and iridocyclectomy in 1 of the 7 patients who were in the observation or sector iridectomy group initially. Histopathologic examination revealed spindle cell in 27, mixed cell in 6 and epithelioid cell type melanomas in 2 of the 35 cases who underwent iridectomy, iridocyclectomy, and/or enucleation. The mean follow-up was 3.2 years and the mortality rate was found to be 2.4% during this period. One patient who died of metastases had epithelioid cell type melanoma. **Jpn J Ophthalmol 1998;42:281–285**

Key Words: Epidemiology, histopathology, iris melanoma, management.

Introduction

Iris melanomas comprise between 3 and 10% of all malignant melanomas of the uvea.[1] It is generally agreed that they are relatively benign. Signs of malign transformation include change in color, increase in size, pupil distortion, new vessel formation, ectropion uveae, sector cataract, and glaucoma.[2]

Iris melanomas appear to involve the inferior portion of the iris.[3] They grow either into the anterior chamber or along the iris surface, ultimately invading the angle and ciliary body. The localized iris melanoma usually appears as a well-demarcated, variably pigmented, irregular, elevated mass. On the other hand, diffuse melanomas are the result of widely scattered areas of neoplasia and they carry a more severe prognosis.

Malignant melanomas of the iris can exhibit several clinical and histopathologic variations. There are certain questions that arise in studying these tumors. Even the matters of what shall be called "melanoma" and when to use the terms *benign* and *malignant* are often subjects for debate. A series of 41 malignant melanoma of the iris is presented in this study, with a discussion of clinical and histologic characteristics, management, and prognosis.

Materials and Methods

Between 1964 and 1996, 41 patients with iris melanomas were diagnosed and treated in the Eye Clinic of the Tumor Department of Ankara University. Histopathologic examinations were made in the Pathology Department of the same university. Of the patients, 20 were men and 21 women. They were all Caucasians. Their ages ranged between 5 and 75 years with a mean age of 44.6 years.

The diagnosis of iris melanoma was made by obtaining a careful history and performing slit-lamp biomicroscopy, gonioscopy, and a complete ocular examination. Periodic observation was recommended in some of our patients at the time of initial diagnosis until definite evidence of growth was established. We followed these patients with anterior segment photographs at 6-month intervals. Surgical iridec-

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Table 1. Clinical Findings at Initial Examination (41 Cases)

Clinical Findings	Number of Cases	%
Iris mass	29	70.7
Iris mass + IOP	8	19.5
Iris mass + pupillary distortion	3	7.3
Iris mass + anterior staphyloma	1	2.5
Total	41	100.0

IOP: intraocular pressure.

tomy was curative in circumscribed melanomas. We used a modification of Stallard's technique for iridectomy. Circumscribed melanomas that extended posteriorly into the ciliary body were treated by iridocyclectomy. On the other hand, enucleation was the treatment of choice at initial examination in patients who had a diffuse melanoma that was too extensive to be managed by other methods and that produced secondary glaucoma that could not be controlled with surgery.

The mean follow-up period was 3.2 years, ranging from 3 months to 16 years.

Results

All the patients in our series had a pigmented lesion on the iris, which is the most common presenting clinical feature of an iris melanoma (Table 1). Eight (19.5%) of these 41 patients had secondary glaucoma, 3 (7.3%) had pupillary distortion, and 1 (2.5%) had anterior staphyloma as well as iris melanoma.

Eleven (26.8%) patients were initially treated by enucleation (Table 2). Four (36.4%) of these had secondary glaucoma resistant to medical treatment, 2 (18.2%) had a ring melanoma and 4 (36.4%) had extensive ciliary body involvement. The remaining 1 (9.0%) had anterior staphyloma.

Table 2. Treatment Modalities Employed in 41 Eyes of 41 Melanoma Cases

Treatment	Number of Eyes	%
Enucleation	11	26.8
Observation	6	14.6
Iridectomy	11	26.8
Iridocyclectomy	6	14.6
Iridectomy + enucleation	4	9.7
Observation + enucleation	1	2.5
Observation + iridocyclectomy	1	2.5
Observation + iridectomy + enucleation	1	2.5
Total	41	100.0

Iridocyclectomy was performed in 6 (14.6%) patients. In all of these 6 patients melanomas were extending into the ciliary body.

Fifteen (36.5%) patients who had a melanoma confined to the iris were managed by a sector iridectomy. During the follow-up period, 2 (13.3%) of these melanomas continued to grow and 2 (13.3%) extended into the ciliary body. Enucleation was performed subsequently in these 4 eyes.

Observation with periodic anterior segment photography was the management of choice in 9 (22%) patients. In 2 (22.2%) of these 9 patients, evidence of growth was established and enucleation was performed. In one of them, iridectomy was performed first and enucleation subsequently. The intervals between the initial diagnosis and enucleation was 3 and 59 months, respectively. Iridocyclectomy was performed in another patient on the 124th month of periodic observation because of secondary glaucoma and ciliary body involvement.

No treatment-related complication was observed intraoperatively or postoperatively. All tumors treated surgically (iridectomy, iridocyclectomy, or enucleation) were histologically confirmed as iris melanomas. Twenty-seven of these 35 lesions were found to be spindle cell, 6 were mixed cell and 2 were epithelioid cell type melanomas (Figure 1). Spindle type lesions were composed of elongated cells with plump nuclei, clumping of the nuclear chromatin, and peripheral margination and prominent nucleoli. Mitotic activity was present but not marked. There was a high nuclear-cytoplasmic ratio. Cytoplasm of most of the cells contained melanin pigment (Figure 2). A fascicular pattern was found in most of them. In epithelioid type lesions; tumor cells grew in sheets and

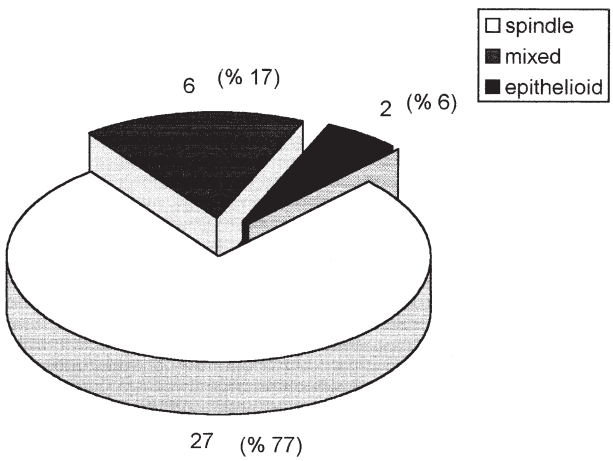

Figure 1. Histopathologic evaluation in 35 patients.

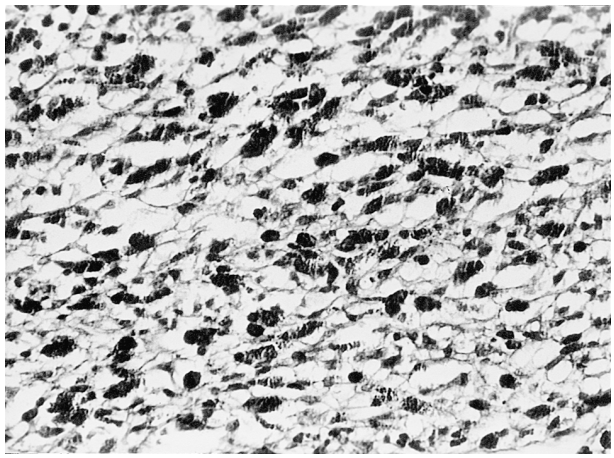

Figure 2. Malignant melanoma with heavily pigmented spindle cells (hematoxylin and eosin, original magnification ×200).

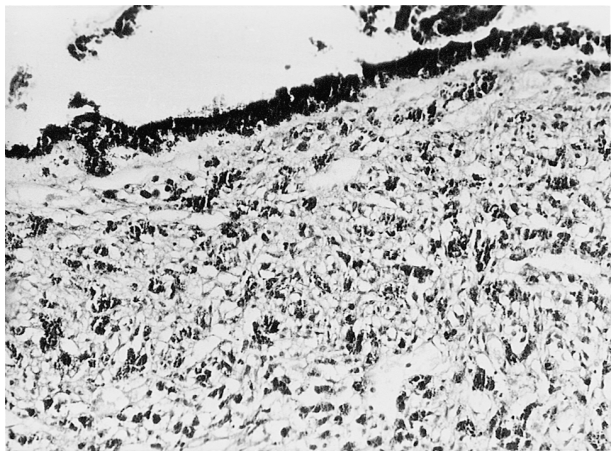

Figure 4. Malignant melanoma with pigmented mixture of cells (hematoxylin and eosin, original magnification ×100).

nests and they displayed a high nuclear-cytoplasmic ratio. The nuclei were large and had eosinophilic nucleoli (Figure 3). Depending on the degree of tumor cell pigmentation, macrophages were variably present. In mixed type lesions, there was a mixture of malignant spindle cells with plump nuclei containing prominent nucleoli and larger, more polyhedral cells with glassy cytoplasm and large nuclei possessing eosinophilic nucleoli. Mitotic figures could always be identified (Figure 4).

In this study, only 1 patient died during the follow-up. This patient had a melanoma with ciliary body involvement and was initially treated by enucleation. He had liver and gastrointestinal metastasis and died 3 years after treatment. Histopathology showed epithelioid tumor.

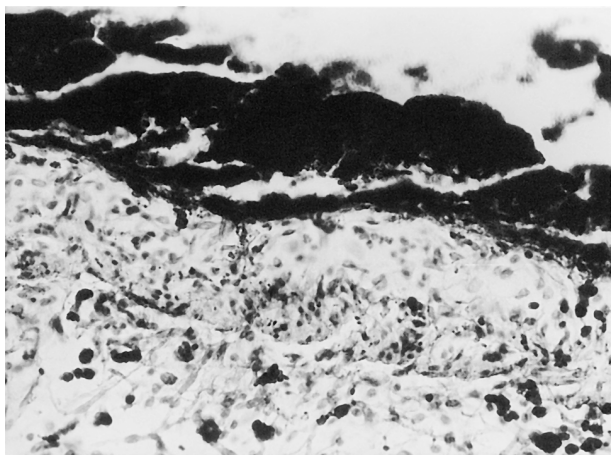

Figure 3. Epithelioid cell melanoma (hematoxylin and eosin, original magnification ×200).

Discussion

Because the iris is the most easily observed part of the eye, changes in color, distortion of the pupil, and/or other abnormalities are noted early. This may account for the discovery of iris melanomas in an age group younger than the groups in which melanomas of the ciliary body or choroid are found. If the tumor is hidden in the extreme periphery of the iris, it may not be detected early. It may extend around the angle causing glaucoma as an initial problem. Tumors in this location will often invade the ciliary body early or even extend outside the globe by way of Schlemm's canal.[4] In our study, a pigmented lesion on the iris was noted in all patients, but only 70.7% of them were aware of it at the initial examination. Ocular pain and/or blurred vision was the prominent symptom in 29.3% of the patients (Table 3).

Like other melanocytic uveal tumors, there is a definite predisposition for iris melanomas to occur in light-skinned white persons. Men and women appear to be affected in nearly equal proportions.[5] The av-

Table 3. Symptoms of Cases

Symptoms	Number of Cases	%
Change in iris color	22	53.6
Change in iris color + decrease in visual acuity	5	12.2
Change in iris color + pain	2	4.9
Decrease in visual acuity	6	14.6
Pain	5	12.2
Decrease in visual acuity + pain	1	2.5
Total	41	100.0

IOP: intraocular pressure.

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erage age at diagnosis has been reported to range from 40 to 47 years.[6,7] In our series, of the 41 patients, 48.8% were men and 51.2% women. Male:female ratio was 0.95. The average age was 44.6, but 24.4% of the patients were in the 51 to 60-year age group.

A number of lesions can clinically simulate a malignant melanoma of the iris. Failure in diagnosis can sometimes lead to unnecessary ocular surgery or even enucleation. Ferry reported 24 pseudomelanomas in a series of 69 eyes that were enucleated because of suspected iris melanoma, a diagnostic error rate of 35%.[8] Shields and coworkers[9] reviewed the records of 200 patients with an iris lesion suspected of being a melanoma. On clinical evaluation, 24% of the lesions met the criteria for the diagnosis of iris melanoma and the remaining 76% were diagnosed as pseudomelanomas.

With better understanding of the clinical behavior of iris melanomas, their management has become more conservative. Years ago, clinicians treated most iris melanomas by enucleation, but it has become recognized that iris melanomas can have a better prognosis and that surgical iridectomy is often curative.[3,10,11] In more recent years, there has been an increasing tendency to manage iris melanomas by periodic observation rather than by surgical intervention.

Observation with periodic anterior segment photography is the management of choice for most iris melanomas, since many of these tumors are stationary lesions that have no tendency to grow. As Territo and co-workers[12] indicated, only 4.6% of the suspicious melanocytic iris lesions showed clinical evidence of enlargement within 4.7 years after initial diagnosis. Examination every 6 months with slit-lamp photography is the most appropriate approach until growth is clearly documented. Gonioscopic examination is extremely important during observation of iris melanomas. If active growth can be established, an iridectomy is indicated if the tumor is localized and does not involve other structures. In our series, we performed sector iridectomy in 15 (38.5%) of the patients at initial visit. All these patients had melanoma confined to the iris and surgical procedure was planned according to the size and the extent of the tumor. During the follow-up, 4 (26.7%) of these required enucleation due to recurrence.

Iridocyclectomy is indicated in cases with ciliary body involvement and melanoma that is producing a progressive cataract, subluxation of the lens, vitreous hemorrhage, or secondary glaucoma.[5] Iridocyclectomy was performed in 7(17.1%) of the patients in this study. In 6 of these cases, iridocyclectomy was the initial treatment. The other patient was followed-up for 124 months, but iridocyclectomy was performed because of secondary glaucoma and extensive ciliary body involvement. Iridocyclectomy provides the means for potentially excising the tumor and preserving useful vision in the treated eye. Complications include hemorrhage, vitreous loss, dislocated lens, cataract, iridocyclitis, secondary glaucoma, and retinal detachment. In 1977, Forrest, Keyser, and Spencer[13] reviewed the outcome of patients who underwent iridocyclectomy and reported that there was minimal surgical morbidity, good visual outcome, and excellent survival with this procedure. In another study by Memmen and McLean,[14] long-term results of iridocyclectomy to remove a lesion of the iris or ciliary body in 52 patients were evaluated. Visual outcome was generally good, surgical morbidity was rare. They observed cataract, secondary glaucoma, vitreous loss, retinal detachment, vitreous hemorrhage, and retinal hole in a small number of their cases. In eyes from which tumors were removed by iridocyclectomy in our series, no treatment-related complication occurred and all patients followed have done well.

There are fewer indications for enucleation for iris melanoma today than in the past. Enucleation for an iris melanoma should be considered only if the tumor is too extensive to be managed by other methods or if the eye has no salvageable vision because of either the tumor or an unrelated cause. In this study, 17 of the 41 (41.5%) eyes were enucleated. Enucleation was performed initially in 11 (26.8%), following observation or iridectomy in 6 (14.6%) of the patients. The higher enucleation rate in this study is not surprising because our series included patients who were referred to us late and who had an advanced stage of the disease.

The prognosis in patients with iris melanoma is very favorable. A report by Noor Sunbar and colleagues[15] indicated a mortality of 4% in iris melanoma patients. The mortality rate from metastasis in Memmen and McLean's series was 22%.[14] This was significantly higher than the 3% reported by Giesse and Robertson.[16] Ashton found no tumor-related deaths.[6] Rones and Zimmerman[3] reported that only 3/67 patients with iris melanomas died during the follow-up interval and that none of these deaths was proved by autopsy to be related to the tumor. In our study, the mortality rate was 2.4%. Only 1 patient died because of metastasis during the follow-up. This patient had an enucleation for iris melanoma invading the ciliary body; death occurred 36 months after the surgery. The histopathologic diagnosis was epithelioid cell

type melanoma. Pure epithelioid cell melanomas in the iris are extremely rare and have a poor prognosis. A few studies with limited number of patients have noted more deaths in patients with epithelioid cell as compared with those with pure spindle cell melanomas.[17] In a retrospective clinicopathologic study of 189 iris and iris and ciliary body lesions originally diagnosed as melanomas, 87% of lesions were reassigned to six benign categories and 13% were assigned to three malignant categories, there were no tumor related deaths.[18] The authors also pointed out that cytologically benign pigmented iris tumors could show some growth, invade the angle, and increase intraocular pressure.

The latency between treatment and detection of metastases is also different between iris and posterior uveal melanomas.[19] Kersten and associates[17] noted the mean interval between treatment and metastatic diagnosis was approximately 8.5 years, and only 3 of 13 patients died less than 5 years after ocular surgery. The interval between enucleation and death was 3 years in our patient.

Consequently, for many years it has been recognized that iris melanomas are relatively benign tumors. They should be treated conservatively until the signs of active growth occur. If unequivocal growth is documented, surgical intervention may be justified according to the size and the extent of the tumor. The better prognosis of iris lesions has been attributed to earlier detection. In melanomas that show diffuse infiltration and are of epithelioid cell type, the mortality rate appears to be high.

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