UVEAL MELANOMAS IN BLACK PATIENTS: A CASE SERIES AND COMPARATIVE REVIEW

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Uveal melanomas are rare in black patients. Of a total of 2586 patients with the diagnosis of posterior uveal melanoma who were managed in the Oncology Service at Wills Eye Hospital from 1974 to 1987, 10 patients (0.39%) were black. Data on patient age (mean: 53.9 years), sex (male-to-female ratio: 7:3), and relative frequency of disease between black (0.39% of total cases) and white patients were similar to that of previous reports. The distinguishing characteristics (incidence, risk factors, complications, and prognostic indicators) of uveal melanoma in black versus white patients also were reviewed. (*J Natl Med Assoc.* 1995;87:709-714.)

Key words • uveal melanoma • intraocular tumors • malignancies

Uveal melanoma is the most common primary malignant intraocular tumor among whites. The annual incidence of this tumor in the white population has been estimated to be approximately six cases per million persons in the United States.[1] The annual incidence of uveal melanoma in blacks in the United States is not known precisely but appears to be substantially lower, probably in the range of 0.64 to 0.86 cases per million persons[1] (assuming that the anatomically unspecified ocular tumors were all intraocular choroidal melanomas).

A review of more than 3000 pathologic specimens of uveal melanomas from the Armed Forces Institute of Pathology (AFIP) revealed only 24 that were obtained from black patients.[2] Similar findings have been reported in surveys of African populations.[3-7] A South African study uncovered one case of uveal melanoma in a black patient compared with 150 cases among the minority white population. The risk for developing a uveal melanoma is similarly lower in races of intermediate pigmentation.[1,8-10] This article reviews uveal melanoma in black patients and summarizes the clinical and histopathologic findings and follow-up information in 10 black patients with uveal melanomas.

PATIENTS AND METHODS

The Wills Eye Hospital Oncology Service records from 1974 to 1987 were reviewed to identify all black patients diagnosed with a uveal melanoma. Table 1 summarizes patient characteristics including age at diagnosis, presenting symptoms, and presenting best-corrected visual acuity. The clinical diagnosis of uveal melanoma was made in every case on the basis of comprehensive ophthalmic and physical examinations, and include appropriate ancillary testing.[11,12] When the clinical diagnosis could not be made on ophthalmoscopy alone, ultrasonography (Figure 1), fluorescein angiography, computed tomography, magnetic resonance imaging, and intraocular fine needle aspiration biopsy were used when indicated.

The degree of tumor pigmentation, size of the tumor, and location of the tumor (position of the most anterior margin relative to the equator and ora serrata) (Table 2)

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TABLE 1. PATIENT CHARACTERISTICS

Patient No.	Age (Years)	Sex	Symptoms	Visual Acuity
1	44	Male	VA change	6/12
2	35	Male	VA change	6/60
3	47	Male	VA change	6/18
4	63	Male	VA change	No light perception
5	50	Female	VA change	6/6
6	56	Female	VA change	Count fingers
7	62	Male	None	6/6
8	83	Female	VA change	NA
9	39	Male	RD	6/7.5
10	60	Male	VA change	6/12

Abbreviations: VA = visual acuity, NA = not applicable or not reported, and RD = retinal detachment.

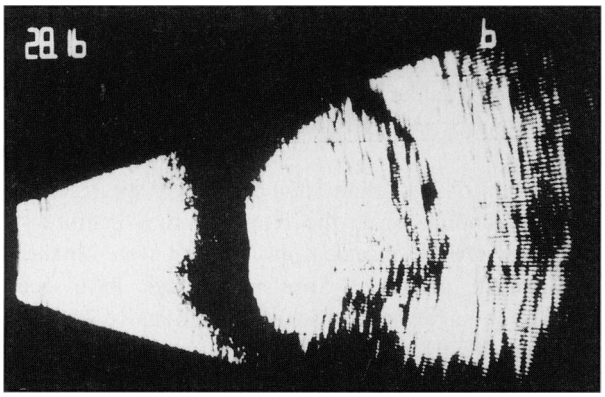

Figure 1. B-scan ultrasound of a large, dome-like choroidal melanoma.

TABLE 2. TUMOR CHARACTERISTICS

	Tumor		
Patient	Location	Pigmentation	Thickness (mm)*
1	AE	Yes	9.3
2	PE	Yes	4.0
3	PE	Yes	3.4
4	CB	Yes	12.0
5	PE	No	5.7
6	CB	Yes	15.6
7	PE	Yes	3.8
8	PE	Yes	NA
9	CB	Yes	8.1
10	CB	Yes	7.2

Abbreviation: NA = not applicable or not reported.
*Average thickness: 7.68 mm.

were all recorded, as were the method of treatment and response to therapy (Table 3). The pathologic features of the tumors managed by enucleation and those evaluated by fine needle aspiration biopsy also were tabulated and summarized. The clinical course of each patient after diagnosis and treatment until death or recent follow-up (April 1989) was reviewed.

Table 4 summarizes the tumors' histopathology according to the modified Callender classification. Callender[13] originally described two spindle cell lines (types A and B), fascicular, epithelioid, mixed, and necrotic cellular subtypes. While both types A and B are "spindle" in shape, they are distinguished by the presence of nucleoli and mitoses in type B, which are absent in type A. The presence of palisading nuclei, in either spindle type, further classified them as fascicular. Larger, round to ovoid, pleomorphic cells, with large oval to polygonal nuclei and decreased cellular cohesiveness describes the epithelioid subtype. The mixed cell line is comprised of a combination of varying amounts of both the spindle and the epithelioid cell lines.

When the proportion of viable cells is small enough to preclude the aforementioned classification, the tumor is classified as "necrotic." The modified Callender classification combines both spindle cell types with the fascicular cell line under the single "spindle" category. The relative long-term prognosis decreases as the tumor cellular subtype changes from spindle to mixed to epithelioid (prognosis of the necrotic subtype being approximately equal to that of the mixed cell line).[2]

RESULTS

Out of a total of 2586 patients diagnosed with posterior uveal melanoma, 10 (0.39%) were black. The age of the patients at diagnosis ranged from 35 to 83 years (average: 53.9 years). There were seven men and three women. Nine of the 10 patients were born in the United States; the other patient came from the West Indies. Eight of the 10 patients presented with complaints of decreased vision. One patient was asymptomatic. The best-corrected visual acuity in the affected

TABLE 3. TREATMENT AND FOLLOW-UP

Patient No.	Treatment		Radiation Side Effects	Length of Follow-Up (Years)	Status
	Initial	Secondary			
1	Plaque radiation	Enucleation	Cataract	7	Well
2	Plaque radiation	Enucleation	Retinopathy	5	Well
3	Enucleation	—	NA	0.5	Well
4	Enucleation	—	NA	0.5	Well
5	Plaque radiation	Enucleation	Retinopathy	1	Well
6	Enucleation	—	NA	3	Dead*
7	Plaque radiation	—	NA	5	Well
8	Refused treatment	—	NA	Lost	?
9	Observation	—	NA	1	Dead†
10	Plaque radiation	—	Retinopathy/ neovascular glaucoma	4	Well

Abbreviations: NA = not applicable or not reported.
*Cause of death: lung carcinoma.
†Cause of death: metastatic uveal melanoma.

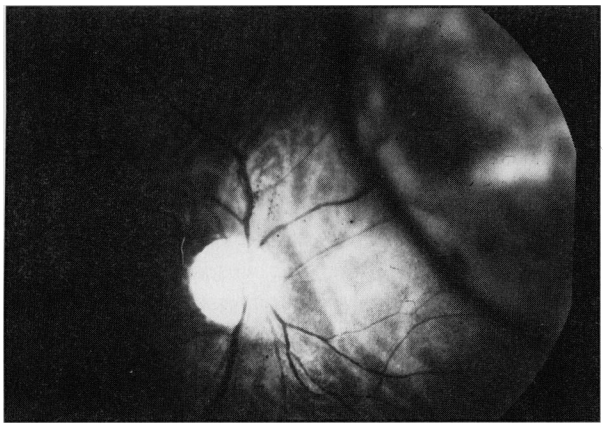

Figure 2. Large, elevated (out-of-focus) choroidal melanoma in the nasal posterior pole.

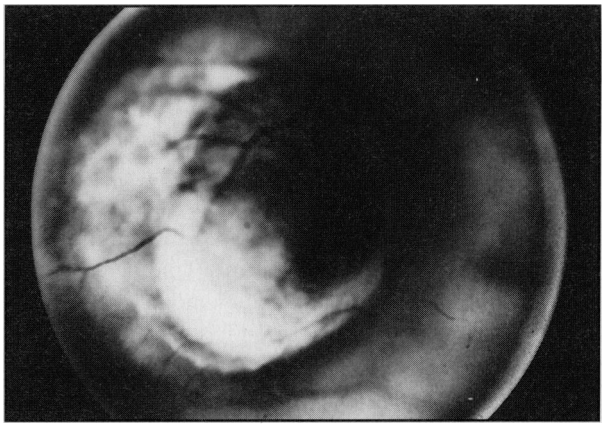

Figure 3. Subretinal hemorrhages (black) and exudation (white) after iodine^{125} therapy. Note the thin, dark, retinal vessel coursing over the oval-shaped tumor and surrounding exudates. The view is hazy secondary to the radiation-related retinovitreitis.

eye ranged from 6/6 to no-light-perception (median: 6/12). None of the patients had a family history of an eye tumor or cutaneous malignant melanoma. One of the patients had ocular melanocytosis in the eye that developed the tumor.

The location of the anterior tumor margin was anterior to the ora serrata in the ciliary body in four eyes, between the ora and equator in one eye, and posterior (Figure 2) to the equator in five eyes. Nine of the 10 tumors were darkly pigmented ophthalmoscopically, and one of the tumors had prominent orange pigment clumps on its surface. Several of the tumors were associated with serous retinal detachment. Seven of the tumors had a smooth, dome-shaped, cross-sectional contour, while three had broken through Bruch's membrane to assume a mushroom-like contour. The thickness of the tumors ranged from 3.4 to 15.3 mm (mean: 7.6 mm; standard deviation: 4.11 mm).

Management

Primary treatment consisted of enucleation for three patients and episcleral plaque radiotherapy for five patients (four patients received cobalt^{60} and one patient received iodine^{125}) (Figure 3 and Table 3). Three of five plaque-treated patients eventually required enucleation of the involved eye. One patient was managed on observation, and one patient refused therapy.

TABLE 4. TUMOR HISTOPATHOLOGY

Patient No.	Method	Cell Type	Bruch's Membrane Breaks	Extraocular Extension
1	Enucleation	Necrotic	Yes	No
2	Fine needle aspiration/ enucleation	Spindle	No	No
3	Enucleation	Mixed	No	No
4	Enucleation	Epithelioid	Yes	Yes
5	Enucleation	Necrotic	No	No
6	Enucleation	Mixed	Yes	No
7	NA	NA	No	No
8	NA	NA	No	NA
9	Fine needle aspiration	Spindle	No	No
10	Fine needle aspiration	Mixed	No	Yes

Abbreviations: NA = not applicable or not reported.

One of the 10 patients, at 1 year follow-up, died of autopsy-diagnosed metastatic uveal melanoma. In the remaining patients, follow-up ranged from 6 months to 7 years (median: 3 years). The first, fifth, and seventh year "patient follow-up retention rates" were 90%, 30%, and 10%, respectively.

Management considerations and modalities are numerous, challenging, and constantly advancing. When and how to use the various treatment options (periodic observation, enucleation, orbital exenteration, modified enucleation and exenteration, radiotherapy, photocoagulation, local resection, diathermy, cryotherapy, photoradiation, hyperthermia, and chemotherapy) is beyond the scope of this article and has been described in detail elsewhere.[11,12,14]

DISCUSSION

Uveal melanomas can be lethal, although they rarely occur in blacks. Physicians are best positioned to avoid missing such a serious diagnosis by studying its salient characteristics. Several studies have demonstrated a marked difference in the frequency of uveal melanoma in black patients compared with whites.[1-7,15] Margo and McLean[15] found 39 black patients with uveal melanomas out of 3876 total patients with uveal melanomas referred to the AFIP up to 1975. The Third National Cancer Survey reported a conservative annual incidence of uveal melanomas in blacks of 0.64 cases per million persons.[1]

With regard to risk factors for the development of uveal melanomas, the degrees of uveal pigmentation epidemiologically appear to be protective in blacks compared with whites.[1,4,16] This correlation parallels that of cutaneous melanomas.[17-22] Based on this apparent protection, the widespread and varied racial heterogeneity of blacks should lead to a relative frequency intermediate to that of assumed homogeneous white and black populations. Indeed, the white-to-black ratio for uveal melanoma has been reported as 8-15:1[1,16] in the United States and as 80:1 in South Africa.[4] This suggests that mixed racial ancestry may be a possible risk factor for black Americans.

There is strong epidemiologic evidence that intense sunlight exposure increases the risk of development of cutaneous melanomas and that somehow the increased pigmentation in blacks is protective.[1,20-22] The evidence linking sunlight exposure with subsequent development of posterior uveal melanomas is weaker than that for cutaneous melanomas.[23-25] Lee and Merrill[26] found the rate of ocular melanoma to be higher in the southern than in the northern United States. However, a more recent study found no correlation between frequency and latitude.[1]

In contrast to uveal melanoma, oculodermal melanocytosis or nerve of Ota occurs with equal or greater frequency in blacks than whites.[11,27-31] While there appears to be an increased risk of developing a uveal melanoma in white patients with ocular and oculodermal melanocytosis, this same risk has not been established clearly in nonwhites.[32] There is only one published report of a black patient with ocular or oculodermal melanocytosis who developed a uveal melanoma.[33] One of the patients in our series had an ocular melanocytosis that developed uveal melanoma. Again, whether this increased the patient's risk for developing the malignant ocular tumor is unclear.

The ocular morbidity due to associated complications also appears to be higher in blacks compared with whites. Margo and McLean[15] found that blacks were more likely to have inflammation and secondary

glaucoma prior to enucleation. There are at least two plausible reasons for this. First, the higher rate of ocular morbidity may be related to the observed higher frequency of tumor necrosis in black versus white patients.[15] Second, this increased ocular morbidity may be related to a clinically significant delay (diagnosis unsuspected prior to enucleation) in making the diagnosis in blacks.[15] This delay in diagnosis, for whatever reason, may have prognostic significance and deserves further investigation. One of the 10 black patients in this series had both associated intraocular inflammation and secondary glaucoma. The tumor in this patient was epithelioid but not necrotic. However, there appeared to have been significant delay between the onset of symptoms and the initial presentation/diagnosis as the patient presented with no-light-perception vision and a large tumor (12 mm). This patient underwent primary enucleation.

While tumor histopathology, size, location, and scleral invasion are all general prognostic indicators, only tumor histopathology has an additional, race-specific, prognostic value. Margo and McLean[15] found an increased mortality rate in blacks with the presence of necrotic or epithelioid-type cells within the tumor compared with whites. Poorer prognosis is associated, in both white and black patients, with the presence of varying proportions of epithelioid cells, noniris uveal tumor locations, large tumor size, and scleral involvement.[11] We were unable to make any comparisons between this series and previous reports due to certain study limitations noted below. Case examples that both support and do not support the above prognostic trends can be found in this series. In the patient who died, the tumor was located in the ciliary body, was pathologically a mixed-cell type melanoma, and had broken through Bruch's membrane (which are all poor prognostic indicators).

In terms of overall survival, it is known that blacks with some malignant tumors, including cutaneous melanomas, tend to fare worse than whites.[34,35] However, no significant difference exists in the overall (excluding tumor-tissue subtyping) death rates for uveal melanomas in blacks and whites.[15]

Several obstacles became evident while conducting this review:

- the small number of cases, due to the inherently low frequency of this disease in blacks,
- the oncology service's uncertain "region-specific" racial population base, secondary to its internationally broad referral base,
- the study's nonrandomized, retrospective nature due to the ethical dilemma of prospectively randomized treatment options in a potentially fatal disease,
- the limited patient follow-up retention, and
- the short follow-up period for this study, which is secondary to the lack of examiner influence over patient follow-up in a retrospective study design.

Despite these limitations, certain observations can be made. This study agrees with previously reported black-to-white, relative-frequency ratios for patients with uveal melanoma, sex preponderance, and patient-age data. We found a small relative frequency of 0.39% in blacks, which is similar to the previously reported value of 0.63%[2] (24 blacks to 3828 nonblacks). Yanoff and Zimmerman[36] reported a male-to-female ratio of 6:4, which is similar to our finding of 7:3. Earlier studies report a median age of 55 years,[37,38] which is similar to our finding of an average of 53.9 years.

Raivio[38] reported 5-, 10-, and 15-year survival rates of 65%, 52%, and 46%, respectively. Simply looking at the numbers alone, our study reveals a 1-year survival rate of 86% (6 patients alive out of 7 patients whose status was known up to 1 year of follow-up). However, the study's limited patient follow-up retention, short follow-up period, and small number of cases make it difficult to comment on the significance of our survival rates. Others have found no difference in the overall death rates from uveal melanomas in blacks and whites.[15]

SUMMARY

The distinguishing characteristics of uveal melanoma in blacks and whites were compared. Such salient features exist with regard to incidence, certain possible risk factors, associated secondary complications, and certain prognostic indicators. The relative frequency of uveal melanomas in black patients in this series was similar to those reported by pathologic laboratory referral practices. Age and sex data reported here were similar to those reported previously. However, while similar to other reports, the survival rates in this series must be interpreted with caution.

Finally, the authors wish to foster a reasonable diagnostic and referral threshold in all physicians. This is important as the differential diagnosis of uveal melanoma is broad,[39,40] the diagnostic and treatment options can be complex,[11,12,14,15] and the risk of serious morbidity and mortality exists in black as well as white patients.[15,39]

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