Prognosis of Uveal Melanoma in Patients With Oculodermal Melanocytosis

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Ocular melanocytosis is a congenital melanocytic condition that manifests with hyperpigmentation of the sclera, uvea, and orbit.[1] This condition is estimated to affect 0.04% of the white population.[1] Oculodermal melanocytosis (ODM), or nevus of Ota, includes the above features with additional dermal pigmentation of the periocular skin and temporal fossa. Within the white population there is a known relationship between the presence of ODM and the development of uveal melanoma. Studies have documented that patients with ODM have early onset of melanoma, occurrence of melanoma ipsilateral to ODM, and sector-specific development of melanoma in sectoral ODM.[2] More recent studies have estimated that 1 in 400 white people with ODM develop uveal melanoma during their lifetime.[3] Herein, we describe a case of uveal melanoma in an elderly patient with ODM and discuss the associated risks.

CASE REPORT

A 72-year-old white man with lifelong heterochromia manifesting with brown iris of right eye (OD) and blue iris of left eye (OS) was unaware of the risks of the asymmetric ocular pigmentation of ODM. The patient presented to his optometrist with blurred vision and photopsia OD. Examination revealed visual acuity of hand motions OD and 20/70 OS. Intraocular pressure was 12 mm Hg in each eye. Nuclear sclerosis and cortical spoking accounted for moderate reduced visual acuity in both eyes (OU). The left eye was otherwise unremarkable.

External examination of OD disclosed slate-blue scleral pigmentation and dark brown iris with velvety surface consistent with ocular melanocytosis (Figure 1). Funduscopically, diffuse, dark brown choroidal melanocytosis OD with scattered drusen contrasted sharply with the relatively blonde OS. In the affected eye, there was retinal detachment with an underlying mushroom-shaped, amelanotic choroidal melanoma. The melanoma measured 14 mm in diameter and 9 mm in

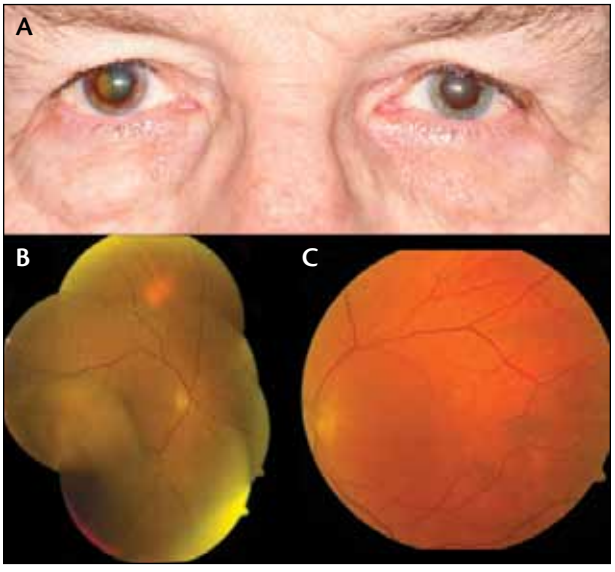

Figure 1. A 72-year-old white man with ocular melanocytosis and uveal melanoma in the right eye (OD). External photograph depicting right heterochromia and visible uveal melanoma OD (A). Fundus OD displayed choroidal melanocytosis and uveal melanoma 14 mm in diameter and 9 mm in thickness (B). Note the extensive drusen. Fundus OS was normal (C).

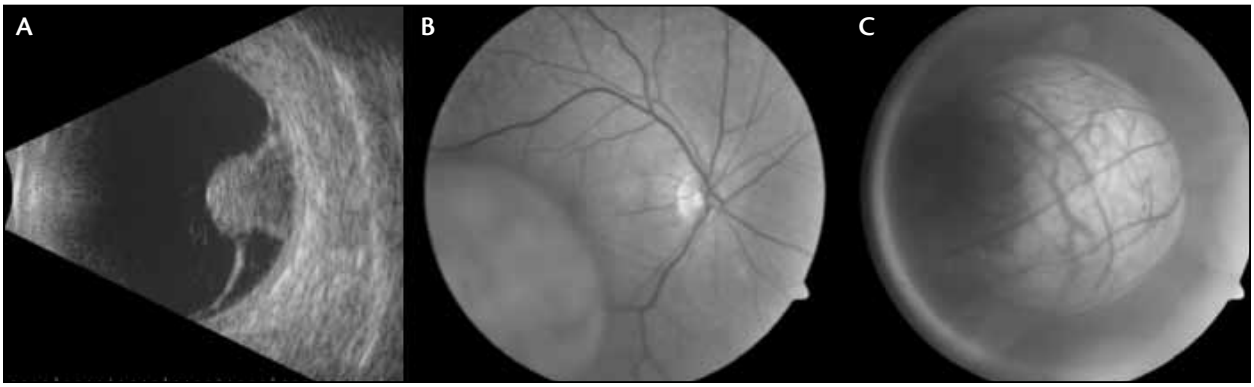

Figure 2. Uveal melanoma imaging. Ultrasonography OD showed a mushroom-shaped choroidal melanoma 9 mm in thickness (A). Fluorescein angiogram late frame documented double circulation (B).

thickness, located in the macular region (Figure 2). The final diagnosis was mushroom-shaped choroidal melanoma arising from ocular melanocytosis. Treatment consisted of I-125 plaque radiotherapy with apex dose at 7000 cGy. Following plaque treatment, panretinal photocoagulation (PRP) and quarterly bevacizumab (Avastin, Genentech) injections were provided to minimize radiation-induced visual acuity loss.

DISCUSSION

ODM affects 0.04% of the white population[3] and 1.4% of the uveal melanoma (UM) population.[4] In other words, ODM is 35 times more prevalent in the uveal melanoma population than the general white population.[4] In a study of 56 patients with ODM and uveal melanoma, Singh et al[3] found the lifetime prevalence rate uveal melanoma in white patients with ODM to be 2.6×10^{-3}, or, otherwise stated, approximately 1 in 400 white people with ODM develop uveal melanoma during their lifetime. In the general population, it is estimated that lifetime risk for uveal melanoma is 1 in 13 000 persons.[3] In our patient, the melanocytosis remained unrecognized to the patient, as he was unaware of the significance of heterochromia. The uveal melanoma was detected at a large size (14 mm diameter, 9 mm thickness) in this elderly man. One might speculate that proper annual monitoring of this at-risk patient could have detected the melanoma at an earlier point when the tumor was a smaller size.

Sector or partial melanocytosis is a less common form of melanocytosis that affects only a portion of the iris, choroid, or both.[5] In a study of 89 patients with sector melanocytosis, Shields et al[5] found iris involvement in 65% of cases with a mean of 6 clock hours involvement, and they noted choroidal involvement in 54% with a mean of 5 clock hours involvement. Of the 89 patients with sector melanocytosis, 7 presented with uveal melanoma, all within the area of partial melanocytosis.[5] Both patients with complete melanocytosis and those with sector melanocytosis should be routinely monitored for uveal melanoma, particularly within the region of excess pigmentation.[5] Subtle findings such as shallow subretinal fluid or a few clumps of orange pigment could be important identifying features of underlying melanoma in these cases. Optical coherence tomography and fundus autofluorescence are key diagnostic tools to early detection of melanoma when the tumor might be minimally apparent clinically.

TABLE 1. RISK OF METASTASIS OF UVEAL MELANOMA AT 5 AND 10 YEARS IN PATIENTS WITH AND WITHOUT OCULAR MELANOCYTOSIS BY KAPLAN MEIER ESTIMATES.

Years	Metastasis rate from uveal melanoma in patients with melanocytosis (n = 230)	Metastasis rate of uveal melanoma in patients without melanocytosis (n = 7642)	Probability value
5	27%	15%	$P < .001$
10	48%	24%	$P < .001$

Shields CL, Kaliki S, Livesey, M, et al. Oculo(dermal) melanocytosis is associated with higher rate of uveal melanoma metastasis. 2012; Submitted for publication.

In a more recent evaluation on prognosis of melanocytosis, Shields et al[6] evaluated risk for metastasis of uveal melanoma based on the presence or absence of ocular melanocytosis. In a retrospective analysis of 7872 patients with uveal melanoma, they documented that patients with ODM (230/7872; 3%) had a metastatic rate 1.6 times higher than patients without ODM, with risk varying by location (Table 1). Furthermore, the risk for metastasis was 2.8 times higher for patients with iris melanocytosis, 2.6 times higher with choroidal melanocytosis, and 2 times higher with scleral melanocytosis.[6] In that series, the only factor predictive of metastasis and death in patients with ocular melanocytosis was increasing tumor thickness.[6]

In conclusion, patients with ODM should be routinely followed on a 6-month basis with widely dilated fundus examination, as they carry an increased risk for uveal melanoma and subsequent doubled risk for metastasis. All patients with ODM should be clearly informed of the importance of this condition and the need for lifelong ophthalmic follow-up. Early detection of uveal melanoma is critical for minimizing metastatic risk and improving life prognosis. ■

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1. Shields JA, Shields CL. *Intraocular Tumors.* 2nd ed. Philadelphia: Lippincott Williams & Wilkins, 2008:140-141.

2. Shields CL, Kaliki S, Furuta M, Mashayekhi A, Shields JA. Clinical spectrum and prognosis of uveal melanoma based on age at presentation in 8,033 cases. *Retina*. 2012;32(7):1363-1372.

3. Singh AD, De Potter P, Fijal BA, et al. Lifetime prevalence of uveal melanoma in white patients with oculo(dermal) melanocytosis. *Ophthalmology*. 1998;105(1):195-198.

4. Gonder, JR, Shields, JA, Albert DA, et al. Uveal malignant melanoma associated with ocular and oculodermal melanocytosis. *Ophthalmology*. 1982;89(8):953-960.

5. Shields CL, Qureshi A, Mashayekhi A, et al. Sector (partial) oculo(dermal) melanocytosis in 89 eyes. *Ophthalmology*. 2011;118(12):2474-2479.

6. Shields CL, Kaliki S, Livesey, M, et al. Oculo(dermal) melanocytosis is associated with higher rate of uveal melanoma metastasis. 2012; Submitted for publication.