

Metastases From Small Choroidal Melanoma: Facts and Figures

BY MELISSA MURPHY; NINA NI, MD; AND CAROL L. SHIELDS, MD

The differentiation of small choroidal melanoma from nevus can be challenging. Despite the minute size, small choroidal melanoma can carry substantial risk for metastatic disease and death. The larger the tumor is the greater the risk for death. In this report, we illustrate a striking case of a small melanoma, one that could have easily been misconstrued for a choroidal nevus, that lead to the death of a patient within 4 years of diagnosis.

CASE PRESENTATION

A white woman aged 58 years presented with nasal visual acuity loss in her right eye. Her past medical history was unremarkable and she reported no family history of malignancies. On ocular examination, best corrected visual acuity was 6/21 in her right eye and 6/6 in her left eye. External and slit-lamp examinations were within normal limits in both eyes. Fundoscopy in her right eye revealed an oval-shaped melanocytic choroidal lesion in the macular region measuring 7 x 7 mm in basal dimen-

sions and 2.5 mm in thickness, with an acoustically hollow appearance on ultrasonography. There was associated subretinal fluid and overlying orange pigment (Figure 1A). These findings were consistent with a small choroidal melanoma.

The patient was treated with 125I plaque brachytherapy with 7811 centigray to the apex of the lesion and 18626 centigray to the base over a period of 94 hours, followed by transpupillary thermotherapy (TTT) consolidation post plaque removal. In the subsequent 3 years, she received eight more sessions of TTT for marginal recurrence of the melanoma. Complete regression of the tumor to an atrophic scar 3 years after initial diagnosis was noted (Figure 1B). Despite primary tumor control, routine computed tomography (CT) several months later revealed multiple hypoattenuating lesions throughout the liver, confirmed by biopsy to be uveal metastases.

The liver metastases were treated with four cycles of immunoembolization with granulocyte-macrophage colony-stimulating factor, four cycles of chemoemboliza-

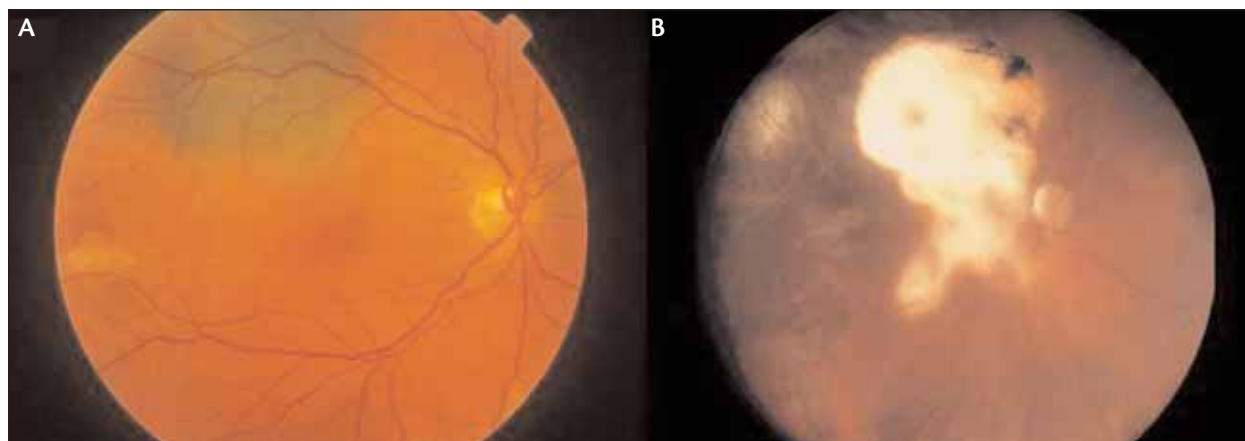


Figure 1. A white woman aged 58 years presenting with visual deficit in the right eye secondary to small choroidal melanoma. Fundus photograph of the right eye showing a small choroidal melanoma measuring 7 x 7 mm in diameter and 2.5 mm in thickness and with overlying orange pigment and subretinal fluid (A). Fundus photograph of the same eye following plaque radiotherapy and TTT showing local tumor control at 30-month follow up (B).

TABLE 1. RISK FACTORS ASSOCIATED WITH METASTASES FROM SMALL CHOROIDAL MELANOMAS.⁵

Clinical Feature	% Metastases with Feature	Relative Risk	P Value
Thickness (0-0.1 mm vs 1.1-3.0 mm)	5	8.8	0.004
Growth (absent vs present)	11	3.2	0.003
Posterior margin of tumor (not touching disc versus touching disc)	9	2.9	0.003
Symptoms (none vs blurred vision)	5	1.9	0.06

tion with carmustine, and one intrahepatic arterial infusion of fotemustine. The patient continued to experience disease progression despite liver treatments and eventually passed away from metastatic disease 42 months after the initial diagnosis of choroidal melanoma, and 10 months after the discovery of metastases.

DISCUSSION

Choroidal melanoma is the most common intraocular malignancy in adulthood, with an age-adjusted incidence of six cases per 1 million annually in the United States.¹ Metastases can arise from melanomas of every size. Shields and colleagues evaluated 8,033 eyes with uveal melanoma and found that rates of metastasis for small melanomas up to 3.0 mm in thickness were 6%, 12%, and 20% at 5, 10, and 20 years, respectively.² In comparison, medium melanomas (3.1-8.0 mm) were associated with metastatic rates of 14%, 26%, and 37%, and large melanomas (>8 mm) with metastatic rates of 35%, 49%, and 67%.² Although several local treatments are effective in controlling the primary malignancy, survival rates from secondary metastases are grim with a median survival rate of approximately 6 months.³

With regard to improving patient outcomes, distinguishing benign choroidal nevi from lesions with risk factors for growth and metastasis is critical. Risk factors predictive of growth of a nevus into a melanoma can be recalled by the mnemonic TFSOM (To Find Small Ocular Melanoma), whose letters indicate Thickness >2 mm, subretinal Fluid, Symptoms, Orange pigment, and Margin <3 mm from the optic disc.⁴ For small choroidal lesions, the best independent predictors of metastases are tumor

thickness (>1 mm), tumor growth, posterior margin touching the optic disc, and symptoms of blurred vision (Table 1). According to the same study, the two risk factors of tumor thickness and symptoms, as seen in our patient, was associated with an 8% risk of metastases.⁵

Management of these malignant lesions is directed to offer best prognosis. Certain small melanomas may be managed with laser photocoagulation or TTT alone. For medium-sized melanomas, a recent Collaborative Ocular Melanoma Study (COMS) report showed that 125I brachytherapy and enucleation are associated with similar rates of metastases at 12 years.⁶ As choroidal melanomas most commonly metastasize to the liver (91%), lung (28%), and bone (18%),³ it is also important that patients have systemic follow-up with a combination of screening modalities including liver function tests and chest and abdominal imaging. The patient presented in this article illustrates the importance of continuing regular systemic evaluation even after the primary tumor has regressed.

Over recent years, the detection of small uveal melanomas has increased and hopefully will ultimately lead to improvement in survival rates.⁵ Careful surveillance of all choroidal melanocytic lesions for the above outlined red flags followed by prompt treatment may represent an important step toward the much anticipated improvement in patient outcomes. ■

Support provided by the Retina Research Foundation of the Retina Society in Cape Town, South Africa (CLS) and the Eye Tumor Research Foundation, Philadelphia, PA (CLS).

Melissa Murphy is a medical student at Trinity College in Dublin, Ireland.

Nina Ni, MD, is a recent graduate from Yale School of Medicine in New Haven, CT.

Carol L. Shields, MD, is the Co-Director of the Ocular Oncology Service, Wills Eye Institute, Thomas Jefferson University. She is a Retina Today Editorial Board member. Dr. Shields can be reached at +1 215 928 3105; fax: +1 215 928 1140; or via e-mail at carol.shields@shieldsoncology.com.

The authors have no financial interests to disclose.



1. Shields JA, Shields CL. Posterior Uveal Melanomas: Clinical Features. In: Shields JA, Shields CL. *Intraocular Tumors: A Text and Atlas*, 2nd ed. Philadelphia, PA: Lippincott Williams and Wilkins, 2008;86.
2. Shields CL, Furuta M, Thangappan A et al. Metastasis of uveal melanoma millimeter by millimeter in 8033 consecutive eyes. *Arch Ophthalmol*. 2009;127:989-998.
3. Diener-West M, Reynolds SM, Agugliaro DJ, et al. Screening for metastasis from choroidal melanoma. *J Clin Oncol*. 2004;22:2438-2444.
4. Shields CL, Furuta M, Berman EL, et al. Choroidal nevus transformation into melanoma. *Arch Ophthalmol*. 2009; 127:981-987.
5. Shields CL, Shields JA, Kiratli H, et al. Risk factors for growth and metastasis of small choroidal melanocytic lesions. *Ophthalmology*. 1995;102:1351-1361.
6. Collaborative Ocular Melanoma Study Group. The COMS randomized trial of iodine 125 brachytherapy for choroidal melanoma. *Arch Ophthalmol*. 2006;124:1684-1693.