Find Melanoma Early, Save a Life

The challenge is to identify small melanoma using known clinical risk factors.

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Early detection and treatment of choroidal melanoma are crucial for patient survival. Damato et al evaluated 3072 patients with choroidal melanoma from the Liverpool Ocular Oncology Center and found a mean tumor basal diameter of 12.1 mm and mean thickness of 4.1 mm. They observed that patients who were younger at the time of treatment tended to have smaller and less extensive tumors with a lower degree of malignancy and better prognosis. They concluded that treatment when the tumor is small can prevent melanoma growth, dedifferentiation, and metastatic disease. This important report underscored the impact of early detection and treatment of choroidal melanoma.

The challenge in detection of early melanoma is to distinguish it from benign choroidal nevi, which can be the same size, color, and appearance, but which remain stable. Medium and large choroidal melanoma can be recognized readily with ophthalmoscopy and ultrasoundography, but the real challenge is to identify small melanoma using known clinical risk factors. The hope with early detection and treatment is to avoid micro-metastatic disease to the liver and lungs that can often precede detection of intraocular melanoma. Shields et al evaluated 8033 eyes with uveal melanoma at Wills Eye Hospital, Philadelphia, and found that increasing tumor thickness was significantly associated with a higher risk of metastasis. These authors suggested that recognition and treatment of melanoma when small, with thickness of less than 3.0 mm—or, better yet, less than 2.0 mm—is ideal for avoiding metastasis.

We describe a case of a small choroidal melanoma referred with the diagnosis of choroidal nevus but imaging features strongly suggesting melanoma.

CASE REPORT

A 72-year-old white woman noted blurred vision inferiorly in the left eye over 3 months (Figure). Medical history was remarkable for breast cancer that was treated with bilateral mastectomy and chemotherapy. Metastatic disease was absent.

On ophthalmic examination, visual acuity was 20/20 in the right eye and 20/30 in the affected left eye. Intraocular pressures and anterior segment examination were normal in each eye. The right fundus appeared normal. Fundus examination of the left eye showed a small, variably pigmented choroidal lesion, located superotemporal to the optic disc. The lesion measured 7.0 mm in diameter and demonstrated a central pigmented portion surrounded by an amelanotic, barely visible rim. Overlying shallow subretinal fluid and orange pigment were clinically suspected. On fundus autofluorescence, hyperautofluorescence of orange pigment on the tumor surface was confirmed.

Enhanced-depth imaging optical coherence tomography (EDI-OCT) revealed shallow subretinal fluid without evidence of retinal edema or degeneration. A slightly elevated choroidal mass with homogeneous appearance, deep optical shadowing, and compression of normal choroidal vascular structures was apparent deep in the retinal pigment epithelium. On EDI-OCT, the mass measured 7.0 mm in basal diameter, and thickness was estimated to be 1.2 mm. Ultrasonography demonstrated a thin, hollow choroidal mass measuring 2.0 mm in thickness (combined retina and choroid) and without extracocular extension.

From these findings, a diagnosis of small choroidal melanoma was suspected due to the presence of seven out of eight risk factors predictive of small choroidal melanoma. These factors included presence of subretinal fluid, associated symptoms, lesion location within 3.0 mm of the optic disc, ultrasonographic hollowness, absence of drusen, and absence of halo. The only risk factor that was lacking was tumor thickness greater than 2.0 mm. With seven risk factors, each weighing in at an approximate relative risk of 3, this patient carried a substantial risk for the mass to grow into a larger mass. The patient was presented with management options including a period of observation for documentation of growth or intervention with transpupillary thermotherapy, iodine-125 plaque radiotherapy, or enucleation. After discussion of these options, plaque treatment was...
selected. A custom-fit, notched iodine-125 radioactive plaque with a posteriorly loaded radiation field measuring 11 mm on a gold plaque of 15 mm was provided. The tumor apex received a total radiation dose of 7000 cGy over 94 hours. The patient was advised to continue systemic monitoring for metastatic disease with physical examination and liver function tests twice yearly, plus magnetic resonance imaging and chest radiographs yearly.

**DISCUSSION**

This was a particularly challenging case that highlighted the importance of distinguishing choroidal melanoma from choroidal nevus. Despite often similar size, color, and configuration of nevus and melanoma, melanoma tends to manifest signs of activity such as lipofuscin (orange pigment) and fresh subretinal fluid with intact photoreceptors that appear shaggy, presumably from macrophages aligning on the posterior retinal surface. More chronic fluid generally shows photoreceptor retraction (stalagmite appearance) or complete loss of photoreceptors (cleft appearance).

Distinguishing small choroidal melanoma from nevus depends largely on the presence of associated clinical risk factors. In an analysis of 2514 consecutive cases of choroidal nevus, most referred under suspicion for small melanoma and managed at an ocular oncology service, documented growth was detected overall in 180 cases (7%). Using Kaplan-Meier estimates, growth was detected in 8.6% of those followed 5 years and 12.8% of those followed 10 years. A mnemonic was devised to assist in remembering clinical features that suggest small choroidal melanoma as follows: “To Find Small Ocular Melanoma Using Helpful Hints Daily” (TFSOM-UHHD) where:

- **T** = Thickness of tumor greater than 2.0 mm;
- **F** = Fluid subretinal;
- **O** = Orange pigment overlying the tumor;
- **M** = Margin of tumor 3.0 mm or less to the optic disc;
- **UH** = Ultrasound hollow;
- **H** = Halo absent; and
- **D** = Drusen absent.

In this case, the patient demonstrated seven of the designated risk factors, and the eighth factor of thickness over 2.0 mm was borderline. The calculated relative risk for this patient, based on published results (drusen not included) was $3 \times 2 \times 3 \times 2 \times 3 \times 6 = 648$ times greater chance for growth compared with a lesion without these risks.

Based on an analysis regarding the power of various combinations of risk factors using the five initial risk factors (TFSOM), the relative risk for growth was 1.9 if only one factor was present, 3.8 if two factors, 7.4 if three factors, 14.1 if four, and 27.1 if all five factors were present. Specific combinations of factors were found to portend better or worse prognosis. For example, small choroidal melanocytic lesion with the combination of thickness greater than 2.0 mm, subretinal fluid, and orange pigment was found to be associated with tumor growth in 40% of cases at 5 years. The worst combination of factors was thickness greater than 2.0 mm, symptoms, and (Continued on page 41)
margin near the optic disc, which led to growth in 69% of cases at 5 years.\(^5\)

Melanoma prognosis depends on several factors, including tumor size and genomic alterations. Shields et al studied 8033 patients with uveal melanoma and noted that increasing tumor thickness correlated with Kaplan-Meier analysis, in that each millimeter increase in tumor thickness was associated with a 5% increased risk for metastasis.\(^4\) Damato et al assessed a cohort of 452 patients with choroidal melanoma who had genetic testing and found that chromosomal aberrations accumulated with tumor growth, likely predisposing the patient to higher risk for metastasis.\(^7\) Both reports emphasized the importance of tumor detection at an early point when the tumor is small, even less than 1.0 to 2.0 mm, as in the case presented here.

**CONCLUSION**

We have described a patient with a small symptomatic choroidal melanoma, which was best detected by autofluorescence and OCT. Early detection while the tumor was small allowed the patient to receive prompt treatment while hopefully still at low risk for systemic metastasis.

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