Choroidal and Retinal Tumors in Adults: Choroidal Melanocytic Lesions

Part two of a four-part series on guidelines for diagnosing and treating ocular lesions.

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In the first article of this series (Choroidal and Retinal Tumors in Adults: Vascular Tumors of the Retina, June 2011, page 76), we discussed vascular tumors of the retina. In this second article, we describe the clinical features, diagnosis, and treatment of three types of choroidal melanocytic lesions.

CHOROIDAL NEVUS

Choroidal nevus (Figure 1), the most common primary intraocular tumor,1 is a benign tumor that arises from melanocytic cells derived from the neural crest. Choroidal nevi are more common in white people, with 4% of the population having at least one.1 Malignant transformation into melanoma is possible; therefore, choroidal nevi should be monitored even though the rate is 1 in 4,000.2 As noted below, certain risk factors are associated with a higher risk of transformation.

Clinical features. Most choroidal nevi are congenital, but they usually do not become pigmented and clinically detectable until after childhood. They can be pigmented, amelanotic, or partially pigmented. Although the majority of choroidal nevi are asymptomatic, approximately 11%, either subfoveal or located near the fovea, become symptomatic later due to subretinal fluid and choroidal neovascularization.3

Diagnostic approaches. There is little difference in the diagnostic and prognostic values of fluorescein angiography (FA) or indocyanine green (ICG) angiography. Choroidal nevi can vary from hypo- to hyperfluorescence. Most benign choroidal nevi do not have prominent intralesional blood vessels, whereas most choroidal melanomas do. Fundus autofluorescence (FAF) is useful because it detects orange pigment, one of the most relevant risk factors for a growing tumor.4 Ultrasound can be used for baseline thickness measurements and to determine acoustic hollowness, a prognostic factor that is associated with the nevus possibly being malignant.

Differential diagnoses. The differential diagnoses of choroidal nevus include choroidal melanoma, metastatic carcinoma, choroidal hemangioma, choroidal osteoma, schwannoma, subretinal or suprachoroidal hematoma, congenital hypertrophy of the retinal pigment epithelial (RPE) cells, and reactive hyperplasia of the RPE.

Management. Asymptomatic choroidal nevus does not require treatment. In symptomatic cases with choroidal neovascularization or subretinal fluid, laser photocoagulation, photodynamic therapy, or transpupillary thermotherapy can be used; however,
these cases should be referred to a specialist because they are often symptomatic due to malignant transformation.\textsuperscript{5} All lesions should be monitored for early detection of malignant transformation. Clinical factors that are statistically predictive of growth of choroidal melanocytic tumors include thickness greater than 2 mm, subretinal fluid, presence of symptoms, orange pigment, tumor margin within 3 mm of the disc, hollowness on ultrasonography, lack of halo, and lack of drusen.\textsuperscript{5-8} Patients with choroidal nevi showing no risk factors should initially be examined every 12 months. Those with one or two risk factors should be monitored every 4 to 6 months. Patients with three or more risk factors should be evaluated at a reputable center for management alternatives and possible treatment because of the high risk of ultimate malignant transformation.\textsuperscript{6}

**MELANOCYTOMA**

Melanocytoma is an unusual congenital and non-hereditary variant of melanocytic nevus that is classically located on the optic disc.\textsuperscript{9} Usually there is a surrounding peripapillary choroidal nevus. Melanocytoma can also be located in the iris, ciliary body, or choroid. It is usually composed entirely of maximally pigmented, polyhedral nevus cells. Melanocytoma is, by definition, never amelanotic.

**Clinical features.** The mean age at diagnosis is 50 years, and melanocytoma does not appear to have a predilection for lightly pigmented races.\textsuperscript{10} Melanocytoma is almost always unilateral and appears as a dark brown to black lesion, affecting the optic disc and the peripapillary area. Optic disc melanocytomas have feathery edges that extend along the nerve fiber layers. Malignant transformation is uncommon. Ocular melanocytosis can be seen in patients with melanocytoma, especially in more pigmented individuals. But melanoma is also more common in persons with melanocytosis, so careful evaluation by an expert is indicated.

**Diagnostic approaches.** FA typically shows hypofluorescence of the lesion, but it is not very useful for differentiating melanocytoma from melanoma.

**Differential diagnoses.** Uveal nevi and melanomas are the main differential diagnoses.

**Management.** Fundus photography and clinical evaluation must be done once or twice a year, as malignant transformation into a melanoma is rare but possible.\textsuperscript{11}

**POSTERIOR UVEAL MELANOMA**

Posterior uveal melanoma is the most common primary malignant intraocular neoplasm in adults.\textsuperscript{12} It arises from melanocytes in the posterior uveal tract. These lesions can be pigmented, amelanotic, or partially pigmented. It is believed that uveal melanomas can arise from preexisting nevi. Early detection and treatment of uveal melanoma when the malignancy is small may reduce the risk for metastasis and increase survival.\textsuperscript{13}

Many of these tumors arise from mutations in the GNAQ pathway. This is different from skin melanomas, many of which arise from mutations in the BRAF pathway. Additionally, there are two forms of uveal melanoma, one which has monosomy 3 by fluorescence in situ hybridization (FISH) analysis and class 2 by mRNA analysis, and another which has disomy 3 by FISH and class 1 by mRNA analysis. Monosomy 3 class 2 melanomas have a high probability of developing metastases, and disomy 3 class 1 melanomas have a very low tendency to metastasize. The more malignant class 2 type is associated with braca associated protein-1 mutations.

**Clinical features.** Clinically, class 1 and class 2 appear the same; class 2 lesions tend to be thicker and more anterior in location, but only biopsy can distinguish the two types.\textsuperscript{14} Ciliary body melanoma is usually a dome-shaped mass associated with external signs such as sentinel vessels or an epibulbar pigmented lesion, which is a sign of extrascleral extension.\textsuperscript{15} Erosion into the anterior chamber via the iris root can be seen by gonioscopy
TAKE-HOME MESSAGE

- Choroidal nevus is a benign tumor that can transform into melanoma. Choroidal nevi, either subfoveal or located near the fovea, may become symptomatic due to subretinal fluid and choroidal neovascularization.
- Melanocytoma is classically located on the optic disc but can also be found in the iris, ciliary body, or choroid.
- Posterior uveal melanoma arises from melanocytes in the posterior uveal tract.

and in advanced cases by direct slit-lamp examination. Ciliary body melanoma can also be diffuse, presenting as a ring melanoma with raised intraocular pressure (IOP). Thus, ciliary body melanoma must be ruled out in the presence of iris heterochromia and unilateral raised IOP in heavily pigmented eyes. Choroidal melanoma (Figure 2) usually presents as a solitary, dome-shaped or sessile tumor, although multicentric lesions can occur. Prominent clumps of orange pigment are frequently present. Exudative retinal detachment and tumor-associated retinal pigment epitheliopathy can lead to vision loss.16

Diagnostic approaches. Ultrasound A- and B-scans usually reveal a solid dark mass with low internal reflectivity and characteristic hollowness. FA and ICG usually reveal prominent intrascleral blood vessels. FAF is useful to highlight the presence of lipofuscin. Computed tomography (CT) and magnetic resonance imaging (MRI) are occasionally used to image uveal melanomas, although the technology is not specific or sensitive. CT shows pronounced contrast enhancement, and MRI shows a mass hyperintense in T1 and hypointense in T2. When positron emission tomography (PET) is done to determine the presence of clinical metastases, the primary medium and large uveal melanomas can sometimes be fluorodeoxyglucose (FDG) avid as well. Early detection of choroidal melanoma is crucial. The risk factors for growth and metastases are discussed in the nevus section above.

Differential diagnoses. Differential diagnoses of uveal melanomas includes choroidal nevus, metastatic carcinoma to the choroid, choroidal lymphoma, exudative age-related macular degeneration, subretinal or suprachoroidal hematoma, choroidal hemangioma, posterior nodular scle- 

lary thermotherapy, charged particle radiation, plaque brachytherapy, other radiation methods such as stereotactic radiosurgery, gamma-knife and cyberknife methods, local resection, enucleation, orbital exenteration, and combinations of these options.17 Plaque brachytherapy is the most commonly used option. An oculon- colist should decide what procedure should be done.

CONCLUSION

Subsequent installments in this series will examine choroidal metastases, intraocular lymphomas, vascular tumors of the choroid, and other tumors. ■

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