# Leading Simulators of Choroidal Melanoma

BY WILLIAM R. SHIELDS; AND CARLOS G. BIANCIOTTO, MD

Each year in the United States, approximately 2,500 patients diagnosed with uveal melanoma. This life-threatening malignancy represents the second most common primary site for melanoma, after cutaneous melanoma. Uveal melanoma leads to metastasis and death in approximately 40% of patients on long-term follow-up, so accuracy of diagnosis and proper management are important.[1] Not all patients referred to an ocular oncology center for the diagnosis of melanoma, however, actually have melanoma. In reality, referral for pseudomelanoma is not uncommon, and a recent report described 1,739 patients sent to an oncology center for the management of melanoma, were found to have a simulating lesion rather than melanoma.[2] Herein, we report an elderly Asian woman with one of the more common pseudomelanomas.

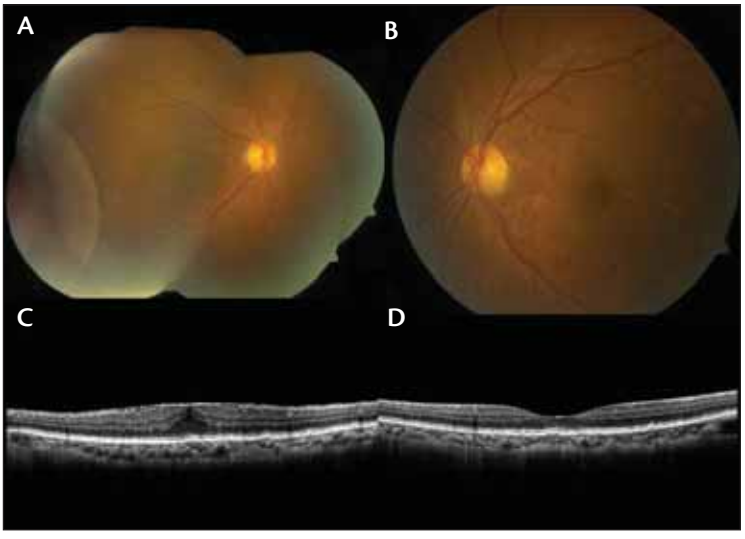


**Figure 1. Color fundus montage of the right eye (OD) showing a dome-shaped temporal mass with associated drusen near the fovea (A). Color fundus photograph of the left eye (OS) depicting drusen temporal to the fovea (B). Optical coherence tomography (OCT ) shows an epiretinal membrane OD (C). OCT with a normal foveal contour OS (D).**

## CASE DESCRIPTION

An Asian woman, aged 69 years, presented with a 10-day history of photopsia and floaters in the right eye. Ophthalmic evaluation disclosed a pigmented tumor in the right eye, and the patient was urgently referred for treatment of "choroidal melanoma."

Upon referral, history revealed that the symptoms were preceded by severe vomiting from gastric upset. The patient had no previous ocular history. Medical history revealed non-insulin–dependent diabetes mellitus, hypertension, hypothyroidism, and congestive heart failure. Medications included daily aspirin (81 mg). At presentation, visual acuity was 20/40 in the right eye and 20/25 in the left eye. The anterior segment was unremarkable in both eyes. Fundus examination of the right eye demonstrated a dome-shaped pigmented subretinal mass located temporally and measuring 12 mm in diameter and 5 mm in thickness (Figure 1). There was overlying subretinal fluid and there were no signs of orange pigment (lipofuscin). Macular drusen were present, and diffuse peripheral retinal pigment epithelial (RPE) changes were found in both eyes. Fundus examination of the left eye disclosed additionally two focal retinal hemorrhages of 1 mm in diameter and located in the inferotemporal periphery. There was no visible scarring from previous macular degeneration, trauma, or polypoidal choroidal vasculopathy. B-scan ultrasonography of the right eye depicted an acoustically hollow mass without spontaneous vascular pulsations, and medium to low internal reflectivity on the A-scan. Optical coherence tomography (OCT) showed an abruptly elevated mass in the right eye with no visibility of the underlying RPE or choroid due to optical shadowing. A coincidental epiretinal membrane was noted in the right eye. Fluorescein angiography (IVFA) revealed a markedly hypofluorescent mass in the right eye, deep to the retina, and nonfluorescence in all phases, strongly sugges-

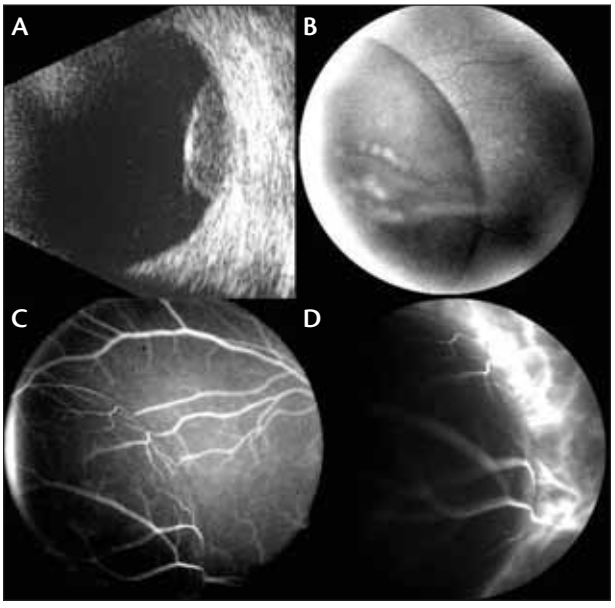


**Figure 2. B-scan ultrasound showing acoustic hollowness of the lesion with a dome-shaped configuration (A). Autofluorescence OD with hypofluorescence at the level of the mass (B). Fluorescein angiogram OD in the arteriovenous phase demonstrating hypofluorescence of the lesion temporally without intrinsic vascularity (C). Late phase of indocyanine green angiography with marked hypofluorescence (D).**

tive of subretinal or sub-RPE hemorrhage. Indocyanine green (ICG) angiography showed nonfluorescence and no sign of polypoidal choroidal changes (Figure 2). Our diagnosis was subretinal hemorrhage from Valsalva retinopathy vs peripheral exudative hemorrhagic chorioretinopathy in an elderly Asian woman. To more definitively confirm the lack of melanoma, fine needle aspiration biopsy (FNAB) for cytologic analysis was performed using a 27-gauge needle through a pars plana approach. At the time of biopsy, the mass showed immediate collapse to 20% of its original size, suggestive of blood removal. Cytology confirmed red blood cells only, with no malignancy.

## DISCUSSION

Pigmented tumors deep within the retina can represent an assortment of benign or malignant neoplastic conditions such as choroidal nevus, choroidal melanoma, cutaneous melanoma metastasis to the choroid, hemorrhagic choroidal tumors, RPE tumors, and others.[1-3] In addition, non-neoplastic conditions can manifest as a pigmented subretinal mass, most often hemorrhage under the retina, under the RPE, and within the choroid.[4] In such cases, it is important to understand the underlying reason for hemorrhage, whether it be trauma, blood dyscrasia, macular degen-

**TABLE 1. LEADING SIMULATORS OF CHOROIDAL MELANOMA.***

| Types of Pseudomelanoma | Number (%) of All Patients with Pseudomelanoma |
|---|---|
| Choroidal nevus | 851 (49%) |
| Peripheral exudative hemorrhagic chorioretinopathy | 139 (8%) |
| Congenital hypertrophy of the retinal pigment epithelium (RPE) | 108 (6%) |
| Retina or RPE hemorrhagic detachment | 86 (5%) |
| Circumscribed choroidal hemangioma | 79 (5%) |
| Age-related macular degeneration | 76 (4%) |
| RPE hyperplasia | 42 (2%) |
| Optic disc melanocytoma | 37 (2%) |
| Choroidal metastasis | 34 (2%) |
| Choroidal detachment hemorrhagic | 29 (2%) |
| Total number of pseudomelanomas | 1739 |

* Information gathered from Shields JA, Mashayekhi A, Ra S, Shields CL. Pseudomelanomas of the posterior uveal tract: The 2006 Taylor R. Smith Lecture. *Retina.* 2005;25(6):767-771.

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eration, polypoidal choroidopathy, retinal macroaneurysm, Valsalva retinopathy, or other conditions.[1-4]

The management of uveal tumors begins with an accurate diagnosis.[1-3] The treatment of choroidal malignant melanoma is far different from the management of a benign nevus or subretinal hemorrhage.[1-4] Furthermore, patient prognosis can be markedly threatened with melanoma but not with nevus or most other benign conditions. Hence, the clinician should be confident of the diagnosis before embarking on therapy. [5]

Past studies, with less experienced clinicians and more rudimentary imaging equipment, revealed that eyes with pseudomelanoma were occasionally unnecessarily enucleated.[2-3] More recent studies have shown that mistaken enucleation at experienced ocular oncology centers is now rare.[1,6] However, the problem of pseudomelanoma still exists in the general ophthalmic community, as shown in this case and in published reports.[1-4]

In 2005, a review of 12,000 patients referred for presumed uveal melanoma disclosed that 1,739 (14%) were found to have pseudomelanoma with inaccurate referral diagnosis.[2] Fortunately, that large group of pseudomelanomas were spared treatment, as the diagnosis was established as pseudomelanoma by experienced clinicians before melanoma therapy was instituted. In that group of pseudomelanomas, there were 54 different conditions that simulated melanoma. The most common simulators were choroidal nevus (n=851 cases; 49%), peripheral exudative hemorrhagic chorioretinopathy (n=139; 8%), congenital hypertrophy of the retinal pigment epithelium (n=108; 6%), hemorrhagic detachment of the retina or RPE (n=86; 5%), circumscribed choroidal hemangioma (n=79; 5%), and age-related macular degeneration (n=76; 4%) (Table 1).[2]

The problem of pseudomelanoma can challenge any clinician, and, in this case, the referring physician was an experienced, well-trained retina specialist. Also in this case, the salient features suggestive of melanoma included the pigmented appearance, dome-shaped configuration, and acoustic hollowness on B-scan ultrasound. However, there were important features that were much less consistent with melanoma, including the patient's Asian background, abruptly elevated mass with crisp margins, lack of dependent subretinal fluid, lack of spontaneous vascular pulsations on B-scan ultrasonography, and the lack of fluorescence on both IVFA and ICG. The definitive confirmation of nonmelanoma was made on FNAB.[5]

There are several diagnostic tools for evaluation of choroidal melanoma to assist the clinician in achieving an accurate diagnosis. The most important tool is experienced recognition of the salient and subtle features of melanoma and pseudomelanoma with indirect ophthalmoscopy. Other tools for confirming melanoma include transillumination shadowing, ultrasonographic hollowness on B-scan and low internal reflectivity on A-scan, ultrasonographic visibility of intrinsic vascular pulsations, IVFA evidence of intrinsic tumor vascularity, OCT evidence of subretinal fluid, autofluorescence findings of activated bright lipofuscin, and magnetic resonance imaging with enhancement of solid tumor. Despite these tools, uveal melanoma and pseudomelanoma can display atypical presentations, rendering the differentiation challenging. In these cases, FNAB can definitively establish the diagnosis.[5] ■

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