An 81-year-old White woman reported to our office with a complaint of vision worsening in her left eye for a duration of 2 months. She noticed that her left eye had also become slightly more light-sensitive, accompanied by a mild dull ache from inside her eye.

BCVA was 20/25+2 OD and 20/400 OS. Anterior segment examination revealed sectoral injection of the superior to superotemporal conjunctival vessels of the left eye.

It was apparent that the iris root was pulled away from its normal limbal insertion (Figure 1). Further examination of the iris root suggested strongly that the ciliary body had proliferated enough to displace the iris at the root and the ciliary body proliferations had begun to fill the angle. Gonioscopy revealed an atypical superior temporal angle with a large brown mass between the iris and the choroid 0.5 mm nasally (Figure 2).

Dilated fundus evaluation revealed a posterior IOL displaced slightly inferonasally and a large melanoma of what seemed ciliary body in origin. Sentinel vessels were apparent in the superior to superior temporal quadrant of the episclera, especially apparent after other vessels were blanched with phenylephrine instillation. The melanoma extended posteriorly with maximum diameter of about 10.2 mm on B-scan ultrasound (Figure 3). Peripheral retinal evaluation also revealed an associated serous retinal detachment.

**DIAGNOSIS AND MANAGEMENT**

The patient was diagnosed with a ciliary body–based melanoma and referred urgently to retinal oncology. The mass was further classified as an iridociliochoroidal melanoma after fine needle biopsy. The patient was scheduled for enucleation and additional workup for metastases.

No evidence of metastatic disease was found within the chest, intrapelvic or intraabdominal areas on CT imaging. Complete blood count (CBC) and differential, comprehensive metabolic panel, and lactate dehydrogenase were all within normal ranges.

Histologic analysis was performed on the enucleated eye (Figure 4). Spindle-shaped melanocytes comprised the majority of the tumor, with rare epithelioid cells. Lymphocytic infiltration was present. The tumor did not break through the sclera. A central cavitation indicated that necrotic changes were starting. Light microscopy also revealed invasion of the iris root, trabecular meshwork, melanocytes, and macrophages in the trabecular meshwork opposite the primary tumor site.
The timeline of this case from the first appointment to enucleation was 7 days: initial detection, diagnosis, referral to a retinal physician who specializes in ocular oncology, consultation, oncology workup, and enucleation. Within 13 days of the initial appointment, the pathology department had completed its assessment of the specimen and other testing.

**DISCUSSION**

The uveal tissue of the eye consists of three structures: iris, choroid, and ciliary body. Choroidal melanomas represent 85% of uveal melanomas, 10% are ciliary body, and 5% iris tissue. Extrapolating from known incidence of ocular tumors, a ciliary body–based melanoma has a US incidence of about one in 1 million persons per year.

**Testing**

Initial testing for metastases includes liver panels, CBC with differential, and chest x-ray. If any of these are abnormal, further testing, such as liver ultrasound, and PET/CT scan or MRI of the chest and abdomen, is required. It is not uncommon to order this entire battery of tests as soon as a suspicious lesion is detected. Fine-needle biopsy may be used transsclerally to confirm the presence of a malignancy.

**Differential Diagnoses**

Differential diagnosis for choroidal melanoma should include choroidal hemangioma, choroidal metastases, choroidal osteoma, choroidal neurofibroma, peripheral melanocytoma, benign lymphoid tumor, extramacular disciform lesion, posterior scleritis, localized choroidal detachment with hemorrhage, congenital hypertrophy of retinal pigment epithelium (RPE) cells, RPE hyperplasia, RPE window defect, hemorrhagic retinal detachment, retinoschisis.

**Risk Factors**

Common risk factors for choroidal melanoma include White race of Eastern European decent, light iris color, blond hair, oculodermal melanocytosis, genetic factors, and occupational associations. Unlike with cutaneous melanomas, evidence regarding sunlight exposure sparking melanotic growth is weak at best. Race seems to prevail as the most significant risk factor, as uveal melanomas are reported to be 150 times more common in Whites than in Blacks. About two-thirds of uveal melanomas arise in Whites of European descent, who comprise only 13% of the global population.

**AT A GLANCE**

- Intraocular melanomas are rare in everyday practice, but it is important to understand their incidence, origin, morphology, treatment methods, and overall outcomes.

- Diagnosis of choroidal melanoma can be facilitated by B-scan ultrasound, blood work, fine-needle biopsy, and other imaging techniques.

- Efficient, integrated medical care is essential in caring for patients with choroidal melanoma.
Patients with choroidal melanomas are symptomatic 75% of the time, with flashes, floaters, or decreased visual quality as their main symptoms.\textsuperscript{6} Uveal melanomas are increasingly prominent in an aging population, with peak incidence at around 70 years. At this age, the incidence jumps to 24.3 per million for men and 17.8 per million for women. Less than 1% of uveal tumors are found in individuals less than 20 years old.\textsuperscript{2}

Small malignant melanomas of the uveal tissue can be difficult to differentiate from benign nevi clinically. Colors may range anywhere from a lighter off-white to a dark brown to black, including greens, oranges, and yellows.\textsuperscript{3}

**Prognosis**

Ciliary body tumors often have a poorer prognosis than choroidal tumors, which may be due to delayed diagnosis. Ciliary body melanomas can invade the anterior chamber, causing seeding and in some cases iris heterochromia.\textsuperscript{5} The 5-year survival rate of ciliary body melanoma is hard to determine due to the rarity of the lesion.\textsuperscript{7} For anyone with a metastatic uveal melanoma, survival rates are poor, with a median of less than 6 months.\textsuperscript{8}

The 5-year survival rate is 84% for small choroidal melanoma, 68% for medium, and 47% for large.\textsuperscript{7}

Ciliary body melanomas commonly present as elevated dark brown lesions seen on peripheral fundus examination. Associations include sentinel episcleral vessels, segmental cataracts, IOL displacement, and in some cases extension into the sclera. Anterior segment photography, along with ultrasound biomicroscopy, can aid in determining size, location, color, surface characteristics, depth, and vascularity.\textsuperscript{4}

A key prognostic factor is cell typing using the Callender classification system.\textsuperscript{9} In this system, as modified by McLean et al in 1978, tumor cells are histologically classified into types and subtypes: spindle A, spindle B, mixed, and epithelioid. Subcategories of tumors are spindle cell nevus, spindle cell melanoma, mixed cell melanoma, and mixed spindle and epithelioid.\textsuperscript{10}

Spindle cell tumors have a better prognosis than those with epithelioid, mixed, or necrotic cells. The 15-year survival rates after enucleation are 100% for spindle cell nevi, 72% for spindle melanomas, and 37% for mixed, epithelioid, and necrotic cell type tumors.\textsuperscript{5}

Using both diameter (largest basal diameter or LBD) and thickness, tumors are graded from 1 to 4.\textsuperscript{4,11} Kaplan-Meier survival estimates can then be derived. Using this grading of LBD and thickness, metastasis rates were two, four, and eight times higher in stages 2, 3, and 4 when compared with stage 1 (Figures 5 and 6).\textsuperscript{11}

Diagnosis of a small ocular melanoma versus a choroidal nevus can be difficult due to many overlapping features. A choroidal nevus, as defined by the Collaborative Ocular Melanoma Study (COMS), is a melanocytic choroidal lesion ≤ 5 mm in largest basal dimension and ≤ 1 mm in apical height.\textsuperscript{12} Anything larger should be classified as a small choroidal melanoma. Choroidal nevi have a prevalence of 4.6% to 7.9% in the US population, according to recent studies.\textsuperscript{13}

A retrospective medical record review including 2,514 referred choroidal nevi suggested a 7% risk of transformation into choroidal melanoma. The same study also suggested risk factors that can be predictive of nevus growth. Factors include thickness > 2 mm, any subretinal fluid, symptoms, orange pigment, nevus margin within 3 mm of the optic disc, ultrasonographic hollowness, absence of halo depigmentation, and absence of drusen.\textsuperscript{14} A nevus with no risk factors showed 3% chance of growth at 5 years, 38% with one risk factor, and 50% with three or more risk factors.\textsuperscript{14}

Other prognostic factors include mitotic activity, extracocular extensions, location (ciliary body tumors worse than choroidal), chromosomal abnormalities, loss of human leukocyte antigen (HLA) expression, size and variability in nucleolar size, necrosis, pigmentation, lymphocytic infiltration, and melanophagic infiltration.\textsuperscript{10}

**Genetics**

Genetically, uveal melanoma can have loss of chromosome 3, 1p, 6q 8, 9p, or gain of 1q, 6p, or...
8q18. Chromosome 3 has been a determining factor, as its loss has been shown to reduce survival rate from 100% to 50%. Gene expression profiling has been used to classify uveal melanoma into class 1 and 2 subtypes. Disomy 3 and gain of 6p make up class 1; whereas monosomy 3, 1, and 8p with a gain of 8q make up class 2. Class 2 gene expression profiles have been associated with poorer prognosis. Monosomy 3 or trisomy 8q have very poor prognosis, whereas loss of HLA-1 expression is deemed to have a better survival rate.

The most prominent gene implicated in a metastatic role in uveal melanoma is BAP1 on chromosome 3. Other genes including SF3B1 and EIF1AX have been associated with better prognosis. Genes that are present in both choroidal melanoma and choroidal nevi are GNAQ and GNA11, but the roles they play in nevi growth and metastasis are uncertain. The 5-year survival rate of ocular melanoma, if the melanoma does not spread outside the eye, is 85%. Largest tumor diameter (LTD) seems to be the best prognostic indicator, just as important as cell type. These prognostic predictions are calculated assuming that the affected eye had already been enucleated. The Table shows survival rates at 5 years, 10 years, and 15 years for all uveal melanomas.

### Treatment
The goal of treatment for choroidal melanoma is to preserve vision and prevent metastasis. Treatment of the primary tumor is guided by size, location, general health of the patient, and patient preference. Therapies for uveal melanomas include brachytherapy, charged-particle radiation therapy, photocoagulation, transpupillary thermotherapy (TTT), photodynamic therapy, photocoagulation, plaque therapy plus hyperthermia, cryotherapy, local resection, and enucleation. If the lesions are small, observation may be indicated.

Most cases in the United States are treated with plaque brachytherapy, although charged-particle radiotherapy, proton beam therapy, and surgical excision have been shown to be effective. Brachytherapy and external charged-particle beam therapy have been used for treatment of small to medium-sized tumors. Regular ocular examination should be performed following brachytherapy to assess for cataract, exudative retinal detachment, radiation retinopathy, papillopathy, and other radiation-induced damage.

Charged-particle radiation therapy is used to treat medium to large tumors that may not be good candidates for brachytherapy. Significantly improved local control, eye preservation, and disease-free progression with charged-particle therapy as compared to iodine-125 in treatment of choroidal or ciliary body melanoma was demonstrated in a randomized trial.

Laser photocoagulation of tumor tissue is associated with a high rate of complications. TTT, using an infrared laser to penetrate the surface of the tumor, is suitable only for small tumors or marginal recurrences following proton therapy.

Transretinal or transscleral local resection can be performed, but complications include retinal detachment, vitreous hemorrhage, local recurrence, and iatrogenic tumor spread. Enucleation was long thought the treatment of choice until the COMS shed light on survival rates for patients with medium-sized tumors who were enucleated and those treated with iodine-125. Vision-sparing treatments should be considered unless, in selected cases, there is little

### Table. A Survival Rates per LTD After Enucleation of the Affected Eye

<table>
<thead>
<tr>
<th>SIZE</th>
<th>DIMENSIONS</th>
<th>5-YR SURVIVAL</th>
<th>10-YR SURVIVAL</th>
<th>15-YR SURVIVAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small</td>
<td>&lt; 11 mm</td>
<td>86%</td>
<td>76%</td>
<td>70%</td>
</tr>
<tr>
<td>Medium</td>
<td>11–15 mm</td>
<td>66%</td>
<td>51%</td>
<td>43%</td>
</tr>
<tr>
<td>Large</td>
<td>&gt; 15 mm</td>
<td>56%</td>
<td>41%</td>
<td>35%</td>
</tr>
</tbody>
</table>

### Common Risk Factors for Choroidal Melanoma Include White Race of Eastern European Decent, Light Iris Color, Blond Hair, Oculodermal Melanocytosis, Genetic Factors, and Occupational Associations.
probability of retaining vision. When enucleation was elected as a first line therapy, however, patients had less anxiety during follow-up visits than patients treated with brachytherapy. The 10-year survival rate was 17% following iodine-125 brachytherapy and 18% following enucleation.

BE AWARE OF WHAT’S RARE

Although intraocular melanomas are rare in everyday practice, it is important to be educated on their incidence, origin, morphology, treatment methods, and overall outcomes. Primary eye care providers should stress to all patient populations the importance of yearly dilated eye examinations.

Systemic workup and monitoring with oncology services should be continued for a lifetime after successful eradication of a choroidal melanoma. Early detection is crucial to discover the conversion of a nevus to melanoma. Efficient, integrated medical care is essential in caring for patients with choroidal melanoma. Understanding basic concepts such as those reviewed here can help to analyze difficult choroidal lesions.