Comment. In our patient, the clinical suspicion of transretinal seeding by a uveal melanoma raised by SD-OCT could be confirmed histologically. Primary choroidal melanoma with retinal perforation and extension into the vitreous (Knapp-Rönne type) is a rare entity occurring in about 1 in 250 of uveal melanomas. Detection of retinal perforation is valuable owing to increased risk of recurrent vitreous hemorrhage after radiotherapy and increased likelihood of rhegmatogenous retinal detachment after transscleral local resection.

However, early recognition of Knapp-Rönne melanoma can sometimes be a clinical challenge because ophthalmoscopic assessment, and even echography with a resolution of approximately 100 µm, might sometimes be too imprecise for imaging of focal retinal perforation. In contrast, conventional OCT produces cross-sectional images with approximately 10-µm resolution for visualization of microstructural alterations in retinal diseases as well as of the overlying retina in choroidal tumors. Recently, SD-OCT technology has improved resolution up to 3.5 µm per pixel.

Using this technique, we could detect spherical bodies in the vitreous and, particularly, adjacent to the tumor apex where the overlying retina was completely obliterated. Although SD-OCT allows no exact differentiation between melanoma cells, melanomacrophages, or clusters of blood cells, our clinical findings presumed a Knapp-Rönne melanoma that could be confirmed histologically.

In the future, SD-OCT might become a helpful tool for clinical detection of vitreous seeding from uveal melanomas.

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Clinical Detection of Melanoma-Associated Spongiform Scleropathy by Ultrasound Biomicroscopy and Its Correlation With Pathological Diagnosis

Ciliary body and choroidal melanoma account for greater than 90% of all uveal melanomas. Extraocular extension is an important prognostic factor in uveal melanoma and has been described in 8% of eyes enucleated in the Collaborative Ocular Melanoma Study. Infiltrating solid tumors may cause cellular and degenerative changes in connective tissue surrounding the tumor, contributing to tumor cell invasion. For these reasons, characterization of scleral changes adjacent to the tumor may be relevant to tumor invasion.

Melanoma-associated spongiform scleropathy (MASS) is a histopathological entity described as an area within the sclera adjacent to a choroidal or ciliary body melanoma where collagen fibers appear to have disintegrated into loose fibers. Melanoma-associated spongiform scleropathy is observed in approximately one-third of eyes with uveal melanoma. Biochemical analyses of MASS show decreased collagen and amino acids and increased glycosaminoglycans and water uptake. This degradation process, mediated by matrix metalloproteinases, may weaken the structural barrier and facilitate local tumor invasion. Alyahya observed MASS in 91% of eyes with tumor invasion, in contrast to 23% of eyes without. We report for the first time the clinical detection of MASS by ultrasound biomicroscopy (UBM) in ciliary body melanoma, with histopathological correlation.

Report of a Case. A 44-year-old man presented with painless decreased vision in the right eye for several months. Visual acuity was 20/25, and on dilated examination a melanocytic ciliochoroidal mass was identified abutting the lens (Figure 1A). Gonioscopy showed a pigmented mass invading the anterior chamber angle (Figure 1B).

B-scan ultrasound showed a large dome-shaped mass involving the ciliary body that measured 5.4 mm in thickness. There were cystic spaces in the lesion. A-scan demonstrated medium reflectivity with a decrescendo pattern. Ultrasound biomicroscopy showed intralesional cavities. The inner one-fourth of the sclera adjacent to the base of the tumor was hypechoic compared with the outer three-fourths of the sclera (Figure 2A). The thickness of the sclera over the lesion was deemed to be normal.

Diagnosis of a medium-sized, malignant, ciliochoroidal melanoma was made, and enucleation was performed. Gross examination showed a pigmented superotemporal ciliary body mass measuring 6 × 9 × 4 mm. The ciliary body melanoma was composed of spindle B and epithelioid melanoma cells, with large cavities containing eosinophilic exudate. Tumor cells were noted in the anterior chamber angle and iris root (Figure 2B) and extended to the inner sclera only. The inner sclera adjacent to the tumor showed a pale staining area relative to E. Kruse, MD
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the outer sclera and neighboring scleral regions (hematoxylin-eosin staining [H-E], Figure 2B). High-power examination showed a feathery appearance of the inner sclera and dot morphology of collagen fibers in contrast to the normal interlacing collagen fiber bundles in the surrounding sclera (H-E, Figure 2C). The diagnosis was ciliary body melanoma with MASS.

Comment. Ultrasound biomicroscopy has been a valuable tool in the detection and management of anterior segment and ciliary body tumors. Careful assessment of UBM characteristics of the tumor-scleral interface enables the detection of intrascleral invasion and small extraocular tumor extension. Owing to the irregular arrangement of its collagen fibrils, the sclera produces ultrasound backscatter that results in uniform high reflectivity. The region of lower reflectivity involving the inner scleral layers adjacent to the tumor corresponded to MASS seen histopathologically. The observed low reflectivity likely relates to loose arrangement of collagen fibrils and increased water content. As MASS is a non-inflammatory degradation process of scleral collagen that may facilitate tumor invasion, this observation may lead to larger studies to assess whether the clinical detection of MASS by UBM might have clinical or prognostic significance.

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Retinoma Underlying Retinoblastoma Revealed After Tumor Response to 1 Cycle of Chemotherapy

Retinoma is a benign, elevated, gray, translucent retinal mass with cottage cheese–like calcification and hyperpigmented retinal pigment epithelium. Histopathological features include abundant fleurettes and nonproliferative cells. We report a case in which an underlying retinoma was revealed by collapse and massive vitreous dispersion of the overlying unilateral retinoblastoma after 1 cycle of chemotherapy. Pathological analysis of the enucleated eye confirmed retinoma.

Report of a Case. A 2-year-old boy had leukokoria in the left eye. The left eye contained group D retinoblastoma, an endophytic posterior pole tumor with inferior vitreous seeding (Figure 1A). The right eye appeared unaffected.

Because there was potential for useful vision, treatment with chemotherapy followed by laser therapy was initiated. Three weeks after 1 cycle of systemic carboplatin-etoposide–vincristine sulfate treatment with high-dose cyclosporine (Toronto Protocol), the main tumor showed marked reduction in size, revealing a translucent mass with moderate calcification overlying chorioretinal scarring (Figure 1B). However, the main active retinoblastoma had dispersed widely into the vitreous including anterior to the ora serrata inferiorly, so the eye was enucleated.

Pathological examination showed a solid posterior tumor tapering into the inner nuclear layer of the retina (Figure 2A). The residual retinal lesion had numerous fleurettes, consistent with retinoma (Figure 2B). Fleurette-rich regions were not reactive to Ki-67 and p53 antibodies, and mitotic figures were rare. At the edge of the gap in the tumor from which the necrotic vitreous seeds had emerged, small, round retinoblastoma cells with little cytoplasm and no fleurettes stained positive for Ki-67, indicating proliferation and p53. The vitreous contained necrotic cellular debris. The optic nerve, optic nerve head, subarachnoid space, and choroid were free of tumor.

We previously reported that molecular analysis of this retinoblastoma showed a homozygous splice mutation (IVS12 + 1G>A); blood DNA had 2 normal RB1 alleles. Staining for pRb was negative, while the p73 tumor suppressor and senescence marker p16INK4a were highly expressed (case 5 in supplementary Table 2 from our previous article).

Comment. We concluded that the active retinoblastoma (Figure 1A) arose from retinoma (Figure 2B) originating in the inner nuclear layer of the retina (Figure 2A). Chemotherapy killed the dividing retinoblastoma cells, which collapsed into the vitreous. The nondividing translucent retinoma was unaffected by chemotherapy but became evident only after chemotherapy (Figure 1B). This retinoma shows all of the described features: clinical, histopathological, and molecular.

Clinically, retinoma is a translucent intraretinal mass with calcification and/or choroidal scarring that remains benign for the lifetime of the individual in 1.5% to 10% of predisposed persons. Several examples of clinically recognized retinoma that progressed to retinoblastoma have been documented. The transition from retinoma to retinoblastoma is usually so rapid that the benign lesions are rarely observed clinically, but we have previously shown that they are relatively common in eyes removed for retinoblastoma. Most eyes enucleated for retinoblastoma do not undergo therapy prior to removal, so the underlying retinoma is usually hidden by the proliferating tumor (Figure 1A).

Figure 1. Retinoma discovered in a retinoblastoma eye removed after the main active tumor dispersed throughout the vitreous following 1 cycle of chemotherapy. A. The child had unilateral macular retinoblastoma (International Intraocular Retinoblastoma Classification group D) and was treated with chemotherapy (Toronto Protocol), with the possibility of saving the eye. B. A strong response to 1 cycle of chemotherapy resulted in “melting” of the original tumor but massive vitreous seeding. Collapse of the active retinoblastoma revealed a mass with features of retinoma (chorioretinal scarring, translucent mass, and calcification). Because the other eye was healthy, the affected eye was removed 3 weeks after the chemotherapy.