45, PNL2, melan-A, tyrosinase, and MITF, but negative for iron stain.

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-Rønne 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-Rønne 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 tu-

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. Extrascleral 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. Recently, SD-OCT technology has improved resolution up to 3.5 µm per pixel.

Using this technique, we could detect spheroid 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-Rønne 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.
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 extrascleral 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 corresponds 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.

Correspondence: Dr Yücel, Ophthalmic Pathology Laboratory, University of Toronto, St Michael's Hospital, 30 Bond St, Shuter Wing 5-038, Toronto, ON M5B 1W8, Canada (yeni.yucel@utoronto.ca).

Financial Disclosure: None reported.

6. Noble J, Qazi FA, Lakosha HK, et al. Extrascleral extension in association with...
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 taping 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 p75NTR 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 (choriocapillaris scarring, translucent mass, and calcification). Because the other eye was healthy, the affected eye was removed 3 weeks after the chemotherapy.