Iris and Ciliary Body Melanomas

Ultrasound Biomicroscopy With Histopathologic Correlation

Flavio A. Marigo, MD; Paul T. Finger, MD; Steven A. McCormick, MD; Raymond Iezzi, MD; K. Esaki, MD; H. Ishikawa, MD; Jeffrey M. Liebmann, MD; Robert Ritch, MD

Objective: To correlate ultrasound biomicroscopic images of iris and ciliary body melanomas with their histopathologic features.

Methods: Ultrasound biomicroscopy was performed in 3 cases of iris melanoma and in 3 cases of ciliary body melanoma. Cross-sectional ultrasound biomicroscopic images were compared with findings from clinical examination and light microscopy to evaluate associations between their histopathologic, surface, and internal ultrasound characteristics. Unique images of intrastromal and obscured posterior tumor margins were visualized by ultrasound biomicroscopy.

Results: Results of this study revealed that ultrasound biomicroscopy offers an accurate method to evaluate tumor shape, reflectivity, and local invasion. Neoplastic tissue had only medium echogenicity. Enlarged vessels were correlated to echolucent spaces in the iris stroma. Anterior tumor margins were found within the iris stroma, within the anterior chamber angle, and on the endothelial surface of the cornea. Posterior tumor extension was noted to encroach onto the lens, into the sclera, and serious peripheral retinal detachments were associated with ciliary body tumors.

Conclusion: Ultrasound biomicroscopic images correlated well with histopathologic features of anterior uveal melanomas including shape, reflectivity, and local extension.

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MELANOMA IS the most common primary uveal malignancy.1 Iris and ciliary body melanomas compose approximately 15% of the cases.2 Compared with posterior uveal melanomas, iris melanomas tend to be smaller and visible, so they are detected early and metastasize infrequently.2,3 In contrast, ciliary body melanomas are considered more malignant. Unlike iris melanomas, they are hidden behind the iris and cannot be visualized until they are relatively large. The potential of a tumor to metastasize and, therefore, therapeutic decisions, are influenced by size, extension, tumor location, and growth patterns.1,6 However, complete visualization is usually impossible when the tumor is located behind the iris.

Although conventional ultrasonography may provide additional information about tumor size and location, its resolution is limited.2,5,6 In contrast, high-frequency ultrasound biomicroscopy (UBM) provides high-resolution, cross-sectional images in which the tumor surface, internal reflectivity, and tumor borders can be visualized.6,8-11 The clinical application of UBM in the management of anterior segment tumors has been described.1,6,9,11 Unfortunately, there are few published reports revealing histopathologic correlations of normal and abnormal UBM images.6,11-13 Such studies will improve the interpretation of UBM images. This study provides unique clinical, pathologic, and UBM correlations, focusing on internal tumor characteristics and extension into surrounding structures.

REPORT OF CASES

CASE 1

A 79-year-old woman was examined because of a suspected iris melanoma in the right eye. Visual acuity was 20/80 OD. Slit-lamp examination revealed a pigmented iris lesion in the superonasal quadrant near the pupillary border (Figure 1A). Ectropion uveae and a sector cataract were associated with the tumor. Gonioscopy revealed no evidence of pigment dispersion.

Ultrasound biomicroscopy showed a fusiform thickening of the midperipheral and pupillary portions of the iris and a large hypoechoic “cystic” area in the posterior
PATIENTS AND METHODS

PATIENTS

We examined 3 patients with iris melanomas undergoing cataract surgery and concurrently planned excisional biopsy. We also examined 3 patients with ciliary body melanoma in whom enucleation was considered the treatment of choice. In 4 patients (all cases of iris melanoma and 1 enucleation) UBM was performed prior to surgery. To allow imaging of the posterior margin of the lesion, UBM was performed after enucleation in 2 cases of ciliary body melanoma.

UBM EXAMINATION RESULTS

Ultrasound biomicroscopy was performed using a commercially available unit (Paradigm Medical Industries, Salt Lake City, Utah). This system operates at 50 MHz, providing maximum resolution of 50 µm and tissue penetration depth of approximately 4 to 5 mm. The scanner produces a 5 x 5-mm field with a count of 256 lines at a scan rate of 8 frames per second. The probe is suspended from an articulated arm to reduce motion artifacts and lateral distortion is minimized by a linear scan format. For in vivo imaging, scanning was performed with the patient in the supine position using a 20-mm eye cup filled with a saline solution. The enucleated eyes were secured in a mounting cradle after fixation in 10% formalin and submerged within a saline solution bath for scanning. The mounting cradle was manipulated to position the lesion of interest directly under the UBM transducer. The probe was moved perpendicular to the structure to be scanned to obtain longitudinal and transverse sections.

HISTOPATHOLOGIC RESULTS

The specimens collected were immediately fixed in 10% formalin for 24 hours and embedded in paraffin. Sections were stained with hematoxylin-eosin. The histologic preparations were photographed using a microscope (Olympus Vanox; Olympus, Tokyo, Japan). Comparable planes of view and magnification were obtained to correlate with the UBM images.

stoma (Figure 1B-C). An excisional biopsy was performed.

Histopathologic evaluation revealed that the increased iris thickness was caused by infiltration of the stroma by neoplastic melanocytic cells. The hypochroic areas corresponded to enlarged blood vessels found in the posterior iris stroma (Figure 1D).

CASE 2

A 59-year-old man was evaluated for a pigmentated iris lesion in the right eye. Visual acuity was 20/50 OD. Slitlamp examination showed a thick, pigmented, fusiform lesion centered at the 10-o’clock meridian. Ectropion of the lid and cataract were present adjacent to the lesion. Gonioscopy revealed no pigment dispersion on the iris surface, trabecular meshwork, or corneal endothelium. Intraocular pressure and fundus examination results were unremarkable.

Ultrasound biomicroscopy revealed a medium to hypoechoic thickening of the iris stroma in its midperipheral and pupillary zones. The iris surfaces were bowed anteriorly and posteriorly, the anterior surface being more prominent than the posterior (Figure 2A-B). The lesion was considered suggestive of melanoma. Cataract extraction and excisional biopsy of the lesion were performed.

Histopathologic examination revealed that the iris thickening was a result of a plaquelike tumor on the anterior iris surface. It was composed of a mixture of round and spindle-shaped neoplastic melanocytic cells. There were some areas where atypical cells extended into the underlying stroma consistent with the diagnosis of malignant melanoma (Figure 2C).

CASE 3

A 77-year-old man had a velvety, nodular pigmented iris lesion centered at the 3-o’clock meridian in the left eye (Figure 3A). Visual acuity was 20/200 OS. Moderate nuclear sclerotic and dense posterior subcapsular cataractous changes were noted. Intraocular pressure and fundus examination results were unremarkable.

Ultrasound biomicroscopy revealed a medium echoic, nodular lesion arising from the peripheral iris surface (Figure 3B). Dynamic ultrasound examination revealed that with dilation, the tumor moved closer to the ciliary body. At surgery, an excisional biopsy prior to dilation was followed by phacoemulsification and intraocular lens implantation. Histopathologic evaluation revealed the tumor to be an epithelioid-cell malignancy with melanoma cells infiltrating the stroma as nests and single cells (Figure 3B).

CASE 4

A 45-year-old man was examined because of a ciliochoroidal mass in the left eye. Visual acuity was 20/80 OS. Slitlamp examination revealed engorged episcleral sentinel vessels leading toward an iris that was bowed anteriorly.

Tumor infiltration of the iris could be visualized in the peripheral iris in the inferonasal quadrant. After dilation, pigment dispersion was noted on the anterior lens surface and a dark brown mass could be seen behind the iris in the meridian of iris infiltration. Gonioscopy also revealed pigment dispersion onto the trabecular meshwork (inferiorly). Fundus examination revealed a large, vascularized mass extending to 5.0 mm posterior to the equator. Standardized ultrasonography revealed an apical tumor height of 15.6 mm. A clinical diagnosis of uveal melanoma was based on the tumor’s ophtalmoscopic appearance and low-frequency (10-MHz) ultrasound characteristics.

Ultrasound biomicroscopy of the enucleated eye revealed a medium echoic solid tumor within the ciliary body. It had infiltrated the iris root and extended into the anterior chamber angle creating a convex profile. Posterior to the iris, the tumor also extended behind the lens equator (Figure 4A).
Gross pathologic evaluation of the globe showed a large inferior transillumination defect measuring 23.5 × 17 mm. The tumor’s shadow extended from the 4- to 9:30-o’clock meridians. On cut section, a large darkly pigmented tumor with prominent internal vascularization was seen arising from the ciliary body and extending anteriorly to the iris root and anterior chamber angle. Its posterior margin extended 4 mm beyond the equator. Histopathologic examination revealed a mixed-cell uveal melanoma composed of spindle-shaped melanocytic cells with scattered nodules of epithelioid cells (Figure 4B).

CASE 5

A 65-year-old woman was referred for evaluation of a ciliary body tumor in the left eye. She had undergone trabeculectomy (in that eye) 4 years before. Visual acuity was 20/50 OS. Slitlamp examination revealed engorged episcleral sentinel vessels nasally, ectropion uveae inferonasally, and pigment deposition on the iris surface (Figure 5A). Pigment was noted in the trabeculectomy ostium. Tumor infiltration in the inferonasal iris displaced it anteriorly. Pupillary dilation revealed an amelanotic mass arising from the inferonasal ciliary body.

Standard ultrasonography revealed an apical tumor height of 7.4 mm with low internal reflectivity. Its basal dimensions were measured to be 12 × 10 mm by transillumination. Ultrasound biomicroscopy showed a large solid lesion with medium echogenicity in the ciliary body invading the iris root with extension into the anterior chamber angle. Posterior to the iris, the lesion extended past the pupillary margin, partially filling the posterior chamber (Figure 5B). Enucleation was performed.

Gross examination of the globe revealed a transillumination defect extending from the limbus posteriorly in the 7- to 10-o’clock meridians. Histopathologic evaluations revealed a lightly to moderately pigmented, epithelioid cell-type malignant melanoma, arising in a circumferential mixed-cell melanoma of the iris root and ciliary body (ring melanoma) with extension to the iris stroma, trabecular meshwork, and Schlemm canal (Figure 5C). It had eroded through the iris root into the anterior chamber angle. Posterior to the iris, it had encroached on the lens and disrupted the lenticulopupillary axis.

CASE 6

An 81-year-old woman with light perception vision in the left eye was evaluated for a ciliary body tumor. Slitlamp examination revealed a large, darkly pigmented mass...
in the superior quadrant of the ciliary body. The lesion was diagnosed as a uveal melanoma and enucleation was performed.

Ultrasound biomicroscopy of the enucleated eye showed a large solid tumor with medium echogenicity in the ciliary body. There was extension through the iris root to the anterior chamber angle (Figure 6A). A finding of scleral infiltration appeared as a crescent-shaped defect in the sclerochoroidal interface anteroposteriorly (Figure 6A-B). A retinal detachment was also noted along the posterior margin of the tumor, forming a sonolucent space (Figure 6B).

Gross pathologic examination showed an 18 × 17-mm transillumination defect extending from the
10- to 2-o’clock meridians. The tumor extended from the anterior termination of the ciliary body to a position posterior to the equator. Though it infiltrated the iris root, there was minimal infiltration of Schlemm canal and sclera (Figure 6C). Tumor extension through the neural retina and a retinal detachment were also noted. Histopathologic evaluation revealed a mixed-cell uveal melanoma.

COMMENT

There are few reports correlating UBM findings with histopathologic features. Ultrasound biomicroscopy could provide useful information concerning tumor borders and local extension. Tumor extension within anterior segment structures and sclera can be delineated.6,11

Iris melanomas are typically seen as a variably pigmented tumor or diffuse iris thickening in the inferior quadrants.2 In our patients, UBM imaged these lesions either as medium to high echoic fusiform-shaped infiltration of the iris stroma or as nodular lesions (Figures 1 through 3). In Figure 1 and Figure 2, the anterior surface of the iris was displaced resulting in a bowed profile. Since preoperative definition of the depth of tumor invasion into the iris is difficult, it is important that we have found that UBM images correlate well with low-power light microscopy.6 Definition of true tumor margins can only be reached on a cellular basis with higher-power microscopy, but UBM offered a good approximation of those margins. Enlarged iris vessels, as associated with one iris melanoma in this series, were correlated to hypoechoic, cystic spaces in the iris stroma.6,10

Ultrasound biomicroscopy is particularly valuable in the evaluation of ciliary body melanomas, or uveal tumors with ciliary body extension. This is an intraocular location where slitlamp examination, gonioscopy, indirect ophthalmoscopy, and transillumination may not reveal the extent of tumor within the iris and ciliary body stroma. Most small ciliary body melanomas cannot be seen by slitlamp examination, gonioscopy, or indirect ophthalmoscopy. Even if the tumor is detectable by transscleral or transpupillary transillumination, tumor shadows can merge with the ciliary body band. Therefore, UBM provides useful information about tumor extension into the iris and ciliary body.

In these cases, sequential clock-hour imaging of ciliary body melanomas offers an additional method to evaluate lateral tumor spread within the ciliary body. This technique may be of particular value in assessment of the ring melanomas.

In 3 cases, iris extension was characterized by disruption of the iris pigment epithelium or stromal infiltration. Infiltration of the iris was characterized on UBM by disruption of the hyperechoic line representing the iris pigment epithelium (Figures 4 through 6). Iris stromal invasion could be seen as a change in the echogenicity of the affected area as compared with the normal-appearing iris. Disruption of the iris pigment epithelium was a consistent UBM finding that may be useful for early diagnosis of iris and ciliary body tumors.

When invasion of the anterior chamber angle was observed by UBM, there was a loss in the normal acute shape of the angle, which assumed a convex or linear shape (Figure 5B and Figure 6A). In more advanced cases, a tissue with medium echogenicity was seen in the anterior chamber (Figure 4). The scleral spur and the Descemet membrane are important landmarks when evaluating the trabecular meshwork and cornea for infiltration by tumor cells.14 This information is significant when radioactive plaque therapy is being considered. Plaque size and position relative to the tumor and other landmarks can be determined by UBM to provide optimum irradiation of the neoplasm and avoid unnecessary irradiation of normal ocular structures.5,14
Ultrasound biomicroscopy allowed assessment of posterior chamber tumor extension. We found that tumors can extend to the lens equator or lenticular surface. The tumor can eventually encroach and dislocate the lens, disrupting the lenticulopupillary axis, as seen in Figure 5. Therefore, in these cases, UBM can help in planning treatment, showing that complete local resection may not be technically possible to perform.

Serous retinal detachment can be associated with uveal melanoma. In 1 eye of this series (Figure 6B), the detachment could be imaged as a high-intensity line delimiting a small fluid-containing sonolucent space. Scleral extension was seen in 1 case (Figure 6), appearing as a localized loss of integrity in the sclerochoroidal interface and a decrease in the reflectivity of the sclera. Although lacking histopathologic corroboration, a case of intrascleral extension of a ciliary body melanoma was previously reported. As in our case, the authors noted a sonolucent line thought to represent tumor within an emissary canal. Since extrascleral extension of such lesions is considered to worsen the prognosis, the significance of this finding by UBM must be emphasized. If UBM suggests that scleral infiltration is present, full-thickness resection, plaque irradiation, or enucleation rather than lamellar resection or iridocyclectomy should be considered.

Fifty-megahertz ultrasound transducers allow for 50-µm resolution with a penetration (in tissue) of 4 to 5 mm. Therefore, UBM imaging most closely correlates to histopathologic features at a resolution of low-power light microscopy. At this resolution, neither UBM nor histopathologic features were high enough to permit cell-type differentiation. Correlations between ultrasound and histopathologic features are also limited by our ability to match the exact meridians where both pathologic and ultrasound sections were made. Lastly, UBM imaging of tumors beyond 4 mm in depth was impossible due to ultrasound attenuation.

Differentiation between benign and malignant lesions, mainly those located in the iris, is still a challenge. Benign lesions such as nevi can grow and invade adjacent tissues and can even recur after excision. Often such tumor behavior will influence the pathologist’s determination of malignancy. Ultrasound biomicroscopy provides useful information about tumor morphology and growth patterns, but a definitive diagnosis is best reached by histopathologic examination.

This study demonstrates that UBM findings correlate well with the low-power histopathologic appearance of the tumors imaged in this study. Ultrasound biomicroscopy can provide useful information to the eye care specialists who diagnose and treat anterior segment tumors.

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**Figure 5.** Ciliary body melanoma. A, Slitlamp photograph. B and C, Ultrasound biomicroscopy, radial sections. D, Light microscopy (hematoxylin-eosin, original magnification ×6.6). E, Light microscopy (hematoxylin-eosin, original magnification ×40). Slitlamp examination revealed engorged episcleral vessels nasally, ectropion uvea inferonasally, and a mass located behind the iris. Ultrasound biomicroscopy imaged a large ciliary body tumor (TU) invading the iris root near its posterior surface (open arrows). Note interruption of the iris pigment epithelium (solid arrows) and infiltration of iris stroma. The anterior chamber angle is also compromised (arrowhead). Observe scleral spur (*). More than half of the posterior chamber is occupied by tumor.
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Corresponding author: Robert Ritch, MD, Glaucoma Service, The New York Eye and Ear Infirmary, 310 E 14th St, New York, NY 10003 (e-mail: ritch@inx.net).

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