Long-term Survival in a Patient With Uveal Melanoma and Liver Metastasis

Uveal melanoma\(^1\) is the most common primary ocular malignancy in whites and represents 70% of all primary ocular malignancies. In patients with metastatic uveal melanoma, the prognosis for those with initial metastasis to the liver is particularly poor. The median survival of patients who first develop liver metastasis from uveal melanoma is 5 to 7 months, as compared with 18 months for other initial sites of metastasis.\(^2\)\(^-\)\(^4\) This poor prognosis continues despite treatment modalities such as chemoembolization.\(^5\)\(^,\)\(^6\) We report a case of uveal melanoma with initial metastasis to the liver in a patient who survived for more than 5 years after diagnosis of liver metastasis.

Report of a Case. Possible uveal melanoma in the left eye was diagnosed in a 74-year-old white woman with a history of hypertension. The melanoma was discovered after she sought evaluation for decreased visual acuity in that eye. The patient was seen at the Wilmer Eye Institute, Baltimore, Md, September 13, 1993. Examination revealed best-corrected visual acuity 20/30 OD and counting fingers OS. There was a mild afferent pupillary defect with esotropia in the left eye. Examination of the left eye revealed a pigmented ciliochoroidal lesion growing into the lens. The iris was bowed forward temporally. Dilated fundus examination disclosed a cap of retinal detachment over the lesion. Ultrasonography disclosed a large, solid, dome-shaped lesion temporally, which was anterior to the equator, with extension into the ciliary body. The lesion displayed low internal reflectivity. The basal diameter measured 18 × 17 mm, with a maximal elevation of 12.8 mm. Malignant melanoma was diagnosed. As a participant in the Collaborative Ocular Melanoma Study for large-lesion melanoma, she was randomized to undergo enucleation without prior irradiation. The procedure was performed September 24, 1993.

Gross examination of the globe disclosed a mottled gray tumor involving the choroid, ciliary body, and iris periphery. The tumor measured 17 mm at its base and 11 mm in maximum height. Posteriorly, the tumor extended to within 9 mm from the margin of the disc. The lens was molded by the tumor and showed cortical changes. The retina was detached.

Microscopic examination of serial sections disclosed a lightly pigmented tumor of the choroid and ciliary body that invaded the iris leaf and trabecular meshwork (Figure 1). According to the Armed Forces Institute of Pathology modification of the Callender classification, this was a spindle cell malignant melanoma (Figure 2). A count of 40 high-power fields revealed no

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**Figure 1.** Microscopic examination of the globe disclosed a large basophilic tumor (single arrow) arising from the uveal tract, which indented the lens (asterisk) and induced retinal detachment with surrounding subretinal fluid (double arrow) (hematoxylin-eosin).

**Figure 2.** Photomicrograph of melanoma cells revealed a dense collection of cohesive spindle-shaped cells with poorly defined cell borders. Some of the cells exhibited the nuclear folds of the spindle A type (single arrow), while other cells had more distinct nucleoli typical of the spindle B type (double arrow) (hematoxylin-eosin, original magnification ×200).
mitotic figures. The tumor ruptured the Bruch membrane and invaded the peripheral retina. Tumor cells were not seen in the vitreous. There was invasion along a ciliary nerve, with tumor extending close to the surface of the sclera. There was moderate inflammation with lymphocytes at the base of the tumor and within the tumor. Some foci of necrosis, focal hemorrhages, and balloon cells were present within the tumor. Numerous corpora arenacea were seen in the arachnoid surrounding the optic nerve. The final diagnosis was spindle cell melanoma of the choroid, ciliary body, and iris, with invasion of the trabecular meshwork and corresponding retinal detachment.

Follow-up during the next few years disclosed no evidence of local recurrence. In April 1996, physical examination revealed hepatomegaly despite the patient being asymptomatic. Liver function test results were within normal limits, but computed tomography (CT) demonstrated multiple lesions in the lower portions of the liver. Fine-needle biopsy of the liver was performed May 3, 1996. Histopathological analysis disclosed spindle-shaped, melanin-containing cells diagnostic of metastatic malignant melanoma (Figure 3). Dense aggregates of lymphocytes were also observed. Immunohistochemical staining was positive for HMB-45.

Observation was elected. In October 1996, CT showed an increase in metastasis to the rest of the liver. The patient therefore underwent 1 course of chemoembolization. Follow-up CT, including scanning performed in June 1998, disclosed no substantial change in the liver lesions; liver function test results remained within normal limits.

The patient was seen in January 1999 at the Wilmer Eye Institute, where she commented on the loss of skin pigment of the scalp and arms; this was thought to be due to an autoimmune reaction to pigment. There was no sign of local tumor recurrence in the left eye.

On September 30, 1999, the patient underwent sigmoid colectomy, small-bowel resection, cholecystectomy, and liver biopsy at Johns Hopkins Hospital, Baltimore, Md, primarily for removal of adenocarcinoma. Pathological examination results revealed moderately differentiated adenocarcinoma of the sigmoid colon, with lymph nodes negative for cancer and metastatic melanoma of the left and right lobes of the liver. Cholecystitis and cholelithiasis were confirmed. No evidence of small-bowel tumor involvement was found. The patient died June 30, 2001.

**Comment.** The prognosis for patients with metastatic choroidal melanoma is poor. Survival from time of development of systemic metastasis ranged from 1 to 31 months in 1 study. The liver is the most common site of metastasis in choroidal melanoma. This finding remains true despite various therapeutic strategies, such as chemoembolization and hepatic perfusion with melphalan with or without tumor necrosis factor.

In our case, the patient survived more than 7 years after diagnosis of the primary uveal melanoma and more than 5 years after development of metastatic melanoma to the liver. This patient underwent 1 course of chemoembolization of liver metastases, which was performed when CT studies demonstrated metastatic spread within the liver. Subsequent CT demonstrated stability of the liver metastases and prompted speculation about the development of an immune response to the malignancy. The patient developed vitiligo. Only a few cases have been reported of patients with choroidal melanoma and vitiligo. This disorder, thought to have an autoimmune cause, may confer a favorable prognosis for patients with cutaneous melanomas. The patient did not undergo any other therapy for melanoma, although she did undergo surgery for adenocarcinoma of the sigmoid colon. The long-term survival of this patient reinforces the concept that patient-specific factors, such as the possible development of an immune response, can affect the course of uveal melanoma.

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Primary Orbital Melanoma Associated With an Occult Episceral Nevus

Melanomas arising in the orbit can present diagnostic and management challenges to the physician. The pathogenesis of primary orbital melanomas is a matter of some debate. Primary melanomas arising in the orbit are rare, accounting for less than 1% of primary orbital tumors and about 2% of extenterations. Most orbital melanomas arise from the uveal tract, conjunctiva, eyelids, or sinuses, and, infrequently, as metastases from distant primary sites. Approximately 90% of primary orbital melanomas arise from melanocytes found in congenital ocular melanocytosis (including blue nevus and cellular blue nevus), orbital melanocytosis, or oculodermal melanocytosis (nevus of Ota). The presence of melanocytes has also been reported in the optic nerve sheath, orbital fat, extraocular muscles, and orbital peristeum, which theoretically may provide cells of origin for primary orbital melanomas.

Orbital biopsy may be required to diagnose orbital melanoma when no clinical evidence of melanocytosis of the periocular tissues or uveal tract is present. Even with an orbital biopsy, the histopathologic diagnosis can often be difficult, especially if the tumor is amelanotic. We describe a 36-year-old woman who developed a primary orbital melanoma that apparently arose from a previously unreported focus of melanocytes, an occult nevus on the posterior sclera.

Report of a Case. A 36-year-old woman was evaluated for right exophthalmos. The right eye had become increasingly prominent over several years, without pain, diplopia, or change in vision. No history of trauma or systemic medical problems was reported. Magnetic resonance imaging (Figure 1) and computed tomography (Figure 2)