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Isolated Brain Metastasis of Malignant Choroidal Melanoma 27 Years After Enucleation

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Choroidal melanoma primarily metastasizes to the liver. Isolated extrahepatic metastases have rarely been reported and they generally resulted in death within 6 months. We describe a patient who developed an isolated brain metastasis 27 years after his left eye was enucleated for choroidal melanoma. The metastasis was succesfully treated with surgery and radiotherapy. The patient is alive and disease free 3 years after treatment of the metastasis. Posterior location and other clinical and morphologic characteristics of primary choroidal melanoma could explain the unusually long latency of this solitary extrahepatic metastatic disease. Lifelong surveillance to detect early signs of metastasis is mandatory for any patient treated for choroidal melanoma. *Arch Ophthalmol. 1999;117:1553-1556*

Choroidal melanoma is the most frequent intraocular malignant tumor in the adult. Biological malignancy of choroidal melanoma depends on its morphologic and clinical characteristics such as histologic type, presence of fibrovascular loops, mitotic activity, cytomorphometric parameters, tumor size and location, and patient age. Pure spindle cell choroidal melanomas have a limited potential to metastasize.

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The main site of metastases from choroidal melanoma is the liver, and the highest frequency of liver metastasis is within 4 years after treatment of the primary tumor. Three cases of metastatic disease have been reported 36, 40, and 42 years after enucleation.[1-3] Brain metastases of choroidal melanoma are very rare and they usually appear after or concomitant with liver metastases.

We describe a patient who developed an isolated brain metastasis 27 years after his left eye was enucleated for a spindle cell choroidal melanoma. He is disease free 3 years after combined treatment of brain metastasis. To our knowledge, this is the first report of a very late, isolated, apparently succesfully treated brain metastasis from choroidal melanoma.

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CASE REPORT

A 59-year-old man was referred to us for visual disturbances in his right eye. In 1968, at the age of 30 years, his left eye was enucleated owing to an intraocular tumor. Pathological records reported an intact 24-mm left eye containing a 10 × 10 × 3–mm (height) choroidal malignant melanoma composed of a pure spindle cell population. Inconspicuous nucleoli and rare clumps of melanin pigment were detected. Two mitoses in 40 high-power fields were found. The lesion was classified as spindle cell choroidal melanoma, subtype A, according to the original Callender classification.[4] At reevaluation, the tumor was classified as a spindle cell melanoma according to the modified Callender classification[4] (**Figure 1** and **Figure 2**). Sclera and optic nerve were disease free. After uneventful enucleation, the left orbit received external beam irradiation (30 Gy; daily fraction, 2 Gy). The reason for this treatment is unknown. In November 1995, the patient complained of visual

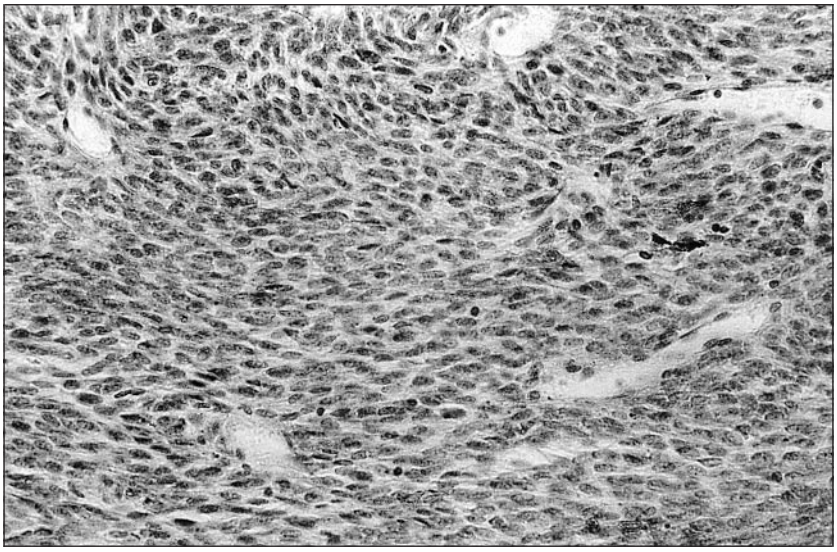

Figure 1. *The choroidal tumor is composed of spindle cells (hematoxylin-eosin, original magnification ×125).*

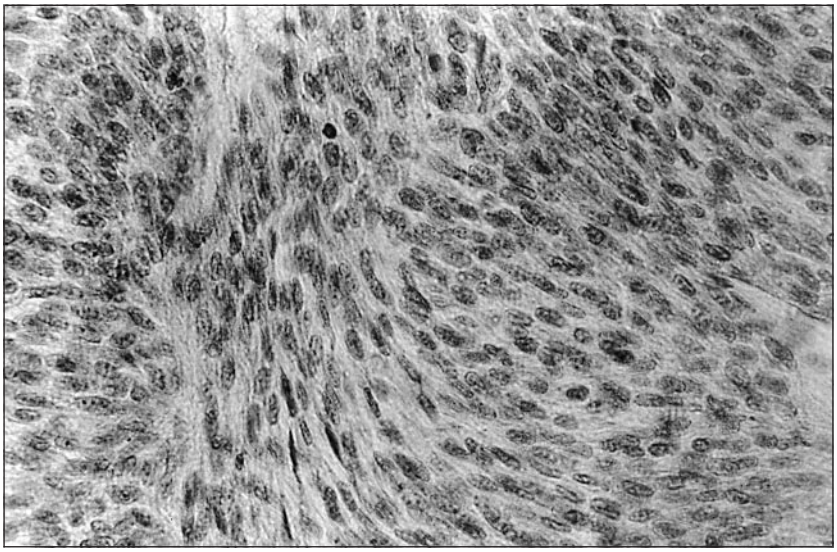

Figure 2. *At higher magnification, nuclei are uniform in size; a limited number of nuclei show distinct nucleoli (hematoxylin-eosin, original magnification ×400).*

disturbances in his right eye and was referred to us.

On examination, best-corrected visual acuity was 20/20 OD and intraocular pressure was 16 mm Hg; anterior segment, fundus, and ocular motility were normal. Visual field examination disclosed a nasal hemianopsia extending to the superotemporal quadrant. On the left side, orbital tissue retraction secondary to enucleation and radiotherapy was found.

The patient underwent a complete medical and oncological evaluation. Liver function test results and tumor markers were negative. Results from chest and abdomen computed tomographic scans and bone scintigraphic scans were normal. Findings of brain computed tomographic scan showed a hyperdense lesion located in the left occipital area (**Figure 3**). Findings from nuclear magnetic resonance imaging, with and without gadolinium enhancement, showed a hyperdense lesion located in the left temporo-occipital region with irregular borders, surrounded by slight edema (hyperintense signal on T1W and hypointense signal on T2W) (**Figure 4**).

Neurosurgical consultation was consistent with a probable primary occipital tumor and the patient underwent surgery on January 1996. The lesion was completely excised macroscopically. The postoperative course was uneventful and the neurological status remained unchanged.

Pathological examination of the excised tumor showed a sharply delimited tumor in the context of normal cerebral parenchyma. Most of the cells were spindle shaped, and rare epithelioid cells were detected. Twelve mitoses in 40 high-power fields were found. All malignant cells were positive for HMB-45 and S100 antigens. No areas of benign melanosis or infiltration of benign-appearing, spindle-shaped nevoid cells were detected in serial sections of the surgical specimens. The tumor was classified as a brain metastasis of malignant melanoma. (**Figures 5**, **6**, and **7**). The postoperative eye examination was unchanged except for the visual field examination, which improved slightly. Brain nuclear magnetic resonance imaging was negative except for the results of surgery in the occipital area.

In March 1996, the patient underwent prophylactic brain irradiation (30 Gy in 10 fractions) without complications. The possibility of a second occult melanoma, for example, in the skin or the subungual or perianal region, was considered but excluded. The patient is now followed up every 6 months. The last examination was performed in November 1998, 3 years after the clinical appearance of brain metastasis. The visual acuity in the right eye was still 20/20 and the anterior and posterior segments were normal. Results of brain nuclear magnetic resonance imaging and chest and abdominal computed tomographic scans showed no signs of tumor recurrence. Results of blood tests were normal.

COMMENT

Metastatic choroidal melanoma is a life-threatening disease with limited life expectancy.[5]

Early metastases (peak at 24 months) are commonly related to the cellular type of the melanoma, with the highest prevalence in patients affected by epithelioid choroidal melanoma.[5] Within 5 years after enucleation, 40% to 70% of patients develop clinically detectable metastases and die within 6 months (the median survival rate is 2 months

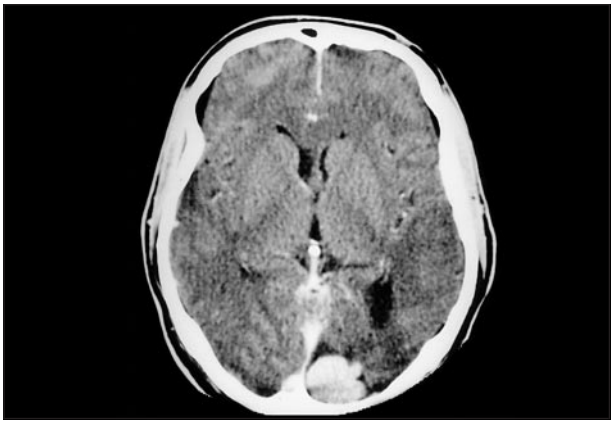

Figure 3. *Cerebral computed tomographic scan showing a hyperdense lesion located in the left occipital area.*

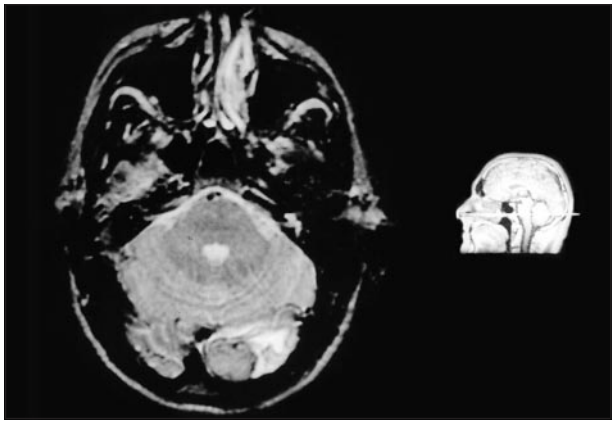

Figure 4. *Nuclear magnetic resonance scan demonstrating the occipital lesion with irregular borders surrounded by slight edema.*

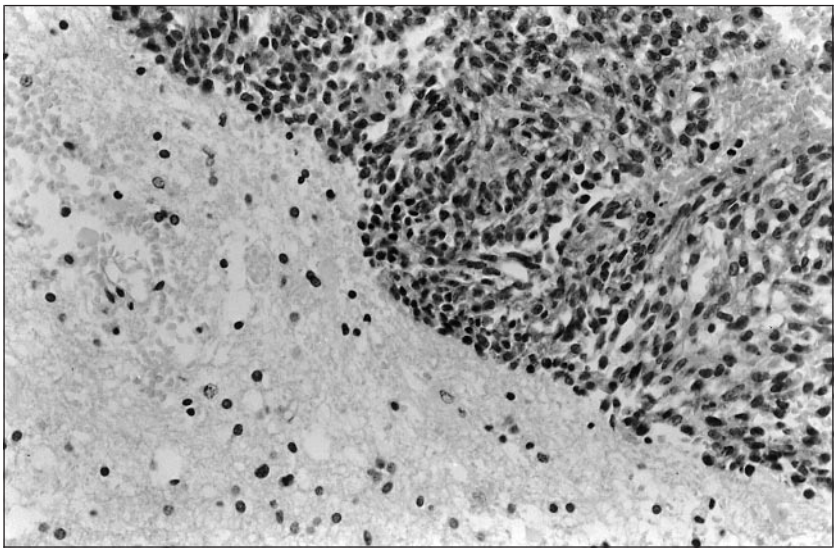

Figure 5. *A sharply delimited, hypercellular neoplastic cell proliferation is seen (top right) in the context of the cerebral parenchyma (bottom left) (hematoxylin-eosin, original magnification ×200).*

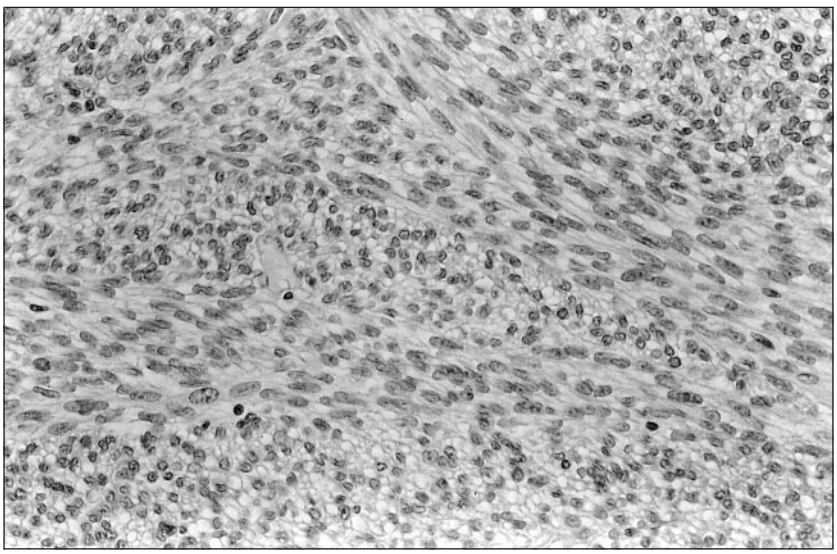

Figure 6. *At higher magnification, the neoplastic cell population exhibits a striking spindle cell morphology. (hematoxylin-eosin, original magnification ×400).*

for patients receiving no treatment compared with 5.2 months for those receiving treatment for metastases).[6] In 1963, Jensen[7] calculated the interval between enucleation and the appearance of metastases and between the appearance of metastases and death. Ten percent of his patients had hepatic metastases. Most metastases occurred 2 to 3 years after enucleation. Another peak of frequency was found 7 to 8 years after the surgical treatment. The interval between metastases diagnosis and death was 6 months or less in 85% of the cases.[7]

Regarding very late metastases, Lorigan et al[2] reported a case in which a patient developed diffuse liver metastases 36 years after enucleation. Coupland et al[1] reported a case of metastatic choroidal melanoma to the contralateral orbit 40 years after enucleation. Shields et al[3] reported a case of orbital recurrence and hepatic metastases 42 years after enucleation of the primary tumor. In his review of the series by Terry and Johns,[8] Chisholm reported 4 cases of metastatic choroidal melanoma more than 20 years after enucleation.[9] The liver, followed by lungs, bone, and skin, is the most common site of metastases. Isolated brain metastases are very rare.[2]

In a clinical and radiologic review of 110 cases of metastatic choroidal melanoma, Lorigan et al[2] found 5 cases (4%) of brain metastases; all of these patients had concomitant hepatic metastases and 4 had multisystemic involvement. Char[10] reported a single case of brain metastasis, without detailed infor-

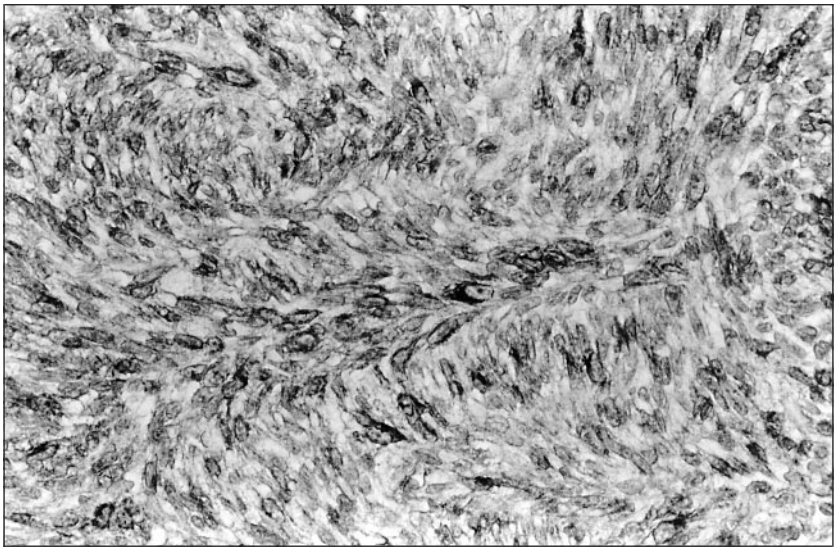

Figure 7. *Immunostaining for the antimelanoma antigen HMB-45 is strongly positive for the spindle cells (immunoperoxidase, original magnification ×400).*

mation, in a series of 41 patients with metastatic choroidal melanoma.

Multiple factors, known and unknown, may influence the prognosis of choroidal melanoma. Most commonly quoted factors are cytologic and histologic parameters of the tumor (spindle vs epithelioid cells, number of mitoses, presence and aspects of nucleoli, and fibrovascular loops); tumor location (most anteriorly located melanoma has worse prognosis) and size (increasing size is a negative prognostic parameter); and extrascleral extension and age at diagnosis (young patients have a better prognosis).[5,7,10,11]

In our case, some features favored a relatively benign prognosis: the favorable histological cell type (pure spindle cells) with minimal atypia and inconspicuous nucleoli, absence of optic nerve and scleral infiltration, posterior location of the lesion, and age at diagnosis. All these elements, and a very long doubling time of the primary tumor and its metastasis (probably greater than the proposed maximum of 350 days)[12] could explain the long latency between enucleation and appearance of the isolated brain metastasis. Unfortunately, we could not perform more in-depth studies of the primary lesion because no histologic blocks were available. Prophylactic orbital irradiation just after enucleation might have influenced malignant cell dissemination. However, preoperative prophylactic radiotheraphy is still being investigated, but seems to have no beneficial effects even if performed before enucleation.

Another intriguing characteristic of this case is the favorable postoperative course: the patient is alive and disease free 3 years after local treatment of brain metastasis.

Metastases from choroidal melanoma commonly have a poor prognosis, with life expectancy generally less than 1 year.[5] However, Gragoudas et al[5] reported that patients receiving some form of therapy for metastatic melanoma survived longer, on average, than those receiving no treatment. Bedikian et al[13] found that survival may be prolonged when the liver is not the primary site of metastases.

In conclusion, patients with choroidal melanoma should be followed up for the remainder of their lives to detect any isolated sign of metastatic disease, and should be treated immediately according to the best clinical protocols available if any signs are found. Moreover, the risk of metastasis exists even when the primary tumor has the most favorable morphologic and clinical characteristics.

Accepted for publication August 17, 1999.

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