

Figure 2. Histopathologic findings. A, Just posterior to the equator, a relatively flat, pigmented, cellular infiltrate is seen within the choroid. The tumor is 500 μm thick and tapers at the ends (hematoxylin-eosin, original magnification $\times 2$). B, The infiltrate displays a dense population of spindle-shaped and epithelioid melanoma cells with pale cytoplasm that demonstrates marked cellular and nuclear pleomorphism. Several small retinal pigment epithelial detachments are seen overlying the tumor (arrows). The retina is artifactually detached and not visible (hematoxylin-eosin, original magnification $\times 20$).

troretinography and antiretinal antibody testing were not performed. Previous cases of vitelliform retinopathy have had some clinical findings consistent with MAR,^{1,2,4,6} while others have not.^{4,5} None of these reports had clinical evidence of choroidal involvement. The vitelliform lesions have been postulated to represent a new paraneoplastic clinical manifestation. The pathologic results in this case argue against a paraneoplastic entity but may suggest a local metastatic cause with subclinical choroidal involvement. Another explanation is that choroidal involvement occurred after the vitelliform lesions with the dissemination of the metastatic melanoma. Further studies are needed to determine the etiology of these vitelliform lesions in metastatic melanoma.

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1. Zacks DN, Pinnolis MK, Berson EL, Gragoudas ES. Melanoma-associated retinopathy and recurrent exudative retinal detachments in a patient with choroidal melanoma. *Am J Ophthalmol.* 2001;132(4):578-581.
2. Palmowski AM, Haus AH, Pföhler C, et al. Bilateral multifocal chorioretinopathy in a woman with cutaneous malignant melanoma. *Arch Ophthalmol.* 2002;120(12):1756-1761.
3. Jampol LM, Kim HH, Bryar PJ, Shankle JB, Lee RT, Johnston RL. Multiple

- serous retinal detachments and subretinal deposits as the presenting signs of metastatic melanoma. *Retina.* 2004;24(2):320-322.
4. Sotodeh M, Paridaens D, Keunen J, van Schooneveld M, Adamus G, Baarsma S. Paraneoplastic vitelliform retinopathy associated with cutaneous or uveal melanoma and metastases. *Klin Monbl Augenheilkd.* 2005;222(11):910-914.
5. Nieuwendijk TJ, Hooymans JM. Paraneoplastic vitelliform retinopathy associated with metastatic choroidal melanoma. *Eye (Lond).* 2007;21(11):1436-1437.
6. Javaheri M, Khurana RN, Bhatti RA, Lim JI. Optical coherence tomography findings in paraneoplastic pseudovitelliform lesions in melanoma-associated retinopathy. *Clin Ophthalmol.* 2008;2(2):461-463.
7. Eksandh L, Adamus G, Mosgrove L, Andréasson S. Autoantibodies against bestrophin in a patient with vitelliform paraneoplastic retinopathy and a metastatic choroidal malignant melanoma. *Arch Ophthalmol.* 2008;126(3):432-435.

Cutaneous Halo Nevi Following Plaque Radiotherapy for Uveal Melanoma

Halo nevi have been described in both dermatology and ophthalmology.^{1,2} Cutaneous halo nevi are found more often in children than adults and are believed to result from an immune response.³ Choroidal halo nevus represents 5% of all choroidal nevi and displays low risk for transformation to melanoma.⁴ The development of cutaneous halo nevi or vitiligo in adulthood can occur following treatment of cutaneous melanoma and correlates with decreased morbidity, presumably due to activation of a systemic immune response.⁵ There have been rare reports of vitiligo and/or cutaneous halo nevi development following enucleation for uveal melanoma.^{6,7} A comprehensive study on choroidal halo nevi found a statistical association with history of skin melanoma.² Herein, we describe a young woman with uveal melanoma who developed a halo ring around numerous pigmented cutaneous nevi following plaque radiotherapy for uveal melanoma.

Report of a Case. A 28-year-old woman with photopsia in the left eye was diagnosed as having choroidal melano-

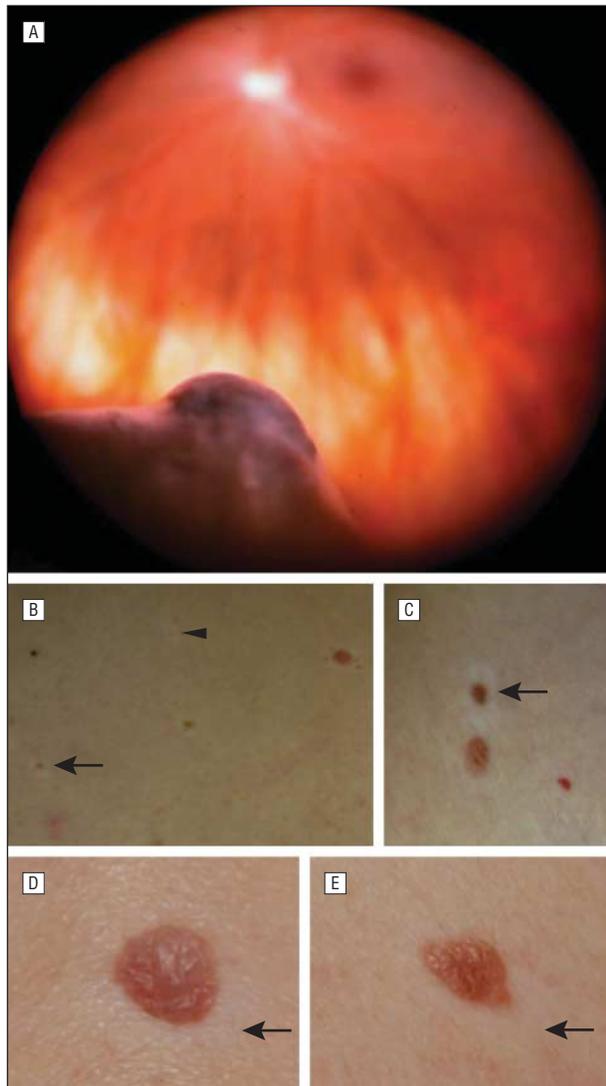


Figure. Cutaneous halo nevi development following plaque radiotherapy for uveal melanoma. A, Wide-angle fundus photograph of the left eye in a 28-year-old woman shows a ciliochoroidal melanoma. B-E, Four months after treatment with iodine 125 plaque radiotherapy, halo (arrows) around multiple cutaneous nevi involving the face, neck, upper chest, and back were documented, with almost complete depigmentation of 1 of the nevi (arrowhead) (B).

noma. There was no history of cutaneous melanoma. Visual acuity was 20/20 OD and 20/25 OS. The melanoma measured 14 mm in basal dimension and 7 mm in thickness (**Figure, A**).

Iodine 125 plaque radiotherapy was performed. Two months after therapy, the patient reported development of a noninflammatory, painless, circumscribed halo around numerous previously pigmented cutaneous nevi, and 1 nevi lost nearly all pigmentation (**Figure, B-E**). At 4 months, the uveal melanoma regressed to 3.7 mm in thickness. Metastatic evaluation findings were negative.

Comment. Cutaneous melanoma can stimulate vitiligo or halo nevi through immune mechanisms. The proposed pathophysiology involves cytotoxic T-cell-mediated immune reaction targeted against antigens shared between normal melanocytes and melanoma cells

such as MART-1, tyrosinase, gp100, TYRP1, and TYRP2.¹ Histopathologically, a lymphohistiocytic infiltrate predominated by CD4 and CD8 T cells has been observed at the margin of such depigmented lesions.¹ Immunotherapeutic strategies for cutaneous melanoma have been attempted based on this observation.¹

In 1968, Nirankari et al⁸ described a 57-year-old man who underwent evisceration for panophthalmitis from undetected uveal melanoma. He developed vitiligo at 9 years and orbital recurrence of uveal melanoma at 11 years, for which orbital exenteration was performed. In 1982, Albert et al⁶ described 2 patients with skin depigmentation following enucleation for melanoma. Case 1 was a 69-year-old man who developed vitiligo 5 years after enucleation, and case 2 was a 36-year-old man who developed cutaneous halo nevi 1 year after enucleation. Albert and colleagues speculated that this represented a heightened host response and more favorable prognosis. In 2004, Duh et al⁷ described a 74-year-old woman with a 12.8-mm-thick uveal melanoma who developed vitiligo 6 years after enucleation. These reports suggest a possible role of the immune system following therapy of uveal melanoma, similar to cutaneous melanoma. We are not aware of other cases of cutaneous halo nevi developing after plaque radiotherapy for uveal melanoma.

The association of cutaneous halo nevus or vitiligo with treated uveal melanoma could be more frequent because these dermal findings can be subtle, as in our case.

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1. Speeckaert R, van Geel N, Vermaelen KV, et al. Immune reactions in benign and malignant melanocytic lesions: lessons for immunotherapy. *Pigment Cell Melanoma Res.* 2011;24(2):334-344.
2. Shields CL, Maktabi AM, Jahnle E, Mashayekhi A, Lally SE, Shields JA. Halo nevus of the choroid in 150 patients: the 2010 Henry van Dyke Lecture. *Arch Ophthalmol.* 2010;128(7):859-864.
3. Rhodes A. Neoplasms: benign neoplasias, hyperplasias, and dysplasias of melanocytes. In: Fitzpatrick TB, Eisen A, Wolff K, Freedberg I, Austen KF, eds. *Dermatology in General Medicine.* New York, NY: McGraw-Hill; 1987: 877-918.
4. Shields CL, Furuta M, Berman EL, et al. Choroidal nevus transformation into melanoma: analysis of 2514 consecutive cases. *Arch Ophthalmol.* 2009;127(8):981-987.
5. Nordlund JJ, Kirkwood JM, Forget BM, Milton G, Albert DM, Lerner AB. Vitiligo in patients with metastatic melanoma: a good prognostic sign. *J Am Acad Dermatol.* 1983;9(5):689-696.
6. Albert DM, Todes-Taylor N, Wagoner M, Nordlund JJ, Lerner AB. Vitiligo or halo nevi occurring in two patients with choroidal melanoma. *Arch Dermatol.* 1982;118(1):34-36.
7. Duh EJ, Schachat AP, Albert DM, Patel SM. Long-term survival in a patient

with uveal melanoma and liver metastasis. *Arch Ophthalmol.* 2004;122(2):285-287.

8. Nirankari MS, Khanna KK, Mathur RP. Uveal malignant melanoma with leucoderma. *J All India Ophthalmol Soc.* 1968;16(2):63-66.

Histopathologic, Immunohistochemical, Ultrastructural, and Cytogenetic Analysis of Oncocytic Uveal Melanoma

The histological findings of malignant melanoma may be highly variable, and the tumor can mimic many other neoplasms.¹ Oncocytic change is defined histologically by abundant, eosinophilic, finely granular cytoplasm due to densely packed mitochondria. Oncocytic change has rarely been described in dermal nevi,² meningeal melanocytoma,³ cutaneous melanoma,^{4,5} or metastatic melanoma.⁶ To our knowledge, we give the first description of exclusively oncocytic uveal melanoma.

Report of a Case. A 73-year-old man visited the outpatient department of ophthalmology with signs of a paracentral scotoma, decreased vision, and metamorphopsia in his left eye for 1 month. Best-corrected visual acuity was 40/40 OD and 20/40 OS. On dilated funduscopy and

ultrasonographic examination of the left eye, a mushroom-shaped hypopigmented subretinal mass was seen superior and temporal to the fovea with a thickness of 7.1 mm, a diameter of 11.4 mm, and medium to low internal reflectivity (**Figure, A**). No atypical cutaneous pigmented lesions were observed. Systemic radiologic evaluation revealed no metastatic lesions. The patient opted for enucleation. After a follow-up of 24 months, there were no signs of metastases.

Sections of the eye confirmed a mushroom-shaped tumor (**Figure, B**) exclusively composed of a trabecular arrangement of epithelioid cells with abundant, finely granular, eosinophilic cytoplasm (**Figure, C**). Mitotic figures were present at 2 per 10 high-power fields. Intracytoplasmic brown pigment stained positive with Masson-Fontana stain. The cytoplasm stained positive with periodic acid-Schiff stain with resistance to diastase treatment. Vascular mimicry with a closed loop pattern was present. The tumor did not show extrascleral extension. Tumor cells stained positive for Melan-A, HMB-45 (**Figure, D**), and tyrosinase, confirming melanocytic lineage. They stained negative for keratin A1/A3, CD56, chromogranin, and synaptophysin, excluding epithelial (neuroendocrine) metastasis.

Ultrastructural studies on formalin-fixed, paraffin-embedded tumor tissue that was deparaffinized, postfix-

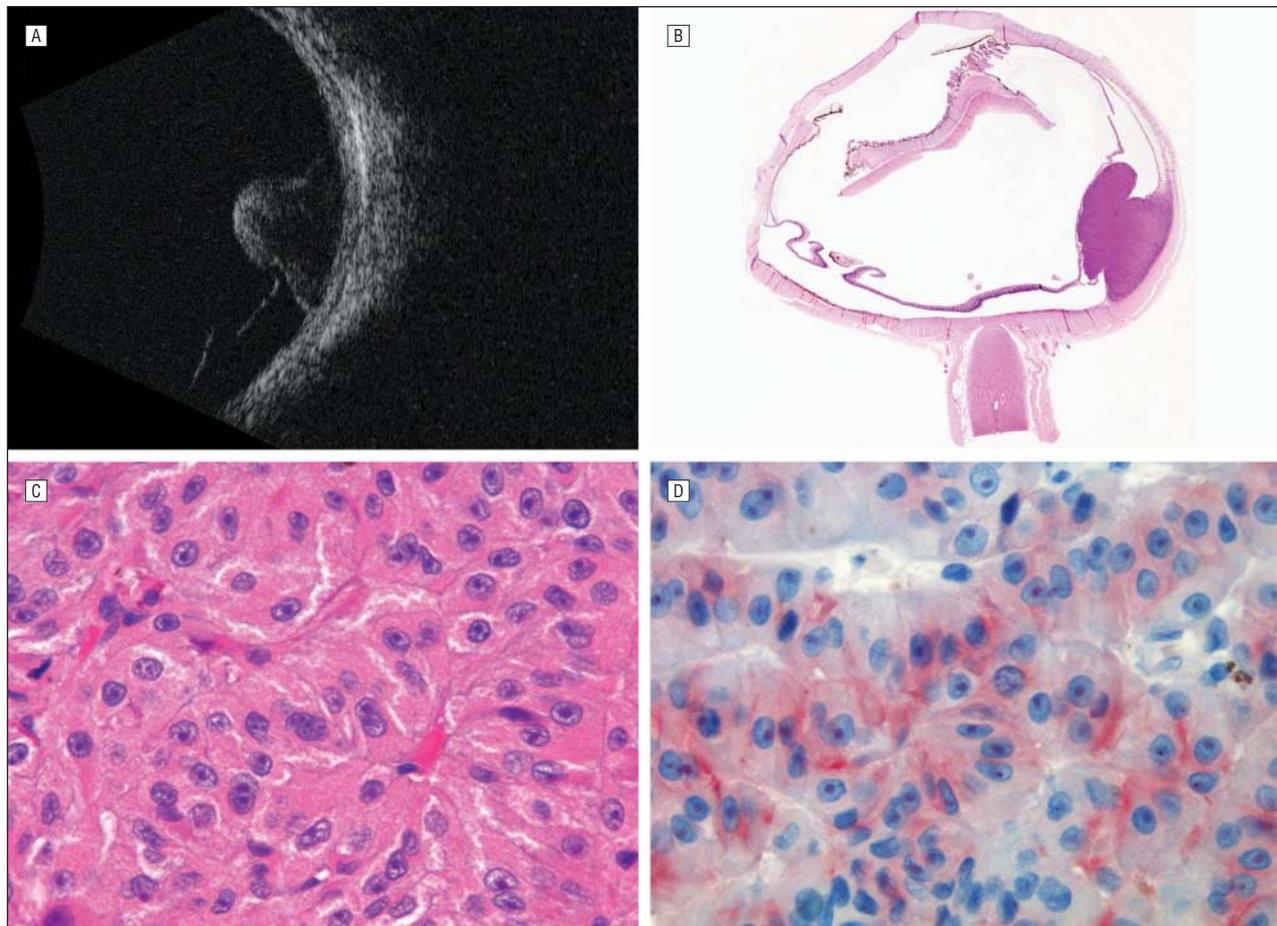


Figure. Ultrasonographic, whole-mount, histologic, and immunohistochemical appearance of the tumor. A B-scan of the tumor (A) and a whole-mount hematoxylin-eosin-stained section (B) of the left eye show a mushroom-shaped subretinal mass in the posterior pole. C, The tumor was exclusively composed of a nested and trabecular pattern of polygonal epithelioid cells with distinct borders and a granular eosinophilic cytoplasm that sometimes contained brown pigment. The nests and trabeculae were surrounded by a delicate capillary network. Nuclei were enlarged with coarse open chromatin and prominent irregular nucleoli (hematoxylin-eosin, original magnification $\times 400$). D, The cells stained positive for the melanocytic marker HMB-45 (original magnification $\times 400$).