

Choroidal Melanoma With Retinal Invasion

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Choroidal melanoma can be associated with invasion into vitreous, retina, optic nerve, sclera, extrascleral tissues, orbit, and intracranial structures.¹⁻⁴ Most of the data regarding local invasion of choroidal melanoma is available from histopathologic studies.²⁻⁴ The Collaborative Ocular Melanoma Study (COMS) provided histopathologic information on 1527 eyes that underwent primary enucleation for choroidal melanoma.² In this cohort, 536 eyes had medium-size melanoma (2.5 to 10 mm in height and 16 mm or less in largest basal diameter), and 991 eyes had large-size melanoma (greater than 10 mm in height or 16 mm in largest basal diameter and 2 mm or greater in height). The microscopic findings regarding melanoma invasive features included rupture of Bruch membrane (88%), scleral invasion (56%), invasion into emissary canal (55%), invasion of the retina (49%), tumor cells in the vitreous (25%), invasion of tumor vessels by tumor cells (14%), vortex vein invasion (9%), and extrascleral extension (8%).² Local invasion of choroidal melanoma generally is believed to be more frequent with larger tumors. Retinal invasion was found in 30.8% of medium-size tumors and 59.0% of large tumors. Despite the relative commonness of microscopic retinal invasion on histopathology, it is not commonly detected clinically. In a large series of 1300 patients with choroidal melanoma with median thickness of 4 mm, less than 1% showed clinical evidence of retinal invasion.⁵ Herein, we report the typical imaging features of choroidal melanoma with retinal invasion.

CASE

A 50-year-old white woman presented with 3 weeks of floaters in her left eye (OS). Past medical history, family history, and ocular history were unremarkable. Ocular examination revealed best corrected visual acu-

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ity (BCVA) of 20/25 in the right eye (OD) and 20/60 OS. Intraocular pressures were 15 mm Hg in both eyes (OU). External and slit-lamp examination OU were unremarkable. Fundus examination OD was unremarkable. Fundus examination OS revealed a mushroom-shaped pigmented choroidal mass, 3 mm from the foveola and 6 mm from the optic disc, measuring 8 mm at its largest basal dimension, with associated subretinal fluid and overlying dark brown retinal invasion (Figure 1A). Fluorescein angiography (FA) displayed blocked fluorescence in the area of retinal invasion surrounded by a rim of hyperfluorescence (Figure 1B). B-scan ultrasonography confirmed a mushroom-shaped, 6.2-mm thick choroidal melanoma (Figure 1C). There was no evidence of vitreous hemorrhage or extrascleral extension. Optical coherence tomography (OCT) showed full thickness replacement of the retina with tumor and abrupt posterior shadowing. These findings were consistent with choroidal melanoma with retinal invasion.

Enucleation vs plaque radiotherapy was discussed with the patient. After informed consent, the melanoma was treated with I-125 plaque radiotherapy with 7000 centigray to the apex and 26 950 centigray to the base over a period of 93 hours. The patient was also started on protocol for protection from radiation complications with 6 planned off-label intravitreal injections of bevacizumab at 4-monthly intervals. At

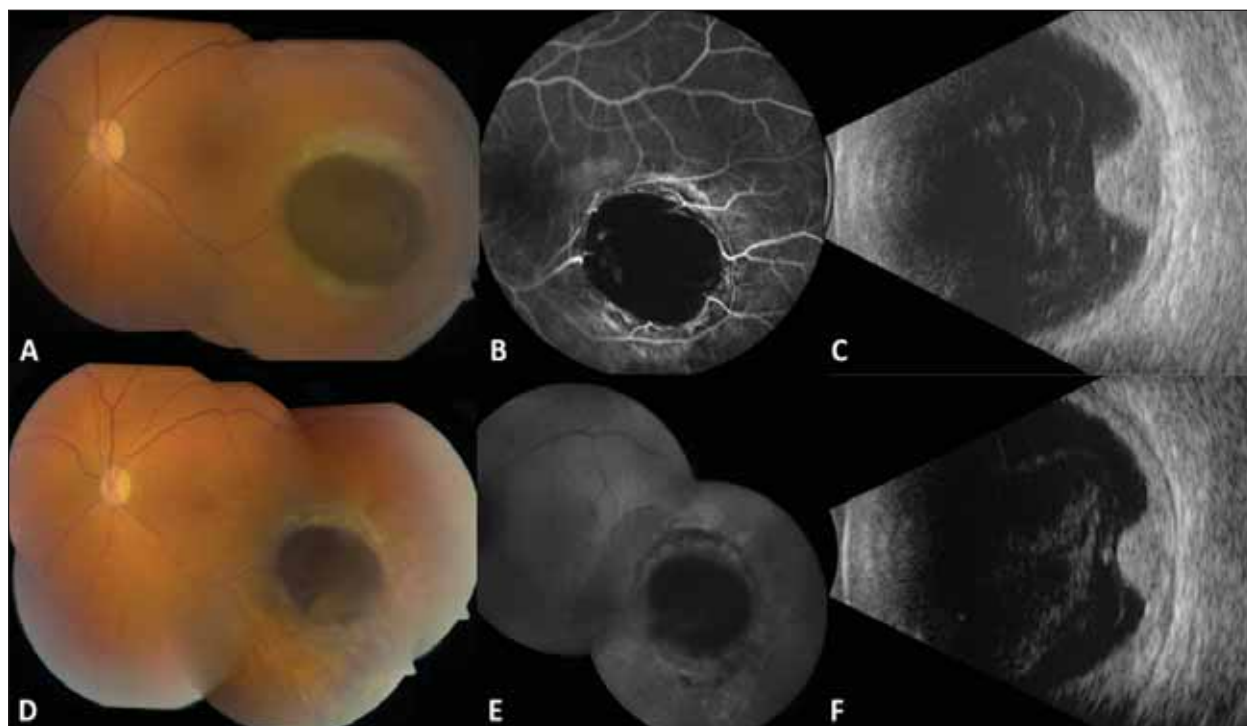


Figure 1. A 50-year-old white woman with (A) fundus image showing choroidal melanoma with retinal invasion; (B) blocked fluorescence at tumor apex, surrounded by hyperfluorescent rim; (C) B-scan ultrasonography demonstrating 6.2 mm thick choroidal melanoma; (D) fundus image showing tumor regression after plaque radiotherapy; (E) fundus autofluorescence showing hypoauteofluorescence at tumor apex; (F) B-scan ultrasonography demonstrating 23% tumor regression.

the 4-month follow-up visit, the tumor had regressed to a thickness of 4.8 mm (Figure 1D-F). Systemic monitoring for metastasis was negative.

DISCUSSION

According to histopathologic studies following enucleation of choroidal melanoma, retinal invasion occurred in 23-50% of cases.⁶⁻⁹ The COMS revealed retinal invasion at a high rate of 49%.² This cohort, however, was composed of mostly large melanoma (65%). In this cohort, 59% of large melanomas and 31% of medium melanomas showed histopathologic evidence of tumor invasion into the retina. Large tumor size ($P < .001$) was statistically predictive of retinal invasion.² Large tumors (>10 mm in height or >16 mm in largest basal diameter) demonstrate a relative risk of retinal invasion of 1.916 ($P < .001$) compared with medium tumors (2.5 to 10 mm in height or <16 mm in largest basal diameter).² Tumor cell type was not predictive of retinal invasion. Spindle, mixed, and epithelioid choroidal melanomas showed equal incidence of retinal invasion between both medium and large melanomas.²

Further study found that irradiated eyes with melanoma show even higher frequency of retinal inva-

sion. In a matched control study by the COMS group regarding histopathologic features in 75 eyes with melanoma that underwent enucleation as a secondary procedure (failed plaque radiotherapy group) compared with 75 eyes that underwent primary enucleation, it was found that the irradiated eyes were more likely to show rupture of Bruch membrane (93% vs 81%, $P < .02$) and retinal invasion (70% vs 30%, $P < .02$).³

Clinically, invasion of the retina can be recognized by a darker, almost black appearance of the melanoma surface, often with a rough appearance to the retinal inner layers, unlike normal smooth retinal contour. Other features of retinal invasion include dilated, tortuous, draining retinal vein (not artery), vitreous hemorrhage, hypofluorescence on FA, and full thickness replacement of retina with tumor on OCT.¹ Eyes with retinal invasion occasionally display dispersed melanoma cells lining the posterior hyaloid as a pre-retinal pigmented membrane, described as "pseudoretinitis pigmentosa."¹⁰

On FA the region of retinal invasion shows nonfluorescence, often surrounded by a ring of hyperfluorescence, as seen in our case (Figure 1B).¹¹ The hyperfluorescence likely represents leakage from damaged

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intraretinal capillaries at the margin of the infiltrated retina.¹¹ In a previous publication from our group, we reviewed FA findings in 99 eyes with choroidal melanoma that displayed retinal invasion, and results showed double circulation pattern (60%), broadened intercapillary spaces (54%), large zones of retinal capillary nonperfusion (35%), blockage of large retinal vessels (25%), and tumororetinal vascular anastomoses (15%).¹² These findings suggest that obliteration of retinal arterioles and venules overlying choroidal melanoma is a reliable marker of retinal invasion.¹¹

Approximately 15% of patients with uveal melanoma require primary enucleation.¹ Traditionally, enucleation is reserved for large tumors in which anticipated vision will be poor with other methods or those with optic nerve or scleral invasion.¹ Presence of retinal invasion is not an indication for enucleation. In our case, the tumor was of medium thickness, at 6.4 mm, and was treated with plaque radiotherapy. Following plaque radiotherapy, choroidal melanoma with retinal invasion can be associated with increased risk for vitreous hemorrhage⁵ and tumor-related lipid exudation, both generally within 2 years following treatment.¹² In an effort to prevent these radiation-related complications, our patient is receiving protocol anti-VEGF (bevacizumab [Avastin, Genentech]) injections.

Prognostically, retinal invasion has been shown to increase the risk for tumor recurrence but not metastasis or death.¹³ A comprehensive clinical study of 8033 eyes with uveal melanoma identified the following factors predictive of metastasis: increasing patient age, ciliary body location, increasing tumor diameter, increasing tumor thickness, deeply pigmented tumor, and the presence of subretinal fluid, intraocular hemorrhage, or extraocular extension.¹⁴ Tumor size (basal diameter $P < .001$ and thickness $P < .001$), older patient age ($P < .001$) and ciliary body location ($P < .001$) were the most powerful predictors of metastasis.¹³

In summary, we describe a case of choroidal melanoma with retinal invasion treated with plaque radiotherapy. Retinal invasion is an important feature of choroidal melanoma related to ultimate risk for vitreous

hemorrhage, dispersion of tumor cells into the vitreous, and tumor recurrence following plaque radiotherapy. ■

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