

# Multifocal Choroidal Malignant Melanoma: At Least 3 Melanomas in One Eye

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**Objectives:** To describe a case of an enucleated eye harboring multiple choroidal malignant melanomas.

**Methods:** Clinical, ultrasonographic, and histopathological evaluations.

**Results:** Meticulous sectioning of the globe did not disclose any structural continuity between the 3 choroidal

melanomas. Fourth and fifth masses were connected to one of the tumors by fibrous tissue and therefore were not considered as additional distinct lesions.

**Conclusion:** Although very rare, a single eye can harbor multiple distinct choroidal melanomas.

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**R**EPORTS documenting the simultaneous presence of more than one primary uveal malignant melanoma are scarce. The lifetime risk of developing bilateral primary uveal melanomas is approximately 1 in 50 million.<sup>1</sup> Bilateral occurrences of uveal malignant melanoma have been described.<sup>1,2</sup> Unilateral double melanomas have been associated with ocular melanocytosis<sup>3,4</sup> and as a syndrome in association with systemic malignant neoplasms.<sup>5</sup> However, other cases of double melanoma do not show any such associations.<sup>6</sup> Volcker and Naumann<sup>7</sup> reported a case of 2 separate choroidal melanomas and 2 uveal nevi in one eye; Pe'er and Bernstein-Lifshitz<sup>8</sup> reported a case of an eye containing both a choroidal and an iridociliary melanoma. Condon and Mullaney<sup>9</sup> reported on the case of an eye harboring a choroidal malignant melanoma, an iris malignant melanoma, and a separate iris benign melanoma.

Only one case of which we are aware in the literature can qualify as true multifocal (>2 melanomas in one eye, as opposed to double) uveal malignant melanoma.<sup>10</sup> However, this case lacks histological proof.

We report a case of a multicentric choroidal malignant melanoma in which serial sections of the enucleated eye prove, beyond any doubt, the presence of at least 3 spatially separated melanomas.

## REPORT OF A CASE

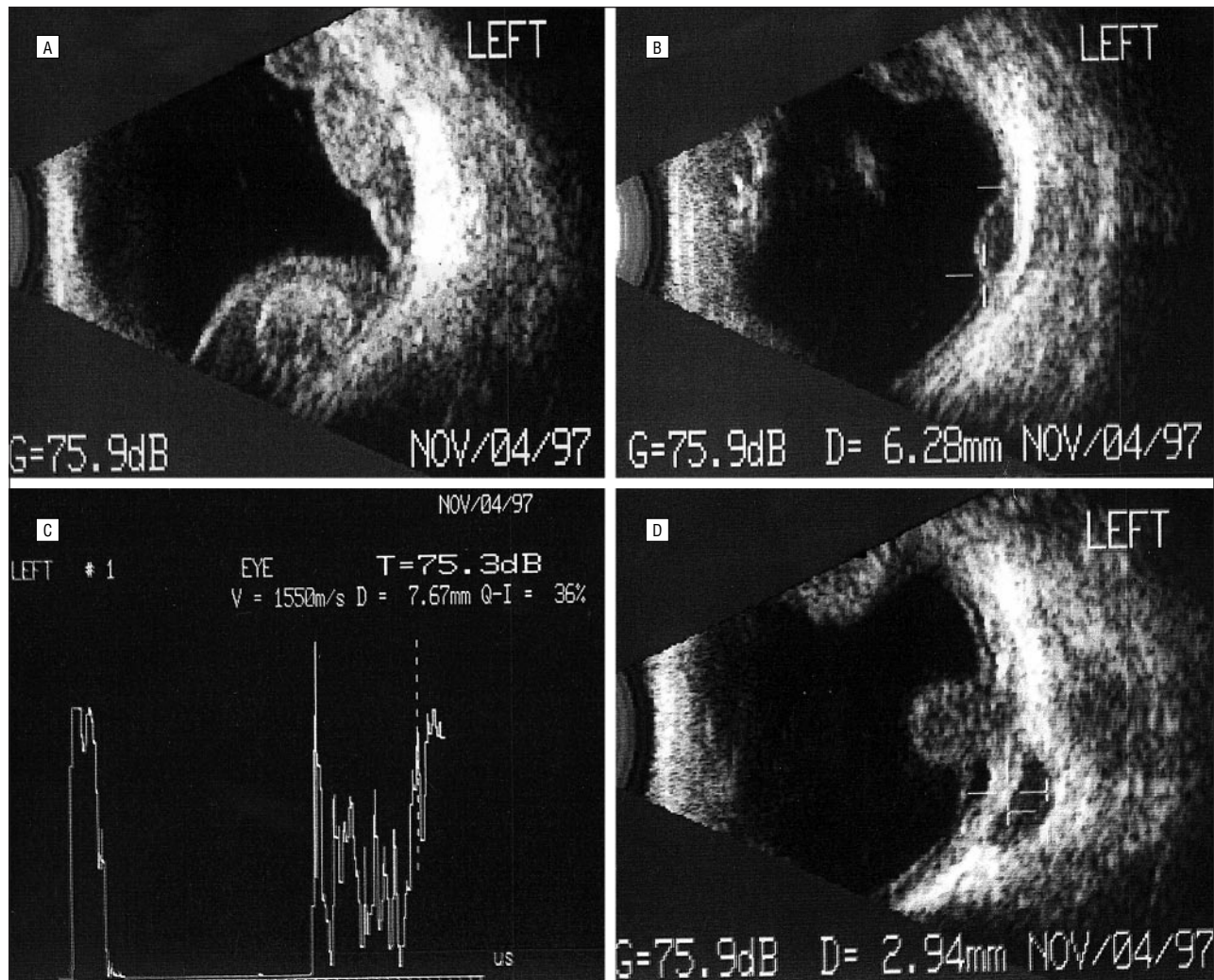
A 79-year-old nondiabetic white man was found to have a dense spontaneous vitre-

ous hemorrhage of the left eye 4 years after uneventful cataract extraction and intraocular lens implantation in both eyes. The ultrasonographic finding of a suspected solid mass component in the posterior segment prompted his referral to our ocular oncology clinic. At the time the patient was receiving low-dose aspirin therapy.

On initial examination, visual acuity OD was 6/7.5 and light perception OS. Anterior segment evaluation was unremarkable (apart from bilateral pseudophakia) and applanation intraocular pressures in both eyes were normal. There was no evidence of ocular or oculodermal melanocytosis. Dilated fundus examination of the left eye revealed a vitreous hemorrhage, a suspected inferior retinal detachment, and a large irregular mass at the superonasal periphery. Repeated observations every several weeks were deemed appropriate since a single solid component could not be accurately delineated ultrasonically in the presence of a massive hemorrhagic choroidal detachment in all 4 quadrants, as well as a dense vitreous hemorrhage.

Four months later, when the hemorrhagic components decreased, multiple solid, elevated lesions were observed clinically as well as on standardized echography (**Figure 1**, A and B). Figure 1, C shows low-medium internal reflectivity (measured as 36%). In addition, the ultrasound examination revealed, for the first time, a small localized extrascleral nodule (Figure 1, D). Findings from systemic evaluation that included liver ultrasound, liver function

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**Figure 1.** Standardized echographic scans. A, Inferiorly: a mushroom-shaped solid mass topped by retinal detachment. B, Tumor No. 3 (compare the ultrasonographic appearance of this small tumor to the gross appearance seen in Figure 2, left cup). C, Standardized A-scan demonstrating low-medium internal reflectivity. No retinal detachment is seen topping tumor No. 1 in this probe orientation. D, A peripheral section through tumor No. 1 showing a small mushroom-shaped solid mass, rimmed by a shallow exudative retinal detachment. An adjacent extrascleral-extension nodule is seen overlying the sclera and measured  $6.5 \times 2.9$  mm.

tests, and a chest radiograph did not disclose any evidence of metastases.

Surgical exploration showed the extrascleral component to be a darkly pigmented nodule overlying the sclera. The eye was enucleated and fixed in buffered formaldehyde solution.

At 9-month follow-up, the patient was free of any distant metastases.

## RESULTS

### GROSS EXAMINATION

The specimen consisted of a firm left eye, measuring  $26.5 \times 25.5 \times 25.5$  mm. By transillumination, a large shadow was seen in the inferonasal quadrant that measured

$23 \times 18$  mm (tumor No. 1). Another smaller shadow was seen in the superotemporal quadrant (tumor No. 2). A heavily pigmented mass measuring  $7 \times 9$  mm was bulging through the sclera at the inferonasal quadrant about 4 mm from the optic nerve. The eye was opened obliquely, superotemporally to inferonasally (**Figure 2**). An intraocular lens implant was seen in the posterior chamber. Multiple lobules of mostly amelanotic tumors were seen in the inferonasal quadrant. Tumor No. 1 measured 13 mm in diameter and 10 mm in maximal height. Tumor No. 2 was bilobular in shape, measured  $8 \times 10$  mm, and was seen in the superotemporal quadrant. Tumor No. 3 was a small, dome-shaped tumor seen in the superonasal quadrant.

The retina in the posterior pole was detached.

### MICROSCOPIC EXAMINATION FINDINGS

Microscopic examination findings revealed an eyeball with multiple uveal melanoma tumors (**Figure 3**). The largest tumor, at the inferonasal part of the eye (tumor No. 1), extended from the pars plana to a point behind the equator. The tumor was seen breaking Bruch membrane in one area and invading the sclera and extending outside of the eyeball into the orbit. This tumor was of mixed-cell type composed mainly of epithelioid cells. There were about 2 to 3 mitoses per 20 high-power-field, and periodic acid-



Schiff staining networks of loops were seen throughout. The retina over all 3 tumors was atrophic, and an associated retinal detachment was seen rimming and at times topping the tumors. Pigment-laden macrophages were seen in the sub-retinal fluid. Immediately behind the main tumor there were 2 small, additional mixed-cell choroidal melanomas that were not directly connected to the larger tumor.

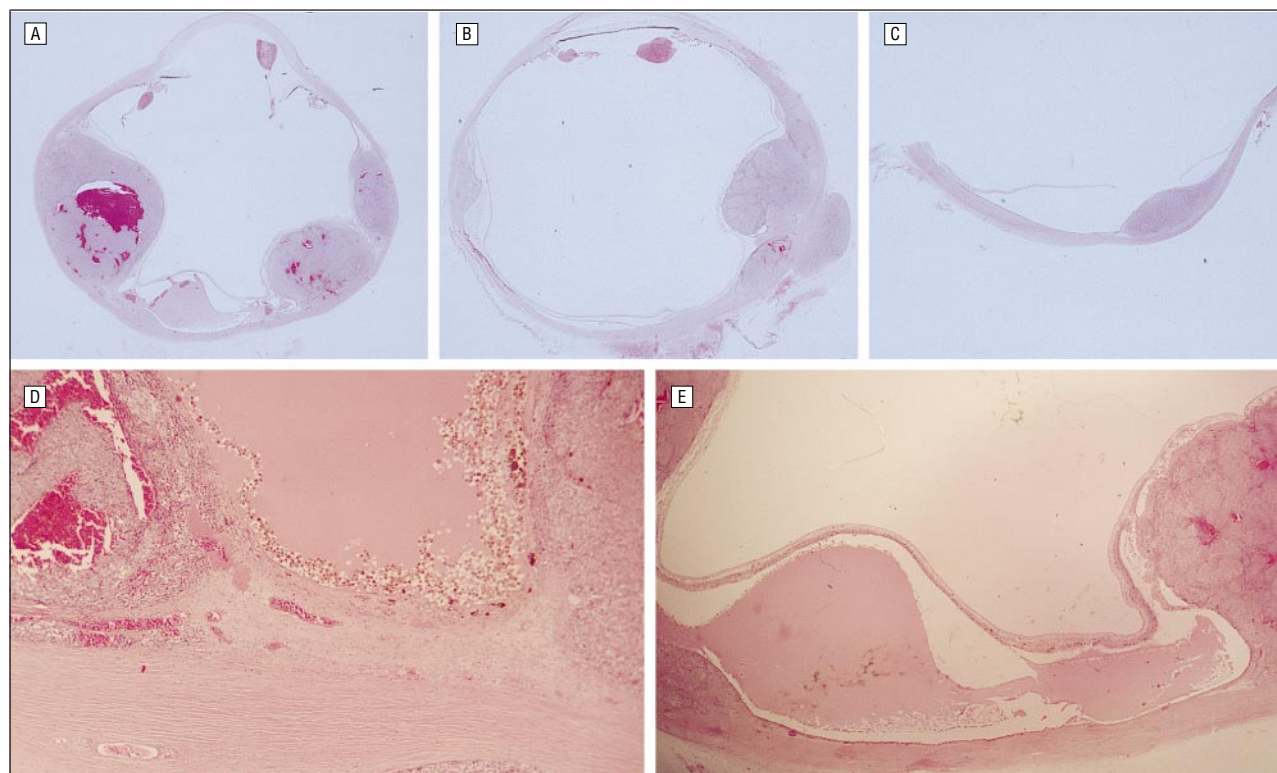
However, because of their close proximity and the finding of a bridge of fibrous tissue, as opposed to normal choroid, bridging the main tumor to the other 2 tumors, we chose not to count these 3 tumors as distinct tumors (Figure 3, D). Another medium-sized bilobular melanoma was seen in the superotemporal quadrant (tumor No. 2). It is of the mixed-cell type and in one area invaded the

sclera only superficially. Another small mixed-cell-type choroidal melanoma was seen in the superonasal choroid (tumor No. 3).

Meticulous serial sectioning of the globe, using hundreds of slides of 7 different blocks, showed areas of normal choroid between the 3 main masses and failed to demonstrate any microscopic connections between them (Figure 3, E), confirming that they were, indeed, spatially separate.



**Figure 2.** Three gross sections of the enucleated eye. A, A cup of the eye showing 2 tumors. On the left, a partially pigmented tumor No. 1. On the right, a bilobular tumor No. 2. B, A pupil-optic nerve section that again shows tumor No. 1 on the right, and tumor No. 2 on the left. A small retinal detachment is seen in the posterior pole between these 2 tumors. C, The other cup of the eye shows the partially pigmented tumor No. 3, surrounded by normal choroid.



**Figure 3.** Microscopic sections. A, A whole-mount picture through the globe showing tumor No. 1 on the left and the bilobular tumor No. 2 on the right (hematoxylin-eosin). B, A whole-mount picture through the periphery of tumor No. 1, showing the extrascleral component, and tumor No. 2 on the left (hematoxylin-eosin). C, A whole-mount picture showing tumor No. 3 (hematoxylin-eosin). D, The area between 2 parts of tumor No. 1 showing a fibrous bridge between these adjacent melanomas (hematoxylin-eosin, original magnification  $\times 10$ ). E, The area between the posterior borders of tumor No. 1 on the right and tumor No. 2 on the left, in their closest proximity, shows normal choroid and exudative retinal detachment above it (hematoxylin-eosin, original magnification  $\times 4$ ).

#### COMMENT

A case in which a patient's eye is harboring more than 2 uveal melanomas is indeed a rare occurrence. We are aware of only one such case, which was reported by Rosen and Moulton<sup>10</sup> in 1953. Within a single eye, 1 large and, in addition, 4 small, flat, discrete tumor nodules were seen in the vicinity of the optic nerve head, both clinically and on findings from pathologic examination. Ciliary body involvement was also observed microscopically. However, as those authors state:

The actual number of lesions cannot be stated inasmuch as serial sections were not made through the whole eye. However, serial sections carried through a portion of the posterior segment which appeared grossly to contain a single moderate-sized tumor of the choroid, reveal two separate and distinct malignant melanomas of the choroid which are in no way connected with any other lesion.<sup>10</sup>

Rosen and Moulton conclude that "At least two of the lesions are completely independent. . . . The exact number of lesions cannot be stated in the absence of serial sections through the whole eye."

Lois et al<sup>11</sup> recently published a case of a 3 separate uveal melanomas in 2 eyes of the same patient. In this unique report, they conclude that "Although histopathologic studies were not available, clinical findings as well as results of ancillary studies were consistent and strongly suggestive of . . ." bilateral choroidal melanomas, as well as a unilateral diffuse iris melanoma in a single patient. They conclude that "it is unlikely that any of these lesions represent metastases from another primary tumor."

We report on a histologically verified case of a single eye harboring at least 3 distinct noncontiguous uveal melanomas. While the simultaneous presence of several choroidal neoplasms may be secondary to metastatic dissemination from a single primary tumor, we feel that this is unlikely. There was neither systemic evidence of metastases at the time of presentation nor any evidence of metastatic disease at 9-month follow-up.

In conclusion, this case represents an eye harboring several spatially separated primary neoplastic tumors. Unfortunately, we are not aware of a genetic or other markers that could unequivocally ascertain whether the distinct tumors originated from a single cell line.

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## From the Archives of the Archives

### A look at the past . . .

To pursue the method for which my plea is made does not necessitate a thorough training in bacteriological technique. A little practice in staining cover-glass preparations both in the usual way and by Gram's method, together with a study of the pictures presented by the gonococcus and the pneumococcus, will enable one, as a rule, to make an immediate diagnosis. When we fail to find the latter in cases at all suspicious, it may be advisable to resort to cultures, but these instances will be in the great minority. To grow the gonococcus will require the aid of a trained bacteriologist, as it is probably the most difficult of all organisms to cultivate on artificial media, but fortunately the appearance of a cover-glass preparation is so characteristic that a mistake is scarcely possible to one having any training in bacterioscopy.

Reference: Kibbe AB. A plea for the more general use of the microscope in diagnosis by ophthalmologists. *Arch Ophthalmol.* 1898;27:373.