

Clinicopathologic correlations in eyes enucleated after uveal melanoma resection with positive surgical margins

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We identified three eyes that had undergone enucleation after transscleral resection of uveal melanoma. Two enucleated eyes with microscopically positive margins of resection exhibited no evidence of residual melanoma and these patients were alive without metastasis with at least four years' follow-up. One eye with a transected melanoma contained residual melanoma and that patient died with metastatic melanoma to the liver three years after enucleation. There appear to be at least two general types of positive surgical margins of resection of uveal melanoma:

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microscopically positive margins and macroscopically positive (transected) margins of resection.

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Currently, there is no evidence that indicates the superiority of any single treatment modality with regard to survival of the patient with uveal melanoma.¹ Local resection may be appropriate for certain ciliary body melanomas or ciliochoroidal melanomas.² Local resection of uveal melanoma is a technically demanding procedure with a high incidence of positive or questionable surgical margins of resection.^{3,4,7} The purpose of this study was to understand the implications of positive surgical margins of resection.

Case Reports

Case 1

A 79-year-old man who had a history of age-related macular degeneration was found on routine ophthalmic examination to have a minimally pigmented tumor in the ciliary body and choroid of his right eye. The patient underwent a lensectomy, cyclectomy and eye wall resection for the tumor. The resected specimen showed a 10 mm diameter X 8 mm thickness minimally pigmented ciliary body/choroidal tumor [Fig. 1].

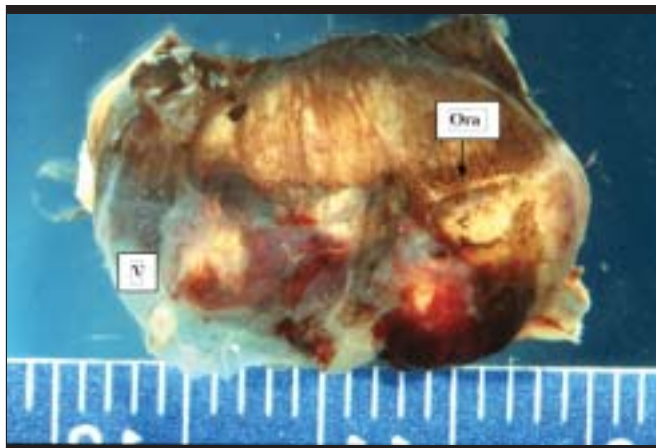


Figure 1: Case 1. The resected melanoma straddles the ora serrata (Ora). The vitreous base (V) is present. There is hemorrhage at the posterior aspect of the tumor

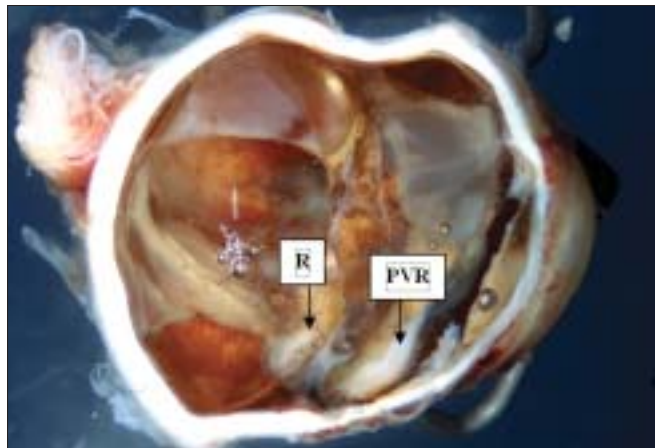


Figure 3: Case 1. The enucleated, aphakic eye contains proliferative vitreoretinopathy (PVR) and detached, gliotic retina (R). There is no grossly apparent residual melanoma

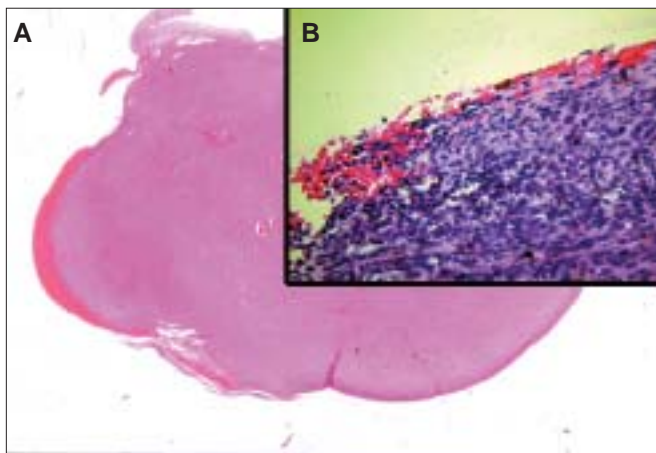


Figure 2: Case 1. A. The lobular tumor is not transected. There is microscopic extension of the resected tumor to its lateral margins. B. Tumor cells and erythrocytes are present at the lateral margin (inset) (H/E, A. 10x, B. 100x)

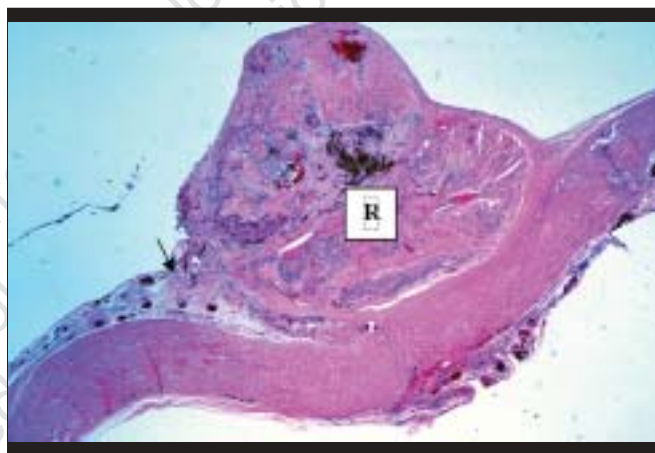


Figure 4: Case 1. The choroid terminates (arrow) in the area of the resected tumor. Detached, gliotic retina (R) is present in this area (H/E, 25x)

Microscopic examination showed a mixed cell type melanoma that extended to the lateral margins of resection, although the tumor was not transected [Fig. 2]. The patient developed proliferative vitreoretinopathy, a tractional retinal detachment, fibrovascular ingrowth and a blind, painful right eye. He underwent enucleation nine months after local resection. The enucleated eye showed no residual melanoma [Fig. 3]. There was redundant, gliotic retina and proliferated ciliary body epithelium posterior to the resected ciliary body [Fig. 4]. There was no residual melanoma. The patient had no evidence of metastatic melanoma four years after enucleation.

Case 2

A 45-year-old man with a two-week history of cloudy vision was found to have a moderately pigmented tumor of the ciliary body and peripheral iris in his right eye. The patient underwent an iridocyclectomy and partial eye wall resection. The resected specimen showed a moderately pigmented 9 mm diameter X 4 mm thickness tumor. Microscopic examination showed an epithelioid cell type melanoma that extended to the posterior and lateral margins of resection, although the tumor was not

transected. The patient developed a vitreous hemorrhage and due to microscopic extension of the melanoma, the eye was enucleated two weeks later. Examination of the enucleated specimen showed the site of iridocyclectomy temporally and no evidence of residual melanoma. The patient had no evidence of metastasis five years after enucleation.

Case 3

A 56-year-old man was found to have a moderately pigmented ciliary body/choroidal tumor in his right eye during a routine ophthalmic examination. A lamellar sclerouveaectomy was performed. The resection specimen showed a 12 mm diameter X 5 mm thickness multilobed tumor [Fig. 5]. Microscopic examination showed a mixed cell type melanoma with the posterior margin of the tumor transected [Fig. 6]. Due to transection of the melanoma, the eye was enucleated two weeks later. The enucleation specimen showed the site of previous sclerouveaectomy temporally with a 3X3mm nodule of residual melanoma [Fig. 7]. Microscopic examination confirmed the residual melanoma [Fig. 8]. An abdominal CT three years after enucleation showed multiple liver nodules, consistent

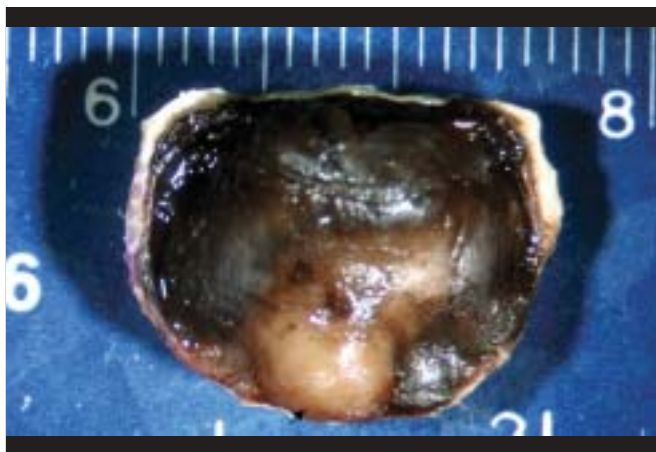


Figure 5: Case 3. The resected melanoma is multilobed. The posterior aspect of the melanoma is transected (arrow)

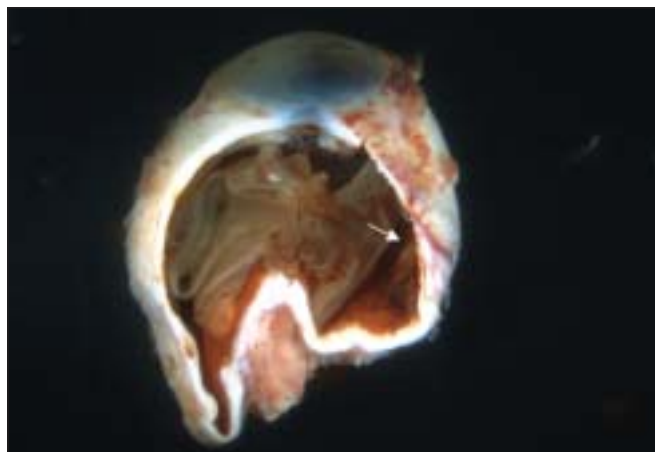


Figure 7: Case 3. A nodule of recurrent (residual) melanoma (arrow) is present in the enucleated eye

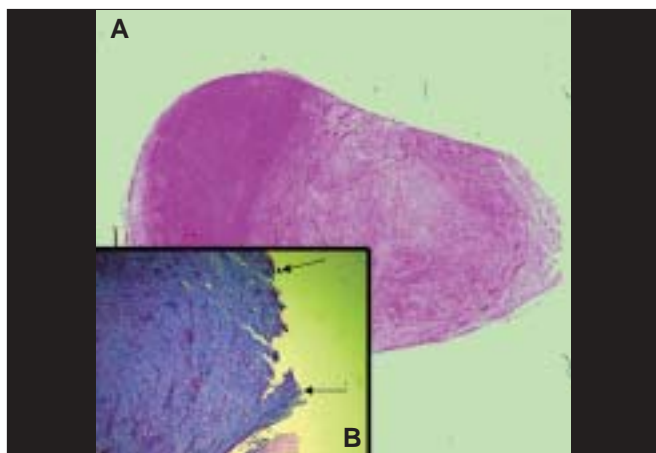


Figure 6: Case 3. A. The resected melanoma is lobular. B. (inset) The area of posteriorly transected tumor (between arrows) is visible on low magnification (H/E, A. 5x, B. 25x)

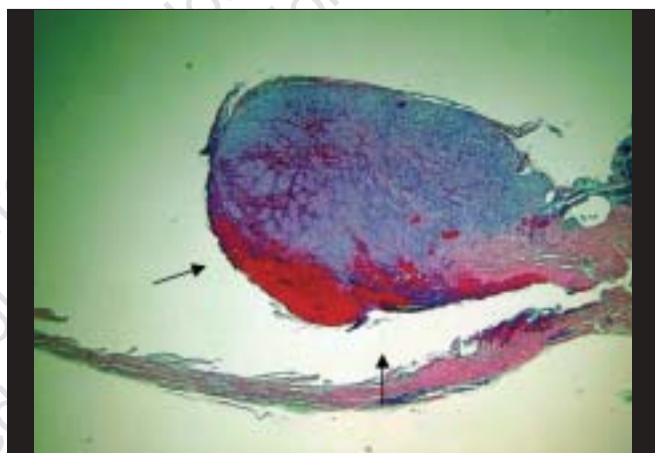


Figure 8: Case 3. The transected portion of recurrent (residual) melanoma is hemorrhagic (between arrows) (H/E, 25x)

with metastatic melanoma. The patient died three years after enucleation.

Discussion

In a matched, case-control study comparing transscleral resection and I¹²⁵ brachytherapy for uveal melanoma, patients who underwent transscleral resection were found to have a significantly smaller risk of developing cataract, vitreous hemorrhage and maculopathy compared to those treated with brachytherapy.⁸ Additionally, rubeosis, glaucoma and optic neuropathy were found only in the brachytherapy group.⁸ Melanoma-specific survival after I¹²⁵ and local resection were comparable. There was greater local tumor control in the I¹²⁵ treated group compared with the locally resected group.⁸

Local resection of uveal melanoma is technically demanding with numerous associated risks including vitreous hemorrhage, retinal/subretinal hemorrhage, ptosis, cataract, retinal detachment, proliferative vitreoretinopathy (PVR), choroidal detachment and persistent corneal edema.⁹ Two series have reported positive or questionably positive margins of excision in 68 of 138 patients (49.3%)⁴ and 174 of 286 (60.8%)⁵ patients.

However, recurrent melanoma was found in only 13 of 138 patients (9.4%)⁴ and 57 of 286 patients (19.9%)⁵ in those series. Other studies have reported similar incidences of recurrence after local resection ranging from 3 to 18%.^{3,6,7} Our laboratory has evaluated 5/12 (41%) resected melanomas with positive surgical margins of resection and 1/12 (8%) that recurred, similar to the published series.^{3,4,7} Although recurrences were probably prevented by additional treatment with brachytherapy in some of those cases, it is clear that positive surgical margins of resection without additional treatment did not lead to persistent (recurrent) tumor in many cases.^{3,4,7} None of the patients in this report had additional treatment for their uveal melanoma.

The relatively high rates of positive surgical margins after local resection of uveal melanoma may be explained by the fact that the uveal tract is a continuous tissue without anatomic barriers that prevent lateral spread of melanoma. Noncontiguous tumor recurrence of uveal melanoma after local resection has been reported.^{8,10} Evaluation of the surgical margins of resection is, at best, a percentage of the margin of the entire specimen. An inadequately sampled margin, multifocal tumor or a separate primary melanoma may account for tumor persistence

(recurrence) after reportedly negative margins. However, melanoma recurs in only approximately 20 to 33% of eyes after local resection with positive surgical margins.^{4,5} This may be due to secondary treatment (i.e. brachytherapy), spontaneous regression of residual melanoma or melanoma extending to but not beyond the surgical margin. Our cases provide examples of two general types of positive surgical margin of excision of uveal melanoma. The first type is the microscopically positive margin, as seen in Cases 1 and 2. The second type of positive margin occurs when the tumor is transected.

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