AMERICAN ACADEMY™ OF OPHTHALMOLOGY

Vitrectomy and Vitrector Port Needle Biopsy of Choroidal Melanoma for Gene Expression Profile Testing Immediately before Brachytherapy

Deepthi M. Reddy, MD,[1,2] *Lauren B. Mason, BS,*[1] *John O. Mason III, MD,*[1,2] *Jason N. Crosson, MD,*[1,2] *Jacob J. Yunker, MD*[3]

Purpose: Transvitreal and transscleral needle biopsy can result in complications including vitreous hemorrhage and retinal detachment. This study evaluated a technique using 25-gauge vitrectomy as an adjunct to needle biopsy immediately before brachytherapy to minimize these complications and preserve good visual acuity.

Design: Retrospective, observational case series.

Participants: Fifty-seven consecutive eyes of 57 patients with treatment-naïve medium choroidal melanomas without extraocular extension from July 2012 through September 2015.

Methods: Fifty-seven consecutive eyes of 57 patients with a clinically diagnosed choroidal melanoma underwent complete 25-gauge posterior vitrectomy followed by transvitrector port fine-needle aspiration biopsy of the tumor immediately before implantation of a radioactive iodine 125 plaque as treatment for the tumor. Cytopathologic analysis was not performed on the tumor aspirates in this study.

Main Outcome Measures: Best-corrected postoperative visual acuity, postoperative complications of the reported technique, implantation tumor development, local tumor recurrence, presence of metastatic disease after surgery, and sufficiency of the tumor aspirates obtained by the reported technique for successful gene expression profile testing and prognostic classification.

Results: Mean preoperative and postoperative visual acuities were similar (20/60 vs. 20/80, respectively). Mean tumor thickness was 5.0 mm (range, 2.5–10 mm) and mean tumor basal diameter was 13.1 mm (range, 7–22 mm). Only 1 of 57 eyes (1.8%) showed a transient vitreous hemorrhage, biopsy yield was 100% for genetic analysis, and no patients showed recurrence or implantation tumor at the vitrector site.

Conclusions: Combined 25-gauge posterior vitrectomy and 25-gauge trans-vitrector port needle aspiration biopsy immediately before brachytherapy is excellent for obtaining tumor aspirate for gene expression profiling while controlling for hemostasis, resulting in few complications. *Ophthalmology 2017;124:1377-1382 © 2017 by the American Academy of Ophthalmology*

Supplemental video available at www.aaojournal.org.

Of the primary intraocular malignancies, uveal melanoma is the most common with an annual incidence of approximately 6 cases per 1 million.[1–3] Even with advancements in the treatment of choroidal melanomas, approximately 50% of patients die within 25 years secondary to metastases.[4,5] Although the diagnosis of classic choroidal melanoma usually can be made based on clinical examination and noninvasive test results, fine-needle aspiration biopsy (FNAB) of the tumor as an additional surgical intervention in combination with sight-preserving brachytherapy, in leu of en bloc tumor resection or enucleation, has emerged as one method accepted for determining metastatic potential. Other methods for determining metastatic potential include 2010 tumor, node, metastasis classification based on tumor characteristics as well as cytopathologic classification of tumor aspirates. With the use of genetic expression profiling (GEP), uveal melanomas can be classified as having low metastatic risk (class 1) or as having a substantially higher risk of clinical metastases developing and leading to death as a result of metastatic disease (class 2) using a polymerase chain reaction–based 15-gene assay.[6] This RNA-based GEP test (Castle Biociences, Inc, Friendswood, TX) has been shown in several studies to be more accurate than the clinical, pathologic, and chromosomal prognostic factors in predicting the likelihood of metastases.[7–11] In addition, it requires a smaller amount of biopsy material for analysis.[6]

Currently, FNAB via a transscleral or transvitreal (without concomitant vitrectomy) route is used to biopsy choroidal melanomas.[12] The transvitreal approach necessitates perforation of the retina and puncturing of the

http://dx.doi.org/10.1016/j.ophtha.2017.03.053
ISSN 0161-6420/17

vascularized choroidal tumor, which can result in traumatic bleeding. The level of the risk does vary with the thickness of the tumor, prominence of blood vessels in the part of the tumor sampled, number of biopsy sites (the greater the number of sites, the greater the risk of bleeding), and the needle gauge used (potential smaller risk of bleeding with smaller-gauge needle used). Additionally, the anatomic sites where the hemorrhage may accumulate (subretinal or intravitreal) depends on whether there is a serous detachment overlying the tumor, the tumor characteristics before biopsy (eruption through Bruch's membrane, retinal invasion, and presence or absence of overlying subretinal or intravitreal hemorrhage). In a series of 140 uveal melanoma biopsy samples obtained via transvitreal approach for FNAB, 46% of the patients demonstrated transient, localized vitreous hemorrhage.[13] Although the vitreous hemorrhage resolved in all of these patients without requiring additional surgery, the postbiopsy hemorrhage may result in temporary vision loss. In addition to vitreous hemorrhage, inadequate sample size is a potential drawback of the transvitreal approach. In a retrospective case series of 34 patients with choroidal melanomas, 35.3% of the FNAB sample yielded an inadequate sample for cytodiagnosis.[14] However, these tumors were small choroidal tumors in comparison with the tumors in this study, which theoretically could contribute to a less-than-adequate sample. It should also be noted that cytopathologic analysis (as in the study mentioned above) is not the same as the GEP conducted in our present study. Moreover, Augsburger et al[15] previously showed that insufficient aspirates (via 2 or more sites sampled) for cytodiagnosis suggest a favorable prognosis, and not necessarily a sampling error. In fact, FNAB may be used concurrently to obtain cellular aspirates for GEP and cytopathologic analysis, and even if the aspirate is insufficient for useful cytodiagnosis, GEP yield may still be sufficient.[16] In comparing the transvitreal approach with the transscleral approach, the transscleral approach has a lower incidence of vitreous hemorrhage. In a series of 24 eyes, Young et al[17] reported vitreous hemorrhage as a complication in 20% of the eyes. The biopsy technique used in the Young et al study, which may be different than that used by other ocular oncologists, also used multiple subretinal needle passes into the tumor, which could contribute to vitreous hemorrhage. Even if the hemorrhage resolves without requiring surgery, the technique still may contribute some compromise to visual acuity. Over the past decade, 25-gauge pars plana vitrectomy (PPV) increasingly has replaced standard 20-gauge PPV for most vitreoretinal surgery. It decreases surgically induced trauma at sclerotomy sites, and consequently reduces postsurgical patient discomfort.[18] The aforementioned benefits allow for more rapid postoperative visual recovery. Like any other procedure, there are risks associated with 25-gauge PPV including, but not limited to, hypotony, retinal detachment, endophthalmitis, and cataract development, as well as progression.[19–21] We report a surgical technique for the biopsy of choroidal melanomas immediately before brachytherapy that includes 25-gauge PPV, FNAB using a 25-gauge needle on a 10-ml syringe, and endolaser for hemostasis to preserve visual acuity after biopsy by preventing transient or non-transient vitreous hemorrhage.

Methods

Institutional review board approval from the University of Alabama-Birmingham Institutional Review Board and informed consent were obtained before collection of patient data. The study complied with the Health Insurance Portability and Accountability Act and adhered to the tenets of the Declaration of Helsinki.

This was a retrospective review of 57 consecutive eyes that underwent a 25-gauge PPV followed by a transvitreal choroidal melanoma biopsy and placement of a radioactive iodine 125 (I^{125}) plaque. The original Collaborative Ocular Melanoma Study classification of tumor size using thickness was used to categorize the choroidal melanomas in this study. All patients with medium classic choroidal melanomas who sought treatment at Retina Consultants of Alabama P.C. from July 2012 through September 2015 and underwent 25-gauge PPV with a transvitreal needle biopsy of the melanoma and subsequent brachytherapy were included. Patients who had small choroidal melanomas or atypical melanomas, who received treatment before initial presentation, who had ciliary body melanomas that required transscleral biopsy, or who required enucleation because of a large choroidal melanoma, extraocular extension, or both at presentation did not undergo the technique being reported.

All patients underwent the same technique (Video 1, available at www.aaojournal.org) and included placement of an I^{125} radioactive plaque. Before the biopsy portion of the procedure, conjunctiva was dissected from the sclera and the location of the choroidal melanoma was determined via transillumination or indirect ophthalmoscopy and was delineated using a marking pen on the sclera. Next, a standard 3-port PPV was performed with 25-gauge instrumentation (Fig 1). Vitrectomy was performed with only the required minimal manipulation of the retinal surface overlying the choroidal melanoma to minimize dispersion of tumor cells into the vitreous cavity. Only a core vitrectomy was performed. A posterior vitreous detachment was not induced if not already present and epiretinal membranes, if present, were not removed because they were not visually significant. Additionally, localized serous retinal detachments overlying choroidal melanomas were not repaired because we have found these typically resolve after brachytherapy. After the PPV, the IOP was increased from 30 to 60 mmHg as a 25-gauge 1.5-inch needle, attached to a 10-ml syringe, was passed through 1 25-gauge cannula to collect the aspirate from the tumor (Fig 2). Although other ocular oncologists use connector tubing between the biopsy needle and the aspirating syringe, in all cases we used a 10-ml syringe without connector tubing. Aspirate was collected from 2 extramacular tumor locations while care was taken to avoid any major retinal vessels. The microscopic cells from both sites were aspirated with the same 25-gauge needle with suction using a 10-ml syringe consecutively, so that the tumor aspirates from both sites were admixed, being careful to apply aspiration only while the needle was within the tumor. Immediately after the aspirate was collected, endolaser cauterized the area around the penetrated retina and choroid and the IOP was reduced from 60 mmHg to 30 mmHg. The ports were removed and sclerotomies were closed with 8-0 Vicryl sutures (Ethicon, New Brunswick, NJ). Although sclerotomies created by 25-gauge cannulas typically are left unsutured, we