Chromosome 3 Analysis of Uveal Melanoma Using Fine-Needle Aspiration Biopsy at the Time of Plaque Radiotherapy in 140 Consecutive Cases

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Reviewing clinical records of patients with uveal melanoma at the Ocular Oncology Service at Wills Eye Hospital, **Shields et al.** *evaluated the feasibility of using fine-needle aspiration biopsy (FNAB) prior to plaque radiotherapy to obtain cells for genetic testing of chromosome 3 abnormalities. Of the 140 eyes sampled, the researchers found monosomy 3 in 44 cases (31 percent) and disomy 3 in 76 cases (54 percent) using DNA amplification and microsatellite assay. Greater tumor basal dimension (P = 0.02) and greater distance from the optic disc (P = 0.02) were factors predictive of monosomy 3. In 20 cases (14 percent), genetic analysis was not possible due to inadequate DNA genomic yield. Although a 30-gauge needle via the transscleral tumor base approach produced adequate DNA yield in just 75 percent of cases, adequate DNA was obtained in 97 percent of cases with a 27-gauge needle via the transvitreal tumor apex approach. Given these results, the researchers concluded that FNAB is capable of providing adequate DNA for genetic analysis of uveal melanoma.*

The purpose of this study, said lead author Carol L. Shields, MD, was simply to show that it is possible, without enucleation, to use fine-needle aspiration biopsy (FNAB) to procure enough cells for genetic analysis.

"We found we were able to get enough cells in 86 percent of cases," said Dr. Shields, despite the fact that 44 percent were small melanomas, 3 mm thick or less. "This means we can use standard techniques like plaque radiation but still provide the patient with genetic testing."

The researchers found one of the biopsy techniques more successful. The pars plana with a transvitreal tumor apex approach makes it possible to witness the needle in the tumor before aspiration. "Using this technique, we were able to get enough DNA for genetic testing in nearly 100 percent of cases," said Dr. Shields.

Since the publication of this paper, said David H. Abramson, MD, it's been shown that the chromosomal abnormality monosomy 3—though an important prognostic stepping-stone—is not the most sophisticated molecular test nor the best predictor of outcome. Evangelos S. Gragoudas, MD, agreed. "There are more accurate techniques, such as gene expression profiling of RNA from these tumors, where the prognosis is almost 100 percent."

"Our study had a different focus—we didn't look at prognosis," said Dr. Shields, who added that "we're all waking up to this treasure hunt for the best prognostic method for uveal melanoma." However, Dr. Shields disagreed that monosomy 3 is an outmoded test. "Although several chromosomes could lead to melanoma, it has been shown to be the most important chromosome for metastatic disease."

With the very short follow-up, this study did not provide meaningful data on survival, said Dr. Abramson, "since melanoma can metastasize over a five-, 10-, 20-, and even 30-year period."

Dr. Gragoudas added that identifying high-risk patients is useful, so they can be enrolled in clinical trials and followed more closely. "At the present time, unfortunately, we don't have good treatment for metastatic melanoma," he said. "So for the individual patient, I'm not sure it will have any effect on survival or management."

Although Dr. Shields said that genetic testing can provide welcome reassurance for some patients, Dr. Abramson countered that the inconclusiveness of prognostic predictors lessens their usefulness. "This is the problem with all prognostic features in cancer," he said. "If a test is not 100 percent predictive and there is no correlation with survival done, then really all you can tell the patient is you did a research test that may help others in the future."

Dr. Abramson also questioned whether the risks justified the knowledge gained from FNAB, especially given the lack of treatment available for uveal melanoma. However, Dr. Shields described complications as minimal: no cases of diffuse vitreous hemorrhage, retinal detachment, or tumor recurrence along the biopsy tract. Transient minor local vitreous hemorrhage at the site of retinal perforation was seen in 46 percent of eyes—a side effect that resolved in two to four months.

Because follow-up was only eight months, it is not yet possible to fully assess the safety of the technique, said Dr. Abramson, who added, "Spread of melanoma from needle biopsy has been previously reported in the ophthalmic literature, and that is something every patient needs to know before agreeing to have this performed."

All three doctors also acknowledged the inherent weaknesses of any biopsy technique used to harvest cells for prognostication—even with gross tumors—where heterogeneous distribution can confound results. "The big question is sampling error," said Dr. Shields. "This is a sample of 20 cells in a tumor that has thousands or millions of cells. Are you getting the most representative cells? We don't know."

—Annie Stuart

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