8:00 AM

Gene Expression Profile (GEP) Classification and Its Relationship to Traditional Clinical Funduscopic and Ultrasound Features in Uveal Melanoma

- Amy C. Schefler, MD
- Ryan S. Kim, BA
- Maria E. Bretana, Ophthalmology
- Eric N. Kegley, BA
- Brandon T. Nguyen, BS

OBJECTIVE The purpose of this study was to examine the association between the gene expression profile (GEP) assay and traditional clinical high-risk features of uveal melanoma.

PURPOSE To determine whether traditional clinical high-risk funduscopic and ultrasound features of uveal melanoma are associated with the gene expression profile (GEP) signature currently used to predict metastatic risk in uveal melanoma.

METHODS This was a retrospective, single-center study of patients with small to medium-sized uveal melanomas treated from 2013-2016 with adequate data for analysis. Eighty-three patients met the criteria for the study. Patients were examined for: drusen/retinal pigment epithelium (RPE) changes, vascularity on B-scan ultrasound, internal reflectivity on A-scan ultrasound, subretinal fluid (SRF), orange pigment, and tumor height. A point system was created to assess the degree of high-risk features of each

tumor. The association of the clinical risk score with the GEP classification (1A, 1B, 2) was then assessed statistically using the Chi-Square Test and the Fisher Exact Test.

RESULTS Sixty-nine patients had complete data on clinical risk factors and were included in the final analysis. Thirty-two patients were classified as GEP Class 1A; 15 as Class 1B; and 22 as Class 2. A lack of drusen/RPE changes was statistically associated with the Class 2 GEP signature ($p<0.001$). All other clinical risk factors as well as a cumulative total risk score did not have a statistically significant association with GEP signature.

CONCLUSION Larger studies are needed, but clinicians should keep in mind that modern genomic data is likely much more predictive of metastatic death than traditional clinical funduscopic assessment in uveal melanoma patients.

TAKE HOME MESSAGE Traditional clinical features of uveal melanoma often used to predict growth and need for treatment may not be as erliable as traditionally thought especially when compared to modern genomic data.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board

8:08 AM

Correlation of Cytogenetic Abnormalities With Clinical Features of Uveal Melanoma in 1059 Patients

- Carol L. Shields, MD
- Emil Anthony T Say, MD
- Murat Hasanreisoglu, MD
- Jarin Saktansate, MD, MD
- Arman Mashayekhi, MD
- Jerry A. Shields, MD
- Arupa Ganguly, PhD

OBJECTIVE To correlate clinical and cytogenetic features of uveal melanoma

PURPOSE To predict cytogenetic profile

METHODS 1059 patients underwent fine-needle aspiration tumor biopsy for cytogenetics

RESULTS Comparison (normal chromosome 3, 6, and 8 vs any 3, 6, or 8 abnormality) revealed significant differences in mean age (55 vs 58 years), ocular melanocytosis (1% vs 5%), ciliary body location (5% vs 11%), mean distance to optic disc (3.3 vs 5.0 mm), and increased mean basal diameter (9.8 vs 12.6 mm) and thickness (3.8 vs 5.9 mm). Tumors classified as small/medium/large showed abnormalities with loss of disomy of chromosome 3 (35%/52%/65%), 6 (15%/34%/51%), and 8 (19%/41%/69%). By comparison (medium/large vs small melanoma), odds ratio (OR) included complete monosomy 3 (3.09), 8p gain (6.16), 8p loss (6.04), and 8q gain (4.87).

CONCLUSION Increasing melanoma size demonstrates greater cytogenetic alterations. Alterations in chromosome 8 show unique correlation with melanocytosis.

TAKE HOME MESSAGE Thank you!

HUMAN RESEARCH This study involves human research.

IRB Approval Status: Approved by institutional review board

8:20 AM

Targeted Uveal Melanoma Therapy: Extended Follow-Up of Radiotherapy Sparing Surgical Ablation For Small Choroidal Melanoma

- Timothy G. Murray, MD, MBA
- Aaron S. Gold, OD

OBJECTIVE This study reports, for the first time, the long term outcomes of primary radiosparing surgical management of small choroidal melanoma

PURPOSE To evaluate the long-term outcomes for direct surgical tumor ablation using a micro-incisional vitrectomy surgical approach (MIVS). Molecular genomics were utilized to direct personalized therapy avoiding radiotherapy. The small cohort of this series was first presented at the ASRS. This study includes the long-term followup of the initial cohort along with the larger consecutive series.

METHODS A consecutive series of 198 patients with small uveal melanoma presenting confirmed by molecular genomic analysis treated with pars plana vitrectomy, membrane peeling, endolaser thermal tumor ablation and intravitreal triamcinolone acetonide. Molecular genomics were determined using gene expression profiling. All patients were evaluated with widefield photography, echography, and ophthalmological examination at baseline, 3, 6, 12 18, 24, 36, 48 and 60 months.

RESULTS 198 patients presented at a mean age of 64 years (41-86 years). Presenting mean VA was 20/100+. Virtually all patients had subretinal fluid (192/198, 96.9%)), 112 patients had enlargement of the tumor mass. Mean tumor apical height was 1.9 mm (1.1-2.9 mm). Mean follow-up was 43 months (6-62 months) and mean VA improved to

20/30. Molecular genomic classification was confirmed in 196/198 patients (99.0%). Two patients had progressive tumor growth and underwent secondary 125-Iodine brachytherapy. Five patients developed post-operative progressive retinal detachment at 3 months and underwent surgical repair with silicone oil tamponade. No cases of significant vitreous hemorrhage, choroidal detachment or endophthalmitis were seen. No cases of tumor metastases were seen during the study.

CONCLUSION Targeted uveal melanoma management of small ocular melanoma using MIVS delivered endolaser tumor ablation achieves excellent tumor control while avoiding radiotherapy in almost all patients. This data documents the first report of extended follow-up with excellently maintained local tumor control utilizing targeted molecular genomics to guide definitive therapy.

TAKE HOME MESSAGE Small choroidal melanoma may be effectively managed with direct surgical laser ablation avoiding radiotherapy when targeted genomics are evaluated.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board

8:28 AM

Long-Term Follow-Up of a 24-Month Study of Ranibizumab for the Prevention of Radiation Vasculopathy

- Ivana K. Kim, MD
- Anne-Marie Lane, MPH
- Monica Oxenreiter
- Evangelos Gragoudas, MD

OBJECTIVE The aim of this study was to evaluate longer-term outcomes of prophylactic treatment with ranibizumab after radiation for choroidal melanomas near the disc or fovea.

PURPOSE A pilot study of ranibizumab administered every 2 months for 2 years after proton beam irradiation in patients with small-medium choroidal melanomas near the optic nerve or fovea suggested visual benefit. Since high risk of radiation vasculopathy remains for at least 3 years after radiation, we evaluated longer-term outcomes of patients who participated in this clinical trial.

METHODS A retrospective review of 24 patients with choroidal melanomas < 15mm in diameter and < 5 mm in height, located within 3 mm of the optic nerve and/or macula who had completed the clinical trial was performed. A group of historical controls meeting the same criteria for tumor size and location with similar length of follow-up was utilized. Outcome measures included the proportion of patients with final visual acuity of 20/40 or better, the proportion of patients with final visual acuity of 20/200 or

better, and the proportion of patients developing radiation maculopathy or papillopathy at the most recent follow-up visit.

RESULTS Median follow-up was 48.3 months. Nineteen patients (79.2%) had at least 3 years of follow-up; 12 patients (50%) had 4-years of follow-up. At the 24-month trial visit, 88% (21/24) of ranibizumab-treated patients had visual acuity ≥20/40 vs. 47% (29/62) of historical controls (p< .001) and 100% (24/24) of ranibizumab-treated patients had visual acuity ≥20/200 vs. 69% (43/62) of controls (p=.001). At the last follow-up visit, 54% (13/24) of ranibizumab-treated patients had visual acuity ≥20/40 vs. 32% (19/59) of controls (p=.054) and 83% (20/24) of treated patients had visual acuity ≥ 20/200 vs. 59.3% (35/59) of controls (p=.03). Six patients received anti-VEGF injections for radiation vasculopathy after trial completion. The proportion of patients with visual acuity of ≥20/200 at the last visit was similar between patients who received subsequent treatment and those who did not (83.3%, both groups). However, 66.7% of untreated vs. 16.7% of treated patients had acuity ≥20/40 (P=.05)

CONCLUSION The potential benefit of prophylactic ranibizumab extends for at least 1 year after discontinuation. A significant proportion of patients appear to retain good vision without continued treatment. However, it is unknown if continued treatment would result in better visual outcomes.

TAKE HOME MESSAGE The efficacy of ranibizumab in preventing vision loss after radiotherapy for choroidal melanoma declines 1 year after discontinuation of prophylactic treatment, but some benefit persists.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board

8:40 AM

Mythbusters: Does Vitrectomy at Time of Brachytherapy in Choroidal Melanoma Influence Survival?

- Tara A. McCannel, MD, PhD
- Colin A. McCannel, MD
- Robert D. Almanzor

OBJECTIVE To evaluate mortality from choroidal melanoma metastasis in patients who underwent vitrectomy at time of iodine-125 brachytherapy for treatment of primary choroidal melanoma.

PURPOSE Vision-saving strategies where silicone oil can be used as a radiation attenuating substance to reduce exposure to non-tumor parts of the eye have been demonstrated to improve vision. However, this strategy remains controversial; there is little data demonstrating the effect of vitrectomy surgery at the time of tumor treatment on metastatic outcome.

METHODS All patients diagnosed with choroidal melanoma and treated with Iodine-125 brachytherapy who underwent concomitant vitrectomy and silicone oil 1000 centistokes placement for radiation attenuation were included. Patients were excluded if there was less than 6 months of clinical follow-up. Records were reviewed to obtain patient demographic information (gender, age), tumor characteristics (tumor height, tumor greatest basal dimension), prognostic information from tumor biopsy and length of follow-up. Overall survival (death from any cause) was recorded. Survival was

compared to results from the Collaborative Ocular Melanoma Study (COMS), where iodine-125 brachytherapy alone was performed.

RESULTS A total of 283 patients who underwent vitrectomy with silicone oil placement at time of iodine-125 brachytherapy for choroidal melanoma treatment were reviewed. There were 103 patients who underwent vitrectomy plus plaque, and 180 who underwent phacoemulsification, intraocular lens placement and vitrectomy plus plaque. Clinical follow-up ranged from 6 months to 7 years (mean 35 months). Average tumor height was 4.93 mm. Average tumor greatest basal dimension was 12.02 mm. Metastasis from choroidal melanoma occurred in 22 patients (7.8%). When only medium sized tumors were analyzed in our study and compared to the COMS medium tumor trial survival rates, there was no significant difference between groups.

CONCLUSION Vision-improving strategies to prevent radiation retinopathy at the time of brachytherapy that involve vitrectomy techniques do not appear to increase the risk of metastatic spread, and may be considered to improve patients' overall visual outcome.

TAKE HOME MESSAGE Vitrectomy at the time of brachytherapy does not increase a patient's metastatic prognosis.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board

8:45 AM

Expanding Clinical Spectrum of Ocular Melanocytomas

- Jerry A. Shields, MD
- Carol L. Shields, MD

OBJECTIVE Ocular melanocytoma was initially described by Zimmerman as a tumor that occurred on the optic disc and had typical clinical and histopathologic features. We report herein subsequent observations on ocular melanocytomas.

PURPOSE The purpose of this presentation is to highlight new observations on ocular melanocytomas that were seen in an ocular oncology service and to describe the expanding spectrum of these tumors based on further clinical and/ or histopathologic observations.

METHODS The charts were searched on patients coded with a diagnosis of melanocytoma. Most of them were also subclassified as a nevus for coding and retrieval purposes because, in reality, melanocytoma is a variant of melanocytic nevus. We reviewed charts of patients seen on our ocular oncology service and specifically identified those that had new findings that were not previously well known in the literature.

RESULTS Iris melanocytoma usually had of a uniform dark brown to black color. A very distinct feature in many cases is a granular multinodular surface that is highly characteristic and quite different from the typical iris nevus. A rare but impressive variant seen in some iris melanocytomas is an extremely large mass that sheds extensive

pigment over the entire iris and in the angle. We have seen 3 such cases of this “giant” choroidal melanocytoma in children in the first decade of life, all of which were confirmed histopathologically. We identified cases that involved the choroid and iris. Iris melanocytomas were found to have very typical clinical findings that are unlike other iris nevi. Many iris melanocytomas showed enlargement but were believed to be benign despite slow growth. In the early part of this study, iris tumors showing growth were treated with surgical removal, but it was eventually found that they were usually benign pathologically despite the growth.

CONCLUSION Our knowledge of ocular melanocytoma has changed greatly in recent years. It is now known that tumor can occur not only in the optic nerve but also in the iris, choroid and ciliary body. The vast majority of melanocytomas are benign and transformation into melanoma is rare.

TAKE HOME MESSAGE Thank you!