Title
EPID-08. PRE-SURGERY IMMUNE PROFILES OF ADULT GLIOMA PATIENTS

Journal
Neuro-oncology, 22(Suppl 2)

ISSN
1522-8517

Authors
Bracci, Paige
Rice, Terri
Hansen, Helen
et al.

Publication Date
2020-11-01

Peer reviewed

EPID-08. PRE-SURGERY IMMUNE PROFILES OF ADULT GLIOMA PATIENTS

Paige Bracci[1], Terri Rice[2], Helen Hansen[2], Stephen Francis[2], Sean Lee[2], Lucie McCoy[2], Pavan Shrestha[2], Gayathri Warrier[2], Jennifer Clarke[2], Annette Molinaro[2], Jennie Taylor[2], John Wiencke[2], and Margaret Wrensch[2]; [1]Department of Epidemiology & Biostatistics, UCSF, San Francisco, CA, USA, [2]Department of Neurological Surgery, University of California (UCSF), San Francisco, San Francisco, CA, USA

Changes in glioma patients' immune profiles over the course of disease may predict outcomes. DNA based immunomethylomics quantifies blood immune cells based on cell specific DNA methylation signatures. To assess changes in immune profiles, we are longitudinally collecting blood samples from glioma patients pre-surgery and at other clinically relevant time points. Here we report patients' pre-surgery immune profiles. All patients underwent biopsy or resection of a presumed new glioma or recurrent lower grade glioma. Blood DNA methylation was assessed with Illumina EPIC methylation arrays. Relative cell fractions of CD4, CD8, B-cells, natural killer cells, monocytes, and neutrophils, were estimated via our validated deconvolution algorithm. Total nucleated cell counts from Nexcelom cytometry were used to compute absolute cell counts. Other measures include total lymphocytes, CD4/CD8 ratio, neutrophil to lymphocyte ratio (NLR), and lymphocyte to monocyte ratio (LMR)). The first 125 participants includes 56 newly diagnosed glioblastomas (GBM), 28 newly diagnosed grade II-III gliomas, and 41 recurrent grade II-III gliomas. Median patient age is 49 years. 53 (43%) had recent dexamethasone exposure. In overall non-parametric analyses, most cell subsets, especially CD4, differed across grade, diagnosis group, WHO classification and dexamethasone exposure. In post-hoc pairwise analyses, immune profiles of IDH wildtype GBM patients who had taken dexamethasone differed from patients with GBM or grade II-III glioma who had not taken dexamethasone; they had clinically relevant and statistically significantly lower absolute CD4 counts, total white cell counts, and percent of total lymphocytes, and higher absolute neutrophil counts, NLR and LMR. However, some dexamethasone naïve GBM patients also had altered immune profiles. Comparisons of relative immune cell fractions with those from 454 non-glioma controls from the UCSF Adult Glioma Study showed that across grade and WHO classification, for the most part, immune profiles of glioma patients not exposed to dexamethasone did not differ from controls.

EPID-09. QUANTIFYING SOCIAL DETERMINANTS OF HEALTH AMONG GLIOMA PATIENTS

Angelica Hutchinson[1], Alexandria Marshall[2], Fang-Chi Hsu[2], Kathryn Weaver[3], Alisha DeTroye[2], Kristin Strickland Houston[2], Annette Carter[2], Michael Chan[4], Christina Cramer[5], Adrian Laxton[2], Stephen Tatter[6], Glenn Lesser[5], Mollie Canzona[6], and Roy Strowd[2]; [1]Wake Forest Graduate School of the Arts and Sciences, Winston Salem, NC, USA, [2]WFBH, Winston Salem, USA, [3]Wake Forest Baptist Medical Center, Winston Salem, NC, USA, [4]Wake Forest University Health Sciences, Winston-Salem, NC, USA, [5]Wake Forest School of Medicine, Winston-Salem, NC, USA, [6]Wake Forest University, Winston-Salem, NC, USA

BACKGROUND: Social determinants of health (SDH) are modifiable factors that contribute to health outcomes. Despite studies linking SDHs with cervical, ovarian, and prostate cancer outcomes, few studies have explored SDHs in glioma patients. We conducted a cross-sectional survey to characterize and contextualize SDHs in glioma patients by community income, rural/urban residence, and treatment status. METHODS: Two validated instruments: PRAPARE (Protocol for responding to and assessing patents' assets risks and experiences) and AHC (accountable health communities instrument) quantified SDHs; along with study-specific supplemental questions. Risk scores were calculated and combined into an overall and domain-specific (economic, education, neighborhood environment, social context, and healthcare) SDH risk, with a higher score being indicative of higher SDH risk. Scores were compared between low-income (LIC) vs high-income (HIC) communities (defined by median household income), urban vs rural (defined by zip code), and active treatment vs surveillance (determined by patient medical record) using Wilcoxon rank-sum test. RESULTS: 100 glioma patients were enrolled: mean age 53 years (range: 22–78); 49% male; 18% oligodendroglioma, 34% diffuse astrocytoma, 38% glioblastoma, 10% other glioma; 68% resided in LICs, 27% in rural zip codes, and 51% were on active treatment. Overall, SDH risk scores were low (mean= 4.43-out-of-38). Scores in the healthcare domain were the highest. Compared to patients from LICs, patients from HICs had higher healthcare risk scores ($p< 0.05$). Surveillance patients had higher overall SDH risk on the AHC than patients in active treatment ($p< 0.05$), with age being a confounder. In multivariable analysis, younger age, and astrocytoma histology were associated with higher social health risk. CONCLUSION: Glioma patients report relatively few SDH risk factors on standardized instruments designed for general clinic populations. The higher health risk observed in patients in HICs and higher AHC risk for those in surveillance will be further explored in planned qualitative analysis.

EPID-10. MITOCHONDRIAL DNA SEQUENCE VARIATION AND RISK OF GLIOMA

Claudine Samanic[1], Jamie Teer[1], Zachary Thompson[1], Jordan Creed[1], Louis Nabors[2], Sion Williams[3], and Kathleen Egan[1]; [1]H. Lee Moffitt Cancer Center, Tampa, FL, USA, [2]University of Alabama at Birmingham, Birmingham, AL, USA, [3]University of Miami Miller School of Medicine, Miami, FL, USA

Malignant gliomas are the most common primary adult brain tumors, with poor prognosis and ill-defined etiology. Mitochondrial DNA (mtDNA) sequence variants and haplogroups have been linked with certain cancers, but research on glioma is lacking. We examined the association of germline mtDNA variants and haplogroups with glioma risk in 1,654 glioma cases and 1,065 controls from a US case-control study, and 427 glioma cases and 1,541 controls from the UK Biobank, all genotyped using the UKBiobank array with 276 tiled mtDNA variants. The analysis was restricted to participants of European ancestry, and risk of glioblastoma (GBM) and lower grade glioma (LGG) was examined separately. Distribution of mitochondrial haplogroups (H/HV,I,J,K,R,T,U,V,W,X) were similar in both study populations, with 46.4% and 48.1% of controls in the US and UK studies respectively, identified as H/HV, the most common haplogroup. In the US study there was an inverse association between haplogroup W and glioma (OR=0.43, 95%CI: 0.23–0.79) when compared with the H/HV haplogroup, which was not seen in the UK study (OR=1.10, 95%CI: 0.49–2.49). In the US study, a significant inverse association was observed with the previously reported mtDNA variant m.14798T > C (PMID: 31323957), resulting in the amino acid substitution F18L, for LGG (OR=0.73; 95%CI: 0.53–0.99) though not for GBM (OR=0.86; 95%CI: 0.66–1.11). In the UK study, the F18L substitution was associated with an increased risk of GBM (OR=1.48; 95%CI: 1.07–2.04), and no association was observed for LGG (OR=0.95; 95%CI: 0.53–1.68). Among cases in the US study with isocitrate dehydrogenase 1 (*IDH1*) status available (747 gliomas), a nonsignificant inverse association of the F18L substitution was observed in glioma cases with wild type (OR=0.72; 95%CI: 0.52–1.01) but not mutant (OR=1.08; 95%CI: 0.70–1.69) *IDH1*. No other common mtDNA variant (minor allele > 5%) was associated with glioma risk in either study. These associations merit further study.

EPID-11. A MULTI-INSTITUTIONAL COMPARATIVE ANALYSIS OF THE CLINICAL, GENOMIC, AND SURVIVAL CHARACTERISTICS OF PEDIATRIC, YOUNG ADULT AND OLDER ADULT PATIENTS WITH IDH-MUTANT GLIOMA

Mary Jane Lim-Fat[1], Jayne Vogelzang[2], Eleanor Woodward[2], Alana McGovern[3], Clement Ma[3], Hasan Al-sayegh[3], Sanda Alexandrescu[3], Ashley Margol[4], Jennifer Cotter[4], Kristina Cole[5], Marilyn Li[5], Emily Owens[6], Amy Smith[6], Stewart Goldman[7], Kristiyana Kaneva[7], Emily Burton[8], Kellie Nazemi[8], Karen Wright[9], Patrick Wen[10], Katherine Warren[1], Mehdi Touat[11], David Reardon[12], Wenya Linda Bi[13], Keith Ligon[14], and Kee Kiat Yeo[1]; [1]Dana Farber Cancer Institute, Boston, MA, USA, [2]Brigham and Women's Hospital, Boston, MA, USA, [3]Boston Children's Hospital, Boston, MA, USA, [4]Children's Hospital Los Angeles, Los Angeles, CA, USA, [5]Children's Hospital of Philadelphia, Philadelphia, PA, USA, [6]Orlando Health Arnold Palmer Hospital for Children, Orlando, FL, USA, [7]Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, USA, [8]OHSU Doernbecher Children's Hospital, Portland, OR, USA, [9]Dana-Farber Cancer Institute/Boston Children's Hospital, Boston, MA, USA, [10]Dana-Farber Cancer Institute, Boston, MA, USA, [11]AP-HP, Hôpitaux Universitaires La Pitié Salpêtrière - Charles Foix, Service de Neurologie 2-Mazarin, Paris, France, [12]Center for Neuro-Oncology, Dana-Farber Cancer Institute, Boston, MA, USA, [13]Department of Neurosurgery, Brigham and Women's Hospital, Boston, MA, USA, [14]Department of Pathology, Brigham and Women's Hospital, Boston, MA, USA

BACKGROUND: Prognostic significance of *IDH*-mutation in glioma is incompletely understood in children and adolescents/young adults (YAs). We compared the clinico-genomic features, outcomes and prognostic factors observed in *IDH*-mutant gliomas across age groups. METHODS: Clinical, histologic and molecular data of patients with *IDH*-mutant gliomas from 8 pediatric institutions (spanning twenty years) and adult patients from two institutions (from 2013–2019) were identified. Patients were grouped as pediatric (< 19y), YA (19y to < 40y) or older adult (≥ 40y). Genomic alterations, including somatic mutations and copy number variants, were captured with institutional next generation sequencing. Factors were compared across age categories using Fisher's exact test or analysis-of-variance. Cox proportional-hazards regression tested factors for association with overall (OS) and progression-free survival (PFS). RESULTS: Of 379 patients, 48(13%) were pediatric, 204(54%) YA and 127(33%) older adult. Histological subtype differed significantly by age group ($p< 0.0001$). YAs