shows a homogeneously enhancing mass with surrounding edema. The imaging differential diagnosis is broad, and includes high grade glioma and neuroinflammatory conditions. Definitive diagnosis therefore requires biopsy. Here we present a case of primary CNS lymphoma that was diagnosed as an acute demyelinating process on initial biopsy. A 68 year old female presented with gait instability and vertigo. MRI showed right cerebellar and right trigonal enhancing lesions. Biopsy revealed an acute demyelinating inflammatory process and she was diagnosed with acute disseminated encephalomyelitis. She was treated with intravenous methylprednisolone followed by oral prednisone with resulting clinical and radiographic improvement. She was re-admitted to hospital 4 months later with encephalopathy. Imaging showed a new enhancing mass in the pericallosal frontal lobes. Repeat brain biopsy showed diffuse large B-cell lymphoma. This case illustrates a highly unusual situation of biopsy-proven central demyelination preceding a primary CNS lymphoma diagnosis. It raises a number of etiopathological questions concerning the coexistence and potential causal relationships between demyelination and lymphoma. Additionally, it highlights the need for repeat biopsy if clinical and radiographic suspicion for lymphoma persists despite an alternative initial biopsy result.

PATH-61. IMMUNOHISTOCHEMICAL PHENOTYPING AND SURVIVAL ANALYSIS OF WHO GRADE II-IV GLIOMAS

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INTRODUCTION: Specific genetic mutations are linked to clinical prognosis in gliomas. There has been increasing demand to understand the association between tissue biomarker expression and survival. Using patient-derived samples, WHO grade II-IV gliomas were evaluated by the protein-staining pattern of molecular markers of interest across tumor grade, and the association between their expression and survival was investigated. METHODS: Tissue microarrays (TMA) containing duplicate 1 mm cores were generated from 78 gliomas (WHO grade II-IV) using an automated TMA system. Immunohistochemistry was performed per the manufactures recommendation to evaluate expression of: Wilms tumor 1 (WT1), platelet endothelial cell adhesion molecule (CD31), adhesion G protein-coupled receptor E5 (CD97), complement decay-accelerating factor (CD55), hypoxia inducible factor 1 subunit alpha (HIF1α), EGF-like module-containing mucin-like hormone receptor-like 3 (EMR3), integrin, and isocitrate dehydrogenase 1 (IDH1). Samples with moderate (+1) or intense (+2) staining to WT1, CD31, CD97, CD55, or HIF1α, or any staining to EMR3 or IDH1 mutation, were considered positive. RESULTS: Of the 78 tumor samples, there were 11 (14%) WHO grade II, 22 (28%) grade III, and 45 (59%) grade IV gliomas. Across grade III gliomas, anaplastic astrocytomas had significantly higher positive WT1 (p=0.04), CD31 (p=0.002) and IDH1 wild-type (p< 0.0001) staining. High-grade (III & IV) gliomas had significantly higher positive staining for WT1 (p=0.013), CD31 (0.024), integrin (p=0.021), and IDH1 wild type (p=0.044). In all gliomas, positive staining for WT1 (p< 0.0001), CD31 (p=0.009), CD97 (p=0.024), EMR3 (p=0.036), and IDH1 wild type (p=0.0006) were associated with worse overall survival. After adjusting for patient age, positive staining for WT1 (p=0.003) was associated with worse overall survival. CONCLUSION: Using immunohistochemistry, unique biomarker staining patterns were identified for WHO grade III anaplastic astrocytomas and for high-grade gliomas. Irrespective of grade, staining for WT1, CD97, CD31, EMR3, and IDH1 wild-type were associated with worse overall survival.

PATH-62. QUANTITATIVE ANALYSIS OF SEX-ASSOCIATED MGMT METHYLATION IN NEWLY DIAGNOSED GLIOBLASTOMA

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INTRO/OBJECTIVE: Glioblastoma (GBM) and MGMT have been reported to have sexual dimorphism. In multiple studies, including our own population-based cohort analysis, females had higher rates of MGMT methylation and improved methylation-associated progression-free and overall survival outcomes compared to males. MGMT methylation is assessed as a mean of five cysteine-phosphate-guanine (CpG1-5) islands (CpG methylation is highly inversely correlated with MGMT RNA expression). The primary objective of this study was to investigate differences in mean and individual CpG methylation by sex. METHODS: 155 patients who underwent first surgical intervention for newly diagnosed GBM at a single tertiary care institution between 2016 and 2018 were reviewed. Of these, 135 patients had available CpG methylation data determined by a clinically validated test using bisulfate conversion followed by PCR and pyrosequencing. MGMT was defined as methylated if the mean of CpG1-5 ≥ 12. The mean of CpG1-5 and each CpG parameter were compared by sex using the Wilcoxon signed-rank test. RESULTS: Overall (mean age 62, 34% female, 42% MGMT methylated), the median (IQR) of mean degree of methylation was 4.0% (2–33) and median CpG1-5 ranged from 3.0 to 4.5%. More females (53.3%) were MGMT methylated than males (37.1%). Females had significantly higher rates of mean methylation compared to males (14.0 vs 3.0%, p=0.046). Females also had higher rates of methylation at each CpG island compared to males CpG1(7.0 vs 3.0%, p=0.15), CpG2(8.0 vs 4.0%, p=0.10), CpG3(9.0 vs 4.0%, p=0.23), CpG4(7.0 vs 3.0%, p=0.047), and CpG5(6.0 vs 4.0%, p=0.097). CONCLUSION: Females had higher rates of mean methylation and methylation of each CpG island compared to males, although only mean and CpG4 methylation values were statistically significant given the limited sample size. Further investigation with a larger cohort is ongoing to elucidate this dimorphism and establish whether sex-specific methylation cut-offs need to be implemented into clinical practice.

PATH-63. TRANSCRIPTIONAL SIGNATURES IN HISTOLOGIC STRUCTURES WITHIN GLIOBLASTOMA TUMORS MAY PREDICT PERSONALIZED TREATMENT SENSITIVITY AND SURVIVAL

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OBJECTIVE: Personalized treatment strategies in Glioblastoma multiforme (GBM) has been hampered by intra-tumoral heterogeneity. The goals of this study were to (1) determine the impact of intra-tumoral heterogeneity on established predictive and prognostic transcriptional signatures in human GBM, and (2) develop methods to mitigate the impact of tissue heterogeneity on transcriptomic-based patient stratification. METHODS: We analyzed transcriptional profiles of GBM histological structures from the open-source Ivy Glioblastoma Atlas Project. To generate these data, infiltrative tumor, leading edge, cellular tumor [CT], perinecrotic zones, pseudopalisading cells, hyperplastic blood vessels and microvascular proliferation were microdissected from 34 newly diagnosed GBM and underwent RNA sequencing. Data from The Cancer Genome Atlas were used for validation. Principle component analysis, network analysis and gene set enrichment analysis were used to probe gene expression patterns. RESULTS: Distinct biological networks were enriched in each tumor histological structure. Classification of patients into GBM molecular subtypes varied based on the structure assessed, with many patients classified as every subtype depending on the structure analyzed. Using only CT to classify subtypes, we identified biologically unique patterns suggesting that proneural and mesenchymal tumors may be more sensitive to chemoradiotherapy and immunotherapy, respectively. Survival outcome predicted by an established multigene panel was confounded by histologic structure. Utilizing CT transcriptomics we developed a novel survival prediction gene signature that identified the highest-risk GBM patients in both CT and bulk tissue gene expression profiles. CONCLUSIONS: Histologic structures contribute to intra-tumoral heterogeneity in GBM. Using mixed-structure biopsy samples could incorrectly subtype tumors and produce invalid patient stratification. Limiting transcriptomic analysis to the CT allowed us to develop a new survival prediction gene signature that appears accurate even in mixed tissue samples. The biological patterns uncovered in the subtypes and risk-stratified groups have important implications for guiding the development of precision medicine in GBM.

PATH-64. PROSPECTIVE, BLINDED PLASMA BASED ANALYSIS FOR DIAGNOSIS OF NEWLY DIAGNOSED GLIOMA

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INTRODUCTION: In patients with newly diagnosed intracerebral lesions, gliomas are often suspected. However, other conditions such as multiple sclerosis, abscess or lymphoma are possible, as well. Furthermore, biopsy can be challenging due to eloquent and/or deep location within the brain. In this prospective, blinded study, analysis of plasma isolated cell-free DNA and exosome mRNA and miRNA from newly diagnosed glioma patients and from cancer-free volunteers was used to predict disease. METHODS: Plasma was drawn from 52 patients with newly diagnosed gliomas (28 high grade glioma (HGG), 10 low grade (LGG)) and 14 patients without documented history of cancer and recent MRI brain which was negative for brain tumor. High quality DNA and RNA was isolated and sequenced using Next Generation Sequencing and Digital Droplet PCR was used for detection and verification of trace molecular artifacts. Multianalyte processing yielded data that was harmonized and interpreted through an