Title

P09.11 Wavelength-specific lighted suction instrument for 5-aminolevulinic acid fluorescence-guided resection of deep-seated malignant glioma

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P09.09 DOES TEMOZOLOIMDE IMPROVES SURVIVAL IN PEDIATRIC GLIOBLASTOMA: A SINGLE CENTER ANALYSIS

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BACKGROUND: Pediatric Glioblastoma (pGBM) is an uncommon entity. The importance of concurrent and adjuvant temozolomide is not known in this subset of patients. METHODS: We retrospectively analyzed our database between 2000 and 2015. All patients were treated with maximally safe surgical resection. This was followed by a uniform treatment schedule of post-operative radiation with concurrent daily temozolomide at 75 mg per meter square. Radiation dose was 60 Gy in 30 fractions planned by 3-dimensional conformal radiotherapy. 4 weeks later, adjuvant temozolomide was started at 150 mg per meter square, day 1 to 5 every 28 days and escalated to 200 mg per meter square if well tolerated. Log-rank test was used to compare survival distribution. The data was analyzed using SPSS v.16. RESULTS: 51 patients were analyzed. Median age was 13 years (Range: 5 to 21 years). 35 males and 16 females were noted. 8 patients had seizures at presentation. Median symptom duration was 3.25 months.29 patients underwent a gross total resection (GTR) while 16 underwent a subtotal resection, 6 patients underwent decompression. 30 patients received concurrent and adjuvant temozolomide. Median PFS was 1.26 years. 1 and 3 year PFS was 54.4% 3 years- 24.6.7%.The median overall survival was 1.45 years. In univariate analysis extent of resection was significantly better favoring GTR (1.45 years vs. 0.96 years; p=0.037) and significance maintained after multivariate analysis p=0.026, HR: 3.069, 95% CI: 1.143-8.238. Survival was better for patients receiving Temozolomide but did not achieve significance, however in multivariate analysis use of Temozolomide was associated with significantly improved survival p=0.036, HR-3.315, 95% CI: 1.078-10.193. CONCLUSIONS: GTR improves survival significantly in pGBM. Temozolomide may have a role in pGBM.

P09.10 THE PROGNOSTIC VALUE OF A NOVEL QUANTITATIVE MGMT PROMOTER METHYLATION SCORE FOR PATIENTS WITH GLIOBLASTOMA

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Evidence continues to solidify the central role molecular markers play in gliomas. Methylation status of MGMT promoter has been shown as a key marker in glioblastoma, predicting response to temozolomide. Traditional testing of MGMT promoter methylation, performed using a methylation specific PCR, yields a binary result; however it fails to consider the multiple potential methylation sites in MGMT's promoter region. A novel quantitative bisulfite Sanger DNA sequencing assay evaluates methylation status at each of the 17 potential methylation sites in the promoter, resulting in a methylation score of 0-17. This novel assay was evaluated for its prognostic role in a cohort of 180 consecutive patients undergoing treatment for newly diagnosed glioblastoma from April 2014 to August 2015. All patients received concurrent chemoradiation with temozolomide. Univariate and multivariate models for overall survival were built along with other established prognostic variables such as age, KPS and extent of resection. The methylation score was predictive of overall survival as a linear model. Stratification into partition groups revealed 3 groups (in order of increasing survival): A)Age greater than or equal to 70, B)Age less than 70 and KPS equal to or less than 70 or Age less than 70 and KPS greater than 70 and MGMT score less than or equal to 8 and C)Age less than 70 and KPS greater than 70, and MGMT score greater than 8. Brier score revealed lower predictive error for the methylation score compared to the traditional binary MGMT promoter methylation assessment, suggesting the methylation score is a more reliable model predicting survival. The methylation score, derived from the bisulfite sequencing analysis, provides a quantitative representation of the degree of methylation in the MGMT promoter. Survival models and partitioning support its role as a prognostic marker for overall survival, and the methylation score being superior to the traditional MGMT promoter methylation analysis in predicting survival in patients with newly diagnosed glioblastoma. Prospective validation and comparison to older/newer techniques including next-generation sequencing are warranted.

P09.11 WAVELENGTH-SPECIFIC LIGHTED SUCTION INSTRUMENT FOR 5-AMINOLEVULINIC ACID FLUORESCENCE-GUIDED RESECTION OF DEEP-SEATED MALIGNANT GLIOMA

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INTRODUCTION: 5-aminolevulinic acid (5-ALA) fluorescence-guided surgery has become a valuable adjunct in the resection of malignant intracranial gliomas. Furthermore, the fluorescence intensity of biopsied areas of a resection cavity correlates with histological identification of tumor cells. However, in the case of lesions deep within a resection cavity, light penetration may be suboptimal, resulting in less excitation of 5-ALA metabolites leading to decreased fluorescence emission. Here, we demonstrate the use of a 400 nm fiber optic light source incorporated into a surgical suction instrument that simultaneously allows for removal of blood products and improvement of tumor fluorescence by providing necessary wavelength-specific illumination to deeper areas of a resection cavity. MATERIALS AND METHODS: A Spetzler™ Lighted Suction Tube (Kogent Surgical, Chesterfield, MO) was connected to a custom-designed 400 nm wavelength emitting light source built using a Luxtec model LX-300 fiber optic illuminator (Integra, Plainsboro, NJ) with a 400 nm filter (Product number #84-781, Edmund Optics, Barrington, NJ) installed in the optical path. The 400 nm lighted suction instrument was used during the resection of the tumor, both for removing blood products and tumor tissue as well as to illuminate areas of the deep resection cavity to probe for remaining areas of 5-ALA positivity. RESULTS: We present the techniques described, including the intraoperative set-up and the equipment utilized. We also describe the use of this technique in several cases of malignant glioma resection. This technique improved the fluorescence intensity of patches of malignant tissue deep within the resection cavity. Light emanating from the instrument did not cause auto-fluorescence when no 5-ALA positive tissue was present. Furthermore, no evidence of photo-bleaching or tissue damage was seen intraoperatively in areas in which the fluorescent light was used. CONCLUSIONS: This technique may further improve 5-ALA's utility in identifying tumor infiltrated tissue for deep-seated lesions. Additionally, this tool may have implications for standardizing the intensity of the blue light exposure on tissues when assessing or quantifying the 5-ALA fluorescence intensity.

P09.12 DURABLE REMISSION WITH TUMOR TREATING FIELDS AS ADJUVANT TREATMENT FOR GLIOBLASTOMA RELAPSE IN A PATIENT WITH GRAD IV HEMATOTOXICITY DURING INITIAL TEMOZOLOMIDE RADIOCHEMOTHERAPY

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We report on a 53 years old female patient who was diagnosed with a left temporal tumor with significant perifocal edema in August 2015. A microsurgical, neuronavigation-guided gross total resection was performed and glioblastoma was diagnosed histologically. On immunohistochemistry, staining for IDH1-mutations was negative. Methylation analysis revealed a methylated MGMT promotor. One month after resection, the patient started a radiochemotherapy with temozolomide (TMZ) 75mg/m^2 per day and radiation fractions of 1.8 Gy with a planned dose of 50.4 Gy and a boost of the tumor region up to a total dose of 60.4 Gy. After 4 weeks the radiochemotherapy was interrupted because of pancytopenia with grade 4 thrombocytopenia (minimal platelets 4000/µl) and grade 3 leukopenia (minimal WBC 1170/µl). The patient was transfused with 8 units of platelets and 6 units of packed erythrocytes. After an interruption of one month WBC were above 2000/µl and platelets above 20000/ml, hence radiation therapy was resumed without concomitant TMZ. On a follow-up MRI in February 2016 a tumor relapse was detected. A second resection of the left temporal tumor was performed and because of a persisting thrombocytopenia with platelets below 100 000/µl, we offered the patient an adjuvant treatment with tumor treating fields (TTF) alone. TTF started in May 2016 and was well tolerated. Except from minor skin reactions, which were managed with ointments, the patient denied any adverse reactions. The latest MRI from September 2016 showed an ongoing remission, and at the most recent clinical follow-up in November 2016 there was no sign of neurological impairment. Hence, the second remission lasts now as long as the first remission, but with a much better toxicity profile of TTF compared to the initial radiochemotherapy. TTF therapy alone might therefore represent an alternative treatment option for patients with relapsed glioblastoma for whom chemotherapy is contraindicated.

P09.13 F-18 FLT PET AND MRI AS OUTCOME PREDICTORS IN GLIOBLASTOMAS FOLLOWING CHEMORADIATION THERAPY

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PURPOSE: To evaluate F-18 fluorothymidine (FLT) PET and MRI as pre-treatment and post treatment biomarkers predicting progression free survival