the tumor at cytotoxic concentrations and efflux pumps found on the epithelial cells of the BBB rapidly pump drugs out of the brain. Convection enhanced delivery (CED) is a drug delivery technique that bypasses the BBB by directly injecting the drug into the tumor site under a pressure gradient. Further clinical implementation of CED requires understanding drug distribution, as optimal drug physico-chemical properties have never been evaluated. METHODS: Sprague Dawley rats underwent a single injection of drug by CED to the brainstem with and without an efflux pump inhibitor. Animals were euthanized at 0, 2, 4, 8, 12 and 24 hours. Their brain drug concentration/distribution was analyzed by MALDI-MSI and plasma drug concentration was measured by LC-MS/MS. RESULTS: Drug distribution and brainstem concentration were increased following BBB efflux pump inhibition compared to no pump inhibition controls. Additionally, efflux pump inhibition resulted in slower drug clearance for those drugs that are known pump substrates. CONCLUSIONS: BBB efflux pump inhibition resulted in a larger volume of distribution, increased drug concentration and slower drug clearance following CED to the brainstem of known efflux substrates.

DDEL-17. TRIPLE INTRAVENTRICULAR CHEMOTHERAPY FOR TREATMENT OF RELAPSED CHOROID PLEXUS CARCINOMA

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Limited evidence for the optimal management of relapsed choroid plexus carcinoma (CPC) exists, with a few case reports involving surgery, radiotherapy and intravenous chemotherapy. However, the safety and tolerability of intraventricular chemotherapy in this setting has not been widely studied. We describe a case where triple intraventricular chemotherapy was administered to a child with relapsed metastatic CPC. A 7-year-old male with a history of CPC presented with relapsed metastatic disease. At initial diagnosis at 4 years of age, treatment involved gross total resection of an intraventricular mass in the left temporal region followed by chemotherapy and autologous stem cell transplantation (SCT) according to HEADSTART II-D. One year after SCT, craniospinal radiation was delivered following radiological relapse, achieving a partial response. Given previous treatment-limiting myelosuppression, intraventricular chemotherapy via Ommaya® reservoir with thiotepa 5mg, etoposide 0.5mg and topotecan 0.4mg twice a week (non-weight-based dosing) was commenced taking into consideration pharmaceutical formulation aspects for optimal intraventricular drug delivery. After six cycles of intraventricular chemotherapy, palliative radiotherapy was administered due to radiological progression. Following completion, weekly triple intraventricular chemotherapy continued for 9 months. The patient remained out of hospital with the main side effects being fatigue and occasional nausea amenable to ondansetron. This case study demonstrates the safety and tolerability of a triple intraventricular chemotherapy regimen used to delay disease progression and prolong quality of life in a child with relapsed CPC in the palliative setting. This could provide an alternative treatment regimen for patients with relapsed disease.

DIFFUSE MIDLINE GLIOMA/DIPG

DIPG-01. REIRRADIATION PRACTICES FOR DIFFUSE INTRINSIC PONTINE GLIOMA

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INTRODUCTION: Diffuse intrinsic pontine gliomas (DIPG) are a leading cause of brain tumor deaths in children. Current standard of care includes focal radiation therapy (RT). Despite clinical improvement in the majority of patients, the effect is temporary and median survival is less than one year. The use of reirradiation and possible benefit has been reported in progressive DIPG, yet standardized approaches are lacking. We conducted an internet-based survey to assess physicians' practices in pediatric DIPG. METHODS: A 14-question REDCap survey regarding re-irradiation practices was emailed to 396 physicians identified through an International Pediatric Neuro-Oncology and Radiation-Oncology database. RESULTS: Response rate was 35% overall (radiation-oncologists, 28%; pediatric oncologists, 57%). Two participants were excluded (did not treat DIPG). Participants included radiation-oncologists (62%), pediatric oncologists (7%), and pediatric neuro-oncologists (29%). Most physicians (62%) treated 1–5 DIPG patients per year, with 10% treating >10/ year. Reirradiation was considered a treatment option in 88%. Progressive disease or worsening clinical status were the most common reasons to consider reirradiation. The majority (84%) considered reirradiation a minimum of 6 months following initial RT. Doses varied, with median total dose 24Gy (range 12–60); 2Gy/fraction (range 1–9). Concurrent use of systemic agents with reirradiation was considered in 46%, mainly with targeted agents (37%), biologics (34%), or immunotherapy (25%). One-time reirradiation was the most common practice (71%). Interestingly, 9% of respondents would not consider reirradiation. CONCLUSION: Although, the vast majority of physicians agree with re-irradiation as a treatment option for DIPG the total doses varied, and further clinical trials are needed.

DIPG-02. USEFULNESS OF BEVACIZUMAB IN MAINTAINING QUALITY OF LIFE AT THE TIME OF DIFFUSE INTRINSIC PONTINE GLIOMA RELAPSE

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INTRODUCTION: Even in the age of molecular diagnosis, diffuse intrinsic pontine glioma (DIPG) is still a dismal disease. The usefulness of bevacizumab for DIPG relapse is reported. SUBJECTS AND METHODS: The treatment and outcomes of 10 patients with DIPG who were treated at our institute since 2001 were retrospectively reviewed. All patients were diagnosed with DIPG by MRI imaging and underwent radiation therapy first. Three cases did not receive chemotherapy at the time of relapse (Untreated Group). In 7 cases, chemotherapy was performed at the time of relapse with ACNU/vincristine or interferon beta (Other Treatment Group), and 2 cases with bevacizumab (Bv Group). The change in the Karnofsky Performance Status Scale (KPS) from the time of relapse was compared. RESULTS: The average overall survival (OS) for all 10 cases was 10.0 months. No prolongation of OS by bevacizumab was observed. However, it was only in the Bv Group that the KPS increased from the time of relapse. Comparison of the KPS at the time of relapse and the KPS after 4 months showed that the Bv Group remained unchanged or increased, while the Untreated Group and the Other Treatment Group decreased. In the Other Treatment Group, hospitalization was required for treatment, and side effects of bone marrow suppression were observed. However, in the Bv Group, outpatient treatment was possible, there were no side effects, and all could be observed at home. CONCLUSION: From the above results, bevacizumab appears useful for palliative treatment for maintaining quality of life after DIPG relapse.

DIPG-03. THERAPEUTIC TARGETING OF TRANSCRIPTIONAL ELONGATION IN DIFFUSE INTRINSIC PONTINE GLIOMA

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Diffuse intrinsic pontine glioma (DIPG) is highly aggressive brain stem tumor and needed to develop novel therapeutic agents for the treatment. The super elongation complex (SEC) is essential for transcription elongation through release of RNA polymerase II (Pol II). We found that AFF4, a scaffold protein of the SEC, is required for the growth of H3K27M-mutant DIPG cells. In addition, the small molecule SEC inhibitor, KL-1, increased promoter-proximal pausing of Pol II, and reduced transcription elongation, resulting in down-regulate cell cycle, transcription and DNA repair genes. KL-1 treatment decreased cell growth and increased apoptosis in H3K27M-mutant DIPG cells, and prolonged animal survival in our human H3K27M-mutant DIPG xenograft model. Our results demonstrate that the SEC disruption by KL-1 is a novel therapeutic strategy for H3K27M-mutant DIPG.

DIPG-04. THERAPEUTIC STRATEGY FOR DIFFUSE MIDLINE GLIOMAS. A SINGLE CENTER EXPERIENCE

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