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INTRODUCTION: Primary central nervous system (CNS) germ cell tumors (GCT) account for 2–3% brain tumors children/adolescents in Western hemisphere. The report aim is to present the results of a Brazilian CNSGCT consortium protocol. METHODS: Since 2013, 45 patients with histologic and/or tumor marker (TM) diagnosis of germinoma with/without HCGβ levels≤200mIU/ml (n=33), four between 100-200mIU/ml and NGGCT (n=12), received carboplatin/etoposide/cyclophosphamide (4–6 cycles), followed by 18Gy ventricular field irradiation and primary site(s) boost. Autologous bone marrow transplant (ABMT) was conducted for NGGCT low responders. RESULTS: Mean age 12.9 years (4.7-20y), 34 males. Diagnosis was made by TM (n=9), surgery (n=19), both (n=15). Two bifocal cases, (-)TM were treated as germinoma. Primary tumor location was pineal (n=20), suprasellar (n=13), bifocal (n=11) and basal ganglia/thalamus (n=1). Fourteen had ventricular/spinal spread. Second-look surgery occurred in 5 patients. For the germinoma group, 26 achieved complete response (CR) after chemotherapy, seven showed residual teratoma/scar. For the NGGCT after 2/4 cycles, four patients showed CR, 2 failure/progression and 6 partial response (4 (-)TM). Two were submitted to ABMT. Radiotherapy was performed as described, except in three. One recurrence to date. Two patients died (endocrinologic complications/progression). Toxicity was mostly grade ¾ neutropenia/thrombocytopenia during chemotherapy. At a median follow-up of 38 months, OS was 100% for Germinoma and 85% NGGCT. CONCLUSION: The treatment is tolerable and VFI dose reduction to 18Gy seems to preserve efficacy. Further follow-up is warranted to assess the NG group and the slow-responder patients.

GCT-59. EPIDEMIOLOGY OF PEDIATRIC INTRA-CRANIAL GERM CELL TUMORS: COMPARING THE INCIDENCE OF INTRA-CRANIAL GERM CELL TUMORS IN THE NATIVE JAPANESE POPULATION AND IMMIGRANT JAPANESE POPULATIONS ABROAD

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Pediatric intra-cranial germ cell tumors (iGCTs) occur at an incidence of 0.6–1.2 cases/million/year in Western countries. The incidence is reported up to 5 times higher in the Japan. It is unknown whether this increased incidence is due to tumor biology or environment. The incidence of iGCTs in children ages 0–19 years was evaluated from 12/1/96-12/1/2016 in stable Japanese immigrant populations living abroad compared to current native Japanese registry data. Medulloblastoma incidence was used as a control to account for assumptions in the data. A review of the Brain Tumor Registry of Japan from 1984–2004 revealed an incidence of 2.5 cases/million/year and a lower incidence of medulloblastoma at 1.1 cases/million/year. Sites outside of Japan included Vancouver, Canada, Lima, Peru, and San Paolo, Brazil and together included a population of 853,174 Japanese persons. Within this population, 0 cases of iGCT were identified over a 20-years. The ratio of medulloblastoma to iGCT cases in Japan was identified as 1:2 while the ratio was 2:1, 6.5:1, and 5:1, respectively, in the other three locations. The data suggests increased incidence in the native Japan may not translate to higher incidence in immigrant Japanese populations abroad and a clear genetic component was not found in this preliminary data set. A more precise and comprehensive study is needed to determine the cause of this difference in incidence. This study also emphasizes the importance of national and state registries and is a call to collaborate on state and country level epidemiology studies.

GCT-60. DEVELOPMENT OF MICROBLEEDING AFTER PROTON THERAPY FOR PATIENTS WITH GERM CELL TUMOR

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BACKGROUND: Proton therapy has been increasingly used to treat pediatric brain tumor. However, there were few reports about radiation-induced cerebral microbleeds(CMBs) and cavernous malformation among these patients. Here we evaluate the incidence and risk factor of CMBs with MR imaging. MATERIAL AND METHOD: We retrospectively identified patients with germ cell tumor treated with whole ventricle irradiation of 30.6 Gy using proton therapy at the Tsukuba University Hospital between 2004 and 2017. CMBs were characterized by examination of MR imaging scan including susceptibility-weighted imaging and T2* weighed gradient-recalled echo sequence. RESULT: The mean age at the time of proton therapy was 14.5 years. The median follow-up duration was 62.3 months. Three patients were treated by local boost in addition to whole ventricle irradiation. CMBs were found in 78% at 5 years, and 88% at 10 years from irradiation. Over 80% of CMBs occurred in area of the brain exposed to 30 Gy. CONCLUSION: This study indicated over 30 Gy irradiation may become a risk factor for development of CMBs. Although the correlation between development of CMBs and cognitive function, proton therapy might have an advantage to reduce late sequelae with decreasing irradiating dose to surrounding normal brain tissue.

GCT-61. CORRELATION OF PATTERNS OF DISEASE RECURRENCE WITH RADIOTHERAPY TECHNIQUES AND DOSE IN INTRACRANIAL GERM CELL TUMOURS (ICGCT): LESSONS FROM THE UK COHORT OF SIOP GCT96 STUDY

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BACKGROUND: There are global variations in radiotherapy approaches for icGCT. An understanding of patterns of disease recurrence correlated with radiation techniques and doses is important in standardising and improving the quality of radiotherapy using high-precision techniques. METHODS AND RESULTS: Data from 20 patients with tumour recurrence after treatment within the SIOP GCT96 study in the UK were analysed. Seven (35%) patients had germinoma and 13 (65%) had non-germinoma. Twelve patients had local recurrence, 5 had metastatic and 3 had local and metastatic disease. Radiotherapy details were retrieved in only 8 patients (40%). Six patients had received focal radiotherapy and two craniospinal radiotherapy. Of the patients who received focal radiotherapy, 4 had recurrence within the radiation portal, one had periventricular recurrence and one had marker-positive recurrence with no radiological lesions. Both patients who received CSI recurred within the CSF space. The main reasons for poor retrieval of treatment details were difficulty in retrieving archived information and that the study was conducted during a period before PACS or electronic radiotherapy records. CONCLUSION: This study highlights the importance prospective data collection and analysis to understand the patterns of recurrence in icGCT. Even within a prospective study, radiotherapy techniques varied between centres. There is therefore an urgent need for centralised radiological review and prospective radiotherapy quality assurance measures in future clinical trials.

GCT-62. DISSECTING INTRATUMORAL HETEROGENEITY OF CENTRAL NERVOUS SYSTEM GERM CELL TUMORS BY SINGLE-CELL RNA-SEQUENCING

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BACKGROUND: Central nervous system germ cell tumor (CNSGCT) is a rare pediatric brain tumor. However, they are found at a relatively high incidence in East Asia. Germinoma is sensitive toward radiotherapy and chemotherapy; however, non-germinoma GCTs (NGGCT) often show poor response. Some cases are a mixture of germinoma and NGGCT (mixed GCT), and they sometimes change histological subtypes at recurrence. Previous report demonstrated that a germinoma and NGGCT component within the same mixed GCT tissue shared the same gene mutation, whereas the genome-wide methylation profiles were distinct from each other. The methylation profiles of germinoma was similar to the primordial germ cells (PGC) at the migration phase, supporting a model that PGC is the cell of origin for CNSGCT. However, tumor heterogeneity hinder information of the mixed bulk RNA-sequence data, causing difficulty in elucidating the mechanism of tumor development. The purpose of this study was to investigate the tumor cells subpopulations at the resolution of individual cells by single-cell RNA-seq. RESULTS: Fresh surgical tumor tissue was immediately dissociated mechanically and enzymatically. Tumor cells are separated from CD45-labelled lymphocytes by FACS, and libraries were generated by Chromium Single cell 3' Reagent Kit. Total of 11 tumor samples were collected and sequenced. Unsupervised Clustering showed individual clusters. One of the clusters had high expression of Oct-4, which is a marker of germinoma. The other clusters showed different subtypes of cells representing the heterogeneity of CNSGCT. Further analysis including a pseudo-time course analysis is underway to identify the lineage of tumor cell development.

GCT-63. STEREOTACTIC RADIOSURGERY FOR RESIDUAL LESIONS OF PINEAL NON-GERMINOMATOUS GERM CELL TUMORS AFTER CONVENTIONAL RADIOTHERAPY: A RETROSPECTIVE STUDY

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OBJECTIVE: To explore the efficacy and safety of SRS for residual lesions of NGGCTs after conventional RT. METHODS: The clinical data of patients with iGCT who were admitted to Department of Oncology, Guangdong Sanjiu Brain Hospital between January 1, 2008 and December 30, 2019 were gathered. Those who were pathologically or clinically diagnosed with NGGCTs, with lesions located at pineal region, limited stage and residual lesions (with a maximum diameter>10mm) of pineal NGGCTs after RT with a total dose of 50-54Gy/25-30f, were eligible for the study. Several indexes such as local control rate, PFS, OS and treatment-related toxicity were analyzed. RESULTS: A total of 27 patients were included; all were male, with a median age of 16 years (range 8–31 years). The patients were followed-up to December 30, 2019, but there were 2 cases lost to follow-up. The median follow-up time was 34 months (range 8–142 months). After a month of treatment with SRS, the ORR and DCR were 71.4% and 95.2%, respectively. During follow-up, 5 cases had radiographic progressions, including 3 cases combined with increased AFP which were diagnosed with local recurrence and 2 cases diagnosed with GTS ; The 3y-PFS and OS were 85.2% and 88.0%.no acute radiation response was found after treatment with SRS, and only one patient had brain neurotoxicity. CONCLUSION: SRS for residual lesions of NGGCTs after RT is proved to be safe and feasible, with well tolerance, which is beneficial for the improvement of local control and the prolongation of survival.

GCT-64. TREATMENT RESULTS IN CHILDREN WITH LOCALIZED CNS NGGCT

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BACKGROUND/OBJECTIVES: Treatment of children with CNS NGGCT remains challenge: 5y OS is 60 – 80%; relapses are very aggressive. DESIGN/METHODS: Between 2003 and 2019, 14 children (median age 10.5, range 4 – 16 years) with localized intracranial NGGCT were treated with RT after induction chemotherapy (focal – 4, WVI+boost – 6, WBI+boost – 3, CSI+boost – 1). Tumor markers were elevated in 13 patients: 6 – AFP, 5 – HCG, 2 – both. One patient with level of HCG 72049 IU/l in serum and 121451 IU/l in CSF received 4 cycles of PEI + CSI 30 Gy with boost 54Gy. RESULTS: At a median follow-up of 4,7 years (range 1 – 16,25 years), 12 patients are alive. 5-year PFS and OS are 77,1% and 85,7%, respectively. Two patients (both AFP and HCG) progressed during RT (1 – focal, 1 – WBI+boost), both died. Two patients with high level of HCG recurred after therapy (WVI+boost – 1, focal – 1), both are alive. The first of them at recurrence (mts of lateral ventricle) received 4 cycles of PEI and RT (WBI+boost). The second patient had level of HCG 620IU/l and initially received focal irradiation 54Gy. At recurrence with distant spinal mts he received HD-CHT with auto-SCT, surgical resection of residual tumor and CSI with boost. CONCLUSIONS: Good results of treatment of localized CNS NGGCT with CSI, WBI or WVI in compare with focal RT show advantages of extended irradiation field. CSI should be considered for patients with extremely high levels of tumor markers and respectively poor prognostic histology.

GCT-65. INCIDENCE AND OUTCOME OF INTRACRANIAL MALIGNANT GERM CELL TUMOURS DIAGNOSED IN WESTERN DENMARK IN THE LAST DECADE

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INTRODUCTION: Intracranial malignant germ cell tumours (iGCT) are rare brain tumours mainly diagnosed in children and younger adults. MATERIAL AND METHODS: A retrospective analysis was performed by chart review of patients treated for iGCT in the northern and central region of Denmark. Teratoma only patients were not included in the study. RESULTS: 20 patients with iGCT were diagnosed from 2008–2019 in Western Denmark. The cumulative incidence was 1.05 per 100.000. The yearly incidence was 0.1 per 100.000. Mean age at diagnosis was 18 years (range 8–36 years), 17 were males and 3 were females. 13 patients presented with germinoma and 7 patients with non germinomateous germ cell tumours (NGGCT). Three patients had disseminated disease, two with germinoma and one with NGGCT. All patients had received radiotherapy and 18 patients were treated with multidrug chemotherapy including platinum and etoposide before irradiation. Two patients experienced recurrent disease, both non disseminated at diagnosis, one patient with germinoma and one patient with NGGCT. Both received salvage treatment including high dose chemotherapy with stem cell transplantation and reirradiation. Two NGGCT patients died, one patient after development of an anaplastic astrocytoma in the radiation field five years after radiotherapy and one patient after intracranial hemorraghe 18 months after salvage treatment for recurrent disease. Overall survival was 90%, 100% for GCT and 71% for NGGCT. CONCLUSION: The outcome of patients with iGCT in Western Denmark was comparable to the literature. A nationwide study of epidemiology and outcome of iGCT in Denmark is planned.

GCT-66. FINAL REPORT OF THE PROSPECTIVE NEXT/CNS-GCT-4 CONSORTIUM TRIAL (GEMPOX FOLLOWED BY MARROW-ABLATIVE CHEMOTHERAPY) IN PATIENTS WITH REFRACTORY/RECURRENT CNS GERM CELL TUMORS

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BACKGROUND: We report the responses, toxicities and long-term outcomes of gemcitabine, paclitaxel and oxaliplatin (GemPOx) regimen administered, in responsive patients, prior to single cycle marrow-ablative chemotherapy (thiotepa, etoposide and carboplatin) with autologous hematopoietic progenitor cell rescue (HDCx+AuHPCR). METHODS: Since De-