hypomethylation in germinoma. However, there were plenty of cases which lacked driver alterations and their pathogenesis is yet to be fully unraveled. Here we aimed to uncover CNSGCT's pathogenesis from a transcriptomic perspective. Genome-wide transcriptional analysis was performed for 58 CNS and 3 testicular GCTs. This demonstrated that germinoma had a transcriptional profile characteristic to primordial germ cells (PGCs) at early embryogenesis, whereas non-germinomatous germ cell tumors (NGGCTs) showed that with differentiation into various tissues. Integration of transcriptome and methylome corroborated the above finding that pluripotency/meiosis-genes were unmethylated and highly expressed in germinoma compared with NGGCT. Co-analysis with transcriptome of various developmental stages of embryonic cells revealed germinoma and NGGCT had similarities in expression to PGC and embryonic stem cells, respectively. Multi-omics analysis with testicular GCTs (n=134) from TCGA showed shared genomic backgrounds between germinoma-seminoma and NGGCT-nonseminomatous GCT (NSGCT) in mutation and methylation profiles, and contrast in the chromosomal instability, which was more highlighted in testicular GCTs. These new insights into molecular profiles of GCTs lead to a better understanding of the complex pathogenesis of GCTs, and will hopefully provide a clue to future development of new treatments.

GCT-53. CASE OF INTRACRANIAL GROWING TERATOMA SYNDROME WITH DIFFICULTY IN TIMING OF RESECTION

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BACKGROUND: Intracranial Growing teratoma syndrome(iGTS) is a phenomenon in which a tumor with a teratoma component grows during treatment, and its pathological tissue is often a mature teratoma. Here we report a case of iGTS in which the timing of surgery was determined by tumor markers and changes in tumor size on MRI images. CASE-REPORT: 11-year-old boy with a short stature. He developed a headache and we found a pineal gland tumor on MRI. Due to obstructive hydrocephalus, an endoscopic third ventriculostomy and biopsy were performed. The pathological diagnosis was mature teratoma, but AFP was elevated at 104.2 ng/mL. Considering NGGCT, we started chemoradiation immediately. Despite the declining AFP, it gradually increased, at which point we suspected iGTS. Resection was considered, but at some point tumor growth had stopped, so radiation therapy and a second course of ICE therapy preceded the resection. Thereafter, the tumor was completely removed, and a third course of ICE therapy was performed. DISCUSSION: The onset mechanism of iGTS has not been elucidated, and its prediction is difficult. Early resection of the tumor is required, but discontinuation of radiation therapy and side effects of chemotherapy also need to be considered. In our case, resection was performed after normalization of AFP and recovery of myelosuppression. The patient followed an uneventful course, but the timing of resection was controversial. CONCLUSION: We experienced a case of iGTS in NGGCT, a mixed tumor with mature teratoma. The optimal timing of the resection was discussed and literature was reviewed.

GCT-55. INTRACRANIAL GERMINOMA ORIGINATING FROM ATYPICAL LOCATION WITH SUBCLINICAL ADH INSUFFICIENCY

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INTRODUCTION: Intracranial germinomas are rare tumors which usually develop in the midline structures and affect in 90% of cases the pineal gland and suprasellar regions. Sometimes they involve basal ganglia, septum pellucidum, and other regions. We report a very unusual presentation of an intracranial germinoma originating from the lateral ventricle. METHODS: A 10-year-old boy presented with a 1-year history of polydipsia and polyuria. During the hypertonic saline test, a low ADH was detected and established the diagnosis of subclinical ADH insufficiency. MRI showed a heterogeneously enhancing periventricular lesion in the lateral ventricle, but no other abnormal findings, including hypophyseal stalk. Initially, the correlation of imaging findings and clinical symptoms were not clear. With suspected subependymoma, tumor removal was performed by small craniotomy. Since the intra-operative pathological diagnosis was germinoma, we performed only partial removal of the tumor. After establishing the histological diagnosis of germinoma, the patient received chemotherapy using carboplatin and etoposide, followed by radiation therapy. MRI showed no recurrence for five years after treatment. RESULTS/CONCLUSION: Our case presents two atypical features. First, intracranial germinoma originating from the lateral ventricle is quite rare. Though the cases with intracranial germinoma originating from septum pellucidum and corpus callosum have been reported, this case is even different. Second, imaging findings did not match clinical symptoms. The cause of subclinical ADH deficiency may be the occult hypophyseal germinoma. In conclusion, we report a 10-year-old case with a very unusual presentation of an intracranial germinoma originating from the lateral ventricle.

GCT-56. ACUTE MYELOID LEUKEMIA FOLLOWING CHEMORADIOTHERAPY FOR INTRACRANIAL GERMINOMA: A CASE REPORT

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INTRODUCTION: Therapy-related acute myeloid leukemia (t-AML) is known as possible complication of chemotherapy, especially topoisomerase II inhibitor, alkylating agents, and platinum agents. Although there are many reports of therapy-related leukemia associated with gonadal germ cell tumor, few cases have been reported on central nervous system (CNS) germ cell tumor. CASE REPORT: A 35-year old gentleman presented with diplopia. CT and MR imaging showed enhancing nodules on his right hypothalamus and around fourth ventricle, and differential diagnoses included sarcoidosis and germinoma. Biopsy for fourth ventricle lesion was performed via transvermian approach, and histopathological diagnosis was germinoma. He was treated by 3 cycles of CARE chemotherapy (carboplatin and etoposide) followed by craniospinal irradiation (CSI, 24Gy). After completion of chemoradiotherapy, he was followed up every half year by MRI, and there had been no evidence of tumor recurrence. Two years after chemoradiotherapy, however, the patient presented with bleeding tendency, which led to the diagnosis of AML. Based on the history of chemoradiotherapy and the presence of t(16;21)(q24; q22), t-AML was diagnosed. Complete remission was successfully achieved by chemotherapy consisting of idarubicin and cytarabine. DISCUSSION: t-AML was diagnosed after chemoradiotherapy in a patient with CNS germinoma probably due to the administration of topoisomerase II inhibitor, etoposide. The prognosis of t-AML is known to be poorer as compared with de novo AML. Therefore, intensive therapy such as allogeneic stem cell transplantation should be considered in younger patients. CONCLUSION: A possibility of t-AML should be kept in mind following chemotherapy for CNS germ cell tumors.

GCT-57. ARE MELATONIN LEVELS A RELIABLE MARKER FOR INTRACRANIAL GERM CELL TUMORS POST TREATMENT DEFICIENCY?

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BACKGROUND: Pineal is the melatonin-producing gland, with this hormone importantly acting as a central and peripheral chronobiotic, antioxidant and in energy metabolism. The urinary dosage of 6-sulfatoxymelatonin (aMT6s), a melatonin metabolite, is an indirect marker to estimate the total melatonin nocturnal production, ranging in clinically normal individuals from 10–50 micrograms(ug). The purpose of this study was to evaluate aMT6s in patients with diagnosis of intracranial germ cell tumors (iGCT) treated at IOP/GRAACC/UNIFESP. METHODS: After an interview to collect data about therapies employed and medications, night urine samples (from 8:00pm to first void in the morning) were collected and analyzed by ELISA. RESULTS: Twenty patients between 5–42 years old (mean 20.9 years), all male, were analyzed. Thirteen patients had diagnosis of Germinoma, 1 with Imature Teratoma, 5 NGGCT and 2 Mature Teratoma. The first site was pineal (N=15) and bifocal (N=5). The treatment was surgery/biopsy/2° look surgery in 17 patients associated with chemotherapy/ radiotherapy, except in 2 (pure teratoma-surgery only) and 1 (chemo only). Three patients had diagnosis by tumor markers treated with chemo only (N=1) and chemotherapy/radiotherapy (N=2). The levels of aMT6s were between 0.2–3.2ug in all participants, except in one (14.8ug-biopsy, chemo and RT). CONCLUSION: aMT6s levels found in most patients are below the expected for the general population suggesting that this is an appropriate marker for pineal tumors with melatonin deficiency. It may contribute to support future studies in this area and adoption of follow-up protocols, with eventual hormone supplementation and consequently improved quality of life.

GCT-58. BRAZILIAN CENTRAL NERVOUS SYSTEM GERM CELL TUMOR CONSORTIUM PROTOCOL

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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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