presented with an AFP >1000 ng/ml at diagnosis. 41 patients were evaluable with a median observation time of 2.4 years; 6/41 received chemotherapy alone. Primary site, histological components (if available), metastatic status and outcome were evaluated. Primary site was pineal in 29/41, suprasellar in 6/41, bifocal 1/41 and other in 5/41 patients. 10/41 patients were metastatic at diagnosis. Four to five courses of standard PEI and radiotherapy (RT) or 2 standard and two intensified PEI (as for SIOP CNS GCT II) were administered in 32 patients. Two received less then 4x PEI and RT, 6 patients <6 years were treated with PEI (either standard or intensified) alone. 16/34 patients with PEI and RT are alive in CR; 2/6 patients without RT survived. Overall, 18/40 (45%) survived. 10–15% of CNS MGGCT are high-risk patients by diagnostic AFP, with the pineal as the main tumour site. Outcome of <50% survival is unsatisfactory. Further research, international cooperation and common data analysis is needed to identify additional risk factors and develop alternative treatment strategies.

GCT-49. EVALUATION OF THE PERIOPERATIVE AND POSTOPERATIVE COURSE OF SURGERY OF PINEAL GERMINOMA ACCORDING TO THE SIOP CNS GCT 96 TRIAL

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INTRODUCTION: CNS germinoma, being marker-negative, are diagnosed by surgical biopsy. Here we evaluate the perioperative status and postoperative complications of patients with pineal germinoma who underwent a primary biopsy or resection, treated according to SIOP CNS GCT 96. METHODS: 235 patients with histologically confirmed germinoma were registered, of which 113 were pineal: 55 were biopsied and 58 underwent primary resection. Initial symptoms, tumour size, complications and neurological status were assessed. 111 patients were evaluable. RESULTS: Pure germinoma was present in 101 patients; 10 had additional teratoma components. The main clinical symptoms at diagnosis were headache (n=98), hydrocephalus (n=93), double vision (n=62), Parinaud syndrome (n=57) and papilloedema (n=44). Tumour size was documented in 81 patients (<2cm, n=14; 2-3cm, n=35; ≥3cm, n=32). 17 patients underwent primary total resection, 14 subtotal resection >50%, 26 subtotal resection <50%, 39 stereotactic biopsy, 11 endoscopic biopsy, 2 open biopsy and 2 not documented. The postoperative neurological status after resection was improved in 23 patients, unchanged in 27, deteriorated in 6 and not documented in one. Clinical status after biopsy improved in 26 patients, was unchanged in 15, deteriorated in 2 and not documented in 11. Postoperatively, 16/57 patients after resection and 5/54 after biopsy developed complications (Parinaud syndrome, double vision and hydrocephalus). CONCLUSION: Although surgical techniques have improved within recent decades, these results support the practice of biopsy over resection for histological confirmation of germinoma arising at the pineal site. Supported in part by German Cancer Aid.

GCT-50. LONG-TERM OUTCOMES OF INTRACRANIAL GERMINOMA IN A SINGLE INSTITUTION

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The treatment for intracranial germinoma has been well-established. Complete removal is not necessary, but radiation therapy is important. As the prognosis of patients with germinoma has become better, side effect of radiotherapy and chemotherapy must be well considered. The aim of this study was to evaluate the outcome of intracranial germinomas at Kyoto University Hospital from 1979 to 2019. 64 patients were diagnosed as intracranial germinoma. Patients with hCG > 100 IU/l and/or AFP > 10 ng/ml were excluded. Patients, who were histologically diagnosed as germinoma without information of hCG and AFP, were included. Follow-up time was from 2 to 486 months (median 136 months). Recently, germinoma patients were diagnosed with biopsy and received low dose whole-ventricle irradiation with intensity modulated radiation therapy (IMRT) (total 24-30Gy) and chemotherapy dominated by platinating agent. 10-year PFS was 80.21% (high dose radiation alone), 86.36% (high dose radiation with chemotherapy) and 100% (low dose radiation with chemotherapy). Many recurrent sites were out of irradiation areas. Late cognitive dysfunction was identified in 6 patients, and 5 of them were treated with high dose radiation. Patients with intracranial germinoma can obtain long-term survival. It is important to prevent recurrence without increasing late iatrogenic complications. Low dose radiotherapy and chemotherapy is highly effective, and it potentially reduces late adverse effects.

GCT-51. IMMUNE CHECKPOINT MOLECULES AND TUMOR INFILTRATING LEUKOCYTES IN THE TUMOR MICROENVIRONMENT ARE ASSOCIATED WITH THE GROWTH OF INTRACRANIAL GERMINOMAS

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The role of immune checkpoint molecules and the tumor immune microenvironment in the development of intracranial germ cell tumors remains unclear. In the present study, we investigated the expression of immune checkpoint molecules, as well as the number of tumor-infiltrating lymphocytes (TILs), in intracranial germinomas to determine whether there were any correlations between the statuses of these immune-related molecules/cells and clinical manifestations in patients with germinoma. The 8 patients were categorized based on the duration between symptom onset and pathological diagnosis into the long-term onset (LTO) group (> 1 year of symptoms, 3 patients) and the short-term onset (STO) group (< 1 year of symptoms, 5 patients). Compared with STO tumors, LTO tumors were significantly associated with a lower ratio of programed cell death ligand-1 (PD-L1)–positive tumor cells ($p = 0.012$), higher number of infiltrating CD3- and CD8-positive lymphocytes ($p = 0.016$, 0.003, respectively), and lower ratio of programed cell death-1 (PD-1)–positive cells per CD8–positive lymphocytes ($p = 0.047$). LTO germinomas were significantly smaller in size than STO tumors and tended to be present in patients with atypical tumor location. Our data suggest that the tumor immune microenvironment, including PD-1/PD-L1 signaling, is associated with the growth of intracranial germinomas. Immune checkpoint inhibitors might be a reasonable treatment option for recurrent germinomas or as replacement for radiotherapy in patients with intracranial germinomas.

GCT-52. TRANSCRIPTOME OF CENTRAL NERVOUS SYSTEM GERM CELL TUMOR REVEALS ITS PATHOGENESIS AND CONTRASTS WITH TESTICULAR COUNTERPARTS IN INTEGRATED OMICS ANALYSIS

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Germ cell tumors (GCTs) are unique neoplasms in that they arise from the migrated cells which were supposed to be directed to gonads. They occur in the central nervous system (CNS), as well as gonadal organs such as testis and ovary. Our genomic analysis revealed that they are characterized by mutations in MAPK and PI3K pathways, chromosomal instability and global

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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