presented with an AFP >1000 ng/ml at diagnosis. 41 patients were evaluated with a median observation time of 2.4 years; 6/41 received chemotherapy alone. Primary site, histological components (if available), metastatic status and initial treatment were evaluated. Primary site was 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. Two received less than 6 patients, and 5 from 6 patients, and 5 from 6 patients were treated with PT (either standard or intensified); 16/41 patients were treated 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 <20% 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 (Z-score, n=14; 2-cm, n=35; >2-cm, n=32); 17 patients underwent primary total resection, 14 subtotal resection ≥50%, 26 subtotal resection >50%, 26 subtotal resection <50%, 39 stereotactic biopsy, 11 endoscopic biopsy, 2 open biopsy and 2 biopsies during resection. Initial symptoms, complications and neurological status were assessed; 111 patients were evaluable. RE-SULTS: 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 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 the 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 effects of radiation therapy 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 chemoreduction dominated by platinating agent. 10-year PFS was 80.2% (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 observed in 4 patients. Complete removal is not necessary, but radiation therapy is important. As the prognosis of patients with germinoma has become better, side effect of chemotherapy must be well considered. Further research, international cooperation and common data analysis is needed to identify additional risk factors and develop alternative treatment strategies.

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 was any correlation between the statuses of these immune-related molecules and cell clones and manifestations in patients with germinoma. The 8 patients were categorized based on the duration between symptom onset and pathological 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 programmed 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 programmed cell death-1 (PD-1)–positive cells per CD8–positive lymphocytes (p = 0.047). LTO germinomas were significantly smaller than STO tumors and were presented more frequently in the anterior symphysis and the pineal region. 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 radiation therapy in these patients.

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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We performed integrative genomic analysis and found that germ cell tumors of the CNS and testis have distinct molecular origins. Tumor microenvironment and immune infiltration in each type were distinctive. We also identified PD-L1–positive tumor cells, higher number of infiltrating TILs, in intracranial germinomas to determine whether there was any correlation between the statuses of these immune-related molecules and cell clones and manifestations in patients with germinoma. The 8 patients were categorized based on the duration between symptom onset and pathological 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 programmed 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 programmed cell death-1 (PD-1)–positive cells per CD8–positive lymphocytes (p = 0.047). LTO germinomas were significantly smaller than STO tumors and were presented more frequently in the anterior symphysis and the pineal region. 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 radiation therapy in these patients.
hypohydration in germinoma. However, there were a few combinations which lacked water administration and their pathogenesis is yet to be fully unraveled. Here we aimed to uncover CNSGCT’s pathogenesis from a transcriptional perspective. Gene-expression transcriptional analysis was performed for 20 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 different expression in specific tissues. Integration of transcriptome and methylome corroborated the above finding that pluripotency/ieiosis-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-semmoma and NGGCT-semmomatus 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: A 13-year-old boy with a short stature. He developed a headache and we found a pineal 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 IEC therapy preceded the resection. Thereafter, the tumor was completely removed, and a third course of IEC therapy was performed. DISCUSSION: The onset mechanism of iGTS has not yet been clarified, and its prediction has not been difficult. Early prediction 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 present case had a favorable course, but the optimal 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 THE LATERAL VENTRICLE. 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 pellicudum and corpus callosum have been reported, this case is even different. Second, our patient did not match clinical symptoms. The cause of subclinical ADH deficiency may be the occult hypohydration in 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 LEUKAEMIA FOLLOWING CHEMORADIOLOGY 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 leukemias 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 hypothalamic, and around fourth ventricle. Imaging findings of pituitary stalk. Initially, the correlation of imaging findings and clinical symptoms 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, the onset mechanism of iGTS was germinoma, we performed only partial removal of the tumor. MRI showed no recurrence for five years after treatment.

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 chronobiologic, anti oxidant and in energy metabolism. The urinary dosage of 6-sulatoxymelatonin (aMT6s), a melatonin metabolite, is an indirect marker to estimate the total melatonin nocturnal production, ranging in clinically normal individuals from 10−50 micrograms/μg. The purpose of this study was to evaluate aMT6s in patients with diagnosis of intracranial germ cell tumors (iGCT) treated at IOPGRAAC/UNIFESP. METHODS: After an interview to collect data about therapies employed and medications, urine samples (from 8:00 pm 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 immature Teratoma, 5 NGGCT and 2 Mature Teratoma. The first site was diagnosed. Complete remission was successfully achieved by chemotherapy and radiotherapy (carboplatin and etoposide) followed by craniospinal irradiation (CSI, 24 Gy). 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, leading to the diagnosis of JAK2V617F (0.8%). 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.