

versity Hospital. All 187 cases were confirmed histologically. RT fields included craniospinal, whole-ventricle (WV), whole-brain (WB), and focal radiotherapy. RT dose was dependent on the M status and combination of chemotherapy. The median follow-up duration was 115 months (range, 3–358). RESULTS: The 10-year overall and recurrence-free survival was 94.5% and 91.4%. The complete response rate after chemotherapy was 62.6%. For the patients with complete response, WV RT 16–20 Gy, and focal boost of 25–36 Gy after upfront chemotherapy showed no in-field recurrence. The causes of death were progression (n=3), 2<sup>nd</sup> malignancy (n=6), treatment-related complications (n=7), and others (n=8). For non-sellar tumors, the rate of hormonal replacement treatment was significantly related to WB RT and WB/WV RT dose  $\geq 30$  Gy ( $p=.030$ , and  $.026$ ). After a latency of the median 20 years, ten patients (5.3%) developed 2<sup>nd</sup> malignancy. WB RT and WB/WV dose  $\geq 30$  Gy were significantly correlated with the 2<sup>nd</sup> malignancy ( $p=.024$ , and  $.004$ ). The rate of severe neurocognitive dysfunction was significantly associated with WB/WV dose  $\geq 30$  Gy ( $p=.027$ ). CONCLUSION: CONCLUSION: RT with or without upfront chemotherapy exhibits the excellent control rate of disease. However, the intensity and volume of RT are critical for managing treatment toxicities. Adaptation and further de-intensification of RT should be followed.

#### GCT-03. TREATMENT OUTCOMES, PHYSICAL DEVELOPMENT AND QUALITY OF LIFE OF PATIENTS WITH BIFOCAL GERM CELL TUMOURS

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BACKGROUND: The optimal radiation field in patients with bifocal germ cell tumours (GCTs) is controversial, especially in non-metastatic cases. Accordingly, we analysed the survival, growth, and health-related quality of life (HRQOL) data of patients with bifocal GCTs. METHODS: The data of 87 patients diagnosed with bifocal GCTs at our hospital during the last 10 years were collected. The WHO AnthroPlus software—used to monitor the growth of persons aged 5–19 years—was employed to calculate the Z-score of height (ZSOH) at diagnosis and the last follow-up. The absolute change in the ZSOH was defined as  $ZSOH_{last\ follow-up} - ZSOH_{diagnosis}$ . The Pediatric Quality of Life Inventory 4.0 was used to evaluate HRQOL. RESULTS: The median follow-up was 49 months (range, 6–134 months). Among 49 patients with non-metastatic germinoma, those receiving cranial spinal irradiation (CSI; n=12) or whole-brain radiotherapy (WBRT; n=34) had comparable disease-free survival (DFS;  $p=0.54$ ), but better DFS than those receiving focal radiotherapy (n=3;  $p=0.016$ ). Furthermore, among 17 patients with non-metastatic non-germinomatous GCTs, DFS was not significantly different between those treated with CSI (n=4) and those receiving WBRT (n=13;  $p=0.11$ ). Twenty-nine patients had paired ZSOH data at both diagnosis and the last follow-up. Patients receiving CSI ( $p=0.026$ ) or  $>40$  Gy ( $p=0.048$ ) experienced a significant decline of absolute change in the ZSOH. HRQOL analysis (n=35) did not reveal difference between patients receiving CSI and those not receiving CSI. CONCLUSIONS: Given the comparable DFS and HRQOL but negative impact on growth, CSI could be spared, especially in patients with non-metastatic bifocal germinoma.

#### GCT-06. DIAGNOSIS OF A RARE CASE OF RECURRENT GERM CELL TUMOR BY CSF PLACENTAL ALKALINE PHOSPHATASE PRESENTING WITH DIFFUSE INTRAAXIAL ABNORMALITY IN THE LOWER BRAINSTEM

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INTRODUCTION: Germ cell tumors in the central nervous system (CNS) typically arise either at suprasellar and/or pineal region, and occasionally at basal ganglia. We report a case of diagnostically challenging, recurrent germ cell tumor presented with diffuse intraaxial abnormality in and across the lower brainstem, which was diagnosed by the elevated placental alkaline phosphatase (PLAP) level in cerebrospinal fluid (CSF). CASE DESCRIPTION: A 28-year-old man had been treated by chemoradiotherapy at the previous hospital for bifocal suprasellar and pineal lesions with the provisional diagnosis of germinoma without histological confirmation. Three years later, he presented with progressive weakness of bilateral extremities for weeks. Magnetic resonance imaging showed a diffuse, bilaterally symmetric high intensity lesion on T2-weighted image with slight contrast enhancement across the ventral side of the medulla oblongata to the upper cervical spinal cord. Serum and CSF hCG, hCG- $\beta$ , and AFP were all negative. Since the image findings were atypical for recurrent germ cell tumor, some kind of myelitis was initially suspected. Therefore, steroid pulse therapy was administered. However, the patient's symptom was still gradually progressing. Then, the CSF PLAP turned out to be positive, indicating the recurrence of germinoma. Accordingly, platinum-based chemotherapy was administered, and the imaging findings, patient's symptoms, and CSF PLAP began to improve. The patient is to be treated with radiotherapy fol-

lowing chemotherapy. CONCLUSION: We report a rare case of CNS germ cell tumor that presented with diffuse intraaxial lesion in the lower brainstem in which examination of CSF PLAP was extremely useful.

#### GCT-08. PROTON BEAM RADIOTHERAPY FOR PEDIATRIC AND YOUNG-ADULT PATIENTS WITH INTRACRANIAL GERM CELL TUMOR

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BACKGROUND: To reduce treatment-related adverse events in pediatric and young-adult patients with brain tumors, proton beam radiotherapy (PBT) has recently been performed instead of conventional X-ray radiotherapy. However, whether PBT is as effective as X-ray radiotherapy has not been sufficiently investigated, especially in patients receiving whole-ventricular irradiation. METHODS: We report a retrospective observation of 15 patients with intracranial germ cell tumors (GCT), who received PBT at our institution from April 2014 to September 2019. We evaluated their clinical course, short-term adverse events, and prognosis. RESULTS/CONCLUSION: Fifteen patients (9 males and 6 females; median age 13 years) who received PBT following induction chemotherapy were analyzed. Nine patients received 23.4–27.0 GyE of whole-ventricular irradiation due to GCT in the pituitary gland, pineal body, or hypothalamic area. Three patients received 23.4 GyE of whole-brain irradiation: one of them had boost irradiation for basal ganglia. Three patients received 30.6 GyE of craniospinal irradiation (CSI). Six of the 15 patients experienced nausea (grade 2, according to the CTCAE version 4.0). Four patients, including two who received CSI, showed myelosuppression: decrease in white blood cell count, lymphocyte cell count, and neutrophil count (grade 3). No other severe short-term adverse events of  $>$ grade 2 was observed in any of the patients. At a median follow-up of 21 months (2–62 months) after irradiation, all patients are alive without recurrence. Our results may be encouraging and further investigations with a larger scale is warranted.

#### GCT-09. HEALTH AND SOCIAL ISSUES IN THE LONG-TERM GERM-CELL TUMOR SURVIVORS

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Germ cell tumor (GCT) is a rare juvenile CNS tumor that is more frequent in eastern Asia. Most survivors require continuous medical care for hormone replacement, maintenance of shunting devices, and late radiation-induced effects. In the present study, we retrospectively analyzed medical records of long-term GCT survivors, and make the health and social issues clear. Ninety-two GCT patients were treated in our institute from 1982 to 2018, and 81 patients, of which medical records are available, are included. The median follow-up period is 12.2 years, and 47 patients (58.1%) are followed for more than ten years. The overall survival rate is gradually decreasing more than ten years follow-up, such as 10-, 15- and 25-years survival are 92.3, 87.7, and 73.3%, respectively. In the long-term follow-up, eight subsequent malignancy and seven cerebrovascular events are recorded. These events occurred 20 years or more after the treatments, and six CNS malignancies were observed in survivors irradiated with 50Gy or more. As social issues, forty-two of 50 adult survivors had been employed after the treatments, but only thirty-four (70.8%) are still working. Of note, only nine (18.8% of adults) survivors got married. All four married women require any hormone replacement, while only one of 4 men requires the replacement. Long-term follow-up of GCT survivors revealed subsequent malignancy and social problems. A recent attempt to decrease the dose of irradiation might overcome some issues. As a conclusion, GCT survivors require a supporting program for not only health but also social issues.

#### GCT-10. CAN HIGH LEVEL SERUM HCG-B BE CONSIDERED EQUIVALENT TO A DIAGNOSIS OF CHORIOCARCINOMA IN PRIMARY CENTRAL NERVOUS SYSTEM GERM-CELL TUMOR?

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**BACKGROUND:** Primary central nervous system (CNS) choriocarcinoma (CC) is very rare and has the poorest prognosis among germ cell tumor (GCT). CC usually has extremely high level (HL) of serum beta-human chorionic gonadotropin (bhCG) over than 1,000 mIU/ml. Some studies assign HL bhCG cases to poor prognosis group even without biopsy. The purpose of this study was to find out if there was a good prognosis subset in the HL bh group. **MATERIALS AND METHODS:** We analyzed 103 cases diagnosed with GCT from 1998 to 2019 in Hokkaido University Hospital and reviewed the literature of CNS CC and bhCG. Survival was assessed using Kaplan-Meier method and log-rank statistics between the group with CC component and that with no CC component but HL bhCG. **RESULTS:** One out of 103 our cases was diagnosed as a mixed GCT with CC component and did not respond to treatment and died 9 months later. Two cases were treated as CC because of HL bhCG (1,226 and 2,739 mIU/ml) despite that the biopsy showed only germinomas and survived (105 and 37 months), that is, no CC component. Combining our cases with 69 cases in the literature, all 7 cases with no CC component but HL bhCG survived but the median survival of the other 65 cases with CC component was 38.2 months ( $P=0.02$ ). **CONCLUSION:** This study has a limitation of selection bias, however, it suggests that patients with no CC component but HL bhCG may have a better prognosis.

#### GCT-12. INTRACRANIAL GROWING TERATOMA SYNDROME: CLINICAL IMPLICATION FROM SINGLE UNIVERSITY EXPERIENCES

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In general, intracranial germ cell tumors (GCT) are sensitive to chemotherapy, radiation therapy, and have favorable outcomes. However, a rare chemotherapeutic retro conversion phenomenon, known as intracranial growing teratoma syndrome (iGTS), shown a poorer prognosis. We analyze the diagnostic characteristics and the result of treatment response for the patients with iGTS treated in our institutes (SNUH and SNUBH, from 1997 to 2019). The electronic medical records and PACS were used for reviewing the clinical information, follow-up MRI images, tumor markers (alpha-fetoprotein, human chorionic gonadotropin, in serum or cerebrospinal fluids), and pathological findings. Out of 328 intracranial GCT patients, seventeen were finally identified as iGTS. Sixteen out of 17 patients were non-germinomatous GCTs, and 1 were germinomas. Initial pathology was common in order of immature teratoma (26.7%), other than immature teratoma (11.5%), and germinoma (0.5%). All of the tumors showed typical 'honeycomb appearance' in their follow-up MRI images. Sixteen out of 17 tumors were surgically resected as 2<sup>nd</sup> look surgery. Among them, 13 tumors were gross totally resected. Twelve were alive without evidence of recurrences during follow-up periods, and the other was dead from the progression of the disease. Among the other than the gross total resection group ( $n=4$ ), two patients were dead, one recurred the tumor, and the other is following up with stable disease after adjuvant radiation therapy. Early detection and total resection of the tumor as possible might be meaningful for favor prognosis, especially in non-germinomatous GCTs patients.

#### GCT-13. THE TREATMENT OUTCOMES OF INTRACRANIAL GERM CELL TUMORS WITH KSPNO PROTOCOL: SINGLE CENTER RETROSPECTIVE ANALYSIS

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Dho et al. (BTRT, 2017) reported that 1.1% (127/11,827) of primary brain tumors are intracranial germ cell tumors (iGCT) in Korea. We analyzed

the epidemiology and treatment results of germ cell tumors in our institution. From 2004 to 2019, among 6494 patients with intracranial neoplasms the 61 (0.9%) patients with iGCTs were enrolled; histologically diagnosed in 50 patients and clinically in 11 respectively. Pediatric patients underwent treatment according to the KSPNO protocol, and adult patients were treated with bleomycin, etoposide, and cisplatin regimens. The median age was 20 years (range: 1–42) and the follow-up period was 7.7 months (range: 10.0–203.4 months), respectively. The tumors arise most frequently in the pineal area ( $n=30$ , 49.2%). There were no significant differences in outcomes between protocols, but in KSPNO protocol group showed lower tumor recurrence rate (11.5% vs. 20%,  $p=0.494$ ) and mortality (0% vs. 5.2%,  $p=0.503$ ). According to the pathological subtype, the outcomes showed statistically significant differences between germinoma and non-germinomatous germ cell tumor (NGGCT) groups. The 10-year progression-free survival was 93.2% and 67.1% in the germinoma and the NGGCT group, respectively ( $p=0.009$ ). The NGGCT pathological type ( $p=0.021$ ) was a significant recurrence associated factor in multivariate analysis. Significant adverse events (CTCAE version 5.0 grade $\geq 3$ ) were showed in 14 patients (7 patients in both KSPNO and other treatment protocol groups). Pure germinoma has a higher survival rate and a lower recurrence rate than NGGCT. And KSPNO protocol might be safe and effective. For appropriate treatment for iGCTs, a multidisciplinary approach might be needed.

#### GCT-14. SECOND-LOOK SURGERY FOR INTRACRANIAL GERM CELL TUMORS

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**OBJECTIVE:** The authors present their experiences of second-look surgery in patients with intracranial GCTs who showed less than complete response despite normalizing or decreasing tumor markers after chemotherapy. **METHODS:** Retrospective review of 14 patients who underwent second-look surgery for an intracranial GCT was performed. **RESULTS:** Of 40 consecutive patients with newly diagnosed intracranial GCTs treated between August 2003 and 2019, 14 patients (35%) underwent second-look surgery. The mean age was 9.2 years. The initial diagnoses were mixed germ cell tumor in 6, immature teratoma in 4, yolk sac tumor in 2, and germinoma 2. Second-look surgery was performed after 1–3 courses of chemotherapy. Magnetic resonance imaging (MRI) at the surgery demonstrated increasing residual tumor in 8 and stable residual tumor in 6. Tumor markers were normalized in 10 and nearly-normalized in 4. Gross total resection was achieved in 12 patients and near-total resection in 2. Histopathology at second-look surgery revealed mature teratoma in 6, immature teratoma in 3, fibrosis with atypical cells in 2, and fibrosis in 3. Eleven patients subsequently underwent additional chemo-radiation therapy according to the initial diagnosis. All patients are alive with no evidence of recurrence with a mean follow-up of 69 months. **CONCLUSIONS:** Second-look surgery plays an important role in the treatment of intracranial GCTs. Surgery may be encouraged at a relatively early phase after chemotherapy when the residual tumor increases or does not change the size despite normalized or nearly-normalized tumor markers in order to achieve complete resection and improve the outcome.

#### GCT-15. INTEGRATED CLINICAL, HISTOPATHOLOGICAL, AND MOLECULAR DATA ANALYSIS OF 190 CENTRAL NERVOUS SYSTEM GERM CELL TUMORS FROM THE IGCT CONSORTIUM

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**BACKGROUND:** We integrated clinical, histopathological, and molecular data of central nervous system germ cell tumors to provide insights into their management. **METHODS:** Data from the Intracranial Germ Cell Tumor Genome Analysis Consortium were reviewed. A total of 190 cases were classified as primary GCTs based on central pathological reviews. **RESULTS:** All but one of the cases that were bifocal (neurohypophysis and pineal glands) and cases with multiple lesions including neurohypophysis or pineal gland were germinomas (34 of 35). Age was significantly higher in patients with germinoma than other histologies. Comparison between tumor marker and histopathological diagnoses showed that 18.2% of histopathologically diagnosed germinomas were marker-positive and 6.1% of non-germinomatous GCTs were marker-negative, suggesting a limitation in the utility of markers or histopathology alone using small specimens for diagnosis. Comparison between local and central histopathological diagnoses revealed a discordance of 12.7%. Discordance was significantly less frequent in biopsy cases, implying difficulty in detecting all histopathological components of heterogeneous GCTs. Germinomas at the typical sites (neurohypophysis or pineal gland) showed a better PFS than those at atyp-