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INTRODUCTION: The prognostic impact of tumour marker (TM) decline rate has been demonstrated for extracranial poor prognostic non-seminomatous/germinomatous germ cell tumours (NGGCT). The current series aimed to assess if this finding can be applied to intracranial primaries. METHODS: Patients were retrieved from the SIOP-CNS-GCT-96 database. They were selected if they had i/assessable values of serum alpha-fetoprotein (AFP) and/or human chorionic gonadotropin (HCG) before and 18 to 28 days after the first course of chemotherapy and ii/ available data for outcome. Decline rate was calculated using a logarithmic transformation and expressed as time to normalization (TTN) as published by Fizazi (JCO 2004). TTN≤ 9 weeks for AFP and ≤ 6 weeks for HCG were considered as favourable decline rate. Prognostic impact of TTN on outcomes was assessed using the log-rank test. RESULTS: Out of 149 patients with NGGCT, 59 were evaluable for both HCG and AFP TTN of whom 44 (74%) had a favourable decline rate. After a median follow-up of 88 months (2–251), 20 relapses and 15 deaths occurred. The 5-year PFS rates were 72% and 60% in patients who had a favourable and an unfavourable TTN, respectively (p=0.15). The 5-year OS rates were 77 % and 69%, respectively (p=0.66). Separate analysis of TTN based only on AFP or only on HCG gave similar results. CONCLUSION: Despite the use of a methodology similar to that used in extracranial NGGCT, no significant impact of serum TM decline on prognosis was observed, but insufficient statistical power cannot be ruled out.

GCT-30. TREATMENT OF PRIMARY INTRACRANIAL GERM CELL TUMORS: SINGLE INSTITUTION EXPERIENCE OF 74 CASES WITHOUT HISTOLOGICAL CONFIRMATION

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BACKGROUND AND OBJECTIVE: Primary intracranial germ cell tumors (PIGCTs) are a group of heterogeneous tumors. It is very difficult to treat those patients without pathological diagnosis. This study retrospectively analyzed the clinical data and outcomes of patients with clinically diagnosed (without histologically confirmed) PIGCTs in SunYat-sen University Cancer Center. METHODS: Patients who were clinically diagnosed as PIGCTs without histological diagnosis through surgical resection or biopsy were included in this study. Patients were analyzed for clinical characteristics, treatment patterns, outcomes and adverse effects. RESULTS: From May 2002 to July 2014, 74 patients clinically diagnosed with PIGCTs received chemotherapy and/or radiotherapy at the Sun Yat-sen University Cancer Center. The median age was 16.5 years old (4–45 years old, majority was teenagers). The most of tumors were found in male, and located in the pineal and suprasellar regions. When the patients were grouped into diagnostic chemotherapy group (57 cases), diagnostic radiotherapy group (5 cases) and gamma knife radiosurgery group (12 cases) based on their initial anti-tumor therapy. The 5-year survival rates were 84.3%, 75.0% and 75.0%, respectively. There was a trend that the chemotherapy group got a better survival. Patients were allocated to secretory tumor group (49 cases) and non-secretory tumor group (25 cases) based on their levels of tumor makers (α-FP and β-hCG). The 5- year survival rates were 80% and 77.8% (P value = 0.966), respectively. CONCLUSION: Clinical diagnosed PIGCT (without histological confirmation) patients may obtain good responses when receiving comprehensive treatments of chemotherapy combined with radiotherapy.

GCT-31. DIAGNOSTIC CAPABILITY OF CSF-PLAP ON INTRACRANIAL GERM CELL TUMOR

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BACKGROUND: Since the majority of intracranial germ cell tumor(GCT) is sensitive for chemoradiation, biopsy specimens are usually tiny and not enough for accurate pathological diagnosis. To supply complementary diagnostic information, a-fetoprotein or human chorionic gonadotropin-b are important biomarkers. Recently CSF-placental alkaline-phosphatase(PLAP) is also reported as an additional biomarker in intracranial GCT. This study's purpose is to evaluate the significance of CSF-PLAP. METHODS: CSF-PLAP was obtained from the patients with the intraventricular and periventricular tumor before any adjuvant therapy. Definitive diagnoses were made by histopathological information and/or their clinical courses; GCT(germinoma or non-germinomatous GCT(NGGCT)) or other tumors. In GCT, the relationship between CSF-PLAP and tumor reduction volume was evaluated. Tumor volumes were calculated on gadolinium-enhanced T1-weighted magnetic resonance imaging before and after initial chemoradiotherapy. RESULTS: Between 2005 and 2019, 42 patients were studied: 24 with GCT and 18 with others. CSF-PLAP value in patients with GCT was significantly higher than those with others: the Specificity was 88% and the sensitivity was 95% at the cutoff value of 8.0 pg/ml. For GCT patients, CSF-PLAP value tended to be higher in germinoma(n=12, mean 4756 pg/ml), compared to the value in NGGCT(n=7, mean 332 pg/ml), although there was no statistical difference. There was a significant positive correlation between initial CSF-PLAP value and tumor reduction volume. CONCLUSION: CSF-PLAP is a useful tumor marker for GCT differentiating from the other tumors located in intraventricular and periventricular region and CSF-PLAP value might correlate with the volume of germinomatous component of the tumor.

GCT-33. A PHASE 2 TRIAL OF RESPONSE-BASED RADIATION THERAPY FOR PATIENTS WITH LOCALIZED CENTRAL NERVOUS SYSTEM GERM CELL TUMORS: A CHILDREN'S ONCOLOGY GROUP (COG) STUDY. IMPACT OF RAPID CENTRAL RADIOTHERAPY REVIEW ON RADIOTHERAPY QUALITY AND PATTERN OF FAILURE FOR NON-GERMINOMATOUS GERM CELL TUMORS

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BACKGROUND: COG ACNS 1123 tested reduced radiotherapy (RT) for non-metastatic, non-germinomatous germ cell tumor (NGGCT) patients. The impact of central review on quality of RT and pattern of failure for NGGCT patients is evaluated. METHODS: Patients who achieved a complete response (CR) or partial response (PR) to induction chemotherapy were eligible for reduced dose and field RT of 30.6 Gy whole ventricular field (WVI) and 54 Gy tumor-bed total dose. An online contouring atlas was available. Within three days of RT start, WVI plans were submitted for rapid central review. Within one week of RT completion, the complete RT record was submitted. Brain and spine MRIs of relapsed patients were centrally reviewed. RESULTS: Between 5/2012–9/2016, 107 eligible patients were accrued and 70 met reduced RT criteria. Rapid RT review was performed for 49 (70%) of 70 patients. Forty-four (89.8%) required no modification. All modifications were completed and plans became compliant. Final central review was performed for 66 evaluable patients: 62 (94%) were per protocol; there were 2 major (1 dose and 1 target) and 2 minor deviations. Eight patients progressed; none had deviations. Median time to progression was 3.54 months (range: 1.7–19.1) from RT start. All failures had a spine component; two also had cranial component: one local progression (within the RT boost volume) and one leptomeningeal disease. CONCLUSION: Providing an online contouring atlas and performing a rapid central review lead to high quality radiotherapy on this prospective trial. The deviations did not contribute to the pattern of failure.

GCT-34. ELUCIDATION OF THE MECHANISMS OF TUMORIGENESIS IN INTRACRANIAL GERM CELL TUMOR BY WHOLE GENOME SEQUENCE

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Intracranial germ cell tumors (iGCT) are heterogenous group of primary brain tumors that consist of various subtype, and driver genetic alterations in iGCTs remain largely unknown. We have previously reported in a study

of whole exome sequence that iGCTs frequently harbored mutations in the KIT gene and its downstream MAPK/PI3K pathway, regardless of tumor subtype. However, no mutations were detected in about one-quarter of germinomas and half of non-germinomatous germ cell tumors. A genome-wide methylation profiling revealed that only germinomas exhibited extreme DNA hypomethylation among iGCTs. Moreover, in mixed iGCT tumors which contained more than one tumor subtypes, each component exhibited distinct methylation status depending on the subtype, while they shared the same mutations. These data suggested that not only mutations in the coding region as previously reported, but also genetic alterations in regulatory regions including promoters and enhancers as well as non-coding RNA genes may be involved in the tumorigenesis of iGCTs. In order to comprehensively search for driver gene alterations, we performed whole genome sequence in 18 paired tumor blood samples from iGCT tumors (16germinomas and two yolk sac tumors (YST)) registered in the Intracranial Germ Cell Tumor Genome Analysis Consortium. In a preliminary analysis of four cases, YSTs harbored a significantly higher number of structural abnormalities, compared with germinomas. Of note, 62 structural abnormalities were clustered within the small genomic region of 95Mb at 1q21-44 in one YST case, suggesting a possibility of chromothripsis. A full analysis of somatic alterations is underway and will be reported.

GCT-35. SALVAGE CRANIOSPINAL IRRADIATION FOR RECURRENT GERMINOMAS

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BACKGROUND: The treatment strategies for recurrence has not been established. PURPOSE: To clarify the tumor control and complications of salvage craniospinal irradiation (CSI) for recurrent germinoma. METHODS: We retrospectively reviewed the medical record. Among 153 germinomas treated in Tohoku University Hospital since 1983, 22 had recurrence of germinoma. At first recurrence, 7 cases received CSI, whereas 15 cases did chemotherapy and/or radiation therapy other than craniospinal field (non- CSI). CSI was performed at 24 Gy/ 12 fractions or 30 Gy/ 25 fractions. RESULTS: CSI had statistically significant better recurrence-free survival rate after recurrence than non-CSI (100% vs 33%, $p<0.001$: log-rank test). In addition, tumor control was obtained in all of four cases with the failure after non- CSI treatments for recurrence. The late complications of these 11 cases were examined. The local dose before CSI was 24- 50 Gy, and the median interval from last irradiation to CSI was 33 months. Median follow- up period after CSI was 126 months. Three patients developed newly developed visual or cognitive deficits. These patients received high-dose irradiation at initial treatment or multiple treatment before CSI. There were no late complications in the cases which had prior chemotherapy and 24 Gy of irradiation to whole ventricle only before CSI. CONCLUSION: Low dose CSI for the first recurrence of germinoma is effective and safe in the cases treated by chemotherapy and low dose irradiation to whole ventricle only.

GCT-36. TREATMENT RESULTS AND RADIATION-INDUCED TUMORS IN CASES OF CENTRAL NERVOUS SYSTEM GERM CELL TUMOR: A LONG-TERM FOLLOW-UP STUDY IN KUMAMOTO PREFECTURE

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INTRODUCTION: Central nervous system germ cell tumor (GCT) is one of the pediatric brain tumors. Although there have been epidemiological studies in the past, long-term prognosis and the late effects remained unclear. In this study, we examined GCT over the past 41 years in Kumamoto prefecture. METHODS: Epidemiological features and complications with radiation-induced tumors were searched in patients diagnosed with GCT in the 41-year period from 1977 to 2018. RESULTS: There were 93 patients diagnosed with GCT. These cases were divided into 14-year periods before and after incorporation of chemotherapy into the treatment, and the results for germinomas were compared. An improvement in the 10-year survival rate from 12 of 23 cases (52.2%) between 1977 and 1991 to 19 of 28 cases (67.9%) between 1992 and 2006 was observed. The 10-year survival rate for germinoma cases that received medical treatment during a more recent 5-year period between 2004 and 2009 increased to over 90%. However, 10.3% of all long-term survivors of GCT developed radiation-induced glioblastoma. The examination results showed that regardless of the tumor type, patients who received a high dose of radiation during their initial treatment developed the complication of radiation-induced glioblastoma within 10 to 25 years after their initial treatment. CONCLUSION: This study suggests that the long-term survival rates for GCT are improving but the rate of radiation-induced glioblastoma in these cases are too high to be ignored. Long-term follow-up of at least 10 years is essential to effectively evaluate the details of treatment for pediatric brain tumors.

GCT-37. PREVALENCE OF AUTISM SPECTRUM DISORDER AND OTHER NEURODEVELOPMENTAL DISORDERS IN PEDIATRIC PATIENTS WITH INTRACRANIAL GERM CELL TUMORS

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PURPOSE/OBJECTIVE(s): Intracranial germ cell tumors (IGCTs) are rare tumors of the central nervous system with peak incidence around puberty. Due to the developmental origins of IGCTs, we investigated the prevalence of neurodevelopmental disorders (NDDs), including autism spectrum disorder (ASD), in our retrospective institutional cohort of patients diagnosed with IGCTs. MATERIALS/METHODS: A retrospective review of medical records was conducted for 105 patients who were diagnosed with IGCTs and treated at Massachusetts General Hospital between 1998 and 2016. All patients with ASD had thorough neuropsychological assessment at the time of radiotherapy that confirmed their diagnoses. RESULTS: Median age at diagnosis was 12.8 years (range: 4.3–21.6) and median follow-up time was 4.7 years (range: 0.4–15.8). Seventeen patients with IGCTs were diagnosed with NDDs prior to cancer diagnoses, including five patients with ASD, and three patients with chromosomal abnormalities, including one patient with Down syndrome. Interestingly, four of five patients with ASD developed pure germinomas, giving an ASD prevalence rate of 6.5% and 2.3% in the pure germinoma and NGGCT cohorts, respectively. All other patients had no known diagnoses of NDDs. CONCLUSIONS: Our study found 17 patients with IGCTs were diagnosed with NDDs prior to their cancer diagnoses. An ASD prevalence of 6.5% in the pure germinoma cohort is more than three-fold greater than the national prevalence, suggesting there may be an association between ASD and pure germinomas. Future prospective studies with larger cohorts are still needed to examine associations between NDDs and ASD and IGCTs.

GCT-38. RELAPSE PATTERNS OF INTRACRANIAL GERMINOMAS BEFORE AND AFTER ENDOSCOPIC ERA

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PURPOSE: We evaluated the relapse patterns of CNS germinomas before and after introducing neuroendoscopic biopsy in 2000. METHODS: We retrospectively assessed the relapse patterns of 57 patients treated as pure germinoma or germinoma with STGC between 1980 and 2019 at University of Tsukuba, partially containing the patients of the previous report (Takano S et al., World Neurosurg, 2015). Median age was 15 y.o.(7y.o.~38y.o.), and men was 80.7%. Tumor locations were pineal 35, sellar 19, basal ganglia 3, others 11. Group A;1980~1999 was 20, and group B;2000~2019 was 37. From 1980 to 1994, whole brain irradiation(WB) 30.6 Gy plus whole ventricle irradiation(WV) 19.8 Gy. From 1995 to 1999, WV 26~30.6 Gy with Chemotherapy(Chem) or Chem alone. Since 2000, Chem for 3 kurr with WV 24~30.6 Gy, and 6–19.8 Gy as local boost to residual lesion. RESULTS: Follow up periods were median 121 M(4.5M~386M; group A), and median 89 M(4 M~231 M; group B). Six patients(30%) recurred in the group A, as ex field 4(1;brain and extramedullary, 1;brain and paranasal sinus, 1;LV & third ventricle, 1;extramedullary), in field 1(LV). Chem only 1(LV & third ventricle). Two patients(5.4%) recurred in the group B, as ex field 2(1;intramedullary, 1;extramedullary). The group A showed CR;18, PR;1, Dead;1(Dissemination), and the group B showed CR;35, PR;1 Dead;1(Encephalopathy). CONCLUSION: WV and Chem prevented extrafield recurrence keeping good quality of life. Neuroendscopy biopsy with ETV did not increase CSF seeding.

GCT-40. PROGNOSTIC FACTORS FOR PATIENTS WITH RELAPSED CENTRAL NERVOUS SYSTEM (CNS) NON-GERMINOMATOUS GERM CELL TUMORS (NGGCTS)

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