ETMR-22. TITLE: DEFINING THE CLINICAL AND PROGNOSTIC LANDSCAPE OF EMBRYONAL TUMORS WITH MULTI-LAYERED ROSETTES (ETMRS), A RARE BRAIN TUMOR REGISTRY (RBTC) STUDY

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ETMR, an aggressive disease characterised by *C19MC* alterations, were previously categorised as various histologic diagnoses. The clinical spectrum and impact of conventional multi-modal therapy on this new WHO diagnostic category remains poorly understood as a majority of ~200 cases reported to date lack molecular confirmation. We undertook comprehensive clinico-pathologic studies of a large molecularly confirmed cohort to improve disease recognition and treatment approaches. Amongst 623 CNS-PNETs patients enrolled in the RBTC registry, 159 primary ETMRs were confirmed based on a combination of FISH (125), methylation analysis (88), SNP and RNAseq (32) analyses; 91% had *C19MC* amplification/gains/fusions, 9% lacked C19MC alterations but had global methylation features of ETMR NOS. ETMRs arose in young patients (median age 26 months) predominantly as localized disease (M0-72%, M2-3 -18%) at multiple locations including cerebrum (60%) cerebellum (18%), midline structures (6%); notably 10% were brainstem primaries mimicking DIPG. Uni-and multivariate analyses of clinical and treatment details of curative regimens available for 110 patients identified metastatic disease (p=0.002), brainstem locations(p=0.005), extent of surgery, receipt of multi-modal therapy including high dose chemotherapy and radiation (P<0.001) as significant treatment prognosticators, while C19MC status, age and gender were non-significant risk factors. Analyses of events in all patients showed respective EFS at 3 and 12 months of 84%(95%CI:77–91) and 37%(95%CI:20–41) and 4yr OS of 27%(95%CI:18–37) indicating despite intensified therapies ETMR is a rapidly progressive and fatal disease. Our comprehensive data on the largest cohort of molecularly-confirmed ETMRs provides a critical framework to guide current clinical management and development of clinical trials.

GERM CELL TUMORS

GCT-02. THE LONG-TERM OUTCOMES AND SEQUELAE ANALYSIS OF INTRACRANIAL GERMINOMA FROM 187 PATIENTS IN THE SINGLE INSTITUTE: NECESSITY FOR THE ADAPTATION OF RADIOTHERAPY DOSE AND VOLUME

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PURPOSE: We aimed to refine the radiotherapy (RT) volume and dose determinant for disease failures and long-term sequelae in the intracranial germinoma. METHODS: The main treatment for intracranial germinoma was craniospinal RT only (n=51) during 1981–1992 and RT with upfront chemotherapy (CRT) (n=152) during 1992–2015 in Seoul National Uni-

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), 2nd 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 ≥ 30 Gy (p=.030, and .026). After a latency of the median 20 years, ten patients (5.3%) developed 2nd malignancy. WB RT and WB/WV dose ≥ 30 Gy were significantly correlated with the 2nd malignancy (p=.024, and .004). The rate of severe neurocognitive dysfunction was significantly associated with WB/WV dose ≥ 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 $|ZSOH_{\text{last follow-up}} - ZSOH_{\text{diagnosis}}|$. 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 >40Gy(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-β, 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 following 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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