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

Masayuki Kanamori[1], Ryuta Saito[1], Yukihiko Sonoda[2], Toshihiro Kumabe[3], and Teiji Tominaga[1]; [1]Department of Neurosurgery, Tohoku University Graduate School of Medicine, Sendai, Japan, [2]Department of Neurosurgery, Yamagata University School of Medicine, Yamagata, Japan, [3]Department of Neurosurgery, Kitasato University School of Medicine, Sagamihara, Japan

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

Takahiro Yamamoto[1], Keishi Makino[2], Hideo Nakamura[3], Jun-ichiro Kuroda[1], Takashi Itoyama[1], Tatsuya Takezaki[1], Kazutaka Ota[1], Naoki Shinojima[1], and Akitake Mukasa[1]; [1]Department of Neurosurgery, Kumamoto University Medical School, Kumamoto, Japan, [2]Department of Neurosurgery, Kumamoto City Hospital, Kumamoto, Japan, [3]Department of Neurosurgery, Kurume University Medical School, Kurume, Japan

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

Kevin X. Liu[1], Roshan V. Sethi[1], Margaret B. Pulsifer[2], Alissa M. D'Gama[3], Beverly Lavally[2], Nancy J. Tarbell[2], Torunn I. Yock[2], and Shannon M. MacDonald[2]; [1]Harvard Radiation Oncology Program, Boston, MA, USA, [2]Massachusetts General Hospital, Boston, MA, USA, [3]Boston Children's Hospital, Boston, MA, USA

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

Takao Tsurubuchi[1], Shingo Takano[1], Ai Muroi[1], Kei Hara[1], Masahide Matsuda[1], Hiroyoshi Akutsu[1], Masashi Mizumoto[2], Hiroko Fukushima[3], Ryoko Suzuki[3], Yuni Yamaki[3], Eiichi Ishikawa[1], Akira Matsumura[1]; [1]Department of Neurosurgery, Faculty of Medicine, University of Tsukuba, Tsukuba, Japan, [2]Proton Medical Research Center, University of Tsukuba, Tsukuba, Tsukuba, Japan, [3]Department of Pediatrics, Faculty of Medicine, University of Tsukuba, Tsukuba, Japan

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)

Mohammad H. Abu-Arja[1], Diana S. Osorio[2], Joseph R. Stanek[2], Jonathan L. Finlay[2], and Mohamed S. AbdelBaki[2]; [1]New York-Presbyterian

Brooklyn Methodist Hospital, Brooklyn, NY, USA, [2]Nationwide Children's Hospital, Columbus, OH, USA

BACKGROUND: Patients with relapsed CNS NGGCTs experience poor outcomes. Our aim to explore prognostic factors that may guide future clinical trials. METHODS: A review of clinical trials that included patients with relapsed CNS NGGCTs was performed. RESULTS: Seventy-four patients were identified; only 14 patients (19%) were long-term survivors. Patients who relapsed >24 months after initial diagnosis had a survival rate of 47% compared with 15% of patients who relapsed in <24 months after initial diagnosis (p= 0.015). Patient with serum/cerebrospinal fluid (CSF) alpha-fetoprotein (AFP) level <25 ng/ml at relapse had a survival rate of 40% compared with 0% among patients with serum/CSF AFP level >25 ng/ml at relapse (p= 0.0015). Patients who achieved complete response/continued complete response (CR/CCR) by the end of therapy had a survival rate of 59% compared with 3% among patients who had less than CR/CCR by the end of therapy (p= 0.0001). Patients who received marrow-ablative chemotherapy followed by autologous hematopoietic cell rescue (HDCx/AuHCR) at relapse had a survival rate of 33% compared with 9% of patients who did not receive HDCx/AuHCR at relapse (p=0.056). The extent of surgical resection, receiving radiotherapy, and beta-human chorionic gonadotropin levels at relapse were not statistically associated with improved outcomes. CONCLUSION: Timing of relapse (>24 months after initial diagnosis), serum/CSF AFP <25 ng/ml at relapse, achieving CR/CCR after treatment were associated with a positive impact on survival. Receiving HDCx/AuHCR at relapse was associated with an improved outcome trend among the patients.

GCT-41. RESPONSE-BASED RADIATION THERAPY IN PATIENTS WITH NEWLY DIAGNOSED CENTRAL NERVOUS SYSTEM LOCALIZED GERMINOMA: A CHILDREN'S ONCOLOGY GROUP (COG) PROSPECTIVE PHASE 2 CLINICAL TRIAL

Ute Bartels[1], Jason Fangusaro[2], Dennis Shaw[3], Aashim Bhatia[4], Arzu Omar-Thomas[5], Shengjie Wu[5], Shannon MacDonald[6], Erin Murphy[7], Mark Souweidane[8], Maryam Fouladi[9], Amar Gajjar[5], Girish Dhall[10], and Soumen Khatua[11]; [1]The Hospital for Sick Children, Toronto, ON, Canada, [2]Aflac Cancer Center, Emory University and Children's Healthcare of Atlanta, Atlanta, GA, USA, [3]Seattle Children's Hospital, Seattle, WA, USA, [4]Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA, USA, [5]St. Jude Children's Research Hospital, Memphis, TN, USA, [6]Massachusetts General Hospital, Boston, MA, USA, [7]Taussig Cancer Institute, Cleveland Clinic, Cleveland, OH, USA, [8]Weill Cornell Medical College and Memorial Sloan-Kettering Cancer Center, New York, NY, USA, [9]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA, [10]The Alabama Center for Childhood Cancer and Blood Disorders at Children's of Alabama, Alabama, AL, USA, [11]MD Anderson Cancer Center, Houston, TX, USA

BACKGROUND: The objective of stratum 2 of COG ACNS1123 was to evaluate children and young adults (3–21 years) with localized central nervous system (CNS) germinoma and investigate whether simplified pre-irradiation chemotherapy followed by response based dose-reduced whole ventricular irradiation (WVI) would maintain a high progression-free survival (PFS) while reducing long term treatment burden. METHODS: Pre-irradiation chemotherapy consisted of 4 cycles of carboplatin and etoposide every 21 days followed by response-based irradiation (XRT). Patients with a complete response (CR) to pre-XRT chemotherapy received 18Gy WVI + 12Gy boost to the tumor bed. Patients with partial response (PR) but less than 1.5 cm residual proceeded to 24Gy WVI + 12Gy boost. All patients were also enrolled on COG ALTE07C1 to prospectively evaluate and longitudinally model the cognitive, social and behavioral functioning. RESULTS: During a total accrual time of 45.5 months from 05/2012 to 06/2018, 137 eligible patients were enrolled. Median age was 14.09 years (4.95–21.46), 73% were male, and 45.26% had elevated βhCG in serum and/or cerebrospinal fluid. Twenty-nine patients (21.17%) did not have tissue biopsy. Eleven patients underwent second-look surgery; 7 had mature teratoma and 4 had non-viable tumor. Eighty-one patients (59.13%) had a CR. There were 4 relapses in patients receiving 18Gy WVI + boost, but no deaths. No unexpected treatment-related events were observed. The estimated 3-year PFS was 94.4 ±2.7% among 74 evaluable subjects. CONCLUSION: This study shows promise in XRT reduction for patients with localized CNS germinoma and CR. Long-term survival outcomes and ALTE07C1 data are being evaluated.

GCT-42. CLINICAL CHARACTERISTICS OF LOCALIZED CENTRAL NERVOUS SYSTEM NON-GERMINOMATOUS GERM CELL TUMORS (NGGCT) PATIENTS ENROLLED ON ACNS1123 WITH RELAPSE: A CHILDREN'S ONCOLOGY GROUP (COG) STUDY

Girish Dhall[1], Shengjie Wu[2], Arzu Onar-Thomas[2], Dennis Shaw[3], Shannon MacDonald[4], Erin Murphy[5], Soumen Khatua[6], Ute Bartels[7], and Jason Fangusaro[8]; [1]University of Alabama at Birmingham, Birmingham, AL, USA, [2]St. Jude Children's Research Hospital, Memphis, TN, USA, [3]Seattle Children's Hospital, Seattle, WA, USA, [4]Massachusetts General Hospital, Boston, MA, USA, [5]Cleveland Clinic, Cleveland, OH, USA, [6]M,D, Anderson Cancer Center, Houston, TX, USA, [7]Hospital for Sick Children, Toronto, ON, Canada, [8]Emory University, Atlanta, GA, USA

ACNS1123 was a Children's Oncology Group Phase 2 study that was undertaken to determine whether irradiation could be safely reduced without impacting survival in a subgroup of NGGCT patients. Between May 2012-Jan 2017, 107 eligible patients were accrued to Stratum 1 (NGGCT stratum). Sixty-six (61.7%) patients achieved a complete/partial response (CR/PR) to induction chemotherapy and received 30.6Gy whole ventricular field irradiation followed by 54Gy tumor-bed boost achieving a 2-year progression-free survival rate of 89% (95% CI:81%-97%) and overall survival rate of 92% (95% CI:86%- 99%). Eight patients progressed; 6 had a spinal relapse and 2 patients had a local plus spinal relapse. Seven of eight patients had marker elevation at relapse and data was not available in one patient. At diagnosis, location was pineal in six cases, suprasellar in one, and bifocal in one case. Four patients had beta HCGβ and AFP elevation and two each had HCGβ and AFP elevation alone at diagnosis. Only two patients had HCGβ or AFP >1000 (HCGβ 3550 in one patient and AFP of 1340 in another). All eight patients were CR by markers; four had radiographic CR and four had a PR. Five patients had surgery at diagnosis: two had embryonal carcinoma, one germinoma, and two mixed germ cell tumor with malignant elements on histology. A consistent significant risk factor could not be identified to explain excess of spinal failures seen in our cohort.

GCT-43. GAIN OF SHORT ARM OF CHROMOSOME 12 IS A MOLECULAR MARKER TO PREDICT PROGNOSIS AND REPRESENTS AN EARLY EVENT IN TUMORIGENESIS IN INTRACRANIAL GERM CELL TUMORS

Kaishi Satomi[1,2], Hirokazu Takami[2,3], Shintaro Fukushima[2], Yoichi Nakazato[4], Shota Tanaka[3], Nobuhito Saito[3], Masayuki Kanamori[5], Toshihiro Kumabe[5], Keiichi Kobayashi[6], Motoo Nagane[6], Toshihiko Iuchi[7], Koji Yoshimoto[8], Masahiro Mizoguchi[8], Kaoru Tamura[9], Taketoshi Maehara[9], Keiichi Sakai[10], Kazuhiko Sugiyama[11], Kiyotaka Yokogami[12], Hideo Takeshima[12], Masahiro Nonaka[13], Akio Asai[13], Ryo Nishikawa[14], Masao Matsutani[15], and Koichi Ichimura[2]; [1]Department of Diagnostic Pathology, National Cancer Centre Hospital, Chuo, Tokyo, Japan, [2]Division of Brain Tumour Translational Research, National Cancer Center Research Institute, Chuo, Tokyo, Japan, [3]Department of Neurosurgery, Faculty of Medicine, The University of Tokyo, Bunkyo, Tokyo, Japan, [4]Department of Pathology, Hidaka Hospital, Takasaki, Gumma, Japan, [5]Department of Neurosurgery, Tohoku University Graduate School of Medicine, Sendai, Miyagi, Japan, [6]Department of Neurosurgery, Kyorin University Faculty of Medicine, Mitaka, Tokyo, Japan, [7]Department of Neurosurgery, Chiba Cancer Center, Chiba, Chiba, Japan, [8]Department of Neurosurgery, Graduate School of Medical Sciences Kyusyu University, Fukuoka, Fukuoka, Japan, [9]Department of Functional Neurosurgery, Tokyo Medical and Dental University, Bunkyo, Tokyo, Japan, [10]Department of Neurosurgery, Shinshu Ueda Medical Center, Ueda, Nagano, Japan, [11]Department of Clinical Oncology and Neuro-oncology Program, Cancer Treatment Center, Hiroshima University Hospital, Hiroshima, Hiroshima, Japan, [12]Department of Neurosurgery, Faculty of Medicine, University of Miyazaki, Miyazaki, Miyazaki, Japan, [13]Department of Neurosurgery, Kansai Medical University Hospital, Hirakata, Osaka, Japan, [14]Department of Neuro-Oncology/Neurosurgery, Saitama Medical University International Medical Center, Hidaka, Saitama, Japan, [15]Gotanda Rehabilitation Hospital, Shinagawa, Tokyo, Japan

Gain of short arm of chromosome 12 (12p) is commonly observed in testicular germ cell tumors (tGCTs) and also seen in intracranial GCTs (iGCTs). However, little is known about the clinical significance of 12p gain in iGCTs. We have collected over 200 fresh frozen tissue samples of iGCTs through the Intracranial Germ Cell Tumor Genome Analysis Consortium in Japan. Firstly, we analyzed DNA methylation profile in 83 iGCTs, 3 tGCTs (seminomas) and 6 normal control samples using Infinium Human Methylation 450K BeadChip array (Illumina, CA, USA) in order to determine 12p gain status. Then, fluorescence in situ hybridization (FISH) study was carried out on 3 mixed iGCT cases using 12p/CEP12 probe (Abbott Molecular, Abbott park, IL, USA). Lastly, 58 iGCTs with clinicopathological information were analyzed for progression-free survival (PFS) and overall survival (OS). Gain of 12p was observed in 100% (3/3) of seminoma, 14% (3/22) of germinoma, 17% (1/6) of mature teratoma, 25% (1/4) of immature teratoma, 55% (11/20) of mixed germ cell tumor, 100% (4/4) of yolk sac tumor, 100% (1/1) of embryonal carcinoma, and 100% (1/1) of choriocarcinoma. In total, 45% (37/83) of iGCT showed 12p gain. Different histological components in each mixed GCT shared the same 12p copy number status within each mixed GCT case. Both PFS and OS were significantly worse in iGCTs with 12p gain (PFS: P=0.027, OS: P=0.0012). Gain of 12p can be a molecular marker to predict prognosis and represents an early event in tumorigenesis prior to histological differentiation in iGCTs.