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Based on results of SIOP CNS GCT 96, patients enrolled in SIOP CNS GCT II with AFP higher or 1000 ng/ml (serum and/or CSF) and/or age less than 6 years with NGGCTs at diagnosis received two standard cycles of PEI and two higher dose PEI courses followed by radiotherapy according to dissemination (54 Gy local RT or 30 Gy CSI/24 Gy tumour boost). Between 2/2012 and 7/2018, 112 patients with CNS NGGCT were registered, of whom 23 were identified as HR patients; 18/23 had an AFP higher or 1000 ng/ml and were older than 6 years. Five children were < 6 years and showed YST elements in histology. of whom 3 received chemotherapy alone due to age. Primary site was pineal in 15/23, suprasellar in 5/23, bifocal in 3/23 patients; 3/23 patients were metastatic at diagnosis and 9/23 patients relapsed. Three years EFS was 0.60±0.10 with a median observation time of 3.96 years. Two recurrences were local, 4 distant (metastatic) and 3 combined, local and distant. HR CNS NGGCTs appeared to benefit from dose intensified PEI, compared with those treated in SIOP CNS GCT 96 with standard dose PEI. These results support the further exploration of this chemotherapy regimen in future clinical trials in such patient groups, including the consideration of delivering three dose intensified courses after one standard chemotherapy course, as is the practice in some groups treating very high risk extracranial GCTs.

GCT-13. KRAS MUTATION IN PEDIATRIC INTRACRANIAL GERM CELL TUMORS

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BACKGROUND: Intracranial germ cell tumors (IGCTs) are rare, highly curable neoplasms. KRAS is a gene in the KIT/RAS signaling pathway, and KRAS mutations were reported in patients diagnosed with IGCTs. OBJECTIVES: To describe clinicopathologic, molecular features of KRAS mutation and treatment outcome of children diagnosed with IGCTs. METHODS: A retrospective review in patients diagnosed with IGCTs at Department of Pediatrics, King Chulalongkorn Memorial Hospital from 2007 to 2019. DNA was extracted from formalin-fixed, paraffin-embedded (FFPE) tissue for the molecular study. Identifies mutations in codon 12,13 and 61 of the KRAS gene was performed by using the real-time PCR technique of the Cobas® test and pyrosequencing method. RESULTS: Eighteen patients were diagnosed with IGCTs (11 males and seven females). Age ranged from 5 to 14 years (median 10.5 years). The diagnosis was germinoma and non-germinomatous IGCTs in 9 patients each. Elevated markers were revealed in approximately 25% of patients. Four patients (2 patients with germinoma and 2 with non-germinomatous IGCTs) had leptomeningeal involvement. All patients underwent tumor biopsy and received neoadjuvant chemotherapy. Radiotherapy was given in 16 patients and craniospinal radiation (CSI) was given only in leptomeningeal metastasis. With the median follow-up of 26 months, overall survival is 88.9% in germinomas and 37% in non-germinomatous IGCTs. Mutation of the KRAS gene was detected by pyrosequencing technique in one patient. The mutation located at codon 61, frequency 38.3% units, nucleotide substitution CAA > CTA and amino acid substitution was Q61L. The patient who carries mutant gene was diagnosed germinomatous germinoma with CSF metastasis and eventually died from treatment-related toxicity. CONCLUSIONS: Our study revealed treatment outcomes of IGCTs in Thai children. We describe KRAS codon 61 mutation in metastasis germinoma patients with poor outcome, support KRAS codon 61 mutation (Q61L) may have a clinical correlation in IGCTs.

GCT-14. THE IMPACT OF RESIDUAL DISEASE ON THE OUTCOMES OF CENTRAL NERVOUS SYSTEM GERMINOMAS – A SINGLE INSTITUTION EXPERIENCE

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BACKGROUND: CNS Germinomas are highly radio-sensitive tumors with an excellent survival rate of more than 90%. The current standard of care combines chemotherapy with reduced-dose radiotherapy to minimize the adverse effects and long-term effects associated with radiotherapy. In the latest Children's Oncology Group clinical trial (ACNS1123 stratum 2), patients with residual or progressive disease following chemotherapy can be considered for a "second-look" surgery to assess tumor viability. Patients with residual disease who do not undergo second-look surgery receive 24 Gy of whole ventricular radiation with a 12 Gy boost compared to 18 Gy plus boost given to patients in complete remission or without viable tumor on second-look. Conversely, the International Society of Paediatric Oncology (SIOP) protocol does not stratify based on response to chemotherapy, and the Korean SMC GCT trial uses 18 Gy CSI plus boost for all patients regardless of chemotherapy response. METHODS: Single center retrospective chart review of germinoma patients treated at St Louis Children's Hospital between 2011 and 2021. RESULTS: We analyzed data for all 15 germinoma patients treated between 2011 and 2021. Five patients had residual disease following chemotherapy. Of these five, one had complete remission at the end of radiotherapy, one had partial response, and three had stable disease. All patients remain relapse-free with time of follow-up ranging between 6.3-109.3 months from the end of therapy (median 24 months). CONCLUSION: None of the five patients with residual disease following chemotherapy demonstrated disease progression following chemotherapy and radiotherapy. Future prospective clinical trials are needed in order to test the possibility of treating germinomas patients who have residual disease after chemotherapy with a low dose of radiotherapy similar to that used in patients with complete remission.

GCT-15. MULTI-INSTITUTIONAL ANALYSIS AND LITERATURE REVIEW OF CENTRAL NERVOUS SYSTEM GERM CELL TUMORS IN PATIENTS WITH DOWN SYNDROME

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BACKGROUND: A standard-of-care has not been established for the management of patients with Down syndrome (DS) who develop primary central nervous system (CNS) germ cell tumors (GCTs) – the most common CNS neoplasm in DS – despite being more susceptible to treatment-related adverse events. METHODS: Data from large academic institutions were collected and a comprehensive review of the medical literature was conducted. RESULTS: Ten patients from six institutions (five USA, one Brazil) were reviewed. Additionally, thirty-one patients were identified in the literature from 1975-2021. Of the 41 total patients, mean age was ten years (range, birth to 35 years); males were predominant (61%). Basal ganglia were the most common tumor location (n=12; 29%), followed by posterior fossa (n=7; 17%). Sixteen patients had non-germinomatous germ cell tumors (NGGCTs) (39%), 14 had pure germinomas (34%), and eight had teratomas (20%); histology was unreported for two (5%). Nine patients (22%) experienced disease relapse, of which four died from tumor progression (one germinoma versus three teratoma). Fifteen patients (37%) experienced treatment-related complications - seven died (four germinoma versus three NGGCT). Of the germinoma patients, two died from chemotherapy-related sepsis, one from post-surgery cardiopulmonary failure, and one from Moyamoya following radiation-therapy (RT) only. Of the NGGCT patients, one died from chemotherapy-related sepsis, one from post-surgical infection, and one from pneumonia following surgery/chemotherapy/RT. Three-year overall survival (OS) was 66% for all histological types - 62% germinoma, 79% for NGGCT, and 53% for teratoma. Three-year OS for patients who received RT or chemotherapy was 71% and 75% respectively. Twenty-seven patients remain alive at latest follow-up (mean follow-up from diagnosis: 46.8 months). CONCLUSIONS: Patients with DS treated for CNS GCTs are at an increased risk of treatment-related adverse events. A different therapeutic approach may need to be considered for this patient population to mitigate treatment-related complications and long-term neurocognitive sequelae.