PATHOLOGICAL CHARACTERIZATION OF CNS GERM CELL TUMORS IN JAPANESE CHILDREN: IMPACT OF MOLECULAR CLASSIFICATION AND CLINICAL OUTCOMES

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CENTRAL NERVOUS SYSTEM GERM CELL TUMORS (GCTs) PRESENT UNIQUE CHALLENGES, INCLUDING VARIATION IN CLINICAL MANIFESTATIONS AND RESPONSE TO TREATMENT. IN THIS STUDY, WE CONDUCTED A CLINICAL AND MOLECULAR ANALYSIS OF CNS-GCTs IN JAPANESE CHILDREN AGED 6 YEARS OR YOUNGER, REGISTERED WITH THE JAPAN CHILDREN’S CANCER GROUP AND THE IGCT CONSORTIUM. DNA METHYLATION ANALYSIS IDENTIFIED EIGHT CASES AS MIXED GCTs, POTENTIALLY INCLUDING YOLK SAC TUMORS. MOLECULAR CLASSIFICATION HELPED INFORM TREATMENT STRATEGIES, INTEGRATING both MEDICAL AND RADIOTHERAPEUTIC APPROACHES. THE 3-YEAR OVERALL SURVIVAL RATES VARIED SIGNIFICANTLY BY DIAGNOSIS: 96% for germinomas, 85% for other GCTs, and 61% for embryonal tumors. FUTURE STUDIES WILL FOCUS ON THE INFLUENCE OF MOLECULAR SUBTYPES ON TREATMENT RESPONSE AND OUTCOMES.
BACKGROUND: Human chorionic gonadotropin (beta-HCG) levels in serum and cerebrospinal fluid (CSF) are critical in the management of patients with germinoma. The threshold for beta-HCG diagnosis is a topic of debate and differs in Europe, ≤50 IU/L, North America ≤100 IU/L, and ≤200 IU/L in Brazil/Japan. METHODS: We conducted a meta-analysis of English-language publications (1990-2023) to assess how beta-HCG cut-off levels impact treatment outcomes. Standard descriptive statistics summarized all data. RESULTS: Forty-nine patients with biopsied germinoma were identified. Eighteen had beta-HCG level of 50-100 IU/L (cohort 1), 21 had 100-200 IU/L (cohort 2), and 10 had >200 IU/L (cohort 3). In cohort 1, treatment with chemotherapy plus radiotherapy was administered to 9 patients. Eight of them received radiotherapy like germinoma treatment (≤30Gy), primarily employing whole ventricle irradiation (WVI). Nine patients received radiotherapy alone with total dose 30-59.6 Gy. Fifteen patients in cohort 2 received chemotherapy plus radiotherapy. Eight of them received radiotherapy ≤30Gy for different fields (WVI = 4, whole brain (WB) = 3, cerebrospinal irradiation (CSI) = 1). In 7 patients the dose of radiotherapy exceeded 30Gy (local radiotherapy – 4, CSI = 3). Radiotherapy alone was used in 5 patients, chemotherapy alone – 1 patient. In cohort 3, radiotherapy only was primarily used. Six patients received CSI (30-54Gy), one – CSI+WB+local radiotherapy (12.8Gy+27.2Gy+50.6Gy). One patient received combined treatment and 2 patients received chemotherapy alone. Relapses occurred in each cohort. In cohort 1 – 2 metastatic relapses (1 after WVI 24 Gy, 1 after radiotherapy >30Gy). Three children from cohort 2, who received chemotherapy plus radiotherapy were diagnosed with relapse (1 after WB 23.4 Gy, 2 after radiotherapy >30Gy). In cohort 3 two metastatic relapses were diagnosed – only after chemotherapy. CONCLUSIONS: Relapse rates across all beta-HCG level are similar. However, study groups are small and treatment regimens vary, warranting further investigation.