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INTRODUCTION: Malignant rhabdoid tumors (MRT) predominantly affect infants. Patients below six months represent a particularly challenging group: intensity of therapy is limited by toxicity to developing organs. Information on prognostic factors, toxicity and long term outcome is sparse. METHODS: Clinical, genetic, and treatment data of 100 patients (less than 6 months at diagnosis) from 13 European countries were analyzed (2005-2020). Tumors and matching blood samples were examined for SMARCB1 mutations using FISH, MLPA and Sanger sequencing. DNA-methylation subgroups (ATRT-TYR, ATRT-SHH, and ATRT-MYC) were determined using DNA methylation arrays. RESULTS: A total of 45 patients presented with ATRT, 29 with extracranial, extrarenal (eMRT) and 9 with renal rhabdoid tumors (RTK). Seventeen patients demonstrated synchronous tumors (SYN). Distant metastases at diagnosis (M+) were present in 27% (26/97). A germline mutation (GLM) was detected in 55% (47/86). Methylation subgroup status was available in 50% (31/62) of ATRT or SYN (SHH=13, TYR=13, MYC=4, SHH+TYR=1). The 5-year overall- (OS) and event free survival (EFS) rates were 23.5±4.6% and 19±4.1%, respectively. Male sex (11±5% vs. 35.8±7.4%), M+ (6.1±5.4% vs. 36.2±7.4%), presence of SYN (7.1±6.9% vs. 26.6±5.3%) and -GLM (7.7±4.2% vs. 45.7±8.6%) were significant prognosticators of 5-year OS, in univariate analysis. Molecular subgroup and survival analyses confirmed the previously described survival advantage of ATRT-TYR. In an adjusted multivariate model clinical factors that influence prognosis were: male sex [HR: 2.1 (1.2 – 3.6)], M+ [3.3 (1.8 – 6)], GLM [HR: 2 (1.1 – 3.6)] and maintenance therapy [HR: 0.3 (0.1 – 0.8)]. CONCLUSION: In this large cohort of homogenously treated infants with MRT, significant predictors of outcome were sex, M+, GLM and maintenance therapy. We confirm the need to stratify which patient group benefits from multimodal treatment, and which patients need novel therapeutic strategies. Biomarker-driven tailored trials may be a key option.

ATRT-06. ATYPICAL TERATOID RHABDOID TUMORS (ATRT): RESULTS FROM A SINGLE INSTITUTION IN BRAZIL - SÃO PAULO UNIVERSITY

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OBJECTIVES: Atypical teratoid/rhabdoid tumor (AT/RT) is a rare, highly malignant tumor of the central nervous system with poor prognosis. Nowadays, multimodal management, including surgery, chemotherapy (CMT), radiation therapy (RT) and Bone Marrow Transplantation (BMT). The aim of this study was to assess the experience and survival in a center of reference of treatment in childhood cancer in Brazil. PATIENTS AND METHODS: Medical records of AT/RT patients who underwent surgery from 2008 to 2020 at a center of childhood cancer treatment (ITACI) in São Paulo University were retrospectively reviewed and statistically analyzed. RESULTS: Eight patients (2 males and 6 females) were presented with AT/RTs. Median age during presentation was 22 months (range, 0 - 6 years). Seven patients (88%) were < 18 months and one patient were >18 months. Tumor location was supratentorial in four patients, infratentorial in 2 patients. Kidney disease as the primary diagnosis in 2 patients (25%). Surgical treatment was performed in 4 patients. Seven children underwent total CMT and 3 children were treated with RT. Only 3 patients underwent Autologous Bone Marrow Transplantation (ABMT). The chemotherapy management protocol of the patients was variable: 2 patients received the EU-RHAB protocol, 2 patients received the HEAD START III protocol, 3 patients received chemotherapy in the ICE regimen (Ifosfamide + Carboplatin + Etoposide) and 1 patient received chemotherapy in the CDDP+CTX+VCR (Cyclophosphamide + Cisplatin + Vincristine) regimen. All patients had episodes of neutropenic fever when they received chemotherapy, requiring hospitalization and use of an antibiotic treatment. Among the 8 patients analyzed, all died. CONCLUSIONS: Despite progress in treatment, AT/RT of the CNS disease or primary kidney disease associated with a lack of standardization in a regimen contributes to the dismal prognosis. There is a high mortality in patients with AT/RT, similar to that found in the literature.

ATRT-07. LOW-GRADE DIFFUSELY INFILTRATIVE TUMOR, SMARCB1-MUTANT: A CLINICAL AND HISTOPATHOLOGICAL DISTINCT ENTITY SHOWING EPIGENETIC SIMILARITY WITH ATRT-MYC

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Most atypical teratoid/rhabdoid tumors (ATRTs) occur in infants, but children and adolescents may also be affected. ATRTs occurring in older patients often comprise the molecular subgroup ATRT-MYC. Recently, central nervous system low-grade diffusely infiltrative tumor with INI1 deficiency (CNS LGDIT-INI1) has been described as a rare low-grade lesion (Nobusawa et al. Am J Surg Pathol 2020;44:1459-1468). Little is known on the molecular relationship of CNS LGDIT-INI1 and ATRT. We therefore further explored a series of six CNS LGDIT-INI1. The median age of the four males and two females was 16 years (range: 10-28 years). All tumors were of supratentorial location and showed low to moderate cellularity, diffuse growth of inconspicuous small SMARCB1-deficient tumor cells and reactive pleomorphic neuronal and glial cells with retained SMARCB1-staining in the background. In addition, two cases also displayed a high-grade rhabdoid component. After DNA isolation, purification and bisulfite conversion, samples were subjected to DNA methylation profiling (MethylationEPIC BeadChip array). Using DNA methylation-based classification and the Heidelberg Brain Tumor Classifier (version v11b4), all tumors were classified as ATRT-MYC (median calibrated score: 0.97). On t-SNE analysis, DNA methylation profiles grouped closely together in proximity to ATRT-MYC. Follow-up information was available for four cases (including the two cases with a high-grade component). Patients received heterogeneous treatments (including chemotherapy according to AT/RT protocols) and experienced stable disease or complete remission after an observation time of three to 56 months. In conclusion, CNS LGDIT-INI1 is a clinically and histologically