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NFS-03. MEDULLOBLASTOMA IN CHILDREN WITH FANCONI ANEMIA: ASSOCIATION WITH FA-D1/FA-N, SHH TYPE AND POOR SURVIVAL INDEPENDENT OF TREATMENT STRATEGIES

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BACKGROUND: Outcome of children with medulloblastoma (MB) and Fanconi Anemia (FA), an inherited DNA repair deficiency, has not systematically been described. Treatment is complicated by high vulnerability to treatment-associated side effects, yet structured data are lacking. This study provides a comprehensive overview about clinical and molecular characteristics of pediatric FA MB patients. METHODS: Clinical data including detailed information on treatment and toxicities of six previously unreported FA MB patients were supplemented with data of 16 published cases. RESULTS: We identified 22 cases of children with FA and MB with clinical data available. Biological subgroup was SHH in all cases with data available (n=9), confirmed by methylation profiling in five patients. FA MB patients exclusively belonged to complementation groups FA-D1 (n=16) or FA-N (n=3). Patients were treated with postoperative chemotherapy only (50%) or radiotherapy (RT)±chemotherapy (27%). 23% did not receive adjuvant therapy. Excessive treatment-related toxicities were frequent. Severe hematological toxicity occurred in 91% of patients treated with alkylating chemotherapy, while non-alkylating agents and RT were less toxic. 14 patients (63.6%) developed 20 other malignancies, of which ten occurred before, five simultaneously with and five after MB diagnosis. Median overall survival (OS) was 1 year (95%CI 0.3-1.9). 1-year-progression-free-survival (PFS) was 26.3±10.1% and 1-year-OS was 42.1±11.3%. Adjuvant therapy prolonged survival (1y-OS/1y-PFS 0%/0% without adjuvant therapy vs. 53.3±12.9%/33.3±12.2% with adjuvant therapy, p=0.006/p=0.086), with no difference whether the patient had received chemotherapy only or RT±chemotherapy. CONCLUSIONS: MB in FA patients is strongly associated with SHH activation and FA-D1/FA-N. Despite the dismal prognosis, adjuvant therapy may improve survival. Non-alkylating chemotherapy and RT are feasible in selected patients with careful monitoring of toxicities and dose adjustments. Unlike in standard MB protocols, focal RT may be considered in FA MB patients. Curative therapy for FA MB-SHH remains an unmet medical need.