HG-80. ISSUES IN THE MANAGEMENT OF CHILDREN WITH BRAIN TUMORS AND BIALLELIC MISMATCH GENE REPAIR DEFICIENCY SYNDROME

Roula Farah1, Farid Maalouf1, Nassim Abi-Chahine1, Hussein Farhat1, Brittany Campbell3, Nataliya Zhukova3, Carol Durno3, Melyssa Aronson4, Cynthia Hawkins3, Eric Bouffet3, and Uri Tabori1; 1Saint George Hospital University Medical Center, Beirut, Lebanon; 2Lebanese American University Medical Center-Rizk Hospital, Beirut, Lebanon; 3Lebanese American University Medical Center-Rizk Hospital, Beirut, Lebanon; 4The Hospital for Sick Children, Toronto, ON, Canada; 5Mount Sinai Hospital, Toronto, ON, Canada

Biallelic mismatch repair deficiency (bMMRD) is a rare cancer predisposition syndrome, presenting in childhood. Affected patients have café-au-lait skin lesions and develop various hematological, gastrointestinal and CNS malignancies. Although guidelines are available for surveillance, there is scarce information about optimal therapy. We report the pedigree, diagnostic studies and clinical course of a consanguinous family with four children, the index case, his sister and two first cousins, affected by the syndrome. The index case developed glioblastoma and T-cell leukemia and died from infection while in complete remission. His sister is under treatment for a high-grade glioma, and his two first-cousins died of their brain cancer. DNA from peripheral blood, saliva and buccal swabs, skin biopsies and paraffin blocks from tumor tissue were used for genetic testing. Both tumor and normal tissue were stained for the presence of the MMR proteins through immunohistochemistry and revealed absence of the PMS2 protein in both tissues. Molecular analysis was performed using Sanger sequencing and MLPA of the 4 MMR genes. A pathogenic, heterozygous mutation was identified in the PMS2 gene (exon15del c.2446-?_2589 + ?del) in the affected children and their fathers. Review of the clinical course of the index case revealed increased morbidity and toxicity compared to other children undergoing therapy on the same protocol. We suggest more adapted treatment protocols for these patients. This family illustrates difficulties encountered in the diagnosis, surveillance and choice of therapy for children affected with bMMRD and the need for increased awareness and more information about this rare but important syndrome.