GATAD2B Gene Microdeletion Causing Intellectual Disability Autosomal Dominant Type 18: Case Report and Review of the Literature.

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Abstract

Pathogenic variants of the GATAD2B gene (1q21.3) are linked to intellectual disability autosomal dominant type 18 (MRD18; MIM 615074), characterized by dysmorphic features, psychomotor and language delay. We present an 11-year-old female patient with intellectual disability and typical clinical characteristics of MRD18. Chromosomal microarray analysis (CMA) revealed a novel CNV, approximately 200 kb in size and showed that the INTS3 and SLC27A3 genes are completely deleted along with the first 10 exons of the GATAD2B gene. INTS3 encodes the integrator complex subunit 3 and is part of the complex that maintains genome stability; SLC27A3 encodes a fatty acid transporter and has been associated with autism spectrum disorder. GATAD2B haploinsufficiency is associated with the phenotype. Furthermore, the girl had other clinical characteristics not previously described, such as emotional instability, calf hypotrophy, hypoplastic digit pads, tapered thumbs, and anterior earlobe crease. This study highlights the importance of the phenotype-genotype correlation using molecular diagnostic techniques, such as CMA, and its impact on precise diagnosis, treatment, prognosis, and genetic counseling for patients and their families.

Mutational profile and EBV strains of extranodal NK/T-cell lymphoma, nasal type in Latin America.

Montes-Mojarro IA, Chen BJ, Ramirez-Ibarguen AF, Quezada-Fiallos CM, Pérez-Báez WB, Dueñas D, Casavilca-Zambrano S, Ortiz-Mayor M, Rojas-Bilbao E, García-Rivello H, Metrebian MF, Narbaitz M, Barrionuevo C, Lome-Maldonado C, Bonzheim I, Fend F, Steinhilber J, Quintanilla-Martinez L.

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Abstract

Extranodal NK/T-cell lymphoma (ENKTL) is an Epstein-Barr virus (EBV) associated lymphoma, prevalent in Asia and Latin America. Studies in Asian cohorts have identified some recurrent gene mutations in ENKTL; however, the mutational landscape of ENKTL in Latin America is unknown. In this study, we investigated the mutational profile and EBV strains of 71 ENKTL cases from Latin America (42 from Mexico, 17 from Peru, and 12 from Argentina) and compared it with Asian cohorts. The mutational analysis was performed by next generation sequencing (NGS) using an Ion AmpliSeq™ custom panel covering for the most frequently mutated genes identified in ENKTL. STAT3 was the most frequent mutated gene (16 cases: 23%), followed by MSN (10 cases; 14%), BCOR (9 cases; 13%), DDX3X (6 cases; 8%), TP53 (6 cases; 8%), MGA (3 cases; 4%), JAK3 (2 cases; 3%), and STAT5B (1 case; 1%). Mutations in STAT3, BCOR, and DDX3X were nearly mutually exclusive, suggesting different molecular pathways involved in the pathogenesis of ENKTL; whereas mutations in MGA, MSN, and TP53 were concomitant with other mutations. Most cases (75%) carried Type A EBV without the 30-bp LMP1 gene deletion. The overall survival was significantly associated with serum LDH level, Eastern Cooperative Oncology Group (ECOG) performance status, International Prognostic Index (IPI) score, and therapy ($p < 0.05$), but not associated with any mutation, EBV strain or deletion in EBV LMP1 gene. In conclusion, mutational analysis of ENKTL from Latin America reveals frequent gene mutations leading to activation of the JAK-STAT pathway (25%), mostly STAT3. Compared to Asian cohorts, BCOR, DDX3X and TP53 mutations were also identified but with different frequencies. None of these mutations were associated with prognosis.