Genotype and phenotype characteristics of west syndrome in 20 Vietnamese children: two novel variants detected by next-generation sequencing

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ABSTRACT

Background: In children with West syndrome (WS), whose treatment is challenging due to drug resistance and poor prognosis, investigation of genetic etiology and genotype-phenotype characteristics might assist in treatment optimization and genetic counseling.

Objectives: In this study, we aimed to present results of genetic analyses and its corresponding phenotypes in a cohort of twenty children with WS in Vietnam.

Methods: Our study was designed as a single-institution retrospective case series, in which consecutive sampling was used to select twenty WS children having undergone genetic testing. Identified variants were investigated individually or as a variant combination by bioinformatics platforms. Clinical data were used to establish the genotype-phenotype correlation and compare clinical characteristics between those with and without genetic causes.

Results: Genetic testing identified at least one variant in 17/20 children. Of all variants, 16 variants (61.5%) were classified as variants of uncertain significance, 4 (15.4%) were likely pathogenic variants, and 5 (19.2%) pathogenic variants. These 26 variants belonged to 21 genes, out of which there were eight candidate genes, including CREBBP, MED25, HDAC8, SCN3A, ABCD, TSC2, COL4A1, and NDUFA10. SCN3A:c.1031+2del and TSC2:c.2700C>G were novel variants. Predicted pathogenic variant combinations were identified in two cases. Compared to three children of unknown etiology, five children with genetic causes had a higher rate of abnormal brain structures, developmental delay, and treatment resistance.

Conclusion: WS has a genetically heterogeneous etiology, and there might be a polygenic susceptibility in some cases. Our findings expand the disease's genotype-phenotype spectrum and support previous results in the literature that genetic etiology poses an unfavorable outcome in WS.

Keywords: West syndrome, infantile spasms, novel variants.