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Identification of 1q21.1 microduplication by microarray analysis in a boy with intellectual disability

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Abstract/Resumo

Chromosomal 1q21.1 region is structurally complex with a presence of large paralogous segmental duplications that make this region susceptible to non-allelic homologous recombination causing a spectrum of recurrent rearrangements, including deletions and duplications. Chromosome 1q21.1 Duplication Syndrome (MIM612475) is a rare genomic disorder caused by microduplications of an approximately 1.35 Mb and includes at least 12 genes. This syndrome has been associated with variable phenotypes including intellectual disability, autism, dysmorphic features, macrocephaly, congenital heart anomalies or normal phenotype. Herein, we report the first case of a boy who presented intellectual disability, behavior disorder, clinodactyly, facial dysmorphism such as frontal bossing and hypertelorism, and low-set ears with paternal inherited 1q21.1 microduplication in Central Brazil. Karyotyping at > 550 band resolution showed a male karyotype (46,XY). Chromosomal Microarray Analysis (CMA) using GeneChip® CytoScanHDTM array revealed paternal inherited 1.92 Mb microduplication at 1q21.1q21.2 (145,895,746-147,819,294) x3, encompassing 13 morbid genes (NBPF10, HYDIN2, NBPF12, PRKAB2, FMO5, CHD1L, BCL9, ACP6, GJA5, GJA8, GPR89B, NBPF11, and NBPF8). Duplication at 1q21.1 region has been reported in phenotypically affected individuals and apparently normal carriers. We detected microduplication at 1q21.1 in an affected boy who his father is asymptomatic. CHD1L gene has been involved with chromatin remodeling as well as DNA damage response and chromatin remodeling has been implicated in developmental and intellectual disability disorders. The HYDIN2 gene, a paralogous segment of the primary ciliary dyskinesia-associated gene HYDIN is exclusively expressed in the brain, and dosage sensitivity of HYDIN2 gene was responsible for the variation in head circumference. NBPF10, NBPF12, NBPF11 and NBPF8 genes are member of the neuroblastoma breakpoint family (NBPF) and copy number variations involving these genes have been implicated in a number of developmental and neurogenetic diseases. The CMA was a powerful and efficient method to identify at the first time in Central Brazil the 1q21.1 microduplication in a boy with intellectual disability and dysmorphic features. Furthermore, it is recommended the family to do genetic counseling to provide information and help to understand about the penetrance and variable expressivity related to this syndrome, the familial implications of genetic contribution to disease and the chance of disease recurrence.

Keyword/Palavras-chave: Intellectual disability; CMA;1q21.1 microduplication

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