1q21.1 Deletions and Duplications in 2 Siblings with Psychiatric Problems

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To the Editor: An 8-y-old girl was admitted for uncontrollable aggressive behavior towards her family members. Two months later, her 6 y old brother was admitted with similar complaints.

The girl was diagnosed with attention deficit hyperactivity disorder (ADHD) and autism spectrum disorder (ASD). She had failure to thrive, mixed expressive and receptive language delay, mild mental retardation (IQ 60), encopresis and enuresis and poor sleep with only 3–4 h per day. She was microcephalic (<3%), small for age (weight and height <3%) and had hyperextensible elbows. She had no other dysmorphic features. Fragile X testing, karyotype, biochemical and metabolic analysis were normal. We followed with a Chromosome Microarray Comparative Genomic Hybridization (CM-CGH) test with Agilent 144 K. The analysis revealed an XX female sex chromosome and a copy number of two for chromosomes 1 to 22, and according to GRCh38/hg38 breakpoints were 0.35 Mb duplication (Chr 1: 145, 670, 852–146, 021, 841), 0.618 Mb deletion (Chr 1: 147, 155, 106–147, 773, 362) at 1q21.1.

Her brother had bilateral sensorineural hearing loss. He was not dysmorphic, was normocephalic (50%), weight and height were 25% and 50% for his age respectively. CM-CGH testing revealed XY male sex chromosome with 1q21.1 duplication and deletion which was similar to his sister.

Their parents were non-consanguineous; their 2 sisters and 2 brothers had hearing loss, one sister had bipolar disorder and one sister had ADHD. Father had depression, 2 maternal aunts and 1 paternal aunt had bipolar disorders.

Unfortunately, parents denied any testing on themselves and any other family member.

The association of recurrent rearrangements in 1q21.1 in variable pediatric phenotypes such as autism spectrum disorders (ASD), ADHD, congenital heart defects, cataracts, micro and macrocephaly, skeletal and genitourinary abnormalities and mild to moderate mental retardation has been shown by different authors [1–5].

Arrangements in this region show variable expressivity and incomplete penetrance. Inheritance is either autosomal dominant or *de novo*. Not testing the other family members is a limitation, but according to DECIPHER, the deleted and duplicated gene regions in our patients are pathogenic. In conclusion, children presenting with psychiatric problems and especially ASD and various physical problems, should be offered microarray testing.

Compliance with Ethical Standards

Conflict of Interest None.

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