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Letter to the Editor

A Case of 17q21.1-q23.2 Microduplication with Autism Spectrum Disorder

Vlachou V[1], Steel D[1], Mankad K[1,2] and Kinali M[1]*

[1]Department of Paediatric Neurology, Chelsea and Westminster NHS Foundation Trust, United Kingdom

[2]Great Ormond Street Hospital for Children NHS Foundation Trust, United Kingdom

***Corresponding author:** Maria Kinali, Department of Paediatric Neurology, Chelsea and Westminster Hospital NHS Foundation Trust, Imperial College, Fulham Road, London, United Kingdom

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An increasingly wide range of genetic associations have been reported for Autistic Spectrum Disorder (ASD). We have come across a case where ASD occurred in association with 17q23.1-q23.2 microduplication, a known genetic cause of Congenital Talipes Equinovarus (CTEV) and, in some cases, additional abnormalities.

17q23.1-23.2 microduplication is a well-documented cause of CTEV [1] and, in many cases, other subtle bony anomalies of the lower limbs [2]. Recently, Peterson et al described a family in which four members carried the mutation and displayed very marked variable penetrance: two females were phenotypically normal; both affected males had CTEV and one had multiple additional congenital anomalies including microcephaly, cardiac defects, seizures and hearing and visual impairment [3]. ASD, however, has never been described in association with this mutation.

Our proband was diagnosed antenatally with severe Congenital Talipes Equinovarus (CTEV), Pirani grade 6 bilaterally. He was treated by the Ponseti method with initial good results, although by the age of four his foot deformities had begun to recur and further treatment was required. Both legs were also noted to have an unusually thin, underdeveloped musculature with weak evertors, and he was generally hypermobile with moderately low tone.

This led to his referral to our Pediatric Neurology service for further assessment.

He was the first child of non-consanguineous Jewish parents, themselves in good health, and the only other prenatal concern was possible polyhydramnios. Motor milestones were slightly delayed: he sat independently at just over eight months and walked at 19 months. Electromyography and nerve conduction studies were normal, as were biochemical investigations and Magnetic Resonance Imaging (MRI) of the brain. MRI of the spine revealed an incidental filum terminale lipoma but no other spinal or intraspinal abnormalities. He was not dysmorphic and no other physical anomalies were detected.

Comparative genomic hybridization microarray revealed a 2.2 MB microduplication of 17q23.1-q23.2. Neither parent carried the microduplication, suggesting that it had arisen de novo. Of note, the proband's mother had a similar unusual appearance of the musculature of the lower leg, although she had not suffered from CTEV.

At four years and five months old, the proband was referred for assessment for ASD as a result of reluctance to interact with other children. His height was on the 95th centile with weight on the 25th centile and head circumference on the 9th. Fine motor and self-care skills were slightly delayed although his language abilities were age-appropriate. He displayed several autistic features: hypersensitivity to sound stimuli and food textures, a typical eye-contact and dislike of change, and stereotyped motor behaviors including hand-flapping and making faces when excited or anxious. Overall, he was felt to meet the criteria for ASD with good potential for learning, previously likely to have been classified as Asperger's syndrome [2].

As the prevalence of ASD is almost 1.5% [4,5] it is not possible to say with certainty whether our proband's microduplication played any causative role in his condition. Given the increasing range of anomalies associated reported to be associated with the mutation, however the possibility is intriguing. The filum terminale lipoma may represent another previously undescribed association. It is possible that this case extends the phenotypic spectrum for this microduplication.

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