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2q23.1 microdeletion involving the MBD5 gene - large deletion associated with a relatively mild phenotype

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BACKGROUND: We report a female patient with a de novo interstitial deletion in chromosome region 2q23.1-23.3 identified by array-CGH. To our knowledge, this is the 6th reported case of a patient with a deletion corresponding to the same genomic region containing the MBD5 gene, a homologue of MECP2, implicated in the pathogenesis of Rett syndrome. **CASE REPORT:** The proband was born at 41 weeks to healthy non-consanguineous Caucasian parents, with a birth weight of 9lb 1oz. She had significant global developmental delay affecting gross motor, fine motor and speech. She developed seizures at 3 years, which were not controlled despite trials of multiple antiepileptics. There was history of regression at age 6, with progressive difficulties with balance, loss of fine motor skills and worsening aggressive behavior. On examination at age 7 years, 3 months, she was profoundly microcephalic (HC << 2nd percentile, 50th centile for 13 months) and of short stature (height at 3rd percentile), while her weight was at the 75th percentile. She had dysmorphic features consisting of low anterior hairline, mild synophrys, almond-shaped eyes, long nasal columella, short philtrum, thin upper lip, and small teeth. On neurological exam, speech was dysarthric but she was able to speak in complete sentences. She demonstrated repetitive hand movements but did not have the wringing movements typical of Rett syndrome. Gait was wide-based and unsteady, and she held her arms in high guard when walking. **Results:** Karyotype, MECP2 testing, chromosome 15 methylation studies, UBE3A sequencing, MRI/MRS brain, and metabolic studies were all normal. BAC microarray revealed a de-novo deletion at 2q23.1 to 2q23.3 with an estimated size between 3.725 - 5.632Mb. **Conclusion:** Published cases of 2q23.1 deletion (Vissers et al 2003, Koolen et al 2004, De Vries et al 2005, De Gregori et al 2007, Jaillard et al 2008) suggest an overlapping region of 250 kb involving the MBD5 gene is responsible for the phenotype. Our patient shares similar clinical features to those reported, including microcephaly, developmental delay, speech impairment, seizure and ataxia. She differs by having milder delay in development, with reasonably preserved speech. Interestingly, she had a larger deletion compared to the reported cases, with telomeric extension involving the CACNB4 gene. This case adds to the phenotypic heterogeneity of the newly described “Angelman-like” or “Rett-like” microdeletion syndrome.