

A 5-Month-Old Boy with Delay in Growth and Development and Decreased Muscle Tone

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CASE DESCRIPTION

A 5-month-old boy was referred to the genetics and neurology services for evaluation of developmental delay, “albinism,” and possible seizures. He was born to a 19-year-old G1P1 (one gestation, one delivery) mother at 36 weeks of gestation via spontaneous vaginal delivery. His birth weight was 2.6 kg (5.7 lbs), and length was 49.5 cm (19.5 in). He had a traumatic delivery and developed left subdural hemorrhage. He was in the neonatal intensive care unit for approximately 3 weeks (his being there was secondary to postnatal respiratory distress and pneumonia), but passed the newborn hearing and extended metabolic screens. During the first months of life, he developed an umbilical hernia and exhibited feeding difficulties. At 4 months of age, he was admitted for evaluation of “spells.” His electroencephalogram was unremarkable. Echocardiography showed normal anatomy and function and a small patent foramen ovale. He had 2 brain MRIs, 1 in the first month, which showed left subdural hemorrhage, and another at 4 months, which showed subarachnoid widening. Ophthalmology evaluated him and ruled out ocular albinism.

His review of systems was significant for abnormal muscle tone, fair skin color, loud breathing, constipation, and gastroesophageal reflux. Family history was unremarkable other than that his mother required speech therapy as a child. His two paternal half siblings and parents were healthy. On physical examination at 5 months of age, his length and weight were below the first percentile, and his occipitofrontal circumference was at the 66th percentile (relative macrocephaly). He was alert and interactive and showed no signs of acute distress. He had a long face with bitemporal narrowing, almond-shaped eyes, and slightly flat nasal bridge. Neurological examination demonstrated truncal hypotonia and increased muscle tone in the lower extremities. His developmental assessment at 5 months of age showed that he was able to control his head and started reaching out and grasping, but did not roll over. He started smiling at 3 months and cooing at 2.5 months. There was no developmental regression. His initial laboratory studies were unremarkable except for mild acidosis with bicarbonate 17–19 mmol/L (reference interval 20–30 mmol/L) and slightly increased ammonia at 108 μ mol/L (reference interval 10–50 μ mol/L).

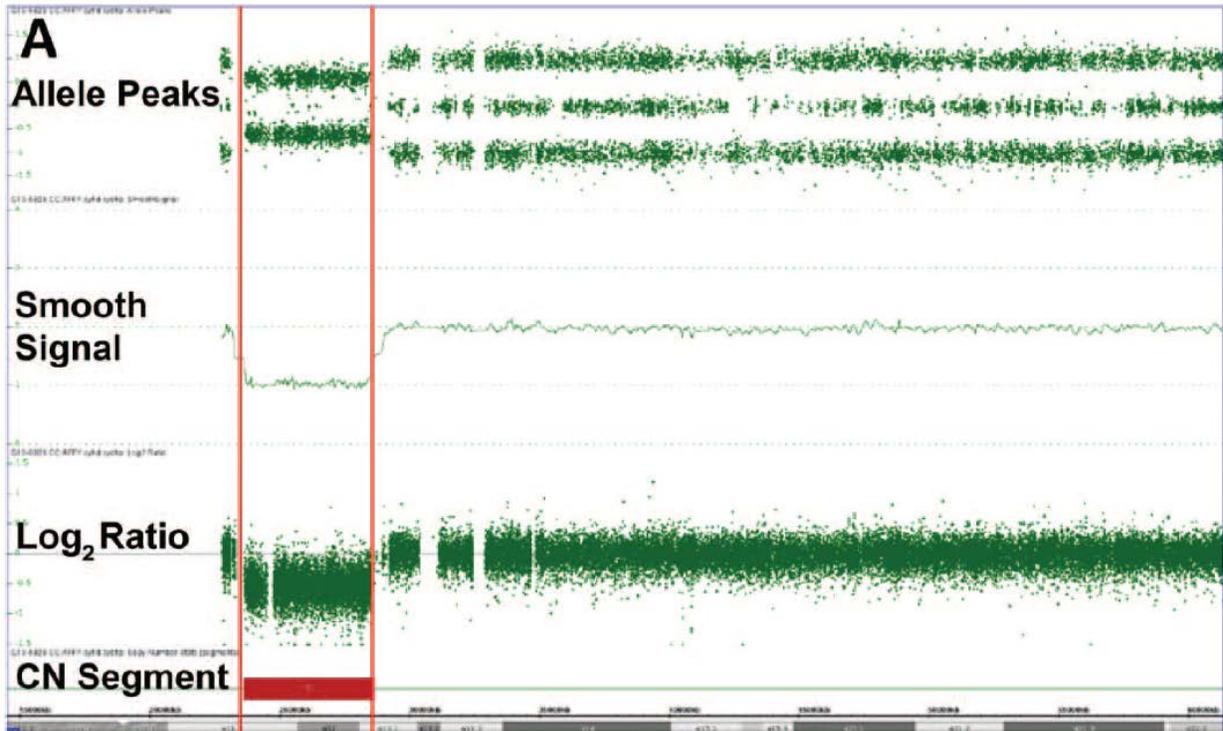
Overall, his neurologic tests and clinical evaluations did not suggest a specific syndrome. In addition, his metabolic workup (acylcarnitine profile, serum amino acids, urine organic acids, and lactate) was unremarkable. Chromosomal microarray analysis (CMA) was performed because the diagnostic yield with CMAs is significantly higher than classic chromosome analysis and professional societies recommend it as the first-tier diagnostic test for patients with unexplained developmental delay/intellectual disabilities or congenital anomalies (1). CMA testing revealed a 5-Mb deletion on 15q11.2q13.1 between genomic coordinates 23,615,768 and 28,644,578 (hg19) (Fig. 2A).

Reference

1. Miller DT, Adam MP, Aradhya S, Biesecker LG, Brothman AR, Carter NP, et al. Consensus statement: chromosomal microarray is a first-tier clinical diagnostic test for individuals with developmental disabilities or congenital anomalies. *Am J Hum Genet* 2010;86:749–64.

Questions to Consider	
•	What 2 genetic disorders are caused by lack of gene expression in 15q11-q13?
•	What are the classic clinical features of these genetic disorders?
•	What laboratory tests should be performed to identify and differentiate between these 2 disorders?

Fig. 2A



Final Publication and Comments

The final published version with discussion and comments from the experts will appear in the January 2015 issue of *Clinical Chemistry*. To view the case and comments online, go to <http://www.clinchem.org/content/vol61/issue1> and follow the link to the Clinical Case Study and Commentaries.

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