A Novel Missense Mutation in Very Long-chain Acyl-CoA Dehydrogenase Deficiency

Very long-chain acyl-CoA dehydrogenase deficiency (VLCADD) is a rare disease [1], and may cause sudden death in infants if undiagnosed [2]. The molecular basis of VLCADD is complicated, with about one hundred mutations reported. VLCADD can now be detected through newborn screening (NBS). Sequence analysis of *ACADVL*, the gene for VLCAD, is used to confirm the diagnosis of VLCADD.

The proband, a girl, was born at 40 weeks of gestation following an uncomplicated pregnancy. Her NBS was performed at 14 days of age in our facility. The result was positive for VLCADD, with a elevated c14:1 level of 4.38 μmol/L (normal, 0.02 to 0.19 μmol/L). Subsequent acylcarnitine profile in a new dried blood spot was tested again by tandom mass spectrometry, and the organic acid profile in urea was tested by gas chromotography mass spectrometry. The samples were sent to a commercial laboratory where the following levels were described: c14:1 of 2.75 μmol/L (normal, 0.02 to 0.25 μmol/L), adipic acid of 114.9 (normal, 0.5 to 5.0), pimelic acid of 24.3 (normal, 0.0 to 9.3), suberic acid of 69.7 (normal, 0.3 to 4.7) and 3-hydroxy sebacic acid of 51.7 (normal, 0.0 to 4.4). During this period, she developed feeding and vomiting. In the evening, her parents found her drowsy in her crib. Combined with laboratory investigations, she was diagnosed with alveobronchiolitis, bloodstream infection, and inherited metabolic disease.

VLCAD gene sequencing of the proband revealed compound heterozygous for the c.1843C>T (p.Arg615*) null mutation and another novel mutation, c.1292A>G (p.Asp431Gly) on the other allele. Targeted mutational analyses were also studied for all family members. Her mother was heterozygous for c.1843C>T (p.Arg615*) and her father was heterozygous for c.1292A>G (p.Asp431Gly). Because VLCADD is an autosomal recessive inherited disease [3,4], this case indicates the *ACADVL* c.1292A>G (p.Asp431Gly) might be a disease-causing mutation in human. In summary, it is essential to find and summarize new mutations in future clinical work because of the diversity of *ACADVL* mutations to provide a theoretical basis for clinical diagnosis.

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