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POSTER

A novel nonsense mutation in the CYP21A2 gene of a Vietnamese patient with congenital adrenal hyperplasia

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Abstract

Inactivating mutations in the CYP21A2 gene which encodes the protein involved in steroid synthesis have been reported in the patients with congenital adrenal hyperplasia (CAH). An infant who diagnosed with the severe phenotype of CAH such as increasing testicular volume, elevating of 17-hydroxyprogesteron, testosterone and progesterone and his family were subjected for genetic studies. Initially, we used PCR and direct sequencing to screen mutations in the CYP21 gene in the proband and his family. We identified a novel nonsense mutation c.374C>G predicts a substitution of serine for a stop codon at codon 125 (p.S125*) within exon 3 in the proband. However, the inheritance pattern of the mutation was not consistent with disease causation because of a heterozygous mutation carrier in father and sibling, wild-type alleles in mother but mutant alleles in proband. This inspired us to find deletions of exon using multiplex ligation-dependent probe amplification (MLPA) assay. In the profiles of MLPA electropherogram, the proband had a large deletion in exon 3, but his mother did not have. It means that the proband inherited a normal allele from his mother and a mutant allele from his father, but the deletion of a normal allele occurred in the proband. Therefore, mutation c.374C>G (p.S125*) in exon 3 in the proband is considered as a heterozygous deletion mutation. In addition, a large deletion in exon 1 in the maternal allele in the proband is observed. Taking together, the proband carried a nonsense mutation accompanied with two deletions in exon 1 and exon 3 in the CYP21A2 gene affect the CAH phenotype severity. These mutations also expand the CYP21A2 mutation spectrum in CAH disorder. This case also highlights the need of caution when interpreting results of molecular genetics and biochemical testing during genetic counseling.

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