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Letter to the Editor

New MCAD Gene Mutation, Not Previously Reported in Other Nations, Found at A1161G in Turkish Population

To the Editor:

Medium chain acyl-CoA dehydrogenase (MCAD) catalyzes the first reaction of the beta-oxidation cycle for 4-10-carbon fatty acids. MCAD deficiency is one of the most frequent inborn metabolic disorders in populations of northwestern European origin [Tanaka et al., 1992]. It is also the most common defect in mitochondrial beta-oxidation in humans. It is an autosomal recessive disorder, which usually presents in infancy. The disease manifests itself in periods of metabolic stress to the beta-oxidation system and may be fatal.

In previous reports, using a polymerase chain reaction (PCR)-based assay for 985A-to-G mutation in the medium-chain acyl-CoA dehydrogenase (MCAD) gene, the following is demonstrated: first, the A985G mutation in exon 11of MCAD gene is present more than 85% of the disease alleles from patients from all over the world; second, the allele frequency of A985G in the general population from most European countries is very high (1/59 in Netherlands, 1/68 in the United Kingdom, 1/74 in Scotland, 1/84 in Caucasian Americans in North Carolina, 1/101 in Denmark, 1/140 in France, and 1/143 in Normandy) [Andresen et al., 1995], but low in the southern part of western and central Europe (1/216 in Turkey, 1/240 in the Czech Republic, and 1/333 in Italy) [Tanaka et al., 1997]; third, these results support the notion of a founder effect in northwestern Europe [Yokota et al., 1991; Gregersen et al., 1993]; and fourth, MCAD deficiency does not play a significant role in the causation of SIDS [Miller et al., 1992; Arens et al., 1993; Ryan et al., 1997].

The prevalence of the 985A-to-G mutation in the medium-chain acyl-CoA dehydrogenase (MCAD) gene among the Turkish population was studied using the PCR/Nco-I method for molecular diagnosis. A frequency study of this common mutation was also conducted on blood samples from 35 healthy newborns and their mothers. Neither heterozygotes nor homozygotes for the 985A-to-G mutation were identified among newborns and their mothers. After considering previous reports, we stopped using the PCR/Nco-I method for molecular diagnosis, and we performed DNA sequencing for that region. We found four A1161G mutations and no A985G mutation in 35 newborns. Because the mutation was heterozygous and the disease was recessive, the effect of the mutation at protein level on the clinical situation could not be studied.

The MCAD gene was cloned and mapped to chromosome 1p21, comprising 12 exons spanning 44 kb of DNA; 80% of hot spots are found on exon 11 for A985G transition, which results in the replacement of lysine by glutamate at codon 304. A total of 26 different mutations have been identified in the MCAD gene but none of these mutations (other than A985G) was counted more often than 1% in variant alleles. However, in our preliminary study, the A1161G mutation was found in 11.4% of the Turkish population, it had not been previously reported in other nations.

The results of the present study fit with previous reports that MCAD deficiency is a common disorder in non-Turkish Caucasians, and quite rare among Japanese [Nagao, 1996.]. Therefore, newborn mass screening for MCAD deficiency using this method would not be practical in Turkey. However, it still seems necessary to investigate a child with fatty acid oxidation disorder for the presence of MCAD deficiency, using both biochemical and molecular genetic methods.

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