Mevalonate Kinase

Alternative Names
MVK
Mevalonicaciduria
Mevalonic Aciduria
Mevalonate Kinase Deficiency

WHO International Classification of Diseases
Endocrine, nutritional and metabolic diseases

OMIM Number
251170

Mode of Inheritance
Autosomal recessive

Gene Map Locus
12q24

Description
Mevalonic aciduria is a consequence of the deficiency of mevalonate kinase (ATP:mevalonate 5-phosphotransferase), the first enzyme after 3-hydroxy-3-methylglutaryl-coenzyme A reductase in the biosynthesis of cholesterol and nonsterol isoprenes. Until January 2004, only 20 cases of mevalonic aciduria have been reported. Data on the phenotype and laboratory indicators of mevalonate aciduria mainly refer to long term observations, and emphasize the absence of hypoglycemia, metabolic acidosis, or lactic academia. In several affected families, prenatal diagnosis has been achieved, and stillbirths or malformed fetuses have been described. Owing to its rarity and unspecific symptoms, mevalonate aciduria is probably underdiagnosed, especially in preterm infants who die early.

Molecular Genetics
The mevalonate kinase gene spans approximately 22 kb and contains 11 exons ranging from 46 to 837 bp and 10 introns varying in size from 379 bp to approximately 4.2 kb. Exon 1 encodes most of the 5-prime untranslated region, exon 2 contains the ATG start codon, and exon 11 contains the stop codon and the entire 3-prime untranslated region. Several natural mevalonate kinase splice variants were detected, resulting in truncated proteins.

Epidemiology in the Arab World

United Arab Emirates
Raupp et al. (2004) described two Arab infants (a female and a male) with mevalonic aciduria. They were born to a consanguineous couple who also had a healthy son. Hepatosplenomegaly, raised levels of C reactive protein, and thrombocytopenia were noted in the female proband. A blood culture taken on day 7 grew coagulase negative staphylococci. From day 12, while being treated, her situation deteriorated and died on day 15 from multiorgan failure. Gas chromatography and mass spectrometry showed urinary excretion of mevalonic acid and mevalonolactone consistent with mevalonic aciduria. On the other hand, the male proband did not show any evidence of infection initially and his platelet count remained normal during the first two weeks. Acinetobacter species was cultured fromendotracheal secretions on day 10. On day 19, his situation deteriorated with thrombocytopenia and raised C reactive protein. After a transient improvement, he developed septicemia caused by coagulase negative staphylococci and died from multiorgan failure at 2 months of age. Mutation analysis was performed on the DNA sample of the male proband and he turned to be homozygous for a T-C transition at nucleotide 104 of the mevalonate kinase gene and causes a L35S change in a conserved sequence of the enzyme. Both the mother and father were heterozygous for the same mutation.
References

Contributors
Ghazi O. Tadmouri: 3.1.2005