

한국인 가족형 LCAT 결손증 환자에서 발견된 프레임시프트 돌연변이

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Identification of Two Novel Frameshift Mutations in Lecithin: Cholesterol Acyltransferase (LCAT) Gene Associated with a Familial LCAT Deficiency Phenotype

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Background : A primary or familial LCAT-deficiency is a rare autosomal recessive genetic disorder caused by the complete or near complete absence of LACT activity. In the present study, we report two previously undescribed molecular alterations in exons 5 and 6 of the LCAT gene in a Korean patient presenting clinical and biochemical features of the familial LCAT deficiency.

Methods : A 25-year-old male patient presented with corneal opacity, absent plasma LACT activity, very low plasma HDL, Apo A-I and A-II concentration, and renal lesions representing global and focal segmental glomerulosclerosis with electrolucent vacuoles of various size with osmiophilic particle cores in the GBM and mesangial areas. To identify a mutation in the LCAT gene, genomic DNA was extracted from white blood cells of the proband and his parents, and all six exons of the LCAT gene were amplified using several sets of primers.

Results : The genomic DNA from the patient demonstrated that the patient has two mutations in exon 5 and exon 6. The same mutation was found only in exon 5 in the DNA of mother whereas the mutation of exon 6 was found in the DNA of his father. In exon 5, a base (G) was inserted after 633 nucleotide from start codon, generating a stop codon after synthesis of unrelated 16 amino acids following 211 amino acids. In exon 6, 8 bases were deleted after 793 nucleotides from start codon, which resulted in the synthesis of truncated of LCAT proteins composed of 251 amino acids of normal LCAT peptides and 17 unrelated amino acids. Both mutations led to a substantial decrease in LCAT activity; the addition of G in exon 5 revealed 35% of the wild type and a deletion of 8 bases in exon 6 resulted in a decrease to 27% of wild type.

Conclusion : These two novel frameshift mutations affect the functional activity of the protein, resulting in undetectable levels of LCAT activity in the patient. These findings provide additional information that may be useful in the genetic for the genetic diagnosis of familial LCAT deficiency and fish eye disease.

Key Words : 가족형 LCAT 결손증, 프레임시프트 돌연변이

Familial LCAT deficiency, LCAT gene mutation