SHORT COMMUNICATION

Rare Variant of Apolipoprotein E (Arg136→Cys) in a Subject with Normal Lipid Values

J. A. HUBÁČEK, J. PIŤHA, Z. ŠKODOVÁ, R. POLEDNE

Institute for Clinical and Experimental Medicine, Laboratory of Atherosclerosis Research, Centre for Experimental Cardiovascular Research, Prague, Czech Republic

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Summary

During the screening of apolipoprotein (apo) E gene polymorphism with PCR and subsequent restriction analysis, we have identified a female carrier with a mutant allele Arg136→Cys. This proband had normal lipid parameters and no history of coronary artery disease (CAD). We did not confirm the previously described connection between apo E Arg136→Cys mutation and elevated lipid levels. In the case of this mutation, other factors (environmental and/or genetic) are important for the development of lipid metabolism disorders.

Key words

Apolipoprotein E • Rare mutation • Lipid metabolism

Apolipoprotein E (apo E) gene determines three common variants – apo E2 (Arg 158 → Cys), apo E3 and apo E4 (Cys 112 → Arg). The frequency of apo E alleles varies among different populations; however, the E3 allele and the E 3/3 genotype are invariably dominant (Davignon et al. 1988, Gerdes et al. 1992, Hubáček and Poledne, 1998). A large number of rare variants has been described (for review see Hubáček et al. 2000).

Apo E, found at first in very low density lipoproteins (VLDL) plays an important role in the metabolism of triacylglycerol-rich lipoproteins and is described as an important determinant of serum cholesterol levels. In common population, higher levels of plasma low-density lipoproteins (LDL) cholesterol is connected with the allele E4 and lower levels with the allele E2 (Davignon et al. 1988). In some cases, homozygosity for apo E2 allele is an important genetic determinant of type III hyperlipoproteinemia.

In apo E polymorphism population screening in the region Benesov (1 % population sample, Hubáček et al. 1999) with the polymerase chain reaction (PCR) and restriction analysis with restriction enzyme Cfo I (Hixson and Vernier 1990), heterozygosity for an uncommon restriction fragment of the size about 110 bp, originated from the loss of Cfo I restriction site in the apo E gene, was found in one proband. This fragment is characteristic for a rare mutation in position 3817 of apo E cDNA (Walden et al. 1994, Feussner et al. 1996).

Through the additional mismatched PCR amplification (primers apo E 3817-A 5´ CGG CTG GGC GCG GAC ATG GAG GAC G, and apo E 3817-B 5´ CAG CTT GCG CAG GTG GGA GGC GAG GT created
a new Rsa I restriction site in carriers of the known rare mutation) and the restriction analysis of the PCR product with Rsa I, carrier of the apo E 2* allele with substitution C387 → T (Arg 136 → Cys) was confirmed. The second allele was the common apo E3 variant.

The proband was a postmenopausal, non-smoker caucasian woman, aged 73, without history of coronary artery disease and with apparently normal lipid values (total cholesterol: 5.17 mmol/l, LDL cholesterol: 2.81 mmol/l, HDL cholesterol: 0.98 mmol/l, apo B: 1.39 g/l) and blood pressure (SBP 139 mm Hg, DBP 87 mm Hg). The proband and her family did not agree with more detailed examination.

In our laboratory, about 3 500 individuals in projects with different designs (Hubáček 2001) have till now been genotyped for common apo E polymorphism. We have already found one family with this mutation in the same geographic region (Hubáček et al. 2000), and although the recent connection between the examined individual and previously described family has not been confirmed, the geographical localization supports the idea that both probands could have had a common ancestor. Thus, we can estimate that the population frequency of this mutation is far lower than 1:1000.

Rare mutations in the apo E gene have very often been described in patients with different types of severe hyperlipoproteinemia.

The apo E 2* allele (Arg136 → Cys) was formerly detected in subjects with a normal and late-onset of type III hyperlipoproteinemia as well as in subjects with normal lipid parameters (Walden et al. 1994, Feussner et al. 1996, Hubáček et al. 2000). Together with our presented results, the apo E allele (Arg136 → Cys) itself in heterozygous form is not sufficient for expression of obvious dyslipidemia.

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**References**


**Reprint requests**

Jaroslav A. Hubáček, IKEM-LVA, Vídeňská 1958/9, 140 21 Prague 4, Czech Republic, fax: 0042 02 41721574, e-mail: jaroslav.hubacek@medicon.cz