

Dominant type III hyperlipoproteinaemia (familial dysbetalipoproteinaemia)

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Dear Editor,

Visser *et al.*¹ describe an interesting case of a dominant form of familial type III hyperlipoproteinaemia (familial dysbetalipoproteinaemia [FD]), based on the presence of a rare APOE1 mutation. Normally, FD patients exhibit homozygosity for APOE2, which is a recessive form of dyslipidaemia, but also requires additional genetic, hormonal or environmental factors for its clinical manifestation, since only a small minority of the carriers of APOE2/E2 develop hyperlipidaemia. The hallmark of this disorder is the accumulation of atherogenic very-low-density lipoprotein (VLDL) and chylomicron remnants which can be demonstrated by an increased amount of cholesterol in the VLDL fraction (ratio of VLDL cholesterol/serum triglycerides > 0.69) after ultracentrifugation.² In addition to the keynotes expressed by the authors regarding their case, I would like to add two special aspects.

1) A very high level of apolipoprotein B (apoB) was measured in the patient, which the authors explained by the presence of a high level of Lp(a). This is most probably incorrect. Lp(a) is indeed an LDL-like particle in which the apoB molecule is covalently linked to a very large glycoprotein known as apolipoprotein (a) (apo a). The level of Lp(a) in plasma varies more than 1000-fold from less than 2 mg/l to more than 2000 mg/l; its measurement depends on the immunoreactivity of the apo(a) component of the protein in Lp(a).³ Lp(a) levels are primarily genetically determined, related to the kringle IV size polymorphism with resulting number of kringle IV type 2 repeats which can vary from 3 to > 40.⁴ The amount of immunodetectable apoB in Lp(a) has been reported to be less than 12%, even when Lp(a) levels were high.⁵ So, there must be another reason to explain the high apoB level in this patient. We have observed earlier a variable conversion of VLDL to LDL in dominant forms of familial dysbetalipoproteinaemia.^{2,6} Patients with APOE3-Leiden

had on average a higher LDL-cholesterol concentration and a higher proportion of cholesterol in the LDL density range (1.019-1.063 g/ml) in n=22 E3-Leiden carriers compared with n=24 E2/E2 carriers (38 ± 8% vs 23 ± 7%, p<0.0001) (Pasch, Stalenhoef, unpublished). This indicates a considerably larger amount of LDL particles in these subjects with dominant FD.

2) The use of the Friedewald formula to calculate the LDL concentration cannot be applied due to the fact that the VLDL composition is abnormal. The authors mention that the therapeutic intervention in the patient resulted in a LDL-cholesterol level of 2.96 mmol/l, which was probably calculated with this formula and is therefore incorrect.

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