Rare disease

Hepatic lipase deficiency in a Middle-Eastern-Arabic male

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Summary

Hepatic lipase (HL) deficiency is a rare genetic disorder that has been associated with premature atherosclerosis despite high plasma *high-density lipoprotein* (HDL) cholesterol concentrations in the affected individuals. The authors describe the clinical and biochemical features of HL deficiency in a young male of Middle-Eastern-Arabic origin. This is the first report of cholesterol ester transfer protein (CETP) activity and mass in HL deficiency in a patient from this ethnic group. While the CETP mass was high, its activity was low, a discrepancy likely due to the abnormal composition of patient's HDL particles.

BACKGROUND

This is a unique case of hepatic lipase (HL) deficiency in a man of Middle-Eastern-Arabic origin with data on cholesterol ester transfer protein (CETP) activity and mass showing discrepancies likely due to the abnormal composition of patient's *high-density lipoprotein* (HDL) particles.

CASE PRESENTATION

A 38-year-old Arab man first presented to our clinic in 2008 with a 14-year history of moderate elevations in concentrations of both triglycerides (2.5 mmol/l) and total cholesterol (5.12 mmol/l). He had a high HDL cholesterol level (2.0 mmol/l). His medical history was unremarkable and he was asymptomatic. The family history was notable for consanguinity (parents are second cousins), hypertriglyceridemia in one sibling and hypertension, hypercholesterolemia and diabetes in his 65-year-old father. The mother, aged 60, had arthritis but no documented dyslipidemia. On examination, the blood pressure was 120/70 mm Hg, pulse rate was 68 beats per min and regular, height was 168 cm, weight was 79.5 kg and BMI was 28.2 kg/m². There were no xanthomas or xanthelasmas. Cardiovascular exam was unremarkable.

Although he was asymptomatic, rosuvastatin therapy (20 mg per day) was started as a prevention measure as Lp(a) and high-sensitivity C reactive protein (hs CRP) were high. Six months later, lipid profile was repeated. Results are shown in table 1.

INVESTIGATIONS

Postheparin plasma HL activity was zero while the lipoprotein lipase activity was 115 nmol/min/ml (normal >90 nmol/min/ml). DNA sequencing of genomic DNA detected one homozygous coding mutation (L334F). This mutation has been previously reported to be dysfunctional

and causative of HL deficiency in a Finnish patient.¹ Lp(a) concentration was three times the upper range of normal. In the absence of data on Lp(a) in his parents, there is no obvious explanation for this finding. This finding further increases this patient's risk for vascular disease,² which is already higher in patients with HL deficiency.

TREATMENT

Rosuvastatin therapy (20 mg per day) was started as a prevention measure as Lp(a) and hsCRP were high. Six months later, lipid profile was repeated.

Outcome and follow-up

There was a significant decrease in atherogenic lipoproteins (*low-density lipoprotein* (LDL)-C and apo B) 6 months after initiating the treatment.

Table 1 Laboratory investigations before and after statin treatment

Analyte (reference range, units)	Baseline	After treatment
Total cholesterol (<5.20 mmol/l)	7.2	3.9
Triglycerides (<1.50 mmol/l)	11.3	2
HDL cholesterol (>0.90 mmol/l)	1.8	1.6
LDL cholesterol	–	1.4
Cholesterol HDL ratio	4.0	2.4
Apo A-1 lipoprotein (>1.10 g/l)	2.4	2.2
Apo B lipoprotein (<1.25 g/l)	1.4	0.7
Apo E genotype	E3E3	–
Lp(a) (<300 mg/l)	1042	–
TSH (0.27–4.20 mU/l)	0.75	–
Fasting glucose (3.6–6.0 mmol/l)	5.0	–
hsCRP (<3.1 mg/l)	5.1	2.2
CETP mass (1–2 µg/ml)	5.4	–
CETP activity (30–50 pmol/l)	4.9	–

CETP, cholesterol ester transfer protein; CRP, C reactive protein; HDL, *high-density lipoprotein*; LDL, *low-density lipoprotein*; TSH, *thyroid-stimulating hormone*.

DISCUSSION

HL is a triglyceride hydrolase located in hepatic sinusoids, and to a lesser extent in the adrenals and ovaries.³ It catalyses the hydrolysis of triglycerides and phospholipids predominantly in HDL and promotes the uptake of triglyceride-rich lipoproteins by hepatic receptors. Previously reported patients with HL deficiency were mostly of European Caucasian descent; some had early coronary heart disease despite high plasma HDL cholesterol concentrations.^{4–8}

HL deficiency is characterised by hypertriglyceridemia and, to a lesser extent, hypercholesterolemia and by relatively high HDL cholesterol levels. The combination of high HDL cholesterol levels in the presence of hypertriglyceridemia with or without hypercholesterolemia, should raise suspicion of HL deficiency as a possible underlying defect. Patients with HL deficiency have no distinct physical features but may have a family history of hypertriglyceridemia or consanguinity. Our patient fits this description. Common primary and secondary causes of hypertriglyceridemia, such as diabetes, hypothyroidism, familial dysbetalipoproteinemia and familial hypertriglyceridemia were excluded.⁹ In our patient, HL activity was absent and he was homozygous for a known loss-of-function mutation in the *LIPC* gene that was previously only found in Caucasian patients. Assay of CETP showed values expected at the high HDL-C level. While the CETP mass was high, its activity was low, a discrepancy likely due to the abnormal composition of patient's HDL particles. Lp(a) concentration was three times the upper range of normal. In the absence of data on Lp(a) in his parents, there is no obvious explanation for this finding. This finding further increases this patient's risk for vascular disease,² which is already higher in patients with HL deficiency.

Learning points

- ▶ HL deficiency has been found in ethnic groups other than Caucasian.
- ▶ Low CETP activity likely reflects the presence of qualitatively abnormal HDL.
- ▶ Rosuvastatin therapy (20 mg per day) could be used as a preventive therapy.

Competing interests None.

Patient consent Obtained.

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