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CASE REPORT

Extremely low HDL and residual cardiovascular risk—a case report

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Abstract

Introduction Extremely low high-density lipoprotein cholesterol (HDL-C) is defined as levels below 20 mg/dL. Association between extremely low HDL-C levels may occur from artifactual, primary monogenic disorders or from secondary causes. We present a 55-year-old known diabetic male with extremely low HDL, in the absence of severe hypertriglyceridemia, with apolipoprotein A1 deficiency and presenting with acute myocardial infarction.

Results Transradial angiography revealed triple vessel disease, for which the patient was medically managed and sent home in a stable condition and is presently on follow-up.

Conclusion Such cases are infrequent and pose a diagnostic challenge.

Keywords Apo AI deficiency · Hypoalphalipoproteinemia · Reverse cholesterol transport · Extremely low HDL · Residual cardiovascular risk

Introduction

In addition to its role in reverse cholesterol transport, high-density lipoprotein (HDL) shows many other protective properties towards atherosclerosis. It has an inhibitory effect on chemotaxis of monocytes, prevents endothelial dysfunction and apoptosis, prohibits low-density lipoprotein (LDL) oxidation, and stimulates the proliferation of endothelial cells and smooth muscle cells. These anti-inflammatory, antioxidative, antiaggregatory, anticoagulant, and pro-fibrinolytic activities are exerted by apolipoproteins, enzymes, and phospholipid components of HDL [1]. HDL also enhances insulin sensitivity and promotes insulin secretion by pancreatic beta islet cells. Elucidation of the HDL proteome has highlighted the "hormonal" characteristics of HDL in that it carries and delivers messages systemically [2]. Low serum high-density lipoprotein cholesterol (HDL-C) is known to be an important component of the metabolic syndrome.

We present a case of extremely low HDL (less than 20 mg/dL) and apolipoprotein A1 (Apo A1) deficiency, presenting with acute myocardial infarction (AMI). Such patients with HDL-C less than 20 mg/dL in the absence of severe hypertriglyceridemia are infrequently encountered in clinical practice and fall below the 5th percentile [3]. The most common pattern of dyslipidemia found in India is a combination of borderline high LDL cholesterol, low HDL cholesterol, and high triglycerides [4]. To our knowledge, there is no documented case from India of extremely low HDL, in the absence of severe hypertriglyceridemia, presenting with AMI.

Case report

A 55-year-old known diabetic male presented to cardiology outpatient department with complaint of recurrent typical chest pain [3–4 episodes] for the last 5 days. His vitals at presentation were as follows: blood pressure 128/80 mm Hg, pulse 70/min, respiratory rate 20/min, normal vesicular breath sounds, normal peripheral pulses, and S1 and S2 heart sounds were audible. His body mass index (BMI) was 19.2 kg/m^2 (18.5–24.9). His abdomen was soft, non-tender, and non-distended, and there was no organomegaly. There was no

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neurological deficit. There was depression of ST wave in V4–V6 leads and elevation of AVR. Echocardiography showed regional wall motion abnormalities in basal inferior lateral wall in left circumflex coronary artery territory, with fair left ventricular systolic function. Left ventricular ejection fraction was 52% (> 55%).

There was no significant allergy history, medication history, and past or family history, except that he was a known case of diabetes mellitus on medication for 6 years. He reported a family history of mildly reduced HDL-C, with his mother and father demonstrating levels of 24 and 27 mg/dL, respectively. He had no family history of cardiovascular disease. He denied taking prescription medications or over-the-counter supplements. He was not a known alcoholic. No significant findings were seen in examination of the skin, eyes, tonsils, and spleen.

The laboratory blood reports at admission were as follows: high sensitive troponin I > 40,000 ng/L (0–19), NT-proBNP 409.7 pg/mL (0–125), CKMB mass 141.55 ng/mL (0–7), hemoglobin 13.6 g/dL (13–17), red blood cell count 4.47 million/μL (4.5–5.5), packed cell volume 40% (40–50), MCV 89.5 femtoliter (83–101), MCH 30.4 pg (27–32), MCHC 34 g/dL (32–36), RDW 14.4% (11–16), platelet count 1.84 lacs/μL (1.00–3.00), total leucocyte count 15000 per μL (4–10), with neutrophils 84% (40–80), lymphocytes 14.5% (20–40), monocytes 1% (0–1), eosinophils 0.5% (1–6), aspartate transaminase 218 U/L (0–35), alanine transaminase 47 U/L (0–45), gamma glutamyl transferase 28 U/L (0–55), alkaline phosphatase 99 U/L (40–130), total protein 6.1 g/dL (6.4–8.3), albumin 4 g/dL (3.5–5), prothrombin time 13.5 s (11–16), glycosylated hemoglobin 6.5% (4–6%). Random plasma glucose, urea, creatinine, electrolytes, and bilirubin were within reference range. His serology reports were negative for HIV, HbsAg, and HCV. 12–14h overnight fasting serum tested the next morning showed the following results: cholesterol 81 mg/dL (0–200), triglyceride 235 mg/dL (0–150), high-density cholesterol 8 mg/dL (35–65), low-density cholesterol 26 mg/ dL (0–100), thyroid-stimulating hormone 4.6 μIU/mL (0.50–8.90), high sensitive C reactive protein 0.9 mg/L (< 3), homocysteine 10.2 μmole/L (5.46–16.2).

Further investigations revealed the following results: total serum lipids: 888.8 mg/dL (450–800), apolipoprotein A1 94.40 mg/dL (110–205), apolipoprotein B 77.40 (55–140), apolipoprotein B/A1 0.82 (0.35–1.0), lipoprotein [a] 24.90 mg/dL (0–30), apolipoprotein E 0.05 g/L (0.023–0.063). Lipoprotein electrophoresis revealed the following results: beta lipoproteins 46 % (38.6–69.4), pre-beta lipoproteins 34.5% (4.4–23.1), alpha lipoproteins 19.5% (22.3–53.5), chylomicrons absent. Urine albumin creatinine ratio and urine routine examination were within reference range.

NCCT whole abdomen and HRCT CHEST showed no significant abnormality, except thin subpleural band in the right lower lobe.

After proper workup and investigations, transradial coronary angiogram was done under aseptic conditions, which showed triple vessel coronary artery disease. There was 70% lesion in the left anterior descending, 50% lesion in the left circumflex, and 100% lesion in the right coronary artery (chronic total occlusion). Medical management was advised and patient discharged in stable condition. He was prescribed fenofibrate 160 mg/day for 6 months, rosuvastatin 10 mg/day for 6 months, niacin 1 g/day for 6 months, and metformin 500 mg/day sustained release tablets to continue. He was also given antiplatelets clopidogrel 75 mg per day and aspirin 150 mg per day for 6 months. He was advised 30–40-min brisk walk for at least 4 days per week and low cholesterol, low carbohydrate diet.

At 6 months follow-up, HDL was 21 mg/dL, triglyceride 132 mg/dL, LDLC 28 mg/dL, and cholesterol 76 mg/dL. He was advised to continue aspirin and rosuvastatin until the next follow-up.

Discussion

Apolipoprotein A1 (Apo AI) is the major HDL protein (65%) and cofactor for lecithin cholesterol acyl transferase (LCAT). Other proteins in HDL include apoA-II, apoC, apoA-IV, and paraoxonase (PON). Mutation, glycation, and oxidative modification of apoA-I destroy the structural and functional integrity of apoA-I and markedly impair its ability to act as substrates for LCAT. Both PON1 and PON3 are almost exclusively associated with HDL, and reduced function of PON cripples their protection of lipoproteins against oxidative modifications [5].

Evaluation of our patient revealed that he had the risk factors of male gender, type 2 diabetes mellitus, low Apo A1 levels, and extremely low HDL with high (though not severely high) triglyceride levels. He presented with acute myocardial infarction. Low HDL is a cause for residual risk for cardiovascular disease, even at LDL levels below 70 mg/dL [6]. Our patient had LDL value at presentation of 26 mg/dL. Residual risk also arises from established risk factors, such as dyslipidemia, high blood pressure, hyperglycemia, inflammation, and unhealthy lifestyles and emerging or newer risk factors [7].

In pathological conditions like diabetes mellitus, as in our patient, oxidative modification and glycation of the HDL protein occur and the HDL proteome changes into a proinflammatory protein. HDL loses its antiatherogenic properties, including reverse cholesterol transport, and oxidative and anti-inflammatory properties and becomes dysfunctional. The relative composition of lipids and proteins and enzymatic activities associated to HDL, such as paraoxonase 1 (PON1) and lipoprotein-associated phospholipase 11 (Lp-PLA2), are altered [8].

Approximately 10% of individuals with extremely low HDL-C levels are heterozygous for mutations in the genes of APOA1, ABCA1, LCAT, or Apo E gene polymorphisms, although data on the risk of atherosclerosis in these individuals are contradictory [9]. We could not perform mutational studies due to financial constraints. Patients exhibiting

extremely low HDL-C often have severe hypertriglyceridemia (triglyceride > 500 mg/dL). HDL-C of less than 20 mg/dL in the absence of severe hypertriglyceridemia, as reported in our patient, arise from severe perturbations in the metabolic pathways of HDL [3]. Compared to isolated low HDL-C, the risk of CVD is 30 to 60% higher when low HDL-C is accompanied by elevated triglyceride [10].

Extremely low HDL levels in the absence of hypertriglyceridemia have also been reported in Tangier disease, anabolic steroid intake, and autoimmune lymphoproliferative disease [3, 11, 12].

Various strategies for increasing levels of HDL or its components and the rationale for these approaches have been documented. Niacin when prescribed at a dose of 1 to 2 g per day can increase HDL-C levels up to 25% [13, 14]. Fibrate therapy lowers triglycerides while raising HDL-C ≈ 10 to 20% [15], and its effects occur via peroxisome proliferator–activated receptor alpha (PPARα) activation. Statins modestly increase HDL-C by 5 to 10% and offset the risk of very low HDL [16].

Conclusion

Case-control studies have reported that there is significant association of acute coronary events with raised apolipoprotein B, total cholesterol, LDL cholesterol, and non-HDL cholesterol and inverse association with high apolipoprotein A and HDL cholesterol. Subjects with HDL-C levels < 25 mg/dL have been shown to have higher mortality than those with HDL levels 26–49 mg/dL [17]. Further large-scale prevalence studies on extremely low HDL and trend studies of risk factor interrelationships in acute myocardial infarction are required. Physicians should be aware of the high possibility of low HDL cholesterol, especially in patients with type 2 diabetes or the metabolic syndrome, and the best treatment options employed to optimize the lipid profile. There is also a need to find a standard method to evaluate HDL functionality and quality, given the challenges posed by the multifarious roles played by HDL.

Authors' contributions All authors contributed to the study conception and design. Moushumi Lodh and Ashok Kumar Parida performed material preparation, data collection, and analysis. Moushumi Lodh wrote the first draft of the manuscript and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Data availability Not applicable.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethics approval Not required for case report.

Consent for participation Informed consent was obtained.

Consent for publication The participant has consented to the submission of the case report to the journal.

Code availability Not applicable.

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