

Title: Is Too Much of a Good Thing a Good Thing?

Extremely high high-density lipoprotein cholesterol with Coronary artery disease, Case report.

Keywords: High-density lipoprotein (HDL), Coronary Artery Diseases, Lipoproteins, Alcohol abuse, Cholesteryl ester transfer protein (CETP).

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Conflict of Interest Statement

The authors: Khalid Sawalha MD and Gilbert-Roy Kamoga, MD, FACP wish to declare there is no conflict of interest.

Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed consent

Verbal consent was obtained directly from the patient.

Abstract

A 52-year-old white female with past medical history of hypertension, Heart failure preserved ejection fraction, anxiety and alcohol abuse presented to the emergency department with chest pain. She was admitted to rule out an acute coronary syndrome (ACS). Her cardiac markers along with her serial electrocardiograms were negative for ACS or pericarditis. Her myocardial perfusion scan did not reveal any reversible coronary ischemia. Due to the persistent nature of the chest pain and its presentation, she was sent for left heart catheterization which showed non-obstructive coronary artery disease with 50% stenosis of the right coronary artery. Upon further testing she was found to have extremely high high-density lipoprotein level of 218 mg/dl (39-61). Whether this extremely high HDL level due to CETP, chronic alcohol abuse or others, we report this interesting case of extremely high high-density lipoprotein to emphasize that serum HDL is not always protective from development of CHD.

Introduction

High-density lipoprotein (HDL) cholesterol is a biomarker inversely associated with an increased risk of coronary heart disease (CHD) events. It is of considerable value in assessing patients' coronary artery disease risk. However, low levels of HDL cholesterol independent of non-HDL cholesterol has not been shown to increase risk of CHD. A 2009 meta-analysis of 108 randomized trials involving nearly 300,000 patients at risk for cardiovascular events found no association between treatment-induced increases in HDL cholesterol with risk ratios for CHD deaths, CHD events, or total deaths after adjustment for changes in low-density lipoprotein (LDL) cholesterol.[1]

HDL is a complex circulating particle with many subspecies that vary in lipid and protein composition.[2] Cholesterol is a major component of the particle and the amount of cholesterol contained in HDL particles can be directly measured; it is referred to as HDL cholesterol. In clinical practice, non-HDL cholesterol, rather than HDL cholesterol, is used to risk stratify patients. On the other hand, extremely high levels of HDL have been associated with high cause mortality in men and women.[3] Therefore, we share this interesting case of extremely high HDL level with its differentials.

Case presentation

A 52-year-old white female with past medical history of hypertension, heart failure with preserved ejection fraction, generalized anxiety disorder and alcohol dependence/abuse for over 10 years presented to the emergency department with retrosternal chest pain associated with nausea. She has family history significant for hypertension, diabetes mellitus type II and coronary artery disease. Her home medications include: Venlafaxine 75 mg, Metoprolol tartrate 12.5 mg and Ambien 10 mg. Vitals upon admission were blood pressure 155/100 mmHg and a heart rate of 110 beats per minute. Her electrocardiogram showed sinus tachycardia with no acute ST-T wave changes. Initial troponin level was negative < 0.012 (ng/ml). Other laboratory data including complete blood count showed WBC 3.9 k/uL (4.5-11.0), RBC 3.60 M/uL (4.2-5.4), MCV 99 fL (80-100). Her Comprehensive metabolic panel was within normal limits. She was admitted for observation in the progressive care unit and made NPO for myocardial perfusion scan in the morning. Further laboratory data showed triglyceride 122 mg/dL (0-149), total cholesterol 265 mg/dL (107-200), LDL 41 mg/dL (0-99), HDL 218 mg/dL (39-61) with repeated level of 200 mg/dL. Her hemoglobin A1C was 5.3% (0-5.99). TSH 1.67 uIU/mL (0.465-4.68), folic acid > 20.0 ng/mL (2.76-19) and vitamin B12 of 197.0 pg/mL (239-931). The trend of cardiac markers was negative. She had myocardial perfusion scan done showing no reversible ischemia. However, due to persistent chest pain, the

decision was made to send the patient for left heart catheterization which showed non-obstructive coronary artery disease with 50% stenosis in the right coronary artery. Later, patient was discharged home along with medical therapy to include: Fish oil 1000 mg Folic acid 1 mg, Atorvastatin 40 mg, Aspirin 81 mg and Thiamine 100 mg with recommendations for further lipidology and genetic testing.

Discussion

High serum HDL cholesterol (>60 mg/dL [1.6 mmol/L]) may be hereditary or associated with conditions such as alcohol abuse, hypothyroidism, phenytoin treatment, and insulin treatment in type 1 diabetes or as a result of regular moderate to intense aerobic exercise. It is usually associated with a lower risk of coronary heart disease (CHD).[4] Several studies have shown that high HDL cholesterol levels are associated with an increased risk of atherosclerosis and cardiovascular events.[5] In these situations, HDL particles are dysfunctional in their antiatherogenic properties.[6] Large HDL particles have a reduced content of anti-inflammatory proteins and lipids that may account for their dysfunctional properties. However, the question is whether the HDL particles are functional in patients with high HDL cholesterol levels. In one series of patients with elevated HDL cholesterol levels who had CHD, it was found that the HDL particles were functionally impaired with regard to antioxidant and anti-inflammatory activities.[5]

Our patient had an extremely high serum HDL lipoprotein levels documented on two occasions and despite the high HDL levels, she had evidence of coronary artery disease although non-obstructive. The first on the differentials is Cholesteryl ester transfer protein (CETP) deficiency as it is integrally involved in HDL metabolism through mediating the transfer of cholesteryl esters from HDL particles to the triglyceride-rich lipoproteins LDL and very low-density lipoprotein (VLDL). Polymorphisms affecting the activity of CETP, such as an isoleucine for valine substitution at codon 405 (I405V) are common. In a study from Denmark, for example, 43 percent of people studied were heterozygous for I405V and 11 percent were homozygous for I405V. [7] Polymorphisms such as I405V that reduce the activity of CETP typically increase plasma HDL-cholesterol concentrations. [8,9,10] Although we didn't test the patient as inpatient, but upon discharge recommendations were for further lipidology and genetic testing as an outpatient.

Second on our list, her long history of 10 years or more of alcohol abuse reported as half a bottle of vodka or whiskey on daily basis is likely responsible for her elevated levels of HDL as alcohol consumption was reported to increase HDL cholesterol levels. [11] From the literature review, it is possible that she has dysfunctional HDL particles that do not confer the protection against CHD that functional HDL particles would. Thus, assessment of HDL function among those with high HDL levels may be an important step in risk assessment for CHD to provide further clinical guidance for our patients.

Other differentials such as hypothyroidism, phenytoin treatment, and insulin treatment in type 1 diabetes or as a result of regular moderate to intense aerobic exercise were ruled out as the patient has TSH level, not on phenytoin or insulin treatment and not active.

Conclusion

We share this interesting case of extremely high serum HDL and how it is not always protective from development of CHD. It has been demonstrated that extremely high levels of serum HDL in both men and women in the general population have high all-cause mortality. Increased risk from CHD is thought to be from dysfunctional HDL particles that maybe more prevalent in individuals with high serum HDL levels. Thus, we should not assume that a high HDL in our patients is always protective.

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