Severe Hypocholesterolemia with Reduced Serum Lipoprotein(a) in a Patient with Visceral Leishmaniasis

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Abstract. We report the case of a 36-yr-old man with visceral leishmaniasis who presented with marked hypocholesterolemia, mild hypertriglyceridemia, severely decreased serum levels of HDL-cholesterol, LDL-cholesterol, apolipoproteins AI and B, and increased serum level of apolipoprotein E. Moreover, serum Lp(a) level was markedly reduced on presentation, which is the first published report on Lp(a) levels in kala-azar. Possible mechanisms for the observed alterations of the serum lipid profile are discussed. (received 25 January 2002; accepted 29 March 2002)

Keywords: visceral leishmaniasis, kala-azar, hypocholesterolemia, lipid disorders, lipoprotein(a)

Introduction

Visceral leishmaniasis, generally called kala-azar, occurs in several Mediterranean countries, and most frequently affects children ≤6 yr of age. Protozoa of the genus Leishmania (species donovani), which are responsible for the disease, are transmitted to humans by the sand fly, Plebotomus argentipes and related species.

Lipid disorders have been described in children with active visceral leishmaniasis [1-5]. The serum lipid profile in most cases is characterized by hypertriglyceridemia with reduced levels of total cholesterol, low density lipoprotein (LDL)-cholesterol, and high density lipoprotein (HDL)-cholesterol. There is one case report that describes an adult patient with kala-azar-associated lipid disorders [6]. Insofar as we can ascertain, serum lipoprotein(a) [Lp(a)] levels have not previously been reported in patients with kala-azar. We report here a patient with visceral leishmaniasis who presented with severe hypocholesterolemia and markedly decreased serum Lp(a) level.

Case Report

A 36-yr-old stockman with an unremarkable medical history was admitted to our clinic because of fever of 6 mo duration, accompanied by sweating and muscle discomfort. On admission, his temperature was 37.4°C, blood pressure 100/70 mmHg, pulse 84/min, and respirations 18/min. The patient appeared cachectic and physical examination revealed marked hepatosplenomegaly.

The patient’s laboratory parameters on admission to our clinic are summarized in Table 1. Serum total cholesterol and triglycerides were determined by an enzymatic colorimetric assay (Olympus AU-600; Diagnostica, Hamburg, Germany). HDL-cholesterol was determined by an homogeneous assay based on polyanionic synthetic polymers and detergents (Olympus AU-600, Diagnostica). LDL-cholesterol was calculated by the Friedewald formula [7]. Serum Apo AI, Apo B, and Apo E were measured by immunonephelometry (Behring Nephelometer BN-100, Behring Diagnostics, Frankfurt, Germany). Serum Lp(a) was measured using a monoclonal anti-Lp(a) antibody technique by an enzyme-linked immunoassay (Macra Lp(a) kit, Terumo Medical Corp., Elkton, MD, USA).

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As shown in Table 2, the patient had severe hypocholesterolemia (total serum cholesterol, 63 mg/dl), with mild hypertriglyceridemia and severely reduced levels of serum HDL-cholesterol, LDL-cholesterol, apolipoprotein AI, apolipoprotein B, and lipoprotein(a); the apolipoprotein E levels were increased.

The patient’s diagnosis of kala-azar was established by bone marrow aspiration and demonstration of intracellular parasites. Antimony gluconate (‘Glucantim’) therapy was started immediately. After two 14-day cycles, a clinical remission was obtained. At 6 wk after initiation of treatment, the patient’s liver and spleen appeared to be normal and his serum lipid profile was essentially within the reference intervals (Table 2).

### Discussion

On admission to our clinic, the patient presented with marked hypocholesterolemia, which was secondary to leishmaniasis, as demonstrated by the normal lipemic pattern after therapy. His serum total cholesterol level is the lowest reported in the literature for an adult patient with kala-azar. Furthermore, the patient exhibited reduced levels of serum HDL-cholesterol, LDL-cholesterol, apolipoproteins AI and B, and lipoprotein(a), whereas his serum triglyceride and apolipoprotein E concentrations were increased. The authors consider that the following mechanisms might explain the patient’s altered lipid profile:

First, an immunological mechanism could be the cause, since autoimmune phenomena have been described in patients with kala-azar, including our case who had a positive direct Coombs test, hypergammaglobulinemia, and elevated serum level of β2-microglobulin. Such a mechanism may account for the dyslipidemia observed in other immunologic disorders, such as systemic lupus erythematosus, multiple myeloma, and macroglobulinemia [6]. Immunoglobins influence lipoprotein metabolism in various ways, such as (a) forming immune complexes between HDL and autoantibodies, which can accelerate HDL degradation [2], (b) interfering with receptor-mediated clearance of chylomicron-remnants, IDL (intermediate density lipoprotein), and LDL, and (c) impairing lipoprotein lipase activity.

Second, sequestration and/or degradation of lipoproteins may occur in the enlarged spleen and liver. For example, HDL binds to the membrane of...
Trypanosoma brucei and the plasmodium of malaria takes cholesterol from its host. In leishmaniasis, the link between HDL and the parasite may reflect sequestration of HDL in the tissues where the parasite accumulates [2].

Third, a decrease in LCAT (lecithine:cholesterol acyltranferase) activity could decrease serum HDL-cholesterol concentration. LCAT activity has been reported to be markedly reduced in patients with kala-azar [4,5]. It has been hypothesized that cytokines released during the acute phase response may have inhibitory effects on LCAT synthesis [8].

Fourth, enhanced activity of the LDL receptor may be provoked by the parasitic infection, due to elevated levels of IL-6 and other cytokines [9]. Additionally, cytokine-induced inhibition of Apo AI synthesis could explain the markedly reduced levels of this apolipoprotein and HDL-cholesterol [5].

Fifth, the observed hypertriglyceridemia may be caused by decreased lipoprotein lipase and hepatic lipase activities, resulting in retardation of VLDL clearance and consequently of the VLDL conversion to LDL, as described in rabbits infected with trypanosoma [10], or possibly to increased VLDL production. The mediators responsible for impaired lipase activity could be the tumor necrosis factor (TNFα), which is elevated in chronic parasitic infections [11], or the elevated levels of Apo E, as discussed below.

Sixth, in agreement with a previous study [4], our patient demonstrated elevated serum Apo E levels (72 mg/dl). This finding may be due to increased Apo E synthesis by the disease-induced activated macrophages. Moreover, excess Apo E accelerates the secretion rate of VLDL-triglycerides and can decrease the efficiency of VLDL lipolysis [12].

Finally, this is the first time that Lp(a) levels are recorded in a patient with visceral leishmaniasis. The Lp(a) level was markedly decreased on presentation and returned to normal by 6 wk later. A recent study demonstrated that Lp(a) behaves as a negative acute-phase reactant during major inflammatory responses in humans [13]. In our patient, serum levels of Lp(a) and LDL-cholesterol responded in parallel. It is unlikely that the diminished concentrations of LDL-cholesterol and Lp(a) were due to increased activity of LDL receptors, because statin-mediated upregulation of these receptors has only minimal effect on plasma levels of Lp(a). On the other hand, cytokines, which play a key role in inflammation and sepsis, have been shown to influence the expression of the apo(a) gene; transforming growth factor-β1 and TNFα, which predominate in severe inflammation, inhibit the expression of the apo(a) gene in primary cultures of monkey hepatocytes [14].

In conclusion, at least in our patient, markedly decreased serum concentration of Lp(a) seems to be an additional feature of visceral leishmaniasis-associated disorders of lipid metabolism.

References


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