Acquired apolipoprotein B deficiency with chronic hepatitis C virus infection

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Chronic hepatitis C virus (HCV) infection is often associated with fatty liver. Apolipoprotein B (ApoB) deficiency is one of the known causes of fatty liver, and acquired ApoB deficiency has recently been reported with HCV infection. We report two patients (47-year-old lady and 48-year-old man) who had asymptomatic transaminase elevation, fatty liver, anti-HCV positive with high viral load (genotype 3). Their lipid profile showed low total cholesterol, low-density lipoprotein, triglycerides and ApoB. One of the patients who received treatment for HCV infection showed improvement in lipid profile and ApoB levels. [Indian J Gastroenterol 2006;25:311-312]

Patients infected with hepatitis C virus (HCV) genotype 3 have more frequent and higher grades of steatosis compared to those infected with other genotypes.1 Hereditary heterozygous apolipoprotein B (ApoB) deficiency is known to cause fatty liver.2

Case 1: A 47-year-old lady was detected to have elevated serum ALT and AST during pre-anesthetic check-up for hysterectomy for uterine fibroids. There was no history of alcohol intake, blood transfusion, surgery or any cause for liver disease. On examination she was non-obese and had no stigmata of chronic liver disease. Per abdominal examination was unremarkable.

Investigations: hemoglobin 9 g/dL (hypochromic, microcytic). Blood sugar levels were normal. ALT and AST levels were 52 and 43 IU/mL (normal up to 40), respectively; rest of the liver profile was normal. INR was 1. Lipid profile showed LDL 43 mg/dL (normal 85-150), triglycerides 47 mg/dL (30-200), apolipoprotein A1 (ApoA1) 99 mg/dL (96-176), ApoB 40 mg/dL (43-126). She was anti-HCV positive, with HCV RNA load >10^6 IU/mL and genotype 3a. HBsAg and HIV tests were negative. Ultrasonography showed fatty liver without evidence of portal hypertension. Isotope liver-spleen scan was normal.

Case 2: A 48-year-old man was detected to have elevated transaminases during routine health check-up. There was no history of alcohol or hepatotoxic drug ingestion, blood transfusion, surgery, autoimmune disease or chronic liver disease. On examination he was non obese without any stigmata of chronic liver disease.

Investigations: hemogram was normal. ALT and AST values were 205 and 97 IU/mL, respectively; rest of the liver profile was normal. Lipid profile showed cholesterol 96 mg/dL, LDL 41 mg/dL, triglycerides 83.2 mg/dL, ApoA1 112 mg/dL and ApoB 35 mg/dL. He was anti-HCV positive; HBsAg and HIV were negative. Ultrasonography revealed fatty liver without evidence of portal hypertension. Isotope liver-spleen scan was normal.

He was treated for 48 weeks with pegylated interferon-alpha 2b (PegInteron; Schering-Plough) and ribavirin. One month following end of treatment his lipid profile showed increase in cholesterol (123 mg/dL), LDL (54 mg/dL) and triglycerides (186 mg/dL), and normalization of ApoB (57 mg/dL). HCV RNA load decreased from 3,293,044 IU/L to undetectable levels; ALT and AST decreased to 87 and 52 IU/mL, respectively.

Hereditary homozygous ApoB deficiency, a rare entity, is associated with syndrome-like abetalipoproteinemia, characterized by fat malabsorption, diarrhea, failure to thrive and ataxia. Heterozygous ApoB deficiency is characterized by typical lipid profile of low levels of cholesterol, LDL, VLDL and triglycerides. It is diagnosed in patients with fatty liver in whom common causes are excluded. ApoB deficiency can be acquired in patients with cirrhosis of liver and is usually associated with decrease in other Apo and lipoproteins.

Acquired isolated ApoB deficiency occurring in hepatitis C infection without advanced liver disease is a recently recognized entity.1 It is correctable on antiviral treatment.

HCV infection is often associated with fatty liver (30%-80%), more commonly in patients infected with genotype 3.1 The mechanism is not clear. Patients with HCV infection with genotype 3 and steatosis present with a lipid profile characteristic of hereditary heterozygous ApoB deficiency. It is postulated that hypobetalipoproteinemia associated with HCV is mediated by HCV core protein, which down-regulates triglyceride metabolism, leading to steatosis.3 Patients infected with non-3 genotype do not show this lipid pattern, and steatosis in them is probably a result of virus-induced insulin resistance.4

Clinically, HCV genotype 3-induced ApoB deficiency correlates with degree of viral load, and is associated with more severe degree of steatosis, increased lobular inflammation and higher grades of fibrosis suggestive of more aggressive disease.5 It also increases risk of hepatocellular carcinoma.6

Low cholesterol levels in a patient with liver disease usually indicates advanced liver disease with poor prognosis. Presence of acquired ApoB deficiency in HCV-infected patients indicates need for treatment for HCV as they are likely to have more progressive disease.

References


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