

• CASE REPORT •

Severe hypercholesterolemia associated with primary biliary cirrhosis in a 44-year-old Japanese woman

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Abstract

A 44-year-old woman developed jaundice and was diagnosed as stage II of primary biliary cirrhosis (PBC). She showed a severely high total cholesterol level. This article focuses on atypical presentations of PBC and the need to test the total cholesterol level of PBC patients.

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CASE REPORT

A 44-year-old gentlewoman was admitted in August 1996 due to a feeling of itching and jaundice. She had no special past history, such as operation, blood transfusion, tattooing or illicit drug use. She did not drink or smoke. There were no particular familial histories such as liver disease or hyperlipidemia. The patient had been on medication for hyperlipidemia, with a daily intake of 10 mg of pravastatin sodium, 12 g of cholestyramine, and 600 mg of ursodeoxycholic acid since one month earlier.

On admission, her height, body mass and body mass index (BMI) were 154.5 cm, 46.0 kg and 19.3 kg/m², respectively. Her physical examination revealed mild anemia and jaundice. Xanthoma was noticed around her eyes, but thickened Achilles tendon was not seen on X-ray examination. Her liver and spleen were not enlarged. There was no pretibial edema in her feet.

Blood test results were compatible with the picture of primary biliary cirrhosis (PBC). The serum bilirubin level was 57 mg/L (normal 2-12 mg/L), direct bilirubin was 42 mg/L (normal <3 mg/L), alkaline phosphatase was 2 362 IU/L (normal 115-359 IU/L), and alanine aminotransferase was 105 IU/L (normal 8-42 IU/L). Prothrombin time was within normal limits at 11.8 seconds. Platelet count was 277×10⁹/L. Renal function was normal. Ultrasound scan showed normal liver size and biliary trees were normal. There were no gallstones or ascites. Intimal medial thickness (IMT) of the right common carotid artery did not show any increase on high-resolution B mode ultrasonography.

Serology tests for hepatitis B and C viruses were negative. Anti-mitochondrial antibody (AMA) and anti-mitochondrial M2 antibody were positive (×320) and 41.5 (normal <7). Anti-

nuclear antibody (ANA) and anti-smooth muscle antibody were both negative. IgG and IgM were 27.42 g/L (normal 8.7-17 g/L) and 11.89 g/L (normal 0.35-2.20 g/L), respectively. Thyroid gland functions were within normal limits at this time.

Her serum total cholesterol level was 13.90 g/L (normal 1.25-2.20 g/L), triglyceride 1.12 g/L (normal 0.35-1.50 g/L), high-density lipoprotein (HDL) cholesterol 1.03 g/L (normal >0.40 g/L), and blood glucose 1.03 g/L. She was positive for lipoprotein X. LCAT was not detectable, compatible with Frederickson type V hypercholesterolemia [apolipoprotein A-I 0.48 g/L (normal 1.26-1.65 g/L), A-II 0.24 g/L (normal 0.246-0.333 g/L), B 1.44 g/L (normal 0.66-1.01 g/L), C-II 333 mg/L (normal 15-38 mg/L), C-III 3.42 g/L (normal 26-46 mg/L) and E 450 mg/L (normal 29-53 mg/L)].

Liver biopsy showed no cirrhosis but revealed compatibility with PBC stage II (according to Ludwig). She was re-started on ursodeoxycholic acid at 900 mg/d and probucol at 500 mg/d. She was diagnosed as subclinical hypothyroidism [TSH 11.5 μIU/mL (normal 0.35-4.94 μIU/mL), free T3 1.45 pg/mL (normal 1.71-3.71 pg/mL) and free T4 8.2 ng/L (normal 7.0-14.8 ng/L)] in April 1999 and 0.05 mg/d of levothyroxine sodium was begun. However, her total cholesterol level remained quite similar to that before treatment as in October 2000 it was still high (10.11 g/L).

DISCUSSION

In PBC patients, a hyperlipidemic state is often observed; however, this case illustrated an unusual presentation of severe hypercholesterolemia. According to Talwalkar and Lindor^[1], up to 85% of patients presented with hypercholesterolemia at diagnosis. However, such a degree of hypercholesterolemia was not observed in many cases. In fact, our survey of more than 100 cases of PBC who visited our clinic revealed only this one case with a level of hypercholesterolemia higher than 10 g/L.

Earlier cross sectional studies reported higher levels of total cholesterol and lower levels of HDL cholesterol in patients with advanced disease compared with those in the earlier stages^[2,3]. On the other hand, Nikkila *et al.*^[4] reported that reduced hepatic synthesis and internal absorption in the terminal stage of PBC might lead to decreased total cholesterol levels. Although high levels of lipoprotein X, comprised of nonesterified cholesterol and phospholipids, were present in the serum of patients with PBC^[5], our patient was at stage II of early PBC, even if her serum bilirubin level was 57 mg/L. Hypothyroidism and subclinical hyperthyroidism often caused hyperlipidemia^[6,7]. In our patient, hypercholesterolemia did not improve after thyroid hormone therapy.

In PBC, marked hypercholesterolemia was not associated with an excess risk of cardiovascular disease, whereas less advanced patients with moderate hypercholesterolemia were exposed to an increased cardiovascular risk^[8]. There is no doubt that a reduction in serum cholesterol levels in PBC patients could be achieved with medical therapy^[9,10], so our patient continued to be observed with medical therapy.

In conclusion, we report a case of severe hypercholesterolemia, not familial, but associated with early-stage PBC. Further studies of severe hypercholesterolemia are warranted.

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