

## Case report

# Primary biliary cholangitis in Thai woman: A case report

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Primary biliary cholangitis or primary biliary cirrhosis (PBC) is a chronic, slowly progressive, autoimmune, cholestatic liver disease. It is globally considered a rare disease. Herein, we presented a 55-year-old Thai woman who gradually developed fatigue and generalized pruritus without fever for four months. Her physical examination revealed only pallor and jaundice, no liver stigmata, and no hepatosplenomegaly; her blood tests showed: Hb 8.1 g/dL, WBC 12,180/mm<sup>3</sup>, platelet 143,000/mm<sup>3</sup>, albumin 2.2 g/dL, globulin 4.0 g/dL, AST 164 U/L, ALT 102 U/L, alkaline phosphatase 384 U/L, total bilirubin 2.8 mg/dL, direct bilirubin 1.3 mg/dL, HBV, HCV and HIV-negative, ferritin 39.9 ng/ml, copper 125 ug/dL, ceruloplasmin 0.27 g/L, urine copper < 1 ug/g creatinine, anti-smooth muscle antibody-negative, anti-mitochondrial antibody-positive 1:1,600, ANA-positive, homogeneous pattern 1:80, centromere pattern 1:1,280, anti-cytoplasmic antibody-positive 1:1,280, alpha fetoprotein 3.16 ng/ml, creatinine 0.55 mg%, and normal coagulogram. Ultrasonography and the computerized tomography of the upper abdomen showed nodularity and heterogeneous parenchymal disease of the liver, no intrahepatic bile duct dilatation, and slight splenomegaly, compatible with cirrhosis. Esophagogastroduodenoscopy showed acute esophageal variceal bleeding that was successfully treated with rubber band ligation. The diagnosis of PBC was concluded and she was treated with ursodeoxycholic acid and propranolol. Within 6 months, her clinical symptoms as well as transaminitis partially improved.

**Keywords:** Primary biliary cholangitis, anti-mitochondrial antibody.

Primary biliary cholangitis or formerly primary biliary cirrhosis (PBC) is a chronic autoimmune inflammatory disease of the intrahepatic bile ducts resulting in periportal inflammation, gradual destruction of the small bile ducts, and cholestasis. Prolonged hepatic cholestasis subsequently leads to cirrhosis and portal hypertension. It presumably results from an environmental trigger in genetically predisposed persons. It predominantly affects females much more than males, and its most frequent presentations are fatigue and pruritus regardless of the disease severity. <sup>(1,2)</sup> PBC can be diagnosed if two of three following criteria are met: 1) biochemical evidence of cholestatic liver disease for at least 6 months duration; 2) positive anti-mitochondrial antibody; and, 3) histopathologic features of PBC on a liver biopsy. <sup>(3)</sup> It usually runs a chronically progressive course and around in half of cases turns from asymptomatic to

develop fatigue and pruritus within 10 years after diagnosis. The only accepted treatment for PBC is ursodeoxycholic acid which can improve the liver biochemistry as well as the pathology of PBC and delay transplantation of the liver. <sup>(4)</sup>

Generally, it is globally considered a rare disease; however, its frequency is variable in different geographic areas, viz., it is much more prevalent in Europe, North America, <sup>(5)</sup> and Great Britain than Australia and Brunei Darussalam. <sup>(6)</sup> In Thailand, PBC has been rarely reported as an unusual cause of cirrhosis. <sup>(7)</sup> Herein, we found one case of PBC who presented with prolonged mild transaminitis.

## Case report

A 55-year-old Thai woman was admitted because of gradually progressive fatigue, pruritus, and mild jaundice without fever for four months. She also had anorexia and noticed some body weight loss. She denied drinking, smoking, or herbal medicine usage. No family member had a problem like her. The physical examination revealed a body temperature of 36.5 °C, pulse rate of 84/min, body weight of 35.5 kg, frank pallor, mild jaundice, no hepatosplenomegaly,

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no liver stigmata and no Kaiser-Fischer's ring, examined by the ophthalmologist, and no xanthoma/xanthelasma.

The blood tests included: Hb 8.1 g/dL, Hct 23.0 %, WBC 12,180/mm<sup>3</sup>, N 53 %, L 45 %, platelet 143,000/mm<sup>3</sup>, MCV 79.3 fL, MCH 27.9 pg, MCHC 35.2 g/dL, RDW 16.6 %, direct anti-globulin test-negative, ferritin 39.9 ng/ml, serum iron 37.7 mcg/dL, TIBC 385 mcg/dL, transferrin saturation 9.8 %, Hb analysis: AE, and Hb E 24.3 %, and Hb A2 3.3 %, serum albumin 2.2 g/dL, globulin 4.0 g/dL, AST 164 U/L, ALT 102 U/L, alkaline phosphatase 384 U/L, total bilirubin 2.8 mg/dL, direct bilirubin 1.3 mg/dL, ceruloplasmin 0.27 g/L (normal 0.2 - 0.6), serum copper 125 ug/dL (normal 70 - 160), urine copper < 1 mcg/g creatinine (normal < 50), anti-smooth muscle antibody (ASMA)- negative, anti-mitochondrial antibody (AMA) - positive 1:1,600, alpha fetoprotein 3.16 ng/ml (normal 1.09 - 8.04); HBV, HCV HIV -negative; antinuclear antibody (ANA) - positive, homogeneous pattern 1:80, centromere pattern 1:1,280, anti-cytoplasmic antibody-positive 1:1,280, coagulation tests-normal, serum cortisol 16.6 ug/dL, Ca 7.9 mg/dL, P 2.3 mg/dL (normal 2.5 - 4.5), Mg 1.5 mg/dL (normal 1.9 - 2.5), creatinine 0.55 mg/dL, fasting blood sugar (FBS) 94 mg/dL, cholesterol 186 mg/dL, normal thyroid function tests, and urinalysis-unremarkable.

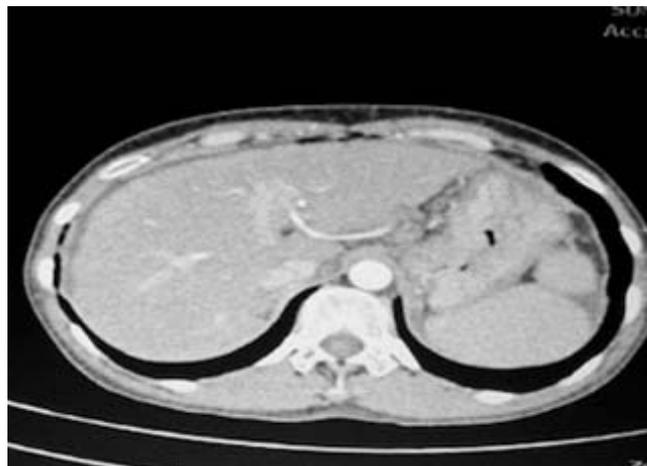
The ultrasonography of the upper abdomen showed a normal size liver with inhomogeneous echogenicity and nodularity, and no dilatation of the

intrahepatic bile duct. Also, splenomegaly and mild ascites were detected. Impression: diffuse parenchymatous disease of the liver, infiltrative tumor could not be excluded.

The multi-detector computerized tomography showed a small sized liver with nodularity and heterogeneous parenchymal density, compatible with cirrhosis; after dynamic contrast study, no enhancing nodule on the arterial or venous phases, mild splenomegaly, and minimal ascites. The gall bladder wall had edema due to ascites. Impression: Cirrhosis with no evidence of hepatocellular carcinoma (Figure 1).

On the 1<sup>st</sup> day of admission, she suddenly developed gross hematemesis with subsequent hypotension. An esophagogastroduodenoscopy performed after blood transfusion found acute variceal bleeding that was successfully treated with a varices ligation band.

She was diagnosed as having PBC with acute variceal bleeding; the other diagnosis was hemoglobin E heterozygosity. Besides variceal ligation, she was continuously treated with ursodeoxycholic acid (UDCA) (150 mg/tablet) 3 tablets a day and propranolol (20 mg a day). Six months later, her pruritic symptom and fatigue were much improved and her blood tests were: albumin 2.0 g/dL, globulin 2.2 g/dL, AST 78 U/L, ALT 49 U/L, alkaline phosphatase 128 U/L, total bilirubin 2.9 mg/dL, direct bilirubin 1.2 mg/dL, Hb 9.0 g/dL, WBC 8,890/mm<sup>3</sup>, and platelet 140,000/mm<sup>3</sup>.



**Figure 1.** Computerized tomography shows small sized liver with nodularity and heterogeneous parenchymal density, compatible with cirrhosis.

## Discussion

The diagnosis of PBC could be made in our case because of the combination of the increased alkaline phosphatase, high titer of anti-mitochondrial antibody (AMA) in the patient who had no extrahepatic bile duct obstruction on the imaging, and no other common causes of cirrhosis<sup>(8)</sup> such as HBV, HCV, alcohol, iron or copper overload.<sup>(9)</sup> Although a liver biopsy was not performed and autoimmune diseases outside the liver such as Hashimoto thyroiditis, Sjogren's syndrome, the high serum globulin<sup>(10)</sup>, high serum cholesterol, and xanthoma<sup>(11)</sup> that could be found in 61.2 % of PBC cases<sup>(12)</sup> were not observed.

AMA is presumably the hallmark of PBC because it is found in around 90% - 95 % of patients with PBC<sup>(13)</sup> although only 61 from a hundred patients with positive AMA tests suffered from liver diseases; 36 with PBC, 19 with different liver diseases of other than autoimmune origin, and 4 with autoimmune hepatitis.<sup>(14)</sup> However, PBC patients with positive AMA mostly present the clinical, laboratory, and liver pathology features and response to treatment similarly to those with negative AMA.<sup>(15)</sup>

Anti-centromere antibody (ACA) is specific for the subset of systemic sclerosis, the so-called CREST syndrome (calcinosis, Raynaud's phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasia) with 25 % frequency.<sup>(16)</sup> However, it is also found in 30 % of PBC patients, 80 % of PBC/systemic sclerosis, and 90 % of limited cutaneous systemic sclerosis cases.<sup>(17)</sup> As for our case, she was initially screened for the causes of chronic hepatitis with a viral study, ANA, and serum copper and ferritin. When the ACA was found positive with high titer, it prompted us to explore autoimmune diseases of the hepatobiliary system and finally PBC was established.

The medical treatment of PBC is UDCA that can decrease the turning rate to the cirrhosis, relieve symptoms, and improve the biochemical response (alkaline phosphatase < 2 times of upper normal limit or decrease to < 40 %, or AST < 2 times of upper normal limit), that would be expected in 6 months or 1 year.<sup>(1)</sup> If not, obeticholic acid or fibrate should be added.<sup>(18)</sup> Our case seemed responsive to UDCA within 6 months, so no other drug was added.

## Conclusion

Primary biliary cholangitis was diagnosed in a Thai woman who had positive ANA, centromere pattern with high titer during having long term hepatitis without

other common causes. Besides the CREST syndrome, anti-centromere antibody should be used to remind a clinician to look for PBC in cases of persistent transaminitis with high levels of alkaline phosphatase.

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