Case Report

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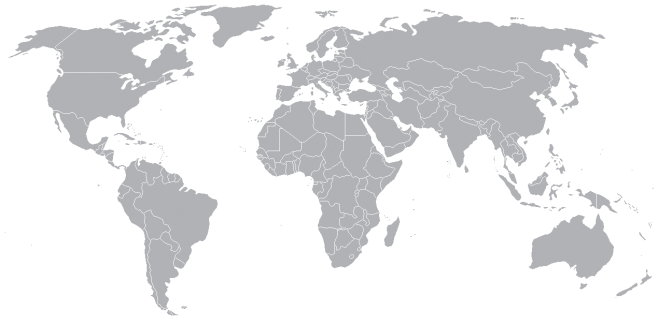

Role of genetics in the Primary Biliary Cirrhosis; with the presentation of the three sisters

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ABSTRACT
Objective: There is growing evidence of genetic susceptibility and environmental factors lead to primary biliary cirrhosis (PBC). In particular, family members of an infected individual can have higher risk of developing PBC. Here we present two of three siblings who did not have any clinical symptoms.
Case: Three siblings, who are 44, 53 and 51 years old respectively, were diagnosed as PBC. One of them excepted and the others were asymptomatic and the 44 years-old women has a known results of PBC such as icteric sclera, ascites, prolonged prothrombin time, elevated INR and splenomegaly. On the contrary, other two sibling did not have symptoms associated with PBC but the screening tests diagnosed PBC.
Discussion: In conclusion that familial PBC is not rare, that it is related to maternally inherited factors. PBC may be initially asymptomatic and therefore family screening is important in the early diagnosis and treatment.
Keywords: Primary biliary cirrhosis; genetic predisposition

INTRODUCTION

Primary biliary cirrhosis (PBC) is an autoimmune liver disease characterized by chronic inflammatory destruction and obliteration of septal and intrahepatic bile ducts and an infiltration of plasma cells and lymphocytes in the portal tracts histologically. It can occur with symptoms including fatigue, pruritus, rheumatic symptoms, skin hyperpigmentation, and right upper quadrant pain (1). Hallmark serologic feature of PBC is the presence of high titer anti-mitochondrial antibodies (AMA). It's peak incidence occurs in the fifth decade of life, and it is uncommon in persons under 25 years of age (2). Genetic, epigenetic, environmental, and infectious factors have been considered important for the development of the disease or its progression from early to advanced stages (3). We report a familial PBC case with three female siblings who lived under similar environmental conditions.

CASE REPORT

Forty-four-year-old sibling was presented with abdominal distension. Physical examination revealed pale conjunctiva, icteric sclera, ascites and splenomegaly. Cholestatic enzyme elevation, hypoalbuminemia, elongation of prothrombin time (PT) and increase at international normalized ratio (INR) were detected parameters at laboratory examinations. Abdominal ultrasonography (USG) showed rough and granular appearance liver, beyond ascites, splenomegaly and upper gastrointestinal tract endoscopy revealed esophageal varices However 53 and 51 year's old other siblings had itching as presenting symptom. Their physical examinations were normal. Laboratory investigations revealed cholestatic enzyme elevation. USG and upper gastrointestinal tract endoscopy findings were normal. AMA M2 was positive and viral hepatitis markers were negative in all cases. Liver biopsies revealed stage 4 PBC at 44-year-old patient and stage 2 PBC at 51 and 53-year-old patients. All three siblings were treated with ursodeoxycholic acid (UDCA) 15/mg/kg/day which resulted in resolution of elevated liver enzymes and disappearance of itching at 51 and 53-year-old patients. Forty four year old patient was managed by endoscopic variceal ligation for esophageal variceal bleeding and was also being treated with propranolol, rabeprazole and spironolactone as well.

DISCUSSION

Primary biliary cirrhosis (PBC) is a presumed autoimmune disease of the liver, which is most commonly diagnosed in women between the ages of 30 and 65. Evidence to date suggests that

immunological and genetic factors might cause the disease (4). However, the concordance of PBC among discordant twin pairs (5), the geographical pattern in prevalence rates (6), and the occurrence of clusters of the disease (7) indicate that environmental factors might contribute to break immunological tolerance and lead to the onset of PBC. Our cases were diagnosed as PBC under the same environmental impact. It has been reported that familial PBC is related to maternally inherited factors, and that the disease tends to present earlier in the

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second generation (8), and is most common in mother-daughter and sister-sister combinations (9). Although the disease is virtually identical in women and men, recent data suggest that X-chromosome monosomy in lymphoid cells is common in women with PBC (10). We diagnosed our patient as PBC then we reached the same diagnosis with clinical family screening in the other two sisters. Results were appropriate with the literature stated on female dominance. Therefore, compared to estimates in the general population, the prevalence of primary biliary cirrhosis in family members of patients with this disease is markedly increased (11). A family history of primary biliary cirrhosis is a predisposing factor for the development of this disease.

In conclusion that familial PBC is not rare, that it is related to maternally inherited factors. Despite all these PBC may be initially asymptomatic (12) and therefore family screening is important in the early diagnosis and treatment.

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