PRIMARY BILIARY CIRRHOSIS

An Autoimmune Liver Disease in Women

© Elaine Moore

This article describes the autoimmune liver disease primary biliary cirrhosis (PBC) including a description of the four disease stages, risk factors for and symptoms of PBC, diagnostic tests and treatment options.

What is Primary Biliary Cirrhosis?

Primary biliary cirrhosis (PBC) is an autoimmune liver disease causing liver inflammation and a gradual destruction of the intrahepatic bile ducts found within the liver. PBC interferes with the liver's ability to break down toxins and it causes cellular changes leading to cirrhosis.

Who is Affected?

PBC is usually diagnosed in people between ages 30 and 60 years, and its incidence peaks in the fifth decade of life. Caucasians from Northern Europe are at a particularly high risk, and 90-95 percent of all PBC cases occur in women. Up to 84 percent of people with PBC are reported to have another autoimmune disorder, and in about 20 percent of cases, the patient has an autoimmune thyroid disorder, usually hypothyroidism.

Environmental Triggers

Suspected environmental triggers for PBC include cigarette smoking, contaminated well water, certain viral or bacterial infections, including the HIV-1 retrovirus and the Epstein-Barr virus, and certain medications, including interferon, estrogen, and chlorpromazine (Thorazine).

Disease Course

Although PBC is considered a slowly progressive disorder, the rate of bile duct deterioration occurs in different rates and with varying degrees of severity in different patients. This article describes the four stages of PBC, symptoms seen in PBC, blood tests used to diagnose PBC, and available treatments.

PBC has four stages, based on cellular changes seen on liver biopsy. However, because the liver is not uniformly affected in PBC, patients can have changes characteristic of all four stages at the same time. Stages are described depending on the most advanced tissue changes seen. For instance, patients with stage 2, 3, and 4 changes will be diagnosed with stage 4 PBC.
Stage 1 changes include inflammatory changes in the portal triad; stage 2 changes include a reduced number of normal bile ducts, and inflammation extending beyond the portal triads into surrounding tissue; stage 3 fibrous changes, which are the first signs of impending cirrhosis, appear; stage 4 is defined by end-stage liver disease with frank cirrhosis and regenerative liver nodules.

Symptoms

A number of different symptoms are seen in PBC. However, at the time of diagnosis, about 60 percent of patients with PBC are asymptomatic, that is, they have no clinically apparent symptoms but are tested for PBC because of elevated liver enzyme levels. Because treatment instituted at this time can halt disease progression, patients who are diagnosed and treated early have a more favorable outcome. In patients who do have symptoms, the most common complaints are itching, which is more intense at night, and persistent fatigue.

Other symptoms in PBC include weight loss, enlarged liver, enlarged spleen, abdominal discomfort, abdominal bloating, bone loss, urinary tract infections in women, finger clubbing, ankle swelling, and depression. Signs of PBC include xanthelasmas, xanthomas, and severe scratching. Xanthelasmas are irregular yellow, fatty nodules or patches on the skin, especially near the eyes, related to elevated cholesterol levels. Xanthomas are similar skin deposits located in the creases of the hands, arms and legs or on the elbows and knees. Severe scratching is related to itching.

Other conditions likely to be seen in people with PBC include gallstones; portal hypertension; esophageal bleeding (varices); sarcoidosis (condition of granulomatous tumors found in the lungs, skin, liver, lymph nodes and bone); Raynaud's phenomenon (blanching or bluing of the hands when exposed to cold); vitiligo (white patches of skin); jaundice; bone loss; bone pain; increased bone fractures; diarrhea; and joint pain. Other autoimmune conditions likely to be seen in people with PBC include rheumatoid arthritis, autoimmune thyroid disease, systemic lupus, scleroderma, celiac disease, and overlap syndromes with autoimmune hepatitis.

Diagnosis

Patients with abnormal liver function tests and signs of bile duct disease are suspected of having PBC. To diagnose PBC, these individuals are tested for the anti-mitochondrial antibody (AMA). Although AMA can show up in low titers in other disorders including Graves' disease, titers of AMA of 1:40 or higher are considered indicative of PBC. Nearly all patients with PBC will have a positive AMA test. Antinuclear antibodies (ANA) are seen in about 50 percent of patients with PBC, including patients who do not have a positive AMA test. The nuclear-rim and nuclear-dot ANA patterns are considered highly specific for PBC.
When diagnosis is uncertain, bile duct imaging tests are used to see if other causes of biliary tract disease such as obstruction may be present. Liver biopsies are used to confirm diagnosis, determine disease severity, and identify the disease stage. Liver function tests are used to monitor disease severity, progression and treatment response. Increased bilirubin levels in PBC are considered a poor prognostic sign and an indicator of advanced disease.

**Treatment**

Patients with PBC are usually treated with medications that reduce itching, such as cholestyramine, rifampin, and ursodeoxycholic acid (ursodiol or UCDA). Ursodiol, which replaces the bile acids that are reduced as a consequence of PBC, is the only drug approved by the Food and Drug Administration (FDA) for the treatment of PBC. Ursodiol reduces progression to cirrhosis and is reported to be effective in up to 80 percent of patients, although it is not effective in patients with advanced disease. Other drugs used for PBC include colchicine, methotrexate, and budesonide.

The best treatment for PBC is still uncertain although ursodiol is considered the primary treatment when used early in the course of PBC. In advanced liver disease, liver transplantation is the only effective treatment. However, AMA are still present after liver transplant and can affect the transplanted liver, causing a recurrent cirrhosis in 30 percent of patients 10 years after transplant.

The copyright of the article PBC Update in Autoimmune Disease is owned by Elaine Moore. Permission to republish PBC Update in print or online must be granted by the author in writing.