PRIMARY SCLEROSING CHOLANGITIS

A Connection with Inflammatory Bowel Disease

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Primary sclerosing cholangitis (PSC) is an autoimmune liver disease that causes bile duct inflammation. PSC often accompanies other autoimmune disorders.

What is Primary Sclerosing Cholangitis?

Primary sclerosing cholangitis (PSC) is a chronic autoimmune cholestatic liver disease (affecting the liver’s ability to excrete bile). Primary sclerosing cholangitis is similar to the autoimmune disorder primary biliary cirrhosis except that in PSC the bile ducts both within and outside of the liver become narrowed due to inflammation and scarring. This interferes with their ability to excrete bile.

Because of the similarities between primary sclerosing cholangitis and primary biliary cirrhosis, patients with symptoms of primary biliary cirrhosis who show no evidence of the antimitochondrial antibodies characteristically seen in this disorder are diagnosed with autoimmune cholangitis, a collective term used to describe autoimmune liver diseases other than primary biliary cirrhosis that affect the biliary system.

Disease Course

The disease course is unpredictable in PSC, but overall it is considered a slowly progressive disorder. Symptoms may remain stable, occur intermittently or progress gradually. Over time, usually a decade or longer, liver failure may occur. And, rarely, patients with PSC may show rapid disease progression to hepatitis, cirrhosis, or fulminant liver failure. In addition, about 1 percent of patients with longstanding advanced cirrhotic liver disease may develop a superimposed tumor of the bile ducts called a cholangiocarcinoma.

Who is Affected?

Unlike most other autoimmune disorders, males are affected more often than females. The incidence of PSC is higher in African-Americans. Although patients of any age, including infancy, may be affected, the peak incidence occurs in the third and fourth decades of life. In recent years, the incidence of PSC in children has dramatically increased.

Other autoimmune disorders are frequently seen in patients with PSC. About 70 to 80 percent of patients diagnosed with primary sclerosing cholangitis have coexisting conditions of inflammatory bowel disease (IBD), and about 25 percent of patients have at least one autoimmune disorder not affecting the liver or colon. In addition, some patients...
may develop PSC after proctocolectomy surgery. About 2.5-7.5 percent of patients with IBD go on to develop primary sclerosing cholangitis. Individuals with primary sclerosing cholangitis may also go on to develop ulcerative colitis.

**Environmental Triggers**

Environmental agents suspected of triggering PSC include bacteria, toxins, viral infections (cytomegalovirus and reovirus), and vaccines.

**Symptoms and Signs**

Patients with PSC may be free of symptoms at the time of their diagnosis. In this case they are usually diagnosed based on abnormal blood test results, primarily elevated levels of the liver enzyme alkaline phosphatase and antibodies to perinuclear antineutrophil cytoplasmic antibodies (p-ANCA). Of interest, recent studies show the presence of p-ANCA antibodies in most patients with inflammatory bowel disease, suggesting a common link in disease development. Increased levels of immunoglobulin G (IgG) and immunoglobulin M (IgM) are also commonly seen in PSC. Early symptoms in patients with PSC include fatigue, itching, and jaundice. Episodes of fever and chills can occur if the bile ducts become infected.

Some patients may have elevated levels of circulating immune complexes, immunoglobulins, and autoantibodies that are not organ specific. Histological and clinical overlap syndromes may exist, particularly with autoimmune hepatitis.

In children, symptoms are highly variable. Patients often do not have symptoms but show liver function blood test abnormalities or an enlarged liver. Alternately, pediatric patients may present with fatigue, itching, fever, intermittent jaundice or weight loss. When progression to cirrhosis is rapid, patients may show evidence of portal hypertension, including accumulations of abdominal fluid (ascites), esophageal bleeding, and enlarged spleen.

**Diagnosis**

Primary sclerosing cholangitis is diagnosed in patients with signs of cholestatic liver disease, such as elevated alkaline phosphatase and gamma glutamyl transpeptidase (gamma GT or GGT) levels and underlying bile duct abnormalities. These abnormalities, are seen on liver biopsy studies along with sensitive imaging tests such as cholangiography, magnetic resonance cholangiography (MRC), ultrasonography, or MRI, which may be accompanied by endoscopy.

Results in PSC include a generalized beading and stenosis or narrowing of the intrahepatic (within the liver) and extrahepatic (outside the liver) biliary tree (bile duct system). However, ultrasound may be normal in as many as 50 percent of patients, and liver biopsy studies may be inconclusive. Therefore, cholangiography remains the criterion standard for establishing the diagnosis of PSC.
PSC, like primary biliary cirrhosis, can be categorized into four stages ranging from mild inflammation to cirrhosis depending on the degree of inflammation seen in tissue studies. However, the stage of PSC has no bearing on the disease course or progression.

**Treatment**

Treatment is directed at controlling symptoms, for instance, reducing symptoms in portal hypertension or reducing itching and malabsorption. None of the treatments used appear to affect the disease course.

Stents and endoscopic balloons are used to dilate the biliary tree. Ursodeoxycholic acid (UCDA) is used to reduce itching, and immunosuppressant medications are used to reduce inflammation. In advanced cases, orthotopic liver transplantation has been used successfully.

**Resources**


What is Primary Sclerosing Cholangitis? American Liver Foundation Information Sheet, 2006.

Elaine Moore, Primary Biliary Cirrhosis on Suite101, http://autoimmunedisease.suite101.com/blog.cfm/primary_biliary_cirrhosis

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