

## **LIVER ABNORMALITIES ASSOCIATED WITH SJOGREN'S SYNDROME**

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### **Introduction**

Sjogren's syndrome is a chronic, autoimmune disease that can affect a number of organ systems, including the lungs, kidneys and liver. When it comes to involvement of the liver, there are three different, separate and distinct liver diseases associated with Sjogren's syndrome: primary biliary cirrhosis (PBC), chronic active hepatitis of the autoimmune type and hepatitis C virus infection.

Both PBC and chronic active hepatitis of the autoimmune type are primary idiopathic immunologic autoimmune disorders; that is, the cause of either is not known. These diseases are manifestations of the body making antibodies against itself, against liver cells. Hepatitis C virus infection, on the other hand, is a distinct entity caused by the hepatitis C virus, a recently described virus.

### **Incidence of Liver Abnormalities**

It appears that the frequency of liver involvement in SS patients may be greater than once thought. A large study done in Europe in patients classified as having primary SS, defined, by these investigators, as symptoms limited to sicca syndrome (dry eyes and dry mouth), found that 25–30% of patients had abnormal liver blood tests. When these abnormalities were evaluated further, 10% of patients thought to have only primary SS were found to have primary biliary cirrhosis (PBC). Another 4% had chronic active hepatitis of the autoimmune type. The important aspect of this study is that even when patients are thought clinically just to have primary SS, they can, in fact, have either of these two autoimmune liver diseases.

### **Sjogren's Syndrome Associated Liver Diseases**

- **Primary Biliary Cirrhosis (PBC)**

This disease is characterized by immune-mediated destruction of small bile ducts inside the liver. We do know a great deal about the features of this disease, and we also have a treatment. One of the remarkable characteristics of the disorder, like many autoimmune diseases, is that it affects primarily females; the vast majority of patients, at least 85%, are women.

It is important to recognize that the disease starts at one point in time, perhaps when patients are in their 20s, 30s, 40s or 50s, and slowly develops over decades. The sequence of events and the order in which patients develop the various manifestations of the disease may vary somewhat, but it is clearly a chronic disease.

The predominant symptoms of primary biliary cirrhosis are itching and fatigue. The itching characteristically occurs all over the body, to varying degrees of intensity, with increased skin pigmentation in the areas of itching, frequently noticeable on the back. There may also be visible cholesterol deposits in the skin.

The simplest way to evaluate whether or not someone with itching has PBC is to perform a routine liver panel blood test. If the itching is caused by PBC, then the tests

will be abnormal. That's how we differentiate the itching of PBC from all the other many causes of itching.

Patients with PBC have abnormal liver blood tests with a distinct pattern, as well as abnormal liver biopsies characteristic of this disease. The liver biopsy tissue should be examined by a pathologist skilled in interpreting liver diseases. At least 20–30% of the patients I see with PBC have had previous liver biopsies that have not been read correctly by the pathologist, simply because the pathologist was not thinking of PBC.

The treatment available for PBC, ursodeoxycholic acid (Actigall), is moderately effective, although its effect on long-term survival, at this point, is not known. Actigall is effective, however, in relieving the symptoms and the biochemical abnormalities of PBC. Use of Actigall began experimentally in this country in 1983, although, prior to that time it had been used in Europe and Japan for other conditions. To my knowledge, there have been no reports of any serious side effects with Actigall. Should the patient's disease advance to the point of requiring liver transplantation, PBC patients, fortunately, do very well.

Regarding the frequency of Sjogren's syndrome in patients with PBC, about one third of patients have symptoms of dry eyes and dry mouth, and about 40% have antibodies characteristically found in Sjogren's syndrome. In a few studies, when more extensive evaluation was done with biopsies of salivary glands, abnormalities were found in 95% of the patients. So, although it may not be clinically obvious, microscopic evidence of Sjogren's syndrome may be very common in patients with PBC.

- Chronic Active Hepatitis of the Autoimmune Type

This liver disease also affects primarily females, in that 85% of the patients are women. It is characterized by abnormal liver blood tests and characteristic features on liver biopsy. Most patients have nuclear antibody and smooth muscle antibody. At least 50% have extrahepatic abnormalities of the skin, arthritis, or Sjogren's syndrome. Immunosuppressive medications are usually very effective in controlling this liver disease.

- Hepatitis C Virus Infection

The third distinct liver disease associated with Sjogren's syndrome is the newly recognized hepatitis virus infection, hepatitis C. For many years, physicians recognized hepatitis occurring after blood transfusion and in IV drug abusers. It was thought to be due to a chronic viral infection. Through sophisticated molecular biology techniques, the virus was identified only five years ago and named hepatitis C virus.

This infection, in humans, almost always becomes chronic, that means the individual cannot get rid of it. Only about 60% of patients with chronic hepatitis C virus infection have abnormal liver blood tests. The others have the infection without abnormalities in liver blood tests, but on liver biopsy, abnormalities of the liver can be found. This chronic infection goes on to progressive liver disease and can result in liver failure. A treatment, alpha interferon, is successful in at least 10–20% of patients.

Since identification of this virus is so recent, a great deal still needs to be understood about its relationship to Sjogren's syndrome. Hepatitis C is diagnosed by the presence of the antibody to the hepatitis C virus in the blood. In one study of 49 patients

with hepatitis C virus infection, salivary gland biopsies were taken to determine if there was evidence of Sjogren's syndrome in the salivary glands. About half of the patients had what was described as lymphocytic capillaritis, an abnormality that is somewhat different from the features seen in classical Sjogren's syndrome. Only a small number of the original group actually had sicca syndrome or the characteristic antibody.

Work on hepatitis C is just emerging, but I suspect that as time passes and we have the opportunity to look at patients with hepatitis C virus infection more carefully, we will identify more Sjogren's syndrome.

### **Diagnosis**

If you are a patient with Sjogren's syndrome and concerned about liver involvement, ask your doctor if specific liver blood testing has been done. A Sjogren's syndrome patient with any liver blood test abnormality should be evaluated further.

Not all doctors are familiar with these specific liver diseases. If your doctor leaves you with questions about whether or not you have a liver problem, and you have abnormal liver blood tests, then it's best to see a gastroenterologist who has been specifically trained in liver disease and can answer those questions. An abnormal liver test, by definition, means there is something wrong with the liver, but sometimes, only a specialist can determine what the problem is, whether it is serious, whether it is related to Sjogren's syndrome and what else needs to be done. In some cases, the abnormality may be due to medications.