Autoimmune Hepatitis

An Autoimmune Liver Disease with Three Subtypes

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Hepatitis is a liver disease characterized by either inflammation or destruction of liver cells. Its causes include drug overdoses, alcohol abuse, viral and bacterial infections, plant and chemical toxins, idiosyncratic reactions to certain drugs, and the autoimmune condition known as autoimmune hepatitis (AIH).

What is Autoimmune Hepatitis?

Autoimmune hepatitis is an autoimmune condition with a disease course similar to that of viral hepatitis. The only way to differentiate autoimmune hepatitis is with laboratory tests. In AIH patients have increased blood levels of gamma globulin and one or more autoantibodies that target the liver.

Who is Affected?

Women represent about 80 percent of all cases of AIH and two major age groups are affected: young people between ages 10 and 20 years; and people older than 55 years. Up to 17 percent of patients with AIH have a second autoimmune disorder, predominantly autoimmune thyroid disease, including both Hashimoto's thyroiditis and Graves' disease. Other autoimmune conditions that coexist with AIH include pernicious anemia, autoimmune hemolytic anemia, rheumatoid arthritis, Sjogren's syndrome, ulcerative colitis, myasthenia gravis, glomerulonephritis, celiac disease, vitiligo, and type I diabetes.

AIH is found worldwide. In the United States, at any given time, approximately 100,000-200,00 cases typically occur with AIH accounting for about 11-23 percent of all cases of chronic liver disease. Occasionally, a prolonged or relapsing condition of hepatitis A may be confused with autoimmune hepatitis.

Environmental Triggers

Environmental triggers of AIH include: the hepatitis A, B, and C viruses; the Epstein-Barr virus (EBV) and the measles virus; Salmonella and Escherichia coli bacteria; the medications halothane, interferon, minocycline, melatonin, alpha methylldopa, oxyphenistatin, and nitrofurantoin; and the herbs black cohosh and Dai-saiko-lo. Interferon therapy used for hepatitis C has occasionally been found to induce latent autoimmune hepatitis.

Symptoms and Signs

The symptoms of hepatitis are the same regardless of the specific type or cause of liver inflammation. Overall, symptoms and signs of hepatitis include fatigue, enlarged liver,
enlarged spleen, jaundice, which is a yellowing of the skin and eyes, low platelet count, fever, malaise, joint pain, nausea and vomiting. In addition, patients with AIH may have acne, puffy facial features, hirsutism (increased facial hair), obesity, pigmented abdominal striae or stretch marks, and absent or decreased menstrual periods. Blood levels of liver enzymes are typically elevated, and in patients with jaundice bilirubin levels are also elevated. Before bilirubin levels become elevated in the blood, bile may be detected in the urine. A positive bile result in a urinalysis assay is often the earliest sign of hepatitis.

**Subtypes and Disease Course**

AIH has three distinct subtypes, types I, II, and III. About 10 percent of patients with AIH, especially patients with subtype I, usually have mild symptoms that wax and wane and spontaneously resolve. Most patients, however, develop a chronic form of AIH that persists, and without treatment, can progress to cirrhosis.

**Autoantibodies**

Autoantibodies seen in AIH include: antinuclear antibody (ANA) with a homogenous pattern primarily seen in subtype I; antibodies to double-stranded DNA (anti-dsDNA); anti-smooth muscle antibody (anti-SMA) primarily seen in type I; anti-liver-kidney microsomal antibody (anti-LKM-1) primarily seen in type II; anti-soluble liver antigen (anti-SKA) primarily seen in type III. Some patients with AIH may also have rheumatoid factor and antiphospholipid antibodies.

**Type I Autoimmune Hepatitis**

Type I AIH primarily affects two specific age groups: young patients between 10-20 years, and adults between the ages of 45 and 70 years. Up to 40 percent of Type I patients have another autoimmune disorder and most patients show a favorable response to steroid medications. About 45 percent of patients with Type I AIH eventually experience liver changes that progress to cirrhosis.

Type I AIH usually have markedly elevated gamma globulin levels; positive smooth muscle antibody (SMA) test results; positive antinuclear antibody (ANA) levels; positive double-stranded (ds) DNA antibody titers; positive perinuclear anti-neutrophilic cytoplasmic (p-ANCA) antibodies; and antiasialoglycoprotein receptor antibodies (anti-GSPR).

**Type II Autoimmune Hepatitis**

Patients with Type II AIH, which primarily affects children between 2-14 years, generally have a more severe course. Type II AIH is rarely seen in adults. About 82 percent of patients with Type II AIH eventually progress to cirrhosis. This may be because their response to steroids is less favorable than that of patients with subtypes I
and III AIH. About 35 percent of patients with Type II AIH have a concurrent autoimmune disease.

Patients with Type II AIH typically have positive test results for LKM type 1 or type 3 antibodies although their test results for ANA and SMA antibodies are negative. In addition, patients with Type II AIH who have antibodies to cytochrome P450 1ID6 are classified as having subtype IIa AIH. These patients, usually children, show a more favorable response to steroid therapy than other patients with Type II AIH. Unlike patients with Type I or III AIH, however, these patients do not experience remission when steroids are withdrawn.

**Type IIb Autoimmune Hepatitis**

Another subtype of Type II AIH known as subtype IIb occurs in older men and is associated with a prior history of hepatitis C virus (HCV) infection. Patients with this subtype are likely to have severe symptoms that are related to chronic HCV infection. Although they do not usually have the cytochrome antibodies seen in Type IIa, patients with subtype IIb AIH show a more favorable response to steroid treatment than other patients with Type II AIH.

**Type III Autoimmune Hepatitis**

Patients with Type III AIH do not have the typical liver autoantibodies seen in patients with Type I AIH. However, some patients with Type III AIH have antibodies to soluble liver kidney antigen cytokeratins 8 and 18 (anti-SKA) or antibodies to soluble liver antigen/liver pancreas (anti-SLA or anti-SLP). About 55-60 percent of these patients have another autoimmune disorder, and about 70 percent of these patients respond favorably to steroid treatment.

**Diagnosis and Treatment**

Autoimmune hepatitis (AIH) is suspected in patients with abnormal liver function test results or symptoms typical of hepatitis who show no evidence of viral hepatitis. Three basic subtypes or varieties of autoimmune hepatitis (AIH) exist: Types I, II, and III. The particular subtype someone has determines the disease course and the best treatment approach. Overall, Type I AIH is the most common type, and AIH occurs in about 8 times as many women as men.

Treatment for patients with AIH, regardless of the subtype, consists of corticosteroids, such as prednisone, which mildly suppress the immune system and reduce inflammation. In about 70 percent of patients, usually patients with Types I or III AIH, the disease goes into a remission with a decrease in symptom severity within two years of starting treatment. If a relapse or return of symptoms occurs, the corticosteroids are resumed. The general rule is to withdraw or taper the steroid dose as liver function tests and gamma globulin levels return to the normal range.
Because corticosteroids can cause a number of undesirable side effects with prolonged use, other immunosuppressant medications may be used along with steroids as corticosteroid-sparing agents to reduce the steroid dose and help relieve symptoms of appetite loss, fever, and fatigue. Other immunosuppressant medications used in AIH include azathioprine, which is considered a mainstay along with prednisone, and also 6-mercaptopurine, cyclosporine, mycophenylate mofetil, and tacrolimus. Patients with suspected viral hepatitis who are treated with interferon typically have a worsening of AIH symptoms. For this reason, proper diagnosis of AIH is important.

In patients with rapidly progressive liver disease and severe symptoms, liver transplants are often recommended in the early disease stages to prevent complications from developing. However, because the autoimmune course of AIH is not improved with transplants, disease symptoms can recur in the grafted tissue. Transplantation has a 1-year survival rate of 90 percent, and a 5-year survival rate of 70-80 percent.


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