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IMPROVEMENT OF LABORATORY DIAGNOSIS OF AUTOIMMUNE HEPATITIS

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ABSTRACT

Autoimmune hepatitis is a complex disease with various clinical, laboratory and histological symptoms. Autoimmune hepatitis is characterized by the presence of hypergammaglobulinemia and autoantibodies against hepatocytes. Timely diagnosis and proper treatment of autoimmune hepatitis leads to remission and prevents the development of liver cirrhosis.

Keywords: autoimmune hepatitis, pathogenesis, laboratory diagnostics.

Many pathogenetic aspects of pathogenetic disorders in chronic liver diseases remain unexplored [18, 27, 31]. One of the most common causes of chronic hepatitis and liver cirrhosis is infection with hepatitis B and C [20, 28, 30]. At the same time, more than 180 hepatotoxic drugs have been identified, of which 6 groups seriously injure the liver. At the same time, 50% of drugs are hepatotoxic, especially in women this effect is more pronounced. Medicines cause hepatocellular damage, even liver necrosis, which is clinically manifested mainly by jaundice, fever, and increased liver enzymes [6].

Over the past two decades, autoimmune diseases of the liver have received increasing attention [17, 29]. Autoimmune liver diseases include primary biliary cirrhosis, primary sclerosing cholangitis, and autoimmune hepatitis (AIG) [8].

AIG is an autoimmune liver disease first described by Waldenstrom in 1953 [16]. AIG can develop at any age, gender, and in all ethnic groups. AIG is a complex disease characterized by a significant diversity of clinical, laboratory and histological manifestations [22].

Autoimmune hepatitis is a complex disease, which is characterized by the presence of hypergammaglobulinemia and autoantibodies against hepatocytes [40]. Autoimmune hepatitis (AIG) is a disease characterized byhypergammaglobulinemia, the presence of autoantibodies against hepatocytes in the blood, morphological signs of hepatitis in histological examination, and a positive response to immunosuppressive therapy [12].

At present, the etiopathogenesis of AIG has not been fully studied, because the main factor in the pathogenesis of AIG is genetic predisposition. The importance of measles viruses, hepatitis A and C viruses, Epstein-Barr virus, and some drugs in the development of AIG has also been mentioned in the literature. At the same time, changes in the primary immune response caused by impaired T-cell immune responses against hepatocyte antigens also lead to the development of AIG[1].

AIG is characterized by progressive hepatocellular inflammation and necrosis that can lead to liver cirrhosis. When diagnosing the disease, alcoholic, toxic, viral hepatitis or genetic liver diseases should be ruled out [13].

The body's immune response works against its own cells [24]. AIG is usually progressive and leads to serious complications [21].

In many cases, patients with a predisposition to autoimmune diseases can develop AIG after infection with the hepatitis virus. This is explained by the subclinical progression of AIG, and when viral hepatitis develops, the disease worsens. At the same time, the presence of hypergammaglobulinemia in AIG can also give a false positive result for viral hepatitis. There are also reports of the development of AIG in some patients after alpha-interferon antiviral therapy for the treatment of chronic viral hepatitis C. Currently, there is an interferon-free treatment strategy for chronic viral hepatitis C, which significantly facilitates treatment, and modern antiviral therapy is characterized by a low number of complications [4].

Clinical manifestations of AIG vary from asymptomatic to fulminant transient hepatitis, depending on the degree of liver cell damage. In 25% of patients, the disease appears without symptoms [3].

In the initial period of the disease, nonspecific complaints such as fatigue, nausea, pain in the abdomen and arthralgia are observed, and AIG is detected incidentally in functional tests of the liver. Some patients show an increase in ALT, AST, sometimes with signs of cholestasis (increased alkaline phosphatase, gamma-glutamyltranspeptidase). In 30% of patients, the disease develops in the form of jaundice, exacerbation of liver diseases, liver cell failure. In one third of patients, portal hypertension syndrome is detected at the stage of liver cirrhosis with symptoms of gastrointestinal bleeding, because the disease is asymptomatic for a long time and is diagnosed only in advanced complications[7].

Autoimmune damage to several organs and tissues in the patient at the same time complicates the process of diagnosis and treatment of AIG. In 25% of cases, patients may have autoimmune thyroiditis, rheumatoid arthritis, systemic lupus erythematosus and other autoimmune diseases simultaneously with autoimmune hepatitis [9].

According to the research of Efe C. and co-authors, 56.4% of patients with autoimmune liver cirrhosis have two, 32.3% three, and 11.3% four autoimmune diseases at the same time. 18.3% of cases had autoimmune thyroiditis. Rheumatoid arthritis, vitiligo, and systemic lupus erythematosus have also been identified [11].

Even now, the diagnosis of AIG is a significant challenge. Exclusion of viral hepatitis V and C, alcoholic hepatitis, and drug-induced liver damage is often the main approach to the diagnosis of AIG [2].

AIG is characterized by hypergammaglobulinemia and an increase in serum IgG. Depending on the level of IgG, the effectiveness of the treatment of AIG can be evaluated. Biochemical changes are not considered a special sign, because these signs can also be found in other liver pathologies. However, despite the histological activity of the autoimmune process, blood biochemical indicators may be normal, which cannot adequately assess the disease state. Therefore, an important part of the diagnostic examination is the identification of autoantibodies. The presence of autoantibodies is important in the diagnosis and classification of AIG. Approximately 70-80% of patients with AIG have antinuclear antibody (ANA) and anti-smooth muscle antibody (SMA) titers of 1:40 or higher. About 34% of patients have an antibody titer <1:40 for type 1 liver and kidney microsomes, and in 20% of patients these antibodies are undetectable [15].

Depending on the antibodies detected, AIG is divided into two types: AIG type 1, which is characterized by an increase in the amount of ANA, anti-smooth muscle antibody (SMA) in the

blood, and AIG type 2, which is characterized by an increase in the amount of LKM1 or anti-LC1. Anti-SLA occurs in both type 1 AIG and type 2 AIG. Type 1 AIG occurs between the ages of 10 and 20 or 45 to 70 years, while type 2 AIG is more common in children between the ages of 2 and 14 [1].

Type first AIG is common and accounts for 85% of all AIG cases. It is characterized by persistent positive serological reactions to ANA and, in many cases, SMA titers of 1:40 or more. Along with SMA, anti-actin antibodies, especially anti-f-actin, are diagnostic of AIG. Anti-f-actin antibodies to actin are undetectable in most clinical laboratories, and anti-f-actin is always present when the SMA titer is 1:320 or higher. In addition, primary sclerosing cholangitis-specific perinuclearantineutrophil cytoplasmic antibodies (RANCA) may also be detected. The titer of RANCA in the blood increases together with the titer of anti-f-actin. ANTI-SLA (antibodies against soluble liver antigen) and ANTI-LP (antibodies against liver-pancreatic antigen) are detected in 10% of AIG type 1 [5].

To date, according to all clinical guidelines, a liver biopsy is considered necessary for the diagnosis of AIG. It is necessary to determine the level of autoimmune inflammation of the liver, the stages of liver fibrosis, and to evaluate the outcome of treatment [21].

The diagnosis of the disease is mainly made after exclusion of other liver diseases after clinical, biological, immunological and histological examinations [10].

In patients with AIG, the goal of therapy is to prevent cirrhosis. In patients with AIG, the timely use of the correct treatment tactics leads to remission, but constant immunosuppressive therapy is required. 50% of patients may develop liver cirrhosis despite the therapeutic effect of corticosteroids [14].

In the acute period of AIG, the risk of liver failure and infectious complications prevails. Complications of immunosuppressive therapy and liver cirrhosis increase during long-term treatment. A recent study showed that patients with AIG had a higher risk of malignant neoplasms outside the liver. In these patients, non-melanoma skin cancer was 5%. Therefore, it is recommended to monitor patients with AIG with liver cirrhosis and to undergo ultrasound examination of the liver every 6 months. [23]. Timely diagnosis of chronic hepatitis and liver cirrhosis and appropriate will reduce the risk of many complications [19, 25, 26].

In conclusion, AIG remains hepatitis of unknown etiology, because many medical institutions do not have special examination methods, and one third of patients are referred after the development of liver cirrhosis. Autoimmune hepatitis can be suspected in any patient with acute or chronic liver disease. 80% of patients have a recurrence of the disease after canceling the treatment.

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