UDC 616.36-092:612.017.1]-036

HEPATIC AUTOIMMUNE DISEASES: SEVERAL ASPECTS OF OVERLAP SYNDROMES

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Annotation: autoimmune liver diseases include autoimmune hepatitis (AIH), primary biliary cirrhosis (PBC), primary sclerosing cholangitis (PSC). The theses highlight some aspects of the cross-syndromes (overlap syndromes) of AIH / PBC and AIH / PSC. The data on clinical symptoms, biochemical, serological, histological criteria that allow to verify the cross syndromes of AIH / PBC and AIH / PSC are presented. Attention is also drawn to the results of magnetic resonance cholangiography. The importance of timely diagnosis of cross syndromes in autoimmune liver diseases lies in the timely correction of immunosuppressive therapy and a change in the prognosis of the disease.

Key words: autoimmune hepatic disorders, antinuclear antibodies, antimitochondrial antibodies, cell antibodies smooth muscle, autoimmune hepatitis (AIH), primary biliary cirrhosis (PBC), primary sclerosing cholangitis (PSC), autoimmune cholangitis (AIC).

Among autoimmune liver diseases, nosological forms are distinguished that have clinical, biochemical, serological and / or histological signs of AIH, symptoms of autoimmune cholestatic disease, PBC, PSC or autoimmune cholangitis (AIC). These symptoms are referred to as overlap AIH / PBC and AIH / PSC. Symptoms of AIH are always identified with these cross-symptoms. Clinical symptoms are intermittent, signs of one or another component of the cross syndrome may prevail, while mild

symptoms of the second component of the syndrome remain [1, p. 2088]. The criteria for overlap syndromes are not clearly defined..

Overlap syndromes between AIH and the pathology that is accompanied by cholestasis (PBC, PSC) is characterized by a progressive course, leading to cirrhosis and liver failure [2, p. 81]. Markers of these syndromes in combination with AIH are considered an increase in the level of alkaline phosphatase (ALP) or the determination of antimitochondrial antibodies (AMA). The lack of results from AIH treatment, which was previously effective, may be the result of joining cross syndrome. In PSC, inflammation of the intrahepatic and extrahepatic bile ducts can be associated with autoimmune diseases of the intestine [3, p. 689]. The diagnosis of overlap syndrome is established if there are clear clinical criteria for AIH and PBC or AIH and PSC. With AIH / PBC, symptoms of PBC are more likely to appear at first, and later signs of AIH join..

AIH with the presence of cholestasis syndrome may be accompanied by damage to the nuclei of cholangiocytes, while the processes of fibrosis progress. PSC and AIC are significant progressive cholongiopathies [4, p. 1593].

Histological examination of liver biopsy specimens more often allows secondary AIH to be recognized in patients with primary cholestatic syndrome. A histological activity index above 4 is usually observed in patients with overlap [5, p. 334]. AIH / PBC is associated with HLA B8 DR3, DR4. Typically, the presence of AMA, antinuclear antibodies (ANA) and antibodies to smooth muscle cell antibodies (SMA).

With AIH / PBC, an increase in the level of aspartate aminotransferase (AST), alanine aminotransferase (ALT) and gamma globulins (characteristic for AIH), as well as an increase in the level of alkaline phosphatase and class M immunoglobulin (IgM), are determined. In 95% of patients with AIH / PBC, AMA, the main marker of PBC, is determined [6, p. 25]. In some patients, in the presence of typical clinical, biochemical, serological and histological signs of PBC, the AMA characteristic of this disease is not detected, but ANA and SMA can be detected. This condition is defined as autoimmune cholangitis (AIH). In the presence of these changes and in

combination with signs of AIH, a separate cross-section AIH / AIC syndrome is sometimes isolated..

Diagnostic criteria for cross-syndrome AIH / PBC::

1) the presence of two or three manifestations of AIH;
2) increased activity to 5 or more norms;
3) increase in IgG level to two or more norms or detection of SMA;
4) according to the results of a histological examination after a liver biopsy, the identification of portal and periportal lymphoplasmocytic infiltration, periportal step and bridge necrosis;наличие двух или трех проявлений PBC;
5) increasing the activity of alkaline phosphatase to two or more norms or gamma-glutamyltranspeptidase (GGTP) to 5 or more norms;
6) AMA detection;
7) according to the results of a histological examination after liver biopsy, periductal infiltration of the portal tracts and destruction of the bile ducts..

A meta-analysis evaluated the diagnostic significance of ANA in patients with AMA-negative PBS. It was shown that ANA have high specificity, but low sensitivity in this pathology [7, p. 959].

In the diagnostic titer, ANA and pANSA are determined with type 1 AIH, and SMA with AIH; hypergammaglobulinemia is simultaneously detected. The presence of HLA B8, DR3, DR4 in patients more often suggests the need for enhanced immunosuppressive therapy, and HLA B8 is a risk criterion for the progression of PBC, and therapy should be continuous. Cross-AIH / PSC syndrome is characterized by the presence of typical histological signs of AIH and PSC (detected by magnetic resonance cholangiography (MRC) or by histological examination). More often at the beginning there are signs of AIH, and much later PSC criteria are determined. The antibody spectrum reflects type 1 AIH. With the progression of the disease, clinical symptoms join the clinical and serological signs of AIH and biochemical criteria for cholestasis appear, with histological examination, fibrotic duct changes.

If the next course of immunosuppressive therapy with AIH was ineffective, the development of PSC should be excluded among the main reasons. Often, the

diagnosis of AIH / PCH is established after MRC in patients with AIH. Typical changes in the intrahepatic bile ducts are detected. In this category of patients, positive ANA typical for AIH in the diagnostic titer and / or SMA, hypergammaglobulinemia, step necrosis, lymphocytic rosettes, moderate or severe periportal or periseptic inflammation according to histological examination after biopsy are determined.

An increase in the level of alkaline phosphatase and ring-shaped structures around the intrahepatic bile ducts is also determined according to MRC, which is typical for PSC. If these changes are not visualized on MRC, then the term small duct cholangitis is used instead of PSC, the diagnosis is confirmed by the results of a histological examination after a liver biopsy. The prognosis for AIH / PSC cross syndrome is more favorable than for isolated PSC, but worse than for isolated AIH.

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