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Variations of Lung Damage in Autoimmune Liver Diseases

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Abstract

Such pathologies as primary biliary cholangitis, primary sclerosing cholangitis and autoimmune hepatitis are recognized as primary autoimmune liver diseases. According to the results of numerous studies and observations over the past decades, it has been recognized that in addition to lesions of the organs of the hepatobiliary system, there are extrahepatic manifestations of the above diseases, namely, lung lesions in the form of focal and interstitial changes. There is also the possibility of their progression with the development of fibrosis and respiratory failure. Currently, the issue of studying autoimmune liver diseases as systemic with multiple organ lesions is being discussed. There is a possibility of a long-term asymptomatic course of the pulmonary process with the development of irreversible changes in patients with autoimmune liver diseases, therefore, it is considered rational to conduct screening studies that allow timely identification and appropriate therapy of this pathology.

Discipline: Medicine.

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1 Introduction

Autoimmune liver diseases are a heterogeneous group in which three main nosological forms are distinguished: autoimmune hepatitis, primary biliary cirrhosis, and primary sclerosing cholangitis [1]. The cause is immune-mediated damage to liver cells - hepatocytes and bile duct cells, which may result in liver failure or cirrhosis of the liver [2]. Over the past decades, many studies have been conducted, according to which it can be concluded that there is a high probability of the development of extrahepatic manifestations of the above autoimmune diseases, namely, damage to the pleura, lungs, and intra-thoracic lymph nodes. Based on these data, we can conclude about the systemic nature of diseases with multiple organ damage [3-5]. It should be noted that when detecting respiratory manifestations in a patient with autoimmune liver disease, differential diagnosis with sarcoidosis, IgG4-associated disease or other autoimmune pathologies is necessary [6]. Some difficulties in differential diagnosis may cause similar clinical and radiological signs, in order to exclude errors, this issue should be approached comprehensively. It would be rational to take a lung biopsy with a further histological, biochemical and morphological examination of the biopsy [7].

Next, options for damage to the respiratory system in the main nosological forms of autoimmune liver diseases will be considered.

2 Cases of Damage in Autoimmune Hepatitis

Autoimmune hepatitis is understood as unresolved inflammation of the liver of unclear etiology, which is characterized by an immune response directed against the liver tissue, which leads to the destruction of the liver parenchyma [8]. This pathology is accompanied by an extensive inflammatory process and the presence of tissue autoantibodies. It is worth noting that in the vast majority of cases there is a response to immunosuppressive therapy. The female sex is considered more predisposed to the disease [9]. The clinic of autoimmune hepatitis is not specific, it is accompanied by astheno-vegetative disorders, joint pain, abdominal pain and jaundice [10,11]. The onset of the disease may be asymptomatic: it is noted in 25% of patients. If we talk about extrahepatic manifestations of autoimmune hepatitis, then we should note isolated clinical cases of interstitial lung diseases, namely lymphocytic interstitial pneumonia and pulmonary fibrosis [12,13]. According to current statistics, respiratory manifestations in autoimmune hepatitis are much less common than previously thought. Therapy with glucocorticosteroids and immunosuppressive drugs successfully reduces the likelihood of pulmonary pathologies [14,15].

3 Cases of Damage in Primary Sclerosing Cholangitis

Primary sclerosing cholangitis refers to idiopathic cholestatic liver disease [16]. The bile ducts are involved in the inflammatory process. Cholestasis is the outcome of granulation tissue formation and fibrous changes (Figure 1).

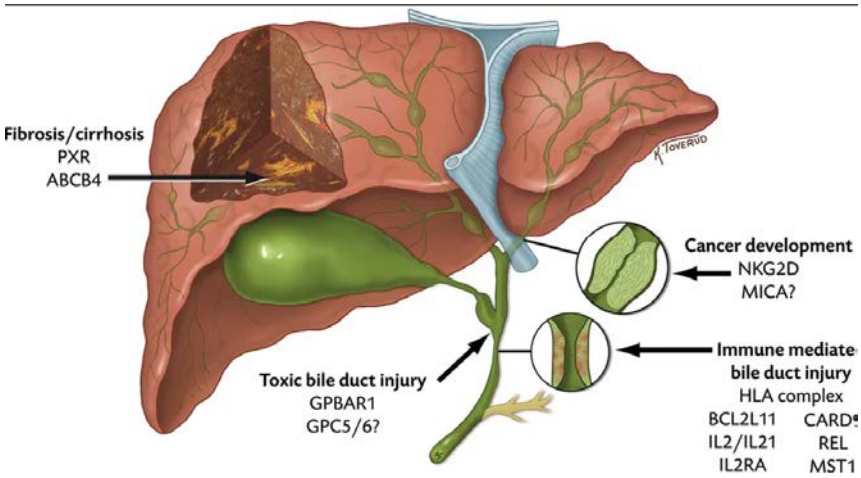

Figure 1: Formation of granulation tissue and fibrous changes

The male sex is more susceptible. An important aspect is intestinal diseases, in particular, ulcerative colitis, in 70-80% of cases it precedes the formation of an autoimmune process in the liver [17]. To confirm the diagnosis of primary sclerosing cholangitis, it is necessary to conduct an endoscopic examination for the presence of corresponding sclerotic or fibrous changes in the bile ducts (Figure 2) [8, 9].

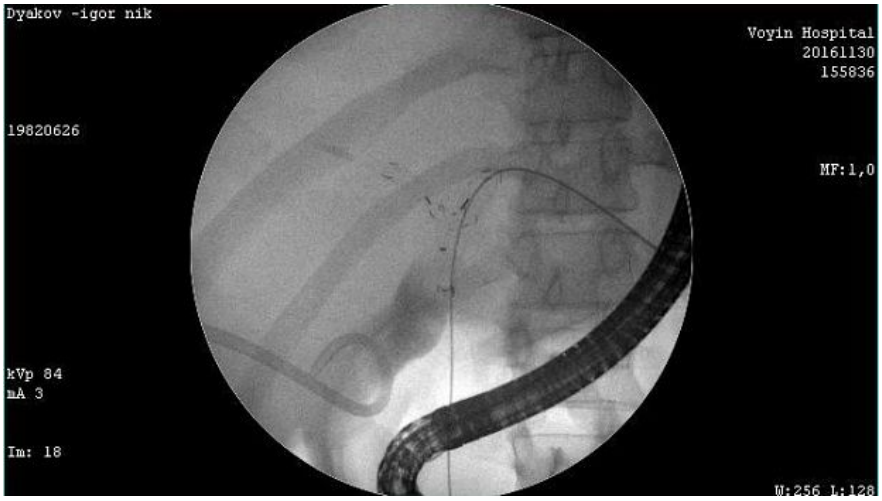

Figure 2: Endoscopic examination for the presence of appropriate sclerotic or fibrous changes in the bile ducts

Lung lesions in primary sclerosing cholangitis are similar to sarcoidosis, and may manifest as the development of interstitial fibrosis, developing pneumonia and hemorrhagic alveolitis [18-20]. To date, there are no uniform clinical recommendations for the effective treatment of respiratory manifestations of this autoimmune liver pathology, but there are a number of studies based on the results of which it is possible to judge the success of the use of glucocorticosteroids and cytostatics. Difficulties in forming a single method of successful therapy lie in the rarity of this pathology, which does not allow for detailed clinical studies [21-25].

4 Cases of Damage in Primary Biliary Cholangitis

Primary biliary cholangitis is a chronic autoimmune liver disease, the outcome of which is cirrhosis and liver failure. This is caused by the inflammatory process, destruction of liver cells and

fibrosis. Middle-aged women are more susceptible to this pathology. This is a case of family inheritance of the disease, it occurs in 4% of first-line relatives and in 63% of identical twins, the risk in the sisters of patients is 14 times higher than the population [26]. There are 3 criteria proposed by the American Association for the Study of Liver Diseases, according to which a diagnosis of primary biliary cholangitis can be established [27]:

1) prolonged (>6 months) cholestasis with increased activity of alkaline phosphatase and/or gamma-glutamyltransferase in blood serum;

2) antimitochondrial antibodies (AMA) in titer >1:40 or AMA-M2 antibodies in any titer;

3) the presence of histological signs of primary biliary cholangitis according to liver biopsy, namely chronic non-purulent destructive cholangitis, often granulomatous, in combination with the destruction of the interlobular bile ducts.

Based on the presence of at least two of the three possible criteria, a diagnosis of primary biliary cholangitis can be fully established. Another important aspect of the correct diagnosis is the exclusion of obstruction [28].

Interstitial lung disease should be attributed to the most common respiratory manifestation of primary biliary cholangitis, but there are also other manifestations listed below [29].

1. Gas exchange disorders.
2. Subclinical alveolitis.
3. Interstitial lung disease:
    - pulmonary fibrosis,
    - lymphoid interstitial pneumonia,
    - nonspecific interstitial pneumonia,
    - obliterating bronchiolitis with developing pneumonia,
    - granulomatous lung disease.
4. Respiratory tract disease.
5. Pulmonary hypertension.
6. Pulmonary bleeding.
7. Pleural effusion.

According to observations, hepatic manifestations of the disease make their debut earlier than extrahepatic ones, however, reverse cases also occur [30].

5 Conclusion

Autoimmune liver diseases can be the cause of various variants of lung pathology, from this it can be concluded that an integrated approach to the diagnosis and therapy of patients in this group is necessary. An important aspect is the control of patients in dynamics due to the high probability of delayed development of pathology of the respiratory system. Due to early diagnosis, timely therapy is possible, which reduces the risk of extrahepatic complications. To date, the variants of lung damage in primary biliary cholangitis are the most studied in comparison with other autoimmune liver lesions. The above-mentioned pathology has a high risk of developing

interstitial lung diseases, therefore it is advisable to recommend a computed tomography of the chest, as well as various tests to assess the functional state of the lungs for the earliest detection of possible lesions of the respiratory system. In the future, research results may also be obtained that will improve approaches to the diagnosis of extrahepatic manifestations in autoimmune hepatitis and primary sclerosing cholangitis. In autoimmune liver lesions, pulmonary lesions have pronounced polymorphism, but the question of the effectiveness of immunosuppressive therapy is still insufficiently studied at present.

6 Availability of Data and Material

Data can be made available by contacting the corresponding author.

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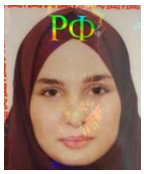

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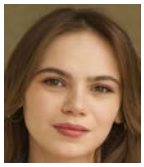

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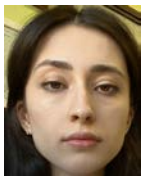

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