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Literature Data on the Effect of Ulceral Colitis on the Liver

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Abstract: Liver diseases can be a complication of inflammatory bowel disease (IBD), such as ulcerative colitis (UC) or Crohn's disease. The liver, which is the body's factory and sewer, produces proteins, breaks down toxins, and produces bile. It can become inflamed if inflammatory bowel disease is not treated properly. Unfortunately, some medications used to treat inflammatory bowel disease can also damage the liver.

Keywords: inflammatory bowel disease (IBD), ulcerative colitis (UC), liver, literature data.

The relevance of the research. Liver disease can be a complication of inflammatory bowel disease (IBD), such as ulcerative colitis (UC) or Crohn's disease. The liver, which is the body's factory and sewer, produces proteins, breaks down toxins, and produces bile. It can become inflamed if inflammatory bowel disease is not treated properly. Unfortunately, some medications used to treat inflammatory bowel disease can also damage the liver. Liver damage is one of the most common extraintestinal manifestations of UC. Of 180 patients with UC, liver damage was found in 58 (32.2%). In patients with UC, there were both liver parenchyma lesions — non-alcoholic steatohepatitis (NASH), autoimmune hepatitis, primary biliary cirrhosis (PBC), and changes in the extrahepatic bile ducts and gallbladder — primary sclerosing cholangitis (PSC), cholelithiasis (CSD). Parenchymal liver lesions were detected in 40 (22.2%) of 180 patients with UC, in 18 (10.0%). In UC, liver parenchyma lesions predominated; out of 58 patients with UC, NASH, autoimmune hepatitis, and primary biliary cirrhosis were detected in 40 (69.0%) patients, and lesions of the extra- and intrahepatic bile ducts and gallbladder were found in 18 (31.0%) patients. Non-alcoholic steatohepatitis develops mainly due to changes in liver cell metabolism against the background of chronic endogenous intoxication, and cholelithiasis develops due to impaired metabolism and chemistry of bile, so these changes can be classified as metabolic. Metabolic lesions of the liver and biliary tract were detected in 43 (23.9%) patients and in 74.2% of patients - lesions of the liver and biliary tract in UC (43 out of 58 patients). [Dorofeev A.E., Dorofeeva A.A 2017].

Gut-activated T lymphocytes in UC patients may contribute to bile duct inflammation, as intestinal-liver endothelial adhesion molecule profiles (vascular address mucosal cell adhesion molecule 1 and vascular cell adhesion molecule 1 expression along with C-C chemokine motif ligand 25 secretion) are similar [Adams D. 2006; Lajsko E et al 2011].

The fact that the expression of Mad-CAM-1 in PSC liver depends on the role of vascular adhesion protein 1 may indicate that modulation of these proteins may influence the progression of PSC [Laylor P et al 2011].

Despite the presence of publications about the effects of experimental ulcerative colitis and its influence on the morphology of the liver, the morphometric changes occurring in the liver during ulcerative colitis are not sufficiently clarified and have not been studied. All this, of course, complicates the correct interpretation of the functional significance of the liver in normal conditions and in pathology.

ETIOLOGY AND PATHOGENESIS The etiology of IBD, including UC, has not been established: the disease develops as a result of a combination of several factors, including genetic predisposition, defects in innate and acquired immunity, intestinal microflora and various environmental factors. Among the factors contributing to the development of UC, one should primarily mention hereditary predisposition. In first-degree relatives of patients with UC, the risk of developing it is 10 times higher

than in the general population. If both parents suffer from UC, the risk of its development in a child by the age of 20 increases to 52%. Genetic studies have shown that twin concordance (the incidence of the same nosological form in both twins) in UC is significantly lower than in Crohn's disease. A positive association has been identified between HLA DR2, as well as certain loci on chromosomes 2 and 6 (to a lesser extent 3, 7, 12 and 16) and the development of UC. The importance of nutrition in the etiology of UC is not as clearly defined as in Crohn's disease. When studying the dietary history, it was found that patients with UC consume less dietary fiber and more refined carbohydrates. There is a hypothesis about the important role of infectious agents, such as mycobacteria, measles virus, chlamydia, and Candida fungi, in the occurrence of UC. Immune impairments in the recognition of bacterial molecular markers (patterns) by dendritic cells, leading to hyperactivation of pro-inflammatory signaling pathways, are an important mechanism for the formation of UC. Also, in UC, there is a decrease in the diversity of intestinal microflora due to a decrease in the proportion of anaerobic bacteria, mainly Bacteroidetes and Firmicutes. In the presence of these microbiological and immunological changes, UC develops under the influence of trigger factors, which include smoking, nervous stress, vitamin D deficiency, a diet with a low content of dietary fiber and a high content of animal protein, intestinal infections, especially C. difficile infection.

The result of the mutual influence of these risk factors is the activation of Th2 cells, overexpression of proinflammatory cytokines, primarily tumor necrosis factor alpha (TNF-α) and 10 cell adhesion molecules. The result of these reactions is lymphoplasmacytic infiltration of the colon mucosa with the development of characteristic macroscopic changes and symptoms of UC. The important role of the autoimmune reaction in the genesis of UC is indicated, in particular, by the typical chronically relapsing course of the disease, extraintestinal manifestations (primary sclerosing cholangitis, hemolytic anemia), detection of autoantibodies to colonocytes and perinuclear cytoplasmic antineutrophil antibodies (pANCA), and the effectiveness of immunosuppressive therapy. However, the autoantigens that would cause the formation of autoantibodies have not yet been clearly identified. One of the potential autoantigens may be the cytoskeletal microfilament protein, tropomyosin. The mechanism of damage to the intestinal mucosa that occurs in UC is complex. The damage involves T-lymphocytes, antibodies and complement, free oxygen radicals and proteases, and changes in apoptosis processes. Various cytokines also play an important role, such as epidermal growth factor, interleukins (IL) and interferon (IFN), in particular IL-1b, IL-2, IL-4, IL-15, IFN-g, as well as neuropeptides, adhesion molecules and intracellular signal. It should be noted that the dynamics of certain immunological parameters (changes in T cells, cytokines, characteristics of antibody formation) have so far been traced only in experimental studies performed on mice with severe combined immunodeficiency syndrome (SCID) and on animals with reproduced genetic changes. Naturally, this significantly complicates the analysis of the results obtained in relation to clinical conditions. [I.V. Dolgalev 2021]

Complications. With UC, various complications are observed, which can be divided into local and systemic. Local complications include colonic perforation, acute toxic dilatation of the colon (or toxic megacolon), massive intestinal bleeding, and colon cancer. Systemic complications. Almost 60% of patients with UC have extraintestinal manifestations. 1. Autoimmune, associated with disease activity: • Arthropathy – arthralgia, arthritis. • Skin lesions – erythema nodosum, pyoderma gangrenosum. • Damage to the mucous membranes – aphthous stomatitis. • Eye damage – uveitis, iritis, iridocyclitis, episcleritis. 2. Autoimmune, not related to disease activity: • Ankylosing spondylitis, sacroiliitis. • Primary sclerosing cholangitis (PSC). • Osteoporosis, osteomalacia. • Psoriasis. 3. Caused by prolonged inflammation and metabolic disorders: • Cholelithiasis. 20 • Liver steatosis, steatohepatitis. • Thrombosis of peripheral veins. • Pulmonary embolism. • Amyloidosis. [I.V. Dolgalev 2021]

Liver lesions in IBD are conventionally divided into three main groups:

1) diseases caused by a pathogenetic mechanism common to IBD:

- ✓ primary sclerosing cholangitis (PSC),
- ✓ overlap syndromes: small duct PSC/pericholangitis and autoimmune hepatitis/PSC,

- ✓ IgG4-associated cholangitis,
- ✓ primary biliary cirrhosis;

2) diseases arising as a result of structural and physiological changes against the background of IBD:

- ✓ cholelithiasis,
- ✓ portal vein thrombosis,
- ✓ liver abscess,
- ✓ granulomatous hepatitis,
- ✓ amyloidosis;

3) diseases associated with adverse effects of drug therapy for IBD:

- ✓ drug-induced hepatitis and liver cirrhosis,
- ✓ reactivation of hepatitis B and C viral infection,
- ✓ liver lymphoma (associated with biological therapy)

The purpose of this article is to study the effect of inflammatory bowel diseases on the liver, as well as to assess the frequency and nature of liver damage in patients with neurological autoimmune bowel diseases.

Result and discussion. *Etiology of ulcerative colitis (UC)*

- ➢ *Multifactorial disease involving:*
- ✓ Genetic predisposition (association with HLA DR2)
- ✓ Defects of innate and acquired immunity
- ✓ Intestinal microflora
- ✓ Environmental factors

Key risk factors

- ✓ Hereditary predisposition (increased risk of development in first-degree relatives)
- ✓ Insufficient dietary fiber intake
- ✓ Smoking
- ✓ Nervous stress
- ✓ Vitamin D deficiency
- ✓ High intake of animal protein
- ✓ Intestinal infections (including C. difficile)

Development mechanisms

- ✓ Activation of Th2 cells and overexpression of pro-inflammatory cytokines (TNF-α, etc.)
- ✓ Lymphocytic infiltration of the colon mucosa
- ✓ Formation of ulcers and other macroscopic changes
- ✓ Impaired apoptosis and damage to the mucous membrane due to free radicals and proteases.

Liver damage in IBD can be caused by:

- ✓ Common pathogenetic mechanism with IBD (PSC, autoimmune hepatitis, etc.)
- ✓ Structural and physiological changes against the background of IBD (cholelithiasis, portal vein thrombosis, etc.)

- ✓ Adverse effects of drug therapy for IBD (drug-induced hepatitis, reactivation of viral hepatitis, etc.)

Dividing liver lesions in IBD into three main groups helps in diagnosis and selection of appropriate therapy.

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