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Collagenoses and cutaneous manifestations of hepar diseases

The diseases of the connective tissue (collagenoses) are systemic diseases that may affect many different organs, including the liver and skin. Diseases with simultaneous cutaneous manifestations are most interesting for dermatologists. The most frequently reported diseases in this group are systemic lupus erythematosus, scleroderma and polyarteritis nodosa. Systemic lupus erythematosus (SLE) is a disease of the immunological type. The production of specific polyclonal antibodies directed against the patient's own antigens is the result of B lymphocyte hyperactivity. Similarly, T lymphocytes play an important role in the pathogenesis of the disease – particularly the disorders in the suppressor subpopulation and the defect of delayed hypersensitivity at a later stage (8).

The probability of the occurrence of disorders in the liver function in patients with SLE is 25-50%. This number does not include cases of hyperbilirubinemia caused by haemolysis connected with SLE or an increase in transaminase activity caused by inflammation of the muscles connected with SLE. An asymptomatic increase in the aminotranspherase activity observed in 10–30% patients with SLE still remains unexplained. In some patients with SLE the level of aminotranspherase activity in the serum changes depending on the severity of the disease. There are reports on the cases of cholestatic hepatitis in relation to the treatment with non-steroid antiphlogistic drugs. Another form of the disease is mild, usually lobulous hepatitis, but sometimes also portal or periportal hepatitis.

The presence of anti-phospholipid antibodies is connected with the thrombosis of the liver veins and with angioembolic disease of the liver. The presence of other changes in the liver in the course of systemic lupus erythematosus such as granulomas, chronic hepatitis and steatosis is rare. There are also reports on a few cases of primary biliary cirrhosis co-existing with systemic lupus erythematosus (5, 6, 9). Some of the authors inform about the presence of lymphadenopathy, splenomegaly and hepatomegaly and even about the rupture of the liver or spleen (8). Budd-Chiari's syndrome (thrombosis of the

liver-veins, portal hypertension, autoimmune hepatitis, itch, cholestasis) can be a clinical symptom of liver damage in SLE (6). In Budd-Chiari's syndrome, ascites occurs in over 90% of the patients and is the most distinctive feature of the syndrome. In 80% of the patients suffering from pains located in the right upper quadrant of the abdomen, hepatosplenomegaly is often present and in some cases, a mild form of jaundice is stated. Encephalopathy, and bleeding from the varices of the oesophagus occur less frequently (10–20% cases), usually in the severe stages of the disease (7).

Virus hepatitis, mechanical jaundice, autoimmune hepatitis, granuloma hepatitis, primary biliary cirrhosis, cryptococcus infections of the liver, chronic hepatitis with IgA or IgD deficiency, porphyria and idiopathic portal hypertension are also decribed as diseases coexisting with SLE (4).

There exists the so-called lupus-like hepatitis similar to systemic lupus erythematosus. This is a form of chronic active hepatitis with systemic symptoms. The results of laboratory studies are partly similar to those in systemic lupus erythematosus – there occur antinuclear antibodies (in 70–90% of cases compared to 99% in SLE). In the course of lupus-like hepatitis there are present antibodies against smooth muscle (SM) antigens (actin F1). Their presence (80–95% of the cases) clearly suggests the diagnosis of lupus-like hepatitis. These antibodies are seldom present in SLE. Similarly, antibodies against ds-DNA seldom occur here (up to 40% of cases, compared to 70% in SLE). In both studied diseases there are the following symptoms: polyclonal gammapathy, fever, its (i. e. the disease's) occurrence in young women, cutaneous lesions and arthritis. Characteristic features of lupus-like hepatitis that allow to differentiate the latter from SLE are: rare occurrence of LE cells (40–50% vs 70% in SLE), lack of sensitivity to light, lack of ulcerative stomatitis, absence of antibodies against Smith's antigen (anti-Sm) and, compared to their presence in SLE in 25% cases, absence of disorders of CUN and of nephritis. Smith's antigen is a small ribonucleoprotein epitope, extremely specific for lupus erythematosus (7).

Diffuse hyperpigementation also accompanies other autoimmune diseases, most frequently – systemic scleroderma. Scleroderma is a disease of a progressive type with characteristic immunological disorders and with the following changes: first sclerodermic and then atrophic changes in the skin, subcutaneous tissues, muscles and internal organs. Patients suffering from scleroderma constitute a varied group where the development of cutaneous changes as well as lesions in the organs take place with different dynamics (2). Damage of blood vessels observed in an early stage of the disease leads to accumulation of activated cells in the perivascular space. Cytokines they produce play an important role in further damaging of the vessel endothelium and its activation. Moreover, cytokines released by activated lymphocytes also induce the process of fibrosis by stimulating fibroblasts to produce collagen and other components of extra-cellular matrix (3).

Sometimes (less than 1% of cases) simultaneous occurrence of scleroderma and primary liver cirrhosis is observed (1, 6). The skin is dark brown, especially in exposed areas. In cirrhosis of the liver with hyperpigmentation also itching of the skin, jaundice and

xanthelasmas occur. Instead, in scleroderma there are observed: hardening of the skin, mostly of the face and circumferential parts of the limbs, less frequently, of the trunk. Other clinical features of scleroderma are: teleangiectases, deposits of calcium in the skin, Raynaud's symptom and trophic ulceration of distal parts of the body.

There are reports on the occurrence of primary sclerosing cholangitis in the course of scleroderma (6). Wojas-Pelc and others (12) stated in 28 patients with scleroderma an isolated significant rise in the concentration of cholic acid in the serum blood with normal ALT and GGT activity, which might suggest the existence of disorders in biotransformation of the liver-cell processes without the damage of the liver. In differentiating the sclerodermic changes with accompanying hyperpigmentation a POEMS syndrome (polyneuropathy; organomegaly of the liver, spleen and lymphatic glands; endocrinic disorders: impotence, gynecomastia; M protein; cutaneous changes) should be taken into consideration. Typical cutaneous changes are: hyperpigmentation, hardening of the skin, hirsutism and angiomas (1).

The changes in the liver in the course of the polyarteritis nodosa are relatively frequent and are the result of both vascular changes in the liver arteries and of B-virus type hepatitis. In 11–60% cases a positive HbsAg, mainly together with a positive HbeAg and the presence of HBV-DNA, is present. The virus antigene can be stated in the walls of affected arteries in the immunofluorescent examination (6). The symptoms may include fever, arthritis, mononeuropathy multiplex (inflammation of several peripheral nerves in different parts of the body), pains of the abdomen, diseases of the kidneys and/or of the heart. Although in some cases an increase in liver-enzyme activity occurs, no clinical symptoms of hepatitis are stated. Diagnosis is based on clinical symptoms and on the arteriographic examination of the arteries of the abdominal cavity and of renal arteries, on which aneurisms and "cork-screw" vessels are visible. The most certain diagnostic method is a histopathological examination of tissues, during which inflammatory changes in the arterioles are stated (7).

In postmortal investigation, in over 40% of the patients with polyarteritis nodosa, the presence of vascular changes in liver arteries is found. However, these changes are seldom observed in clinical examination. Vascular changes lead to closing of the lumen of the artery, which may be a reason of the infarction of the liver or, of subcapsular haematomas with a risk of spontaneous rupture of the liver bag. Vascular changes found in morphological examination of specimens of the liver are rare. A more useful diagnostic method is the vascular examination of liver arteries because in most cases it shows the presence of microaneurysms. Scarcely, an initial symptom of polyarteritis nodosa of the arteries may be acute cholecystitis (6).

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SUMMARY

The authors discuss cutaneous manifestations of some systemic diseases (collagenoses) and their connection with diseases of liver cells.

Kolagenozy i skórne manifestacje chorób komórki wątrobowej

Autorzy omawiają skórne manifestacje chorób układowych, jakimi są kolagenozy, w powiązaniu z chorobami komórki wątrobowej.