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Polymorphism of Hepatic Stellate Cells and their Role in Fibrogenesis

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Annotation. In 1876, stellar cells of the liver (formerly known as lipocytes, Ito cells or perisinusoidal cells) were first described by K.Kupfer and named by him stellate cells. T. Ito discovered fat drops in these cells and found that fat is produced by the cells themselves from glycogen and proved their fat-storing function. However, in 1971, it has been proved that Kupffer cells and fat-storing Ito cellsare completely same and they are kind of "storage" for vitamin A. [1]. stellate cells - perisinusoidal, pericyte-like cells of mesenchymal origin attract attention primarily as effectors of the response with the development of fibrogenesis. In a standard liver, these cells act as a reservoir for retinoids. Most of all the reserves of vitamin A of the human body are located in them [2]. As a result of pericyte-like form, they can also act as regulators of blood flow. One of the most incredible abilities of these cells appears after liver damage. In this situation, stellate cells move from a dormant (normal) state to an activated (damaged) state.

Key words: liver stellate cells, fibrogenesis, morphology, ultrastructure.

Materials and research methods. Classical methods of light and electron microscopy of biopsy specimens and original techniques using ultrathin sections, fixation and staining were used. Intravital liver biopsy was obtained by aspiration liver biopsy in patients with HCV infection (hepatitis C virus) at various stages of liver fibrosis and cirrhosis. Four-point system was used to assess the progressive stage of liver fibrosis, ranging from portal fibrosis (first stage) to liver cirrhosis, with the formation of porto-central vascularized septa and nodular transformation of the liver parenchyma. 4% solution of paraformaldehyde (which was prepared in Millonig's phosphate buffer) was used to fix the liver tissue, then the paraffin sections were stained with hematoxylin and eosin in combination with the Pursl reaction, according to van Gieson with Weigert's staining of elastic fibers with resorcinol-fuchsin, and the PAS reaction was performed.

Research results. Liver stellate cells are located in the perisinusoidal space (Disse) in pockets between hepatocytes and endothelial cells by the presence of large lipid droplets in the cytoplasm, and also have long processes that penetrate deep between hepatocytes. The transformation of "passive" stellate cells, which contain lipo-containing material into fibrogenic, is accompanied by the systematic disappearance of this main morphological marker. It should be noted that the perisinusoidal liver cells in the passive position have a rounded, slightly elongated shape, a rather large nucleus, as well as lipid inclusions that contain retinol. In the passive state of liver stellate cells, the number of lipid cells can reach 30 or more, they are close in size, adjacent to each other, pressing into the nucleus and pushing it to the periphery. [3].

In chronic hepatitis C, the population of liver stellate cells, size, shape and the number of lipid inclusions at the initial stages of fibrosis (0.1) was characterized by pronounced polymorphism. In electron microscopic examination, the population of stellate cells is heterogeneous. Non-uniformity in the electron density of

lipid inclusions was noted not only within one cell, but also between different lipid cells. Also, the nuclei are sharply polymorphic, the length of the cytoplasmic processes varied. At the ultrastructural level, a very small amount of the cytoplasmic matrix was revealed, which is poor in organelles that have membranes, in particular mitochondria, and therefore this phenotype of lipocytes is called "passive". [4].

At stages 2 and 3, the ultrastructure of many liver stellate cells acquired a mixed phenotype - the simultaneous presence of morphological features of both lipid-containing and fibroblast-like cells. At the same time, the cells acquired an elongated shape, the nuclei had deep invaginations of the nucleolemma, a small amount of lipid inclusions, a rather large nucleolus, and an increased volume of the cytoplasm. An increase in the number of mitochondria and ribosomes, as well as lysosomes involved in the degradation of lipid droplets was observed. This process was carried out by the formation of autophagosomes, which were further eliminated by exophagocytosis. And so, during the formation of intralobular perisinusoidal fibrosis with the progressive development of chronic hepatitis C, morphological signs of activation of liver stellate cells were revealed, their transformation from the so-called "passive", accumulating vitamin A, into contractile, proliferating and fibrogenic cells. It should be noted that there was a significant decrease in the number density of lipid-containing stellate cells at the stage of transformation into liver cirrhosis. [5].

Iif there is a acute injury, activation of hepatic stellate cells may play a beneficial role, because the result is an appropriate stromal circuit for regeneration while maintaining the hepatic architecture. [6].

Conclusions. In chronic hepatitis C with the development of liver fibrosis, the numerical density of lipid-containing cells decreases significantly. But, at that time, a certain amount of the population remains a "passive" phenotype in order to carry out metabolic function. In the state of fibrogenic activation, myofibroblast-like stellate cells of the liver have a variety of morphological features, For example, a decrease in the number of lipid inclusions and their further disappearance, focal proliferation of lipocytes, hyperplasia of ribosomes and mitochondria, and the formation of pericellular collagen fibrils in the spaces of Disse. Fibrosis at the level of the central veins, sinusoids, or portal vessels restricts the normal circulation of the liver, and this process leads to a reduction in the metabolically efficient parenchyma, further portal hypertension, and portosystemic shunting. Also, in the spaces of Disse, the growth of connective tissue helps to the disruption of normal metabolic traffic between blood and hepatocytes, thereby it prevents the clearance of circulating macromolecules, and changes intercellular interactions. All of these things ultimately lead to liver cell dysfunction.

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