MORPHOLOGICAL ASPECTS OF HUMAN LIVER HEPATOCYTES IN CHOLESTASIS

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Introduction. As is well known, many liver diseases are accompanied by jaundice, which manifests itself to varying degrees. Among them, mechanical jaundice, which occurs as a result of bile stagnation due to gallstone disease or tumors, occupies an important place. In the literature on intrahepatic cholestasis, there is insufficient material demonstrating the morphological features of intrahepatic cholestasis.

Cholestasis is a pathological condition caused by impaired bile formation and outflow into the lumen of the duodenum, leading to the accumulation of bile pigments in the liver parenchyma. The main principle of distinguishing between types of cholestasis is based on the location of the causes of their development – extrahepatic and intrahepatic [1, 16]. Extrahepatic cholestasis is in most cases caused by obstruction of the bile ducts outside the liver. In intrahepatic cholestasis (IHC), there is no obstruction of the extrahepatic biliary tract, and the immediate causes are as follows: disruption of bile formation mechanisms; disruption of bile transport mechanisms at the hepatocyte level; damage to the intrahepatic bile ducts; a combination of the above causes [2, 17]. Cholestasis may manifest as jaundice, itching, skin xanthomas, or symptoms associated with malabsorption in the small intestine, including deficiencies in nutrients and fat-soluble vitamins A, D, or K. Depending on the location of the damage, BPH is divided into the following morphological variants: intralobular cholestasis (hepatocellular and canalicular) and extralobular cholestasis. Causes of intralobular Biliary Cholestasis: viral, alcoholic, drug-induced, toxic liver damage, benign recurrent cholestasis, intestinal microecology disorders, cholestasis in pregnant women, endotoxemia, liver cirrhosis, bacterial infections, Alagille syndrome, Biliary tract disease associated

with total parenteral nutrition, congestive heart failure, metabolic and other disorders [11-18].

The development of extralobular VPH is based on damage to the epithelium of the bile ducts, impaired patency, metabolism, and composition of bile acids (BA). This type of BPH develops in focal liver lesions (tumors, metastases, abscesses, parasites, Caroli syndrome, Hodgkin's disease, etc.), disseminated lesions (sarcoidosis, tuberculosis, cystic fibrosis); infiltrative liver lesions (leukemia, amyloidosis, storage diseases); inflammatory proliferation of the ducts (primary sclerosing cholangitis – PSC, primary biliary, autoimmune, bacterial cholangitis, graft-versus-host reaction, chronic rejection after orthotopic liver transplantation, hemobilia, biliary tract hypoplasia [12-16].

Unfortunately, literary sources devoted to VPH lack sufficient illustrations based on morphological visualization of the VPH syndrome, which is why we set ourselves the task of eliminating this information deficit to a certain extent.

The aim of the study was to investigate the possibility of migration of the granular component of hepatocyte nucleoli in patients without liver pathology and with liver pathology (to prove the universality of this process in mammals).

The object of the study was the liver of patients with chronic hepatitis (n=20) and extrahepatic diseases (n=16) (autopsy material).

Materials and methods. To solve the tasks set and achieve the goal, clinical materials were used with the application of adequate research methods: general morphological, histochemical (DNA and RNA), morphometric, and static processing methods. In carrying out this work, liver tissue from patients who died of hepatitis (n=20) and patients without liver pathology (n=16) was used, obtained from the morgue of the Tashkent Dental Medical Institute.

Pieces of liver tissue for histological examination were fixed in a 12% solution of neutral formalin and, after standard processing, were embedded in paraffin wax. Sections for histological examination were stained with hematoxylin and eosin, and DNA was detected using Felgen's method and RNA using Brasch's method.

To obtain thin histological sections, a sled microtome was used to produce sections 5-7 μm thick. The histological section was immediately transferred to a microscope slide and deparaffinized, then immersed in a xylene solution. The sections were then stained with a specially prepared hematoxylin solution, which stained the nuclei purple, and the contrast was checked under a microscope. The cytoplasm of the cells was then stained with an acidified alcohol solution of sodium eosin.

After these procedures, the sections were dehydrated in 96˚ and 100˚ alcohol concentrations, clarified by immersion in xylene solution, sealed with Canadian balsam, and covered with a cover glass. After a certain period of air drying, the histological sections were ready for analysis under a microscope. The preparations were photographed using an N-800M microscope under an immersion lens (x100).

The preparations were photographed using a DN-300m microscope with a digital camera attachment connected to a computer. The histological sections were processed using a morphometric method with a special computer program.

Discussions and results. After proving the possibility of nucleolus migration from the nucleus to the cytoplasm in rabbits and white rats, we had to tackle a more complex task, namely, whether this phenomenon occurs in humans. After all, any research is aimed at humans, their well-being, disease prevention, recovery, and ensuring a long life. In this regard, we conducted a study of the livers of patients who died from non-hepatic diseases at the age of 60 to 83 (12 men and 10 women). After general morphological processing, the autopsy material was examined under maximum magnification (immersion x 100) using a modern DN-300 M light microscope with a digital photo attachment.

It should be noted that the human liver has a similar structure to that of other mammals, but differs in some respects. These features include the accumulation of yellow-brown pigment (lipofuscin) in the cytoplasm of hepatocytes, especially around the central vein, and the appearance of minor dystrophic processes in the liver parenchyma.

Dystrophic processes manifested themselves in the form of vacuolar or fatty dystrophy, with varying degrees of severity (fatty dystrophy was more common, while granular and vacuolar dystrophy were rare). In addition, unlike in animal livers, some disorganization of the hepatic plates and sinusoidal capillaries was noted (Fig. 1.A.G). As usual, the hepatic plates are formed by two or three rows of hepatocytes, which are polygonal in shape and contain one or two nuclei in the cytoplasm.

Unlike animal liver cells, human liver cell nuclei are characterized by marked polymorphism, with most nuclei being small to medium in size, along with a small number of large, sometimes giant nuclei (Fig. 1B). In connection with the task at hand, the condition of human hepatocyte nuclei was carefully analyzed.

In cholestasis, an overview image of the histological picture of the liver shows periportal, or more precisely, periductal fibrosis of the liver. Connective tissue proliferation is detected around the triad, and moderate infiltration by lymphohistiocytic elements. The interlobular artery, vein, and bile ducts have a normal structure and, together with the surrounding structures, are clearly separated from the liver parenchyma.

As usual, liver lobules merge with neighboring lobules without clear boundaries, and within the lobule, liver plates and sinusoidal capillaries have a radial orientation, but in some areas this organization is disrupted. Liver cells are polygonal in shape, with oxyphilic cytoplasm and a rounded nucleus in the center. Hepatocyte nuclei are characterized by polymorphism, with small and medium-sized nuclei predominating and large giant nuclei, in which large nucleoli are clearly visible, being rare. In small and medium-sized nuclei, chromatin is evenly distributed throughout the karyoplasm, with some concentration under the nuclear envelope; nucleoli are small and not always detectable. Changes in the nuclei are observed in some hepatocytes.

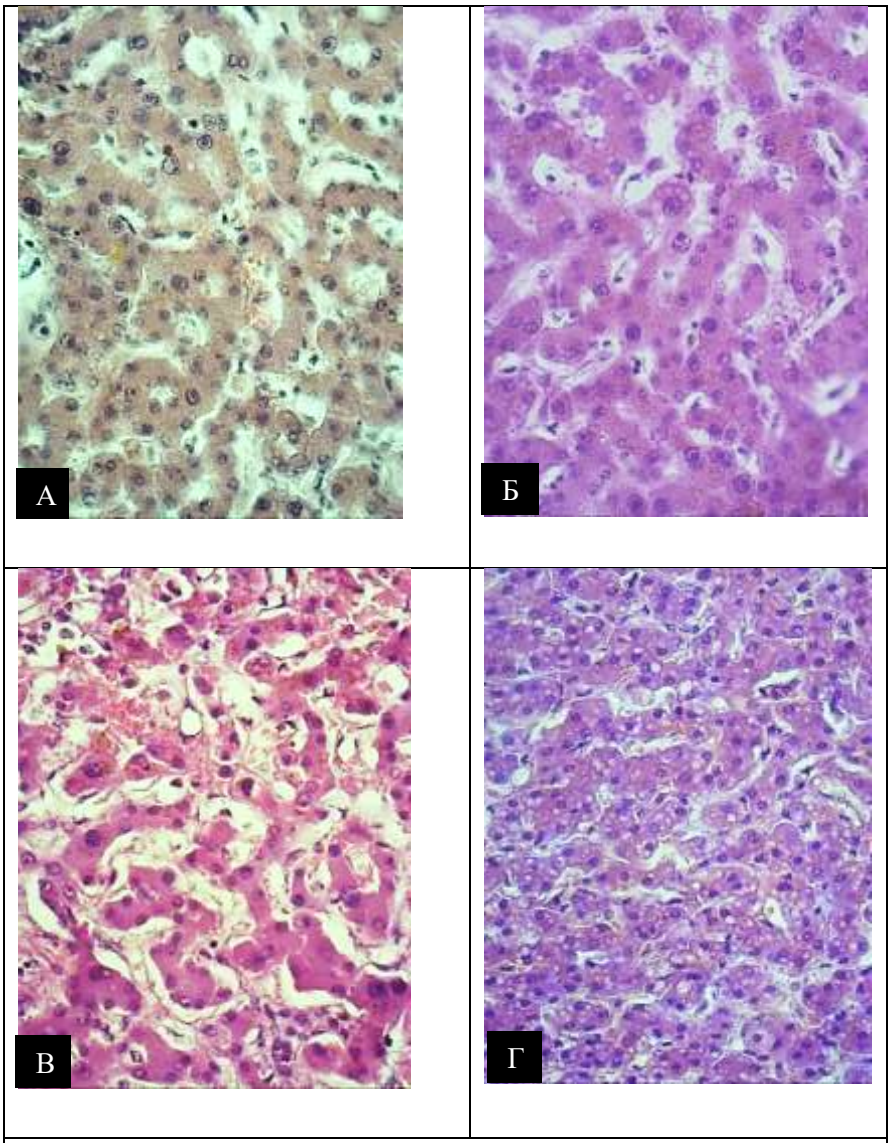

Fig. 1. Overview images of the histological picture of the human liver. Hematoxylin-eosin staining. A. Disorganization of hepatic lamellae and sinusoidal capillaries, vacuolar dystrophy of hepatocytes, nuclear polymorphism. In some large nuclei, the exit of the granular component of the nucleolus from the nucleus is visible (A, B). Small-drop fatty degeneration of hepatocytes (B) and sharp expansion and blood filling of sinusoidal capillaries with hepatocyte atrophy (D). Magnification x 40.

The changes affect the contours of the nuclei, which are deformed or form kidney-shaped growths of the karyolemma. In some cases, the karyoplasm is lightened or, conversely, chromatin condensation is observed with the formation of coarse lumps in the karyoplasm.

In individual nuclei, the nucleolus is sharply swollen and occupies most of the karyoplasm, but its structure is disrupted and the nucleolonema is lightened. Sometimes such vacuole-like structures occupy the entire karyoplasm, after which the nucleus disintegrates, resembling a bubble-like structure.

Ultimately, the devastated nucleus resembles a light bubble in which the nuclear envelope is still preserved but stretched or looks like a thin rim of a ring. Along with well-preserved areas of parenchyma, there are foci of cell necrosis, where the collapse of the stroma reveals the remains of hepatocyte nuclei, and such areas usually merge with the surrounding cells. It should be noted that areas of cholestasis are most pronounced around the central vein.

Bile condensates are detected not only in the lumen of dilated bile ducts, but also in the cytoplasm of centrolobular hepatocytes. Hepatocytes imbibed with bile are detected as large yellow-brown conglomerates. Sinusoidal capillaries are moderately dilated, and Kupffer cells show some activity.

Conclusions. Thus, in cholestasis in the centrolobular zones, areas of cholestasis and foci of necrosis are found, with changes in the nuclei, up to complete disintegration into empty nuclei, which is an indicator of a complete disruption of the regenerative capacity of hepatocytes.

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