MORPHOLOGIC CHANGES IN THE LABORATORY RATS' LIVER IN CASE OF THE DEVELOPMENT OF EXPERIMENTAL AND SPONTANEOUS TUMORS

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Lately the problem of interrelation of tumor and organism attracts much attention of scientists. Necessity of investigation of the liver condition in tumor-carrier organism is the part of this problem, because such information is of great significance for working out of antitumoral therapy.
Keywords: *tumor, rat, liver, hepatocyte*

Actuality. Lately the problem of interrelation of tumor and organism attracts much attention of scientists. Necessity of investigation of the liver condition in tumor-carrier organism is the part of this problem, because such information is of great significance for working out of antitumoral therapy.
Tumor, from very beginning of its development, is connected with the organism, and it exists as a part of the organism. That's why the investigation of the intercommunication of the neoplasm and the organism should not be performed as opposition of the tumor to the organism. It is necessary to determine their interrelation in the form of bilateral connections.
Besides the performance of different vital functions, the liver takes a considerable part in maintenance of normal steroid homeostasis, the disorder of which is able, on the one hand, to cause the malignization of hormone dependent organs, and on the other hand, to intensify malignant disease course. Hence the study of the liver condition in case of the malignant tumor development in the organism, is of great importance. Such data are essential for working out of antitumoral treatment modes.
Information that one can find in the available scientific literature concerns principally with human spontaneous tumors [2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 19, 21]. Data concerned with structural changes in the liver in case of development of experimental tumors are not numerous [1, 17, 18, 20].
Taking into consideration the above mentioned facts we tried to determine the main structural changes in the laboratory rat's liver in case of development of experimental and spontaneous tumors.
Methods. For our investigation we used five groups of the adult males of laboratory rats. Group №1 (control) included five intact animals. Group №2 included five animals that were subjected to subcutaneous introduction of cells of experimental lymphosarcoma. Group №3 included five animals with transplanted intraperitoneal experimental tumor sarcoma 45. Group №4 included five animals with transplanted experimental ovarian tumor. Group №5 included two animals with spontaneous mammary tumor.
Rats of the group №1 were killed on the twelfth day after the beginning of the experiment. Rats of the groups №2, №3 и №4 were killed by the time of full development of the experimental tumors: rats of the group №2 were killed on the fifteenth day, rats of the group №3 were killed on the twentieth day, rats of the group №4 were killed on the twelfth day, rats of the group №5 were killed after their spontaneous tumors were discovered. Livers and tumors were extracted and fixed in solution of formalin. Paraffin sections were stained with hematoxylin-eosin. Histologic specimens were investigated under light microscope.
Discussion. The liver of the rats of control group is characterized by lobulated structure. The most of hepatocytes are polyhedral in shape. Boundaries of the cells are poorly visible, and their cytoplasm is granular. Diameter of the hepatocytes is 13,53±0,35 micrometers. The liver cells are arranged in the form of irregular cords, that ramify and pass from the periphery of lobule to its central vein. Rounded nuclei of the hepatocytes have conspicuous karyolemma and well visible nucleoli and masses of chromatin. Diameter of the nuclei is 7,37±0,29 micrometers. Among the liver cells there are those containing two nuclei (their diameter is more than 23 micrometers) and those containing three nuclei (their diameter is more than 25 micrometers).
Between the cords of hepatocytes there are sinusoids containing numerous formed elements of blood. Internal surface of the sinusoids are lined by endothelial cells that have oval hyperchromatic nuclei. Average diameter of the sinusoids is 7,41±0,39 micrometers. Sinusoids are continuous with central veins the inner surface of which is lined by endothelial cells containing elongated hyperchromatic nuclei.
Connective tissue septa are not prominent hence the lobules are not demarcated. Scanty interlobular connective tissue is made up of thin fibres and cellular elements that surround interlobular blood vessels and bile ducts.
Interlobular veins have wide lumen and thin wall, the inner surface of which is lined by flattened endothelium containing elongated hyperchromatic nuclei.
Interlobular arteries are less in size than veins. They have narrow lumen, their wall is thick due to well developed media.
Interlobular bile ducts are lined by cuboidal and low cylindrical epithelium, the basal membrane of which is not prominent. Boundaries of the epithelial cells are visible. Rounded and oval nuclei are poorly stainable, but their karyolemma is conspicuous.
The liver of the rats of the group №2 is characterized by lobulated structure. The most of the hepatocytes have normal structure. They are polyhedral in shape, their cytoplasm is granular. Their rounded and oval nuclei are characterized by

prominent karyolemma and well visible nucleoli. Diameter of hepatocytes is 18,02±0,75 micrometers, diameter of their nuclei is 8,81±0,25 micrometers.

Some of the liver cells are vacuolated, their nuclei are wrinkled. One can find small empty cavities which were formed in places of entirely destroyed hepatocytes. There are also zones of considerable size that are made up of destroyed hepatic tissue.

Prominent structural difference between central and peripheral parts of the hepatic lobules is not found.

Tumor tissue in the rats of the group №2 is made up of densely arranged malignant cells the boundaries of which are visible. Cytoplasm of the cells is granular. Rounded, oval, bean-shaped, irregular-shaped nuclei have prominent karyolemma and well visible nucleoli. Diameter of malignant cells is 6,51±0,2 micrometers, diameter of their nuclei is 3,86±0,14 micrometers.

Tissue of the tumor contains singly arranged cavities that either are empty or contain unstructured eosinophilic substance within which malignant cells are scattered. Some of the cavities are rounded or oval in shape, their edges are even, they are not more than 85 micrometers in diameter. The other cavities resemble fissures, their lumen is about 140 micrometers.

In some zones of the tumor the malignant cells are arranged loosely and are separated by unstructured eosinophilic substance containing collapsed nuclei of the malignant cells. One can find necrotic zones of different size that consist of unstructured substance within which malignant cells and fragments of nuclei are scattered.

The liver of the rats of the group №3 is characterized by lobulated structure. But considerable destruction changes occur. Such changes are found mainly in the central parts of the hepatic lobules surrounding narrowed central veins the lumen of which contains fragments of collapsed liver cells.

One can often discover well preserved hepatocytes the boundaries of which are invisible. Their cytoplasm is granular, the rounded nuclei have prominent karyolemma and nucleoli. Average diameter of the hepatocytes is 16,9±0,51 micrometers, and diameter of their nuclei is 8,74±0,3 micrometers. Sometimes one can find binucleate cells.

There are numerous small necrotic zones. Many hepatic cells are considerably vacuolated, this fact causes formation of small oval cavities containing wrinkled nucleus and fragments of cytoplasm. There are also small cavities formed in places of entirely destroyed liver cells.

There are also larger cavities formed as a result of destruction of several adjoining liver cells, they contain wrinkled nuclei and cytoplasmic fragments of hepatocytes. One can find singly arranged anucleate cells and zones that are made up of unstructured eosinophilic substance containing wrinkled nuclei.

Tumor in the rats of the group №3 is surrounded by capsule that is made up of numerous cellular elements and of thin fibres. Thickness of the capsule varies in different zones. In the thinnest zones of the capsule (less than thirteen micrometers) its structural elements are densely arranged and oriented along the tumor surface. In those zones the nuclei are small, elongated, hyperchromatic. Average diameter of the nuclei is 3,94±0,16 micrometers. As the capsule becomes thicker its structural elements at first become wavy, then gradually they become irregularly directed. In the thickest zones of the capsule (about one hundred and eighty micrometers) the nuclei are different in size. Here there are both small hyperchromatic nuclei and larger nuclei containing prominent masses of chromatin. Such nuclei are oval and elongated in shape, their diameter is 6,98±0,3 micrometers.

The capsule contains numerous thin-walled vessels that are lined by flattened endothelium. In the thinnest zones of the capsule the blood vessels are found very seldom. As the capsule becomes thicker the number and size of the vessels increase. The capsular vessels penetrate deep into the tumor tissue within which they form dense network.

Malignant cells that are situated under the capsule are closely packed. Boundaries of the cells are invisible. Cytoplasm of many of the cells is vacuolated. Nuclei (that are 8,35±0,2 micrometers in diameter) are densely stained with hematoxylin. The nuclei are rounded, oval, angular, and irregular in shape. Some of the nuclei of the cells situated within the subcapsular zone are destroyed.

Within the deeper zones of the tumor the cells are arranged looser, among them one can seldom find mitotically dividing. The specific gravity of their cytoplasm is increased. In many cells the cytoplasm is vacuolated. Nuclei of the cells are rounded, oval, reniform in shape, their diameter is 10,18±0,4 micrometers. They are characterized by presence of prominent karyolemma and masses of chromatin. The number of nucleoli in the nuclei is one to six. The size of the nucleoli is different, but there is tendency: as the number of the nucleoli increases, their size decreases. However, in some cases a nucleus may contain nucleoli that considerably differ from one another by size.

More deeper zones of the tumor contain numerous destroyed cells. Here one can also find empty cavities formed in places of entirely collapsed cells. The collapsing cells are wrinkled and hyperchromic, their cytoplasm is intensely eosinophilic. Many of those cells have conspicuous boundaries, and they are arranged separately. Their diameter is 10,28±0,3 micrometers , and the diameter of their nuclei 5,01±0,12 micrometers.

The deepest zones of the tumor are made up of necrotic material, that is made up cytoplasmic lumps within which the fragments of nuclei are scattered. In these zones one can find well preserved vessels containing formed elements of blood. The vessels are surrounded by thin adventitia. The wall of some blood vessels is destroyed, in such cases formed elements of blood penetrate between malignant cells.

The liver of the rats of the group №4 is characterized by lobulated structure. Central veins of the lobules are dilated, and their sinusoids are filled with blood.

Many of the liver cells have preserved structure, among them there are binucleate. Their cytoplasm is granular, the boundaries are poorly visible. Rounded and oval nuclei are centrally situated, they are characterized by presence of prominent karyolemma, nucleoli and masses of chromatin. Diameter of the hepatocytes is 17,28±0,6 micrometers, and diameter of their nuclei is 8,9±0,28 micrometers.

Some of the liver cells are destroyed: they are characterized by vacuolation of the cytoplasm, absence of nuclei.

In the liver there are numerous cavities containing fragments of hepatocytes and formed elements of blood.

Ascitic tumor in the rats of the group №4 caused the formation of many mesenteric tumor nodes. Those mesenteric zones, that are situated between tumor nodes, are well vascularized: large arteries have well developed media, large veins are thin-walled. The internodal zones of the mesentery are made up of thin connective tissue fibres. In some cases the fibres are wavy,

in the other cases they interlace forming a network. Cellular elements are situated between the fibres, their oval and elongated nuclei are characterized by presence of prominent karyolemma, nucleoli, and masses of chromatin.

Some of the internodal mesenteric zones contain adipose tissue. Many of the internodal mesenteric zones are infiltrated with the tumor cells.

The metastatic nodes are made up of cells the boundaries of which are not visible. In some of parts of metastases the cells contain granular cytoplasm, and rounded and oval nuclei that have prominent karyolemma and different-sized nucleoli. Diameter of the nuclei is 7,36±0,26 micrometers. Among such cells one can often discover mitotically dividing. In the other parts of metastases the cytoplasm of the cell is densely stained, their hyperchromatic nuclei (that are 5,65±0,2 micrometers in diameter) are rounded, oval, reniform, polyhedral, and irregular in shape. In such parts of metastases there are thin bands of homogeneous eosinophilic substance.

Some parts of the tumor nodes represent unstructured zones within which fragments of nuclei are irregularly scattered.

Some of the metastatic nodes are permeated by blood vessels that are filled with formed elements of blood. The malignant cells gradually destroy the blood vessels, this fact eventually causes small hemorrhages. One can sometimes discover adipose tissue within the metastases.

Numerous tumor cells lie separately from the mesentery. Some of them are arranged singly, such cells have prominent boundaries. The other cells are arranged in groups, their boundaries are indistinct. Some of such separately situated cells contain granular cytoplasm, and rounded or oval densely stained nuclei. Their diameter is 9,36±0,25 micrometers, and diameter of their nuclei is 5,89±0,2 micrometers. The other cells are collapsed.

The liver of the rats of the group №5 is characterized by lobulated structure. Diameter of the liver cells is 15,87±0,62 micrometers, diameter of their nuclei is 8,15±0,17 micrometers. The hepatic tissue is permeated by thin-walled vessels that are filled with formed elements of blood. Sinusoids between the hepatocytes are also dilated and are filled with formed elements of blood, their average diameter is 9,87±0,45 micrometers.

Many hepatic plates are disintegrated due to the collapse of the hepatocytes. Many zones of the hepatic parenchyma is made up of the liver cells that are either devoid of nuclei or contain wrinkled nuclei. In some hepatocytes the preserved nuclei are surrounded by collapsed cytoplasm.

There are some irregular-shaped cavities containing collapsed hepatocytes mixed up with formed elements of blood.

Tumor in one of the rats of the group №5 is made up entirely of connective tissue. In some zones of the tumor the connective tissue consists of thin wavy fibres, and of cellular elements containing rounded, oval, and angular nuclei that are characterized by presence of prominent karyolemma and nucleoli. Diameter of the nuclei is 5,85±0,22 micrometeres. Those zones are permeated by numerous thin-walled vessels that are filled with formed elements of blood.

In the other zones of the tumor the connective tissue fibres are partially homogenized. Numerous cellular elements contain large oval and elongated poorly stained nuclei, the diameter of which is 12,28±0,59 micrometers.

There are vast zones of unstructured substance that contain small cavities in which one can find collapsed nuclei and cytoplasmic fragments of the malignant cells.

In the other rat of the group №5 the neoplasm is surrounded by connective tissue capsule (that is 23,13±0,9 micrometers in thickness), which gives off septa penetrating deep into the tumor tissue. The capsule is made up of thin fibres that lie parallel to the neoplasm surface, and of numerous cellular elements containing poorly stained elongated nuclei. The capsule is permeated by vessels filled with formed elements of blood.

Two types of structurally different zones are determined in the tumor. Some of the zones consist of numerous glandular acini (30,61±1,21 micrometers in diameter), that are arranged in the form of islets separated by the bands of connective tissue. The connective tissue bands are permeated by thin-walled vessels that are filled with formed elements of blood.

Many of the glandular acini in those zones are well preserved. They are lined by simple cuboidal epithelium, the average height of which is 6,11±0,2 micrometers. Hyperchromatic nuclei of the epithelial cells (diameter of which is 4,21±0,13 micrometers) are rounded and oval in shape. Lumen of the glandular acini (diameter of which is 13,88±0,3 micrometers) contains homogeneous secretion. In many cases the epithelial cells are vacuolated. Not infrequently the epithelium is partially or entirely cast-off; in this case well preserved nuclei may either be hypochromatic or have prominent karyolemma and nucleoli. In some cases large drops of secretion are surrounded by collapsed epithelial cells.

Other zones of the neoplasm are made up mainly of connective tissue within which single glands are scattered. Glandular acini and ducts are lined by epithelial cells the boundaries of which are not distinct. The glandular acini are 19,11±0,65 micrometers in diameter, the diameter of the ducts is 12,09±0,5 micrometers. Rounded and oval nuclei of the epithelial cells have prominent karyolemma, nucleoli, and masses of chromatin. Average diameter of the nuclei is 4,52±0,2 micrometers. Surrounding connective tissue consists of thin wavy fibres, and of numerous cellular elements containing oval and elongated lightly stained nuclei the diameter of which is 5,15±0,2 micrometers. These zones of the neoplasm are permeated by large thin-walled vessels filled with formed elements of blood.

Conclusions. Development of experimental and spontaneous tumors in laboratory rats causes conspicuous changes in the liver. Such as disintegration of the hepatic plates as a result of hepatocyte collapse.

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ТӘЖІРИБЕЛІК ЕГЕУҚҰЙРЫҚТАРДАТӘЖІРИБЕЛІК ЖӘНЕ СПОНТАНДЫҚ ІСІКТЕРДІҢ ДАМУЫ КЕЗІНДЕ БАУЫРДА БАЙҚАЛАТЫН МОРФОЛОГИЯЛЫҚ ӨЗГЕРІСТЕР

Түйін: Тәжірибелік егеуқұйрықтарда тәжірибелік және спонтандық ісіктердің дамуы кезінде бауырдың морфологиялық өзгерістерізерттелді. Мүшенің қанға толуы, бауыр бауларының дискомплексациясы, сондай-ақ деструктивті жасушалар мен қанның формалық элементтерінен құралған қуыстардың пайда болуымен сипатталатын гепатоциттердің бұзылыстары анықталды.
Түйінді сөздер: ісік, егеуқұйрық, бауыр, гепатоцит

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МОРФОЛОГИЧЕСКИЕ ИЗМЕНЕНИЯ В ПЕЧЕНИ ЛАБОРАТОРНЫХ КРЫС ПРИ РАЗВИТИИ ЭКСПЕРИМЕНТАЛЬНЫХ И СПОНТАННЫХ ОПУХОЛЕЙ

Резюме: Описаны морфологические изменения в печени лабораторных крыс при развитии экспериментальных и спонтанных опухолей. Были выявлены такие явления. как кровенаполненность органа, дискомплексация печеночных балок, а также разрушение гепатоцитов с образованием полостей содержащих деструктивные клетки печени и форменные элементы крови.
Ключевые слова: опухоль, крыса, печень, гепатоцит