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STRUCTURAL FEATURES OF THE PULMONARY METASTASES IN LABORATORY RATS AND MICE IN CASE OF DEVELOPMENT OF TUMORS OF DIFFERENT TYPE

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At present time the biological modeling of diseases is the most important method of scientific investigation. This fact causes the necessity to create such experimental models (using laboratory animals) that correspond to the mechanisms of human illnesses, and to the mechanisms of recovery. Organization of such experiments is impossible without thorough knowledge of the biology of laboratory animals which represent indispensable constituent of preclinical research.
Keywords: *tumor, cell, lung, rat, mouse*

Actuality. At present time the biological modeling of diseases is the most important method of scientific investigation. This fact causes the necessity to create experimental models (using laboratory animals) that correspond to the mechanism of human illnesses, and to the mechanism of recovery. Organization of such experiments is impossible without thorough knowledge of the biology of laboratory animals which represent indispensable constituent of preclinical research. But biological features of laboratory animals are still poorly investigated. Absence of the necessary information of histologic structure of the different types of tumors in the laboratory animals decreases possibility of the purposeful modeling, and increases the probability of mistaken interpretation of the results of experiments. Information that was found in the available scientific literature is concerned mainly with clinical cases [1, 2, 3, 4, 6, 7, 8, 9, 10, 11, 12, 13, 16, 17, 18]. Datas of the experimental pulmonary tumors are scanty [14, 15]. Information of the tumor metastases of lung in laboratory animals was not found. Taking into consideration the above mentioned facts, we tried to determine structural features of pulmonary metastases in laboratory rats and mice in case of development of different types of tumors.

Methods. For our investigation we used:

a) Three-month-old males of laboratory rats that made up four groups (each group consisted of five animals). The group number one included intact animals. The groups number two included rats subjected to intravenous injection of ten thousand of tumor cells. The group number three included rats subjected to subcutaneous injection of the homogenate of the tumor cells. The group number four included rats subjected to intraperitoneal introduction of five million tumor cells. Concentration of the tumor cells was determined with the help of Gorjaev's count chamber.

b) Adult laboratory mice that made up two groups. The group number five included intact three-month-old mice. The group number six included one mice in which the mammary tumor was found

Rats of the groups number one and number two were killed on the twentieth day of the experiment. Rats of the groups number three and number four were kept till the time of full development of the tumor. Mice of the groups number five and six were killed just after discovery of the mammary tumor.

After the dissection the lungs tissue of the tumor were extracted and fixed in solution of formalin. Paraffin sections were stained with hematoxylin-eosin. Histologic specimens were observed under light microscope.

On the outside the lungs of the control rats (rats of the group number one) are covered by serous tunic that consists of flattened mesothelium (its thickness is 4,13±0,19 micrometers, its cells contains hyperchromatic elongated nuclei) and subepithelial connective tissue layer which is permeated by numerous capillaries. The connective tissue layer consists of a large number of cells having oval densely stained nuclei, and of fibres directed along the surface of the organ. Thickness of the serous tunic is 19,2±1,1 micrometers.

The bulk of the pulmonary parenchyma is made up of alveoles, between which the bronchi of different size are located. The alveoles are lined by flattened epithelial cells containing elongated nuclei. There isn't any prominent difference between the diameter of alveoles situated within the peripheral parts of the lungs (21,1±1,6 micrometers) and the diameter of alveoles situates within the internal parts of the organ (23,63±1,26 micrometers). Besides, there isn't any prominent difference between the density of arrangement of alveoles situated within the peripheral parts of the lungs and of alveoles situated within the internal parts of the organ. Within the peripheral parts of the lungs the number of alveoles in one visual field of microscope (ocular 15, objective 40) is 6,73±0,26, and within the internal parts of the organ the number of alveoles in one visual field of microscope is 7,66±0,33.

Alveoles are separated from one another by thin alveolar septa penetrated by capillaries. The alveolar septa consist of densely arranged cells (that contain rounded and oval nuclei having well visible nucleoli and masses of chromatin) and thin connective tissue fibres. Within the peripheral parts of the lungs the thickness of the alveolar septa is 9,75±0,49 micrometers, and within the internal parts of the organ the thickness of the alveolar septa is 8,73±0,43 micrometers.

Bronchi of any size are followed by blood vessels. Arteries are characterized by well developed smooth muscle of media. Large veins contain valves.

Wall of those bronchi, the lumen of which is eight hundred to one thousand micrometers in diameter, contain plates of cartilage 54,05±3,06 micrometers in thickness. The cartilaginous plates contain oval and irregular-shaped cells that are densely arranged. Those cells have prominent boundaries, diameter of the cells is 15,44±0,8 micrometers. Rounded and oval nuclei of the cells (5,38±0,21 micrometers in diameter) contain well visible nucleoli and masses of chromatin.

Mucous tunic of bronchi of any size forms folds that are made up of epithelium and lamina propria. In the bronchi that are eight hundred to one thousand micrometers in diameter, the height of the folds is 62,01±3,01 micrometers. In the bronchi, that are six hundred and fifty to seven hundred and fifty micrometers in diameter, height of the folds is 103,89±5,09 micrometers. In the bronchi, that are three hundred to four hundred micrometers in diameter, the height of the folds is 60,38±3,01 micrometers. In the bronchi, that are two hundred to two hundred and fifty micrometers in diameter, the height of the folds is 64,35±3,3 micrometers. In the bronchi, that are eighty to one hundred micrometers in diameter, the height of folds is 39,25±1,9 micrometers.

Inner surfaces of the bronchi are lined by pseudostratified epithelium the cells of which contain hyperchromic nuclei that are located within middle and basal parts of the cells. Boundaries between the epithelial cells and the basal membrain are not prominent. In the bronchi, that are eight hundred to one thousand micrometers in diameter, the height of the epithelium is 27,69±1,26 micrometers. In the bronchi, that are six hundred and fifty to seven hundred and fifty micrometers in diameter, the height of the epithelium is 20,36±0,86 micrometers. In the bronchi, that are three hundred and fifty to four hundred and fifty micrometers in diameter, the height of the epithelium is 15,56±0,53 micrometers. In the bronchi, that are two hundred to two hundred and fifty micrometers in diameter, the height of the epithelium is 13,33±0,64 micrometers. In the bronchi, eighty to one hundred micrometers in diameter, the height of the epithelium is 10,8±0,5 micrometers.

Lamina propria of the bronchial mucous tunic consists of numerous cells that contain densely stained nuclei of different size, and of thin connective tissue fibres.

Smooth muscle in the bronchial wall represents bundles of densely arranged smooth muscle cells. The bundles are separated by connective tissue layers. The smooth muscle cells contain poorly stained nuclei that are elongated in shape. The specific gravity of the muscle in the bronchial wall increases as the bronchi become smaller but the thickness of the smooth muscle decreases. In the bronchi, that are eight hundred to one thousand micrometers in diameter, the thickness of the smooth muscle is 73,0±3,6 micrometers. In the bronchi, that are six hundred and fifty to seven hundred and fifty micrometers in diameter, the thickness of the smooth muscle is 41,65±2,0 micrometers. In the bronchi, that are three hundred and fifty to four hundred and fifty micrometers in diameter, the thickness of the smooth muscle is 21,72,±1,08 micrometers. In the bronchi, that are two hundred to two hundred and fifty micrometers in diameter, the thickness of the smooth muscle is 17,94±0,8 micrometers. In the bronchi, that are eighty to one hundred micrometers in diameter, the thickness of the smooth muscle is 7,89±0,3 micrometers.

Bronchial adventitia consists of numerous cells, containing rounded and oval nuclei that are densely stained, and of thin fibres. Connective tissue of the bronchial adventitia is gradually continuous with the adjacent alveolar septa, and with adventitia of the adjacent vessels, that's why boundaries of the bronchial adventitia are not prominent. The walls of the bronchi contain lymphatic nodules occupying all the thickness of the wall and even reach the subepithelial layer.

Lungs of the rats of the group number two and number three contain numerous tumor nodes that are grey in colour. Some of these nodes are situated within the organs, and some of them project out on the surfaces of the lungs. Those nodes were evenly distributed throughout the organ.

In the rats of the group number two the tumor nodes are one to two millimetres in diameter. Each of those nodes is surrounded by connective tissue capsule the structural elements of which are arranged rather densely. Within the capsule there are not numerous tumor cells some of which are present in groups.

Central parts of tumor nodes may be necrotic. In the tumor nodes of the smallest size the necrotic centres frequently are absent. As the size of the nodes increases the specific gravity of the necrotic centres becomes greater.

The smallest tumor nodes are made up of densely arranged cells the boundaries of which are indistinct. Rounded and oval nuclei of the cells are characterized by well visible karyolemma and masses of chromatin. The nuclei are 6,47±0,17 micrometers in diameter. The tumor cells are present in groups separated by thin layers of homogeneous substance.

Next to the necrotic centres almost all the tumor cells have signs if destruction. Necrotic tissue is unstructured and contains fragments of nuclei.

In the tumor nodes of the greatest size the necrotic tissue occupies the most part of the metastasis. Besides, within the peripheral parts of the nodes there are also some small necrotic zones. Intact tumor tissue consists of densely arranged cells the boundaries of which are indistinct. Rounded and oval nuclei of the cells have well visible karyolemma and masses of chromatin. Diameter of the nuclei is 6,2±0,22 micrometers. Tumor cells are arranged in groups separated by wide layers of homogeneous substance.

Among the tumor cells there are those having signs of destruction. The bulk of the destroyed tumor cells are situated next to the necrotic centres.

In the rats of the group number three there are numerous intrapulmonary metastases between which intact tissue of lungs is infiltrated by the tumor cells. Diameter of the metastases varied from thirty-five till two hundred micrometers. Connective tissue capsule around the tumor nodes is not conspicuous.

The most of the tumor nodes are made up of densely packed cells the boundaries of which are not visible. Those tumor cells are arranged in groups separated by thin layer of homogeneous substance. Nuclei of the cells are rounded and oval in shape, they are characterized by distinct karyolemma, nucleoli, and masses of chromatin. Diameter of the nuclei is 7,25±0,3 micrometers. Destroyed cells within those nodes are found very seldom.

There are also some tumor nodes that are characterized by more compact arrangement of cells. Hyperchromatic nuclei of the cells are oval, elongated, or irregular in shape. Diameter of the nuclei is 4,56±0,16 micrometers. Such metastases contain considerable number of collapsing cells. There are also small cavities that remain in places of entirely destroyed tumor cells.

Tumor nodes of the rats of this group may contain blood vessels. Within some of them there are necrotic zones which may be centrally or peripherally located.

Numerous tumor cells migrate from the nodes into the surrounding pulmonary tissue where they destroy blood vessels. The destruction of the vessels causes hemorrhage.

In the rats of the group number four the singly arranged intrapulmonary metastases are rounded in shape, they are about five hundred micrometers in diameter. Those tumor nodes consist of densely packed oval and polygonal tumor cells arranged in groups separated by thin layers of homogeneous substance. Diameter of the tumor cells is 11,5 ±0,29 micrometers, and

diameter of their nuclei is 5,58±0,26 micrometers. Central zones of such tumor nodes are necrotic. Pulmonary tissue situated outside the tumor nodes remains intact.

In the intact mice (group №5) the bulk of pulmonary parenchyma is occupied by alveoles between which the bronchi of different size are found. The alveoles are lined with flattened epithelial cell containing elongated nuclei. There is some difference between diameter of alveoles situated within peripheral zoned of lungs (17,94±0,55 micrometers) and diameter of alveoles situated within central zones of the organ (20,75±1,0 micrometers). There is also difference in the density of arrangement of alveoles in different zones of lungs. In one visual field of microscope (ocular 15, objective 40) in peripheral zones the number of alveoles is 14,3±0,47, and in central zones the number of alveoles is 12,6±0,35.

The alveoles are separated from one another by means of thin alveolar septa. In the peripheral zones of the lungs the alveolar septa are 8,27±0,3 micrometers in thickness. In the central zones their thickness is 6,86±0,23 micrometers. Bronchi of any size are followed by blood vessels. Structural difference between arteries and veins is not conspicuous.

Bronchial mucous tunic forms folds which are made up of epithelium and mucosal lamina propria. The folds are arranged so densely that their contours are not visible that's why it is impossible to determine the height of the epithelial cells. The height of the mucosal folds depends on the diameter of bronchi. In the bronchi that are less than one hundred micrometers in diameter the height of the mucosal folds is 17,0±0,63 micrometers, in the bronchi that are one hundred to one hundred and fifty micrometers in diameter the height of the mucosal folds is 16,8±0,56 micrometers, in the bronchi that are one hundred and fifty to two hundred micrometers in diameter the height of mucosal folds is 17,37±0,59 micrometers, in the bronchi that are more than two hundred micrometers in diameter the height of the folds is 18,25±0,74 micrometers.

Bundles of smooth muscle in the wall of bronchioles is not prominent, and the lymphatic nodules are found very seldom.

In the mouse of the group №6 the pulmonary metastases of the mammary tumor were discovered. The tissue of lungs which is situated between the metastases is destroyed and it is infiltrated by formed elements of blood. But many of the bronchi are preserved structurally. In some bronchioles the epithelium is demolished. Parenchyma of metastases consists of lobules of hyperplastic glandular tissue. The lobules are separated by connective tissue bundles that are made up of densely arranged fibres, and of cellular elements containing hyperchromic nuclei. The connective tissue bundles are permeated with numerous small vessels containing formed elements of blood.

The lobules of the metastases represent the dense clusters of numerous cells. Some of the cells are mitotically dividing. The boundaries of the cells are not visible. Their rounded and oval nuclei either are stained deeply or are characterized by presence of distinct karyolemma, nucleoli, and masses of chromatin. Average diameter of the nuclei is 5,03±0,15 micrometers.

Within the lobules one can often find some zones that are composed of anucleate cells, vacuolated cells, cells the nuclei of which have diluted boundaries, fragments of cytoplasm containing irregularly scattered collapsed nuclei.

Many of the metastatic lobules contain cavities. Some of the cavities are oval in shape, the other cavities resemble fissures. Those cavities may contain considerable clusters of the formed elements of blood.

The main tumor in the mouse №6 is surrounded by connective tissue capsule that is made up of thin irregularly arranged fibres, and of cellular elements containing different shaped hyperchromic nuclei. Average diameter of the nuclei is 4,13±0,14 micrometers. In some zones the capsule is characterized by dense arrangement of connective tissue fibres, and by presence of numerous cellular elements. In the other zones the fibres are arranged loosely, and the cellular elements here are not so numerous; in some cases such zones are infiltrated with the formed elements of blood. Some zones of the tumor surface are surrounded by unstructured granular substance.

The capsule gives off numerous connective tissue bundles penetrating deep into the neoplasm and dividing its parenchyma into lobules. The bundles are permeated by thin walled vessels containing formed elements of blood. Within the bundles the considerable extravascular clusters of blood cells are found.

Peripheral zones of the tumor parenchyma contain glandular acini which are singly lying. Their diameter is 30,12±1,2 micrometers. Their lumen (16,96±0,54 micrometers in diameter) contains densely stained secretion. Those glandular acini are lined by simple epithelium that is 5,65±0,16 micrometers in height. Hyperchromic nuclei of the epithelial cells are different in shape, their average diameter is 3,95 ±0,11 micrometers.

The bulk of the tumor parenchyma is made up of large lobules of hyperplastic glandular tissue. Each of the lobules represents a cluster of numerous densely arranged cells, some of which are mitotically dividing. Boundaries of the cells are not visible. Their round and oval nuclei (5,7±0,22 micrometers in diameter) have prominent karyolemma and very well visible nucleoli and masses of chromatin.

Some of the lobules are composed of numerous glandular acini the lumen of which contains deeply stained secretion.

Central parts of many of the lobules are necrotic, and they represent the fragments of eosiniphilic unstructured substance within which collapsed nuclei are irregularly scattered.

Some of the lobules contain cavities which may be oval in shape (and filled with formed elements of blood) or may resemble fissures. Many of the lobules contain small zones which are made up of either vacuolated cells or cells which have diluted boundaries.

Conclusion. As a result of the investigation it was determined that different types of spontaneous tumors of laboratory mice and rats are characterized by both common structural features and features typical of each types of neoplasm.

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ЗЕРТХАНАЛЫҚ ЕГЕУҚҰЙРЫҚТАР МЕН ТЫШҚАНДАРДЫҢ ӨКПЕСІНІҢ ӘР ТҮРЛІ ІСІК КЕЗІНДЕ МЕТАСТАЗДЫҚ БҰЗЫЛЫСТАРЫНЫҢ ҚҰРЫЛЫМДЫҚ ЕРЕКШЕЛІКТЕРІ

Түйін: Авторлар зертханалық егеуқұйрықтар мен тышқандардың аналық жыныс безінің экспериментальді аффинитетті ісігінің солидті және асцитті түрлерінде және сүт безінің ісігі кезінде өкпе метастазының құрылымдық ерекшеліктеріне сипаттама берген. Аналық жыныс безінің аффинитетті ісігінің әр түрлі енгізу тәсілдерін қолданғанда өкпе метастазының жеке өзіне тән нышандары мен сүт безі ісігінің негізгі ісікпен ұқсастықтары да анықталған.
Түйінді сөздер: ісік, жасуша, өкпе, егеуқұйрық, тышқан

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СТРУКТУРНЫЕ ОСОБЕННОСТИ МЕТАСТАТИЧЕСКИХ ПОРАЖЕНИЙ ЛЁГКИХ ЛАБОРАТОРНЫХ КРЫС И МЫШЕЙ ПРИ РАЗВИТИИ РАЗЛИЧНЫХ ВИДОВ ОПУХОЛЕЙ

Резюме: Авторами описаны структурные особенности лёгочных метастазов у лабораторных крыс и мышей при развитии солидной и асцитной форм экспериментальной перевивной опухоли АфОЯ, а также при развитии спонтанной опухоли молочной железы. Были установлены специфические особенности лёгочных метастазов при различных способах перевивки аффинитетной опухоли яичника, а также структурная схожесть легочных метастазов опухоли молочной железы с основной опухолью.
Ключевые слова: опухоль, клетка, легкое, крыса, мышь