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**STRUCTURAL CHANGES IN THE THYMUS OF LABORATORY RATS IN CASE OF DEVELOPMENT OF EXPERIMENTAL AND SPONTANEOUS TUMORS**

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*It is known that the thymus is an organ regulating immunomorphologic processes in the organism. Reactive changes in the thymus occur in case of oncological diseases. This article describes morphologic reaction of the thymus to the development of some experimental and spontaneous tumors.*

**Keywords:** thymus, rat, tumor.

**Actuality.** It is known that the thymus is an organ regulating immunomorphologic processes in the organism. Reactive changes in the thymus occur in case of oncological diseases. Information that we discovered in the available scientific literature concerns structural changes in thymus in case of chemically induced tumors [17]. We tried to determine structural changes in the rat's thymus in case of intrapulmonic development of the experimental solid ovarian tumor. There is also some information received by means of investigation of the mortuary material [5, 7]. We couldn't find detailed information about structural features of tumors of laboratory animals, though there are data describing clinical material [1, 2, 3, 4, 6, 8, 9, 10, 11, 12, 13, 15, 16, 18, 19, 20].

We investigated influence of experimental and spontaneous tumors on the thymic structure.

**Methods.** For our investigation we used five groups of adult laboratory rat's males. Five rats of the group number one (control) were intact. Five rats of the group number two were subjected to the intravenous transplantation of fifty thousand cells of ovarian tumor. The number of the tumor cells was determined with the help of Gorjaev's count chamber. Five rats of the group number three were subjected to the subcutaneous transplantation of lymphosarcoma cells. Five rats of the group number four were subjected to the intraperitoneal transplantation of sarcoma 45 cells. Two rats of the group number five contained spontaneous mammary tumor.

The rats of the control group were killed on the fifteenth day from the beginning of the experiment. The rats of the groups №2, №3, and №4 were killed by the time of the full development of the experimental tumors. The rats of the group №5 were killed after their spontaneous tumors were discovered.

Thymuses and tumors were extracted and fixed in the solution of formalin. Paraffin sections were stained with hematoxylin-eosin. Histologic specimens were investigated under light microscope.

**Discussion.** Microscopically it was estimated that on the outside the thymus of the control rats is surrounded by connective tissue capsule that consists of numerous cells, and of thin wavy fibres lying parallel to the surface of the organ. The connective tissue cells contain rounded and oval nuclei that are poorly stained, and are characterized by presence of distinct karyolemma and masses of chromatin. Within some zones of the capsule its structural elements are loosely arranged, and among them there are lymphoid cells. Thickness of the capsule is  $19,03 \pm 0,62$  micrometers.

Trabeculae arising from the capsule extend deeply into the substance of the thymus and partially separate

lobules from each other. The trabeculae are penetrated by thin-walled vessels filled with formed elements of blood. Inner surfaces of the blood vessels are lined by thin endotheliocytes containing elongated poorly stained nuclei.

Each thymic lobule has an outer cortex and an inner medulla that differ from one another by density of the lymphoid cell arrangement. The medulla of the adjoining lobules is continuous.

Thickness of the cortex is  $213,33 \pm 10,04$  micrometers. The lymphoid cells in it are very densely arranged, their boundaries are not prominent. Rounded and oval nuclei of the cells are densely stained and are  $3,86 \pm 0,14$  micrometers in diameter.

The epithelial reticular cells are sometimes found between the cortical thymocytes. The epithelial reticular cells contain rounded and oval poorly stained nuclei that have distinct karyolemma and masses of chromatin. The nuclei are  $5,62 \pm 0,21$  micrometers in diameter. The thymic cortex is penetrated by thin-walled vessels filled with formed elements of blood.

Thymic medulla is  $260,0 \pm 7,6$  micrometers in thickness. It is penetrated by numerous small blood vessels. Thymocytes of the medulla are arranged looser, and their nuclei are bigger in size than those of the cortex, the diameter of the nuclei is  $4,45 \pm 0,14$  micrometers.

Epithelial reticular cells of the medulla are found more often, than those in cortex, and some of them are arranged in groups including two to twelve cells. Nuclei of the cells are  $6,9 \pm 0,3$  micrometers in diameter. Among the medullary epithelial reticular cells there are degenerative ones, this fact obviously is the result of the beginning of formation of Hassall's corpuscles.

Completely formed Hassall's corpuscles are found in the cortex of the lobules. The corpuscles are rounded or irregular in shape, they are composed of concentrically arranged epithelial cells. Some of them contain centrally located cavities. Average diameter of the Hassall's corpuscles is  $10,3 \pm 0,4$  micrometers.

In different parts of the thymus of the control rats there are singly present large oval cells ( $11,4 \pm 0,2$  micrometers in diameter). Their cytoplasm is eosinophilic, and their nuclei are centrally situated and densely stained. Those cells resemble plasma cells.

In the rats of the group number two the thymus is surrounded by connective tissue capsule infiltrated by lymphoid cells. Capsular vessels are dilated and filled with formed elements of blood.

Within the lobules of the thymic parenchyma the structural difference between cortex and medulla isn't conspicuous: in all zones the lymphoid cells are arranged

very densely. Boundaries of the thymocytes are not prominent.

In some zones of the lobules the nuclei of the lymphoid cells are densely stained; the diameter of the nuclei is  $3,67 \pm 0,16$  micrometers. In other zones the thymocytes contain poorly stained nuclei that are  $4,56 \pm 0,1$  micrometers in diameter; within those zones there are small cavities that remain in places of the entirely destroyed lymphoid cells. Some zones are made up of homogeneous eosinophilic substance containing fragments of thymocytes.

Thymus of the rats of the group number two is penetrated by numerous dilated blood vessels filled with the formed elements of blood. Hassall's corpuscles are not found. The subcapsular zone of the thymic lobules contain large clusters of cells that resemble the tumor cells. Such clusters of cells are penetrated by numerous dilated thin-walled vessels filled with formed elements of blood. Rounded and oval nuclei of the cells are  $8,77 \pm 0,22$  micrometers in diameter. They have distinct karyolemma, nucleoli, and masses of chromatin.

In the rats of groups number two tumor nodes are located in lungs. They are made up of clusters of densely packed cells. These clusters consist of clusters of cells separated by thin layers of homogeneous substance. Within each group, the cells are structurally similar. Some of the cells possess conspicuous boundaries, and their nuclei contain large masses of chromatin, other cells show figures of mitosis. Hence we can suppose that the clusters of the tumor cells represent isogenous groups, each of which is derived from one maternal cell.

In the rats of the group number two the diameter of the tumor cells is  $8,73 \pm 0,41$  micrometers, and diameter of their nuclei is  $6,16 \pm 0,3$  micrometers. The tumor nodes are penetrated by blood vessels. The walls of the blood vessels are gradually destroyed by surrounding tumor cells. Total destruction of the vascular wall causes bleeding into the tumor tissue. Those zones of the tumor tissue, that are adjacent to the zone of the bleeding, are necrotic.

The tumor nodes are surrounded by connective tissue infiltrated by the tumor cells. Those zones of the lungs which are situated between the tumor nodes are destroyed.

In the rats of the group number three the thymic parenchyma is characterized by dense arrangement of the lymphoid elements within all parts of the organ. Hence the lobular structure and differentiation of cortex and medulla are not conspicuous. Epithelial reticular cells are not visible.

Some of the lymphocytes ( $7,53 \pm 0,3$  micrometers in diameter) have distinct boundaries, their nuclei ( $5,19 \pm 0,2$  micrometers in diameter) are characterized by well visible karyolemma and nucleoli. In other lymphocytes the boundaries are not prominent, and their hyperchromatic nuclei are  $3,4 \pm 0,1$  micrometers in diameter.

Numerous Hassall's corpuscles are rounded, oval, or irregular in shape. Some of the thymic corpuscles represent unstructured eosinophilic mass, the other corpuscles contain clusters of nuclei.

Between the lymphoid cells there are some thin-walled vessels containing formed elements of blood. There are also small cavities filled with homogeneous eosinophilic substance.

Tumor tissue is made up of densely arranged cells boundaries of which are well visible. Cytoplasm of the cells is granular. Nuclei are rounded, oval, or bean-shaped, they are characterized by distinct karyolemma

and nucleoli. Diameter of the tumor cells is  $6,51 \pm 0,2$  micrometers, and diameter of their nuclei is  $3,86 \pm 0,14$  micrometers.

The tumor tissue contains cavities that may be empty and may be filled by unstructured eosinophilic mass containing singly arranged tumor cells. The cavities may be rounded in shape and may represent fissures.

In the rats of the group number four the thymus is surrounded by connective tissue capsule infiltrated by lymphoid cells. Capsular vessels are dilated and filled with formed elements of blood.

Within the lobules of the thymic parenchyma the structural difference between cortex and medulla isn't conspicuous: in all zones the lymphoid cells are arranged very densely. Boundaries of the thymocytes are not prominent.

In some zones of the lobules the nuclei of the lymphoid cells are densely stained; the diameter of the nuclei is  $3,67 \pm 0,16$  micrometers. In other zones the thymocytes contain poorly stained nuclei that are  $4,56 \pm 0,1$  micrometers in diameter; within those zones there are small cavities that remain in places of the entirely destroyed lymphoid cells. Some zones are made up of homogeneous eosinophilic substance.

In the rats of the group number four the tumor is surrounded by connective tissue capsule which consists of numerous cells and thin fibres. The thickness of the capsule is varies in different regions. In the regions where the capsule is thinnest (its thickness is less than thirteen micrometers) its structural elements are arranged densely and are directed along the surface of the tumor. The nuclei of the cells are small, elongated, hyperchromatic. Average diameter of the nuclei is  $3,94 \pm 0,16$  micrometers. As the thickness of the capsula increases its structural elements gradually become wavy and then they become directed in different directions. In regions where the capsule is thickest (its thickness achieves one hundred and eighty micrometers) its connective tissue cells contain both small hyperchromatic nuclei and bigger nuclei containing distinct masses of chromatin. Those nuclei are rounded, oval, and elongated in shape, their diameter is  $6,98 \pm 0,3$  micrometers.

The capsule is well vascularized. In those zones where the capsula is thinnest the vessels in it are discovered very seldom. As the capsule becomes thicker, the number and size of its vessels increases. From the capsule the vessels penetrate deeply into the tumor where they form dense network.

In the peripheral parts of the tumor the cells are densely packed, their boundaries are indistinct. Cytoplasm of many of the cells is vacuolated. Nuclei are hyperchromatic, their diameter is  $8,35 \pm 0,2$  micrometers. Shapes of the nuclei are rounded, oval, polygonal.

Within the internal parts of the tumor the cells are arranged more loosely. Cytoplasm in many of the cells is vacuolated. Nuclei of the cells are  $10,18 \pm 0,4$  micrometers in diameter, they are rounded, oval, or bean-shaped. They are characterized by distinct karyolemma and masses of chromatin. Each nucleus contains one to six nucleoli which are different in size. There is tendency to decrease of the size of the nucleoli within a nucleus while increasing their number. Though there are some nuclei that contain nucleoli which considerably differ from each other in size.

Towards the centre of the tumor the number of destroying cells increases. Nuclei of such cells are wrinkled, and their cytoplasm is brightly eosinophilic. There are also small cavities that were formed in the places of the entirely destroyed tumor cells.

Central parts of the tumor are necrotic.

In the rats of the group number five all parts of the thymus are characterized by very dense arrangement of the lymphoid cells, hence the differentiation of cortex and medulla in the thymic lobules are not distinct. Boundaries of the lymphoid cells are invisible, their rounded, oval, and angular nuclei ( $3,74 \pm 0,12$  micrometers in diameter) are densely stainable. The thymic tissue is permeated by thin-walled vessels that are filled with blood. Epithelial reticular cells in it are not found. Between lymphocytes there are not numerous oval cells containing hyperchromic eccentric nuclei, the cells are about ten micrometers in diameter. Small Hassall's corpuscles are found very seldom, their diameter is not more than 6,5 micrometers.

Some zones of thymic parenchyma are made up of destroyed lymphoid cells. Some of these zones contain homogeneous colloid substance.

In some peripheral thymic zones the lymphoid cells are arranged loosely, their boundaries are well visible. Such cells are  $5,5 \pm 0,17$  micrometers in diameter.

In one of the animal of the group number five the tumor is surrounded by connective tissue capsule (that is  $23,13 \pm 0,9$  micrometers in thickness) that gives off trabecules penetrating deep into the tumor tissue. The capsule is made up of thin fibres that pass along the surface of the neoplasm, and of numerous cells containing poorly stained elongated nuclei. The capsule is permeated with blood vessels.

Inside the tumor one can detect two main types of structurally different zones. Some of the zones are made up of numerous glandular acini that are  $30,61 \pm 1,21$  micrometers in diameter. The acini are arranged in the form of clusters separated by connective tissue bundles. The bundles are permeated with rather large thin-walled vessels filled with formed elements of blood. Some of the glandular acini are very well preserved. They are lined by simple cuboidal epithelium the average height of which is  $6,11 \pm 0,2$  micrometers. Densely stained nuclei of the epithelial cells (the average diameter of which is  $4,21 \pm 0,13$  micrometers) are rounded and oval in shape. Glandular acini (that are  $13,88 \pm 0,3$  micrometers in diameter) have lumen containing homogeneous secretion. Many of the epithelial cells are considerably vacuolated.

Cast-off epithelium is discovered as well, but well preserved nuclei of destroyed epithelial cells are seen within the lumens of glands. Some of the nuclei are densely stained, the other nuclei have prominent karyolemma and distinct nucleoli. There are glands in which large drops of secretion are surrounded by collapsed epithelial cells.

The bulk of some parts of the tumor is made up of connective tissue within which glands are scattered. Acini and ducts of the glands are lined by epithelial cells that have inconspicuous boundaries. Average diameter of the acini is  $19,11 \pm 0,65$  micrometers, average diameter of ducts is  $12,09 \pm 0,5$  мкм. Rounded and oval nuclei of the epithelial cells are characterized by presence of conspicuous karyolemma, distinct nucleoli, and masses of chromatin. Average diameter of the nuclei is  $4,52 \pm 0,2$  micrometers. Surrounding connective tissue is made up of wavy fibres, and numerous cells containing oval and elongated poorly stained nuclei. Average diameter of the nuclei is  $5,15 \pm 0,2$  micrometers. These parts of the tumor contain rather large thin-walled vessels filled with formed elements of blood.

In the other animal of the group number five the tumor consists entirely of connective tissue. In some zones of the neoplasm the connective tissue is made up of thin wavy fibres, and of cells containing rounded, oval and angular nuclei that are characterized by presence of prominent karyolemma and nucleoli. Average diameter of the nuclei is  $5,85 \pm 0,22$  micrometers. These zone of the tumor are permeated with numerous thin-walled vessels filled with formed elements of blood.

In the other zones of the tumor the connective tissue fibres are homogenized. Numerous cells contain poorly stained oval and elongated nuclei that are  $2,28 \pm 0,59$  micrometers in diameter.

There are vast zones that represent poorly stained unstructured substance within which one can find small cavities containing destroyed nuclei of the malignant cells and fragments of their cytoplasm.

**Conclusion.** Development of experimental and spontaneous tumors in rats causes structural changes in thymus. Boundaries between cortex and medulla in the thymic lobules disappear. Many of lymphoid cells collapse.

#### REFERENCES

- 1 Ашуров З.М., Сынебогов С.В., Денисова Л.Б., Варфоломеева С.Р., Инюшкина Е.В. Неходжинская лимфома глоточного кольца Пирогова-Вальдейера // Вестник оториноларингологии. - 2004.- № 4.- С. 54-55.
- 2 Бровкина А.Ф., Сорокина М.Н., Каплина А.В. Внутриглазная злокачественная лимфома // Вестник офтальмологии. - 1990.- Т. 106.- №6.- С. 48-53.
- 3 Вишневская Я.В., Ермилова В.Д., Смирнов А.В., Коробейникова Г.М. Карциносаркома молочной железы (описание 2 случаев) // Архив патологии.- 2. - Т.62.- №1.- С. 37-40.
- 4 Волкова М.А., Рейзингер М.А., Круглова Г.В., Пробатова Н.А. Лимфосаркома с парапротеинемией // Терапевтический архив.- 1980.- Т. 52.- № 2.- С. 107-111.
- 5 Галил-Оглы Г.А., Порошин К.К., Алпченко Л.А., Крылов Л.М. Патологическая анатомия опухолей вилочковой железы // Архив патологии.- 1980.- Т. 42.- В. 11.- С.6-16.
- 6 Далматова И.А., Бастимиева Б.Е. Клинико-морфологические особенности злокачественных лимфом орбиты // Здравоохранение Казахстана. - 1993.- №9.- С. 36-37.
- 7 Догель Л.В. К вопросу о патоморфологии вилочковой железы при миастении // Научные труды Ленинградского института усовершенствования врачей.- Л.: 1971. - В.103.- С. 165-173.
- 8 Заривчатский М.Ф., Иванов С.И., Кулигин А.Г. Первичная лимфосаркома червеобразного отростка // Вестник хирургии им. И.И. Грекова. - 1990.- Т. 145.- № 12.- С. 36-42.
- 9 Коган Е.А., Секамова С.М., Попова И.В., Юшков П.В. Карциносаркома лёгкого // Архив патологии.- 1991.- Т.53.- №2.- С. 67-72.
- 10 Корчмару И.Ф., Яковлева И.А., Гладыш В.В., Бодян В.Д. Неходжинская лимфома клеток мантийной зоны // Вопросы онкологии.- 2000.- Т. 46.- № 2.- С. 236-237.

- 11 Кременецкая А.М., Воробьев А.И., Харазишвили Д.В., Франк Г.А., Воробьев И.А., Капланская И.Б., Кравченко С.К., Моисеева Т.Н., Шкловский-Корди Н.Е., Чернова Н.Г., Лорие Ю.Ю. Гигантоклеточные лимфосаркомы или варианты формы лимфогранулематоза // Терапевтический архив.- 2002.- Т. 74.- № 7.- С. 48-52.
- 12 Лапин Б.А., Яковлева Л.А., Инджия Л.В. Злокачественные лимфомы приматов и принципы их морфологической диагностики (на модели злокачественной лимфомы павианов) // Архив патологии.- 2007.- Т. 69.- № 4.- С.- 38-41.
- 13 Мустяцэ Л.З., Корчмару И.Ф., Яковлева И.А., Робу М.В. Беременность у больной лимфообластной лимфосаркомой в периоде полной ремиссии // Вопросы онкологии.- 1993.- Т. 39.- № 7-12.- С. 325-326.
- 14 Мустяцэ Л.З., Корчмару И.Ф., Яковлева И.А., Робу М.В. Первичная изолированная лимфообластная лимфосаркома головного мозга // Вопросы онкологии.- 1993.- Т. 39.- № 7-12.- С. 325-326.
- 15 Петров Н.Н. Злокачественные опухоли.- Л.: 1932.- Т.1.- 619 с.
- 16 Петров Н.Н. Злокачественные опухоли.- Л.: 1934.- Т.2.- 473 с.
- 17 Селезнёва Т.Н., Гриневиц Ю.А. О морфофункциональных изменениях в надпочечниках и тимусе крыс при химически индуцированном канцерогенезе молочных желёз // Экспериментальная онкология.- 1980.- Т.2.- №3.- С. 37-40.
- 18 Франк Г.А. О клинической морфологии злокачественных лимфом // Терапевтический архив.- 1974.- Т. 46.- С. 60-66.
- 19 Шкондин Л.А., Маликова Н.А., Зверев Г.Р. Случай лимфосаркомы селезёнки // Вестник рентгенологии и радиологии.- 1992.- № 4.- С. 54.
- 20 O'Neill B.P., Glig J.J. Primary central nervous system lymphoma // Mayo Clin. Proc.- 1989.- V. 64.- P. 1005-1020.

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#### **ТӘЖІРИБЕЛІК ЕГЕУҚҰЙРЫҚТАРҒА ЕГІЛГЕН ЖӘНЕ СПОНТАНДЫҚ ІСІКТЕРДІҢ ДАМУЫ КЕЗІНДЕ ТИМУСТА БАЙҚАЛАТЫН ҚҰРЫЛЫМДЫҚ ӨЗГЕРІСТЕР**

**Түйін:** Тәжірибелік егеуқұйрықтарда егілген және спонтандық ісіктердің дамуы кезінде тимустың морфологиялық өзгерістері зерттеліп, тимустың ісіктің өсуіне жалпы реакциясы мен ісіктің белгілі бір түріндегі тимус өзгерістері анықталды. Ісіктің өзіне тән морфологиялық құрамына да сипаттама берілді

**Түйінді сөздер:** тимус, егеуқұйрық, ісік

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#### **СТРУКТУРНЫЕ ИЗМЕНЕНИЯ В ТИМУСЕ ЛАБОРАТОРНЫХ КРЫС ПРИ РАЗВИТИИ ПЕРЕВИВНЫХ И СПОНТАННЫХ ОПУХОЛЕЙ**

**Резюме:** Были изучены морфологические изменения тимуса лабораторных крыс при развитии перевивных и спонтанных опухолей. Были установлены как общие структурные закономерности реакции тимуса на опухолевый рост, так и особенности при развитии каждого конкретного вида опухоли. Описан также морфологический состав самих опухолей.

**Ключевые слова:** тимус, крыса, опухоль.