ActaCAMU
Scientific journal

MERIDIAN
DIAGNOSTIC HOSPITAL

UDK: 616.24 - 006.03 - 07

PATHOMORPHOLOGY AND IMMUNOGISTOCHEMISTRY OF LEIOMYOMATOUS HAMARTOMA OF THE LUNGS

ЎПКАНИНГ ЛЕЙОМИОМАТОЗЛИ ГАМАРТОМАСИНИНГ ПАТОМОРФОЛОГИЯСИ ВА ИММУНОГИСТОХИМИЯСИ

ПАТОМОРФОЛОГИЯ И ИММУНОГИСТОХИМИЯ ЛЕЙОМИОМАТОЗНОЙ ГАМАРТОМЫ ЛЕГКИХ

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Rakhmanova N.S. (2025). PATHOMORPHOLOGY AND IMMUNOGISTOCHEMISTRY OF LEIOMYOMATOUS HAMARTOMA OF THE LUNGS. Actacamu, 10(2), 96–101. https://doi.org/10.5281/zenodo.15641728

Abstract. *The article studies the morphogenesis, pathomorphology and immunohistochemical aspects of leiomyomatous hamartoma of the lung. The objects of study were pulmonary hamartomas examined in the biopsy diagnostics department of the RPAM during 2014-2024. Lung hamartoma has a microscopically polymorphic structure, mainly consisting of bundles of smooth muscles located in different directions, a small amount of fibrosis, adipose tissue, epithelial cells that have undergone various metaplastic and dysplastic changes, located between them, covering the gaps. The marker desmin, which determines the level of differentiation of mesenchymal cells, is expressed in leiomyomatous hamartoma by an average of 17.4%; positive staining of the sarcoplasm and sarcomeres of cells confirms that this marker is localized in myosin, endoplasmic reticulum and mitochondria. Vimentin is located in the intermediate filament of mesenchymal cells, occupies a place in the nucleus, endoplasmic reticulum and mitochondria, is expressed in both the nucleus and sarcoplasm of smooth muscle cells, and is important for maintaining cell shape and providing resistance. to mechanical stress.*

Key words*: lung, hamartoma, chondroid, fibromatous, leiomyomatous, pathomorphology, desmin, vamentin.*

Аннотация. *Ушбу мақолада ўпка лейомиоматозли гамартомасининг морфогенези, патоморфологияси ва иммуногистокимёвий жиҳатлари ўрганилган. Объект сифатида 2013-2023 йиллар давомида РПАМ биопсия диагностикаси бўлимида текширувдан ўтган ўпка гамартомалари ажратиб олинган. Ўпка гамартомаси микроскопик жиҳатдан полиморф тузилишга эга бўлиб, асосан ҳар хил йўналишда жойлашган силлиқ мушак тутамларидан, кам миқдорда фиброз, ёғ тўқимадан, уларнинг орасида ёриқларни қоплаган ҳолда жойлашган ҳар хил метапластик ва диспластик ўзгаришларга учраган эпителий ҳужайралари аниқланади. Мезенхимал ҳужайралар дифференциалланиш даражасини белгилайдиган десмин маркери лейомиоматозли гамартомада ўртача 17,4%да экспрессияланганлиги, ҳужайралар саркоплазмаси ва саркомери мусбат бўялиши ушбу маркернинг миозин, эндоплазматик тўр ва митохондрийларда жойлашганлигини тасдиқлайди. Виментин мезенхимал ҳужайралар оралиқ филаментида жойлашган бўлиб, ядро, эндоплазматик тўр ва митохондрийларда ўрин эгаллаганлиги сабабли силлиқ мушак ҳужайраларнинг ҳам ядро, ҳам саркоплазмасида экспрессияланганлигидан, ҳужайралар шаклини сақлашда, механик таъсиротларга чидамлилигини таъминлашда аҳамиятли ҳисобланади.*

Калит сўзлар: *ўпка, гамартома, хондроидли, фиброматозли, лейомиоматозли, патоморфология, десмин, вамантин.*

Аннотация. *В статье изучены морфогенез, патоморфология и иммуногистохимические аспекты лейомиоматозной гамартомы легкого. В качестве объектов исследования были выбраны легочные гамартомы, обследованные в биопсийно-диагностическом отделении РПАМ в течение 2013-2023 гг. Гамартома легкого имеет микроскопически полиморфное строение, состоящее преимущественно из пучков гладких мышц, расположенных в разных направлениях, небольшого количества фиброза, жировой ткани, эпителиальных клеток, подвергшихся различным метапластическим и диспластическим изменениям, расположенных между ними, покрывающих щели. Маркер десмин, определяющий уровень дифференцировки мезенхимальных клеток, экспрессируется в среднем в 17,4% лейомиоматозных гамартом, положительное окрашивание саркоплазмы и саркомеров клеток подтверждает локализацию этого маркера в миозине, эндоплазматическом ретикулуме и митохондриях. Виментин расположен в промежуточной нити мезенхимальных клеток, занимает место в ядре, эндоплазматическом ретикулуме и митохондриях, экспрессируется как в ядре, так и в саркоплазме гладкомышечных клеток, важен для поддержания формы клеток и обеспечения резистентности. к механическому воздействию.*

Ключевые слова: *легкое, гамартома, хондроид, фиброматозный, лейомиоматозный, патоморфология, десмин, вамантин.*

The aim of the scientific work. Lung hamartoma is a benign tumor arising from at least two types of mesenchymal tissues of the respiratory system. Most often, it arises from tissues of mesenchymal origin, such as connective, adipose, and smooth muscle tissues. The histogenesis of lung hamartoma, according to most scientists, is a neoplasia that begins with the appearance of chromosomal aberrations in the genome of tissues and cells. According to Tomashefski, lung hamartomas are formed by a combination of several mesenchymal tissues, similar to mesenchymomas [3, 4, 5, 7]. They often contain glandular structures. Bateson and co-authors [6] concluded, as a result of a number of studies, that the glandular structures in the hamartoma arise as a result of metaplasia of the alveolar and bronchial epithelium [6, 7, 8]. Fletcher et al [9] examined 17 lung chondroid hamartomas and found chromosomal aberrations in 10, translocations of the 12q-15 gene in four, and q15;q24 in three, confirming the similarity of this condition to uterine leiomyoma.

Lung hamartomas are a common benign tumor and are most often found in people aged 30-70 years, and rarely in the lungs of children and infants. Hamartomas are found in 60-64% of all benign lung tumors. According to various authors, lung hamartomas are found in only 0.025-0.32% of cases at autopsy, and are 2-4 times more common in men than in women. It has been confirmed that peripheral hamartomas are 3 times more often located in the anterior segments, more often in the right lung compared to the left.

Leiomyomatous hamartoma of the lung was described by Cruickshank et al. in 1953. This type of hamartoma is much rarer than chondroid hamartoma [8]. In the literature, this type of hamartoma is called by various names, including “adenoleiomyomatous hamartoma” and “fibroleiomyomatous hamartoma”. Leiomyomatous hamartoma often contains epithelial tissue, with glandular epithelium in 64.5% of cases, hairy epithelium in 28.6%, and rarely basal epithelial cells [1, 2, 7, 9]. Immunohistochemical analysis revealed that the epithelium in the hamartoma contained positive TTF1, SPA, KRT markers, negative p53, CD99, CD34, BCL2, and STAT6 markers, and a Ki67 marker index indicating cell proliferation of 0.2%. Desmin is a protein marker that is initially produced in the embryogenesis of muscle cells, and is actually weakly expressed in muscle cells, and can be strongly expressed only when muscle cells are fully differentiated. Desmin is associated with many structures in the cytoplasm of muscle cells. Desmin is located in the formation of the Z disk of the myosin proteins of the sarcomere, forming a special network. Desmin binds to the sarcomere and connects the contractile apparatus with the nucleus and mitochondria. These ligaments keep the structure and mechanics of the muscle cell intact during contraction. Desmin also plays an important

role in mitochondrial function, including maintaining mitochondrial structure, quantity, and function intact during muscle contraction [8].

Vimentin is a marker of microtubules and actin, important in the structure of the cell cytoskeleton located in the intermediate filaments of tissue and cells with mesenchymal histogenesis. Vimentin is a marker that can be tested to confirm that cells are of mesenchymal origin. In the embryonic development of cells of mesenchymal origin, it is an immunohistochemical marker located in their intermediate filaments. Vimentin is located adjacent to the nucleus, endoplasmic reticulum and mitochondria of mesenchymal cells. Vimentin is important in maintaining the shape of cells and providing resistance to mechanical influences [9].

From the information given above, it is known that the histogenesis, morphogenesis and even pathomorphological changes of leiomyomatous hamartoma of the lung have been little studied. Therefore, in this study, we aimed to study leiomyomatous hamartoma of the lung comprehensively, that is, histogenetically and morphogenetically.

Materials and methods. The results of the study showed that cases of lung hamartoma were isolated from biopsies examined at the Republican Center for Pathological Anatomy of the Republic of Uzbekistan in 2013-2022. During these years, 28 lung hamartomas were isolated from a total of 670 thousand biopsies. 74.5% of the identified cases were men, the rest were women. The average age of the patients was 52.6 years, the youngest patient was 21 years old, and the oldest was 81 years old. Each of these cases was stained using general histological and histochemical methods, and each was given a unique histotopographic description. Of the 28 hamartomas, 17 were chondroid, 5 were fibromatous, and 6 were leiomyomatous hamartomas. Sections were prepared from paraffin blocks and stained with hematoxylin and eosin. Immunohistochemical examination of desmin and vimentin was performed as follows. Histological sections cut from paraffin-embedded blocks fixed in 10% formalin were rehydrated, treated with proteolytic enzymes to preserve tissue proteins at original levels, and heated in a thermostat to dehydrate. For immunohistochemical examination, it was carried out by the method of the Dako company. First, the paraffin sections were deparaffinized and rehydrogenated. The section was held in 1% hydrogen peroxide for 10 minutes to remove any residual water. At room temperature, the primary antibody was dropped, after the section was washed, the secondary antibody was dropped and incubated at room temperature for 15-30 min, washed again, then fixed in peroxidase-activated solution for 5-10 min, after washing again, it was stained in Mayer's hematoxylin for 1-2 min and covered in Canada balsam. The cells of mesenchymal origin, i.e. smooth muscle cells, fibroblasts, macrophages in 6 leiomyomatous hamartoma preparations stained by immunohistochemical method were counted and expressed in brown, and the expression level was calculated as a percentage of 500 cells, desmin averaged 17.4%, vimentin - made 12.6%.

Results. Leiomyomatous hamartoma of the lung has a microscopic polymorphic structure, consisting mainly of smooth muscle bundles located in different directions, with a small amount of fibrosis, adipose tissue, and epithelial cells with various metaplastic and dysplastic changes, covering the gaps between them. When examining leiomyomatous hamartomas microscopically, it was found that their tissue mainly consists of smooth muscle cells forming bundles located in different directions, and their cells are elongated in shape, and their nuclei are oval and elongated. The cytoplasm of smooth muscle cells was found to be eosinophilic, and there were no inclusions in its composition. It was found that there were gaps between the bundles of smooth muscle cells and that they were covered with prismatic bronchial epithelium.

Microscopic examination of leiomyomatous forms isolated from lung hamartomas revealed that the hamartoma of this form is a hamartoma of mixed composition according to histological structure. The presence of smooth muscle tissue structures in the tissue is the main factor to confirm that it is a leiomyomatous hamartoma. In our material, the presence of smooth muscle cells in the hamartoma tissue was confirmed in 6 cases. In most of these cases, it was observed that smooth muscle tissue occupied most of the space of the hamartoma tissue (Figure 1). In this case, it is determined that the smooth muscle cells are of different thicknesses and are arranged in bundles in different directions. It is determined that a large number of blood vessels and nerve fibers are located between the tufts in the longitudinal direction. In the cross-section, it is observed that the tufts of

muscle tulips are surrounded by fibrous tissue. In some places of the muscle tissue, fibrosis and adipose tissue are found to be connected. Since the hamartoma is leiomyomatous, it is confirmed that, along with fibrosis and adipose tissue, there are also islets of connective tissue in its composition. It is known that cracks of various shapes and sizes can appear in the structure of hamartomas, and in most cases these cracks are covered by epithelial cells. It is found that the cracks in the structure of the leiomyomatous hamartoma tissue are mainly covered by prismatic and cylindrical epithelial cells. It has been found that, in addition to the above-mentioned tissues, the structure of the leiomyomatous hamartoma tissue contains islets of connective and adipose tissue.

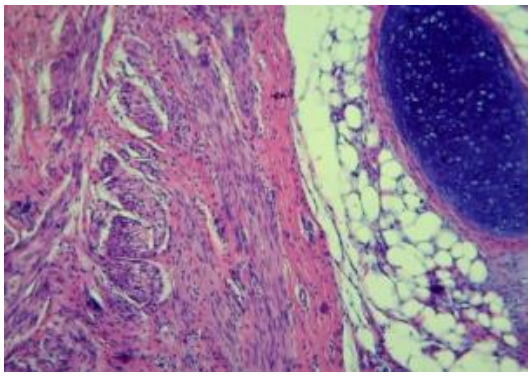

Figure 1. Patient M, 48 years old, had a leiomyomatous hamartoma of the lung composed of smooth muscle, adipose, and adipose tissue. Paint: G-E. Floor: 10x20.

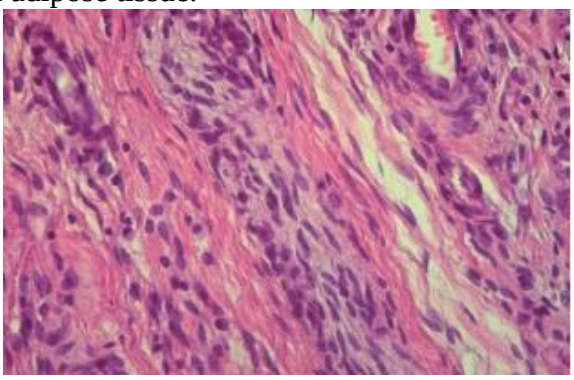

Figure 2. Patient A, 36 years old, had a leiomyomatous hamartoma of the lung, with blood vessels and nerve fibers between parallel muscle fibers. Paint: G-E. Floor: 10x40.

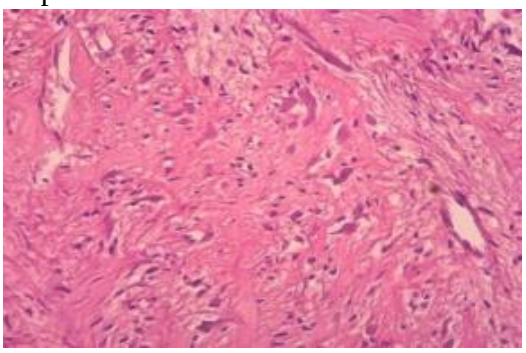

Figure 3. Patient P, 52 years old, leiomyomatous hamartoma of the lung, proteinaceous substance accumulated in the cytoplasm of smooth muscle cells. Paint: G-E. Floor: 10x40.

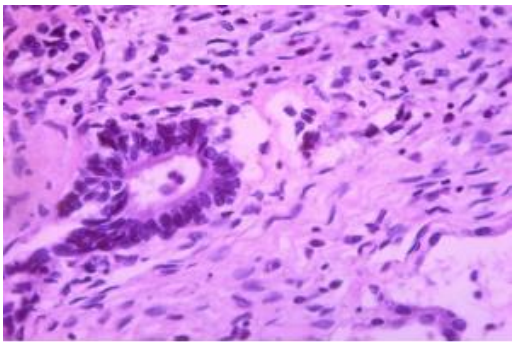

Figure 4. Patient C, 42 years old, leiomyomatous hamartoma of the lung, muscle cells are located in different directions, epithelial gland cells appeared between them. Paint: G-E. Floor: 10x40.

If we study the histotopographic arrangement of smooth muscle cells in the hamartoma, it is found that the longitudinally arranged smooth muscle cells form bundles of various thicknesses, the muscle cells are mainly elongated in shape, the nuclei are also elongated and oval in shape, and the muscle fibers are located in a manner that is interconnected and forms a variety of densities. Between the muscle bundles, connective and nerve fibers of a relatively lighter color in terms of staining are observed (Fig. 2). When examining the smooth muscle tissue under a large microscope objective, it is found that the smooth muscle cells are arranged in bundles in various directions, and between them there are bundles of fibrous tissue. Smooth muscle cells are of various sizes, and some of them are filled with eosinophilic protein and occupy a large area (Fig. 3). Others are found to have relatively small nuclei, round and oval shape, and cytoplasm consisting of pale eosinophilic substance. Swollen connective tissue bundles are found between bundles of smooth muscle cells. When studying the epithelial competences in the leiomyomatous hamartoma, it became clear that the epithelial tissue covering the cracks and creating glandular structures in the interstitial tissue consisted of prismatic and cylindrical epithelium in the area of the cracks (Fig. 4), cells in the areas where the gland cells

ActaCAMU
№2 (10) 2025
ISSN: 2181-4155

appeared it is observed that it is structurally changed due to metaplasia and dysplasia. It is determined that the nuclei of epithelial cells are relatively hyperchromic, oval and elongated in shape.

Results of immunohistochemical examination. The presence of smooth muscle cells, fibroblasts and macrophages, albeit in small quantities, is observed in the mesenchymal genesis of the leiomyoma hamartoma tissue. Since the degree of differentiation of smooth muscle cells is different, it is determined that the protein marker desmin is also expressed at different levels. Cytoplasm and sarcomere of some smooth muscle cells are positively expressed by complete brown staining, while in other cells it is determined that myosin protein is expressed only in granular form in the cytoplasm (Fig. 5). It is also observed to be expressed in fibroblasts and macrophages, which are cells of mesenchymal origin, although at a low level. Among the 500 mesenchymal cells in the 6 cases studied by us, it was found that the amount of cells expressing desmin was on average 17.4%. Thus, during the differentiation process of muscle cells, the desmin marker appears in varying degrees and is expressed to varying degrees, since it is associated with many structures in the cytoplasm of muscle cells.

The second immunohistochemical marker, vimentin, is a marker of microtubules and actin, which are important in the structure of the cell cytoskeleton, located in the intermediate filaments of tissues and cells of mesenchymal histogenesis. Vimentin is a marker that is tested to confirm the origin of cells from the mesenchyme. It is a marker that indicates the degree of differentiation of cells of mesenchymal genesis in the embryonic development of cells and is an immunohistochemical marker located in the intermediate filaments. Vimentin is expressed in the mesenchymal cell nucleus, endoplasmic reticulum, and mitochondria, and is strongly expressed in the smooth muscle cells and fibroblasts surrounding the hamartoma fissures (Fig. 6). It was found to be expressed in an average of 63 out of 500 mesenchymal cells in the hamartoma tissue, i.e., 12.6%. Vimentin is important in maintaining the shape of cells and ensuring their resistance to mechanical stress (Ulirsch J., 2013).

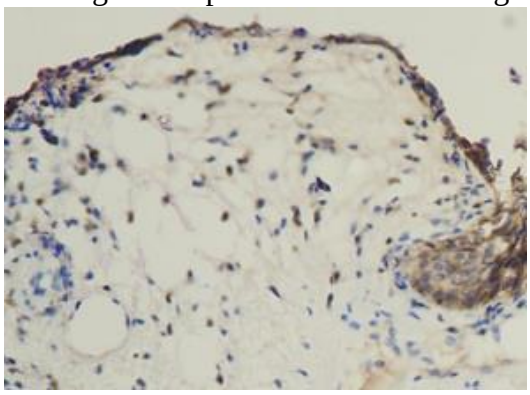

Figure 5. Patient A, 36 years old, leiomyomatous hamartoma of the lung, variable expression of desmin marker in smooth muscle cells. Staining: immunohistochemistry. Floor: 10x40.

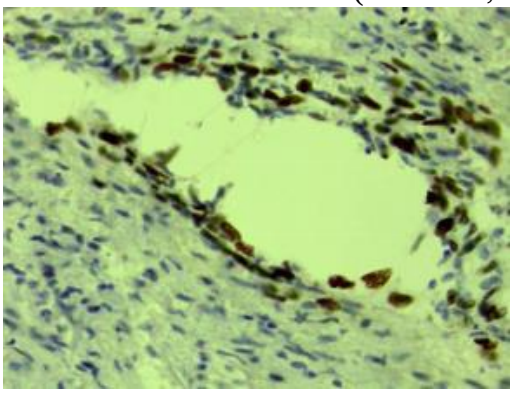

Figure 6. Patient S, 42 years old, leiomyomatous hamartoma of the lung, expression of vimentin in mesenchymal cells surrounding hamartoma tissue fissures. Staining: immunohistochemistry. Floor: 10x40.

Conclusions. Leiomyomatous hamartoma of the lung is found in rare cases, its composition consists of mixed tissues, smooth muscle tissue predominates, epithelial tissue is present in 64.5% of cases.

Lung hamartoma has a microscopically polymorphous structure, mainly from smooth muscle bundles located in different directions, a small amount of fibrosis, adipose tissue, epithelial cells that have undergone various metaplastic and dysplastic changes, located between them, covering the cracks.

Desmin marker, which determines the level of differentiation of mesenchymal cells, is expressed in average 17.4% of leiomyomatous hamartoma, positive staining of sarcoplasm and sarcomere of cells confirms that this marker is located in myosin, endoplasmic reticulum and mitochondria.

ActaCAMU
№2 (10) 2025
ISSN: 2181-4155

Vimentin is located in the intermediate filament of mesenchymal cells, it occupies a place in the nucleus, endoplasmic reticulum and mitochondria, it is expressed in both the nucleus and sarcoplasm of smooth muscle cells, it is important in maintaining the shape of cells and ensuring resistance to mechanical effects.

References:

1. Bulganina, N.A. Diagnosticheckaya convex endosonography pri zabolevaniyax verkhnix otdelov zhudochno-kishechnogo trakta: dis. sugar Med. Nauk: 14.01.17 /14.01.13/ Bulganina Natalya Anatolevna.-M., 2010.- S.64-65.
2. Burkov, S.G. Endoscopic ultrasound examination and diagnosis of stomach pain / Burkov S.G. // Doctor. - 1997. - #2. - S. 9-10.
3. Godjello, E.A. Endoscopic ultrasound examination - a modern diagnostic method of gactrointesinal stromal tumors / E.A. Godjello, N.A. Bulganina, M.V. Khrustaleva // Ultrasound and functional diagnostics - 2013. -№2.-S.78.
4. Egorov, V.I. Gastrointestinal stromal edema dvenadtsatiperstnoy kishki / V.I. Egorov, V.A. Kubyshkin, V.A. Vishnevsky, A.I. i dr. // Surgery. Journal im N.I. Pirogova. - #10. - 2007. - S.66-72.
5. Kravtsov, V.G. Clinical-morphological, immunohistochemical characteristics and criteria for prognosis of gastrointestinal stromal tumors: autoref diss. sugar Med. Nauk: 14.00.15 / Vladimir Grigorevich Kravtsov. - M., - 2007. -S. 23-24.
6. Poddubnaya, I.V. Gastrointestinal stromal tumors (diagnosis, treatment)/ Prakticheskie rekomendatsii // Pod redaktsiey prof. I.V. Poddubnoy. M.: Media Medica. - 2008. 56 - e.
7. Ryabtseva, S.N. Comparative morphological characteristics of gastrointestinal stromal tumors and smooth muscle formation / Ryabtseva S.N., Rogov Yu.I., Smolyakova R.M. i dr.// Oncol. Journal. - 2010. - 42. - (14). - P.50–56.
8. Seryakov, A.P. Gastrointestinal stromal tumors / A.P. Seryakov // RJGGK. - 2010. - 20. - (4). - S. 49–57.
9. Solodinina, E.H. Endoskopicheskaya diagnosis i lechenie podslizistyx obrazovaniy verkhnix otdelov zhudochno-kishechnogo trakta / E.N. Solodinina, Yu.G. Starkov, K. V. Shishin // Sb. thesis of the 13th Moskovskogo mejdunarodnogo congress of surgery. - 2009. S. 286-289.