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MORPHOLOGICAL AND MORPHOMETRIC CHANGES IN THE LUNGS OF 4- AND 7-MONTH-OLD WHITE RATS FOLLOWING INDUCED MAMMARY GLAND CANCER

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✓ ***Resume***

According to statistical data, breast cancer ranks as the leading malignancy among women. Chemotherapy is a chemical treatment method that utilizes drugs with cytotoxic properties to target malignant tumors. However, these chemotherapeutic agents can induce various changes in lung tissue. Lung damage resulting from breast cancer and its treatment is considered one of the most pressing issues in oncology. Therefore, this study investigates the morphological changes occurring in lung tissue as a consequence of breast cancer and compares them with normal parameters.

Key words: lung, breast cancer, morphology, morphometry.

ME'YORDA VA TAJRIBAVIY SUTBEZI SARATONI CHAQIRTIRILGANDAN KEYINGI 4 VA 7 OYLIK OQ ZOTSIZ KALAMUSHLAR O'PKASINING MORFOLOGIK VA MORFOMETRIK O'ZGARISHLARI

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✓ ***Rezyume***

Statistik ma'lumotlarga ko'ra, ko'krak bezi saratoni ayollarning xavfli kasalliklari orasida birinchi o'rinda turadi. Kimyoterapiya kimyoviy usul bo'lib, xavfli o'smalarga qarshi ta'sir etish xususiyatiga ega dori vositalari bilan davolash usulidir. Kimyoterapiyada qo'llaniladigan dori vositalari o'pkada turli xil o'zgarishlar olib keladi. Sut bezi saratoni natijasida o'pka shikastlanishi saraton kasalliklarida onkologiyaning eng dolzarb muammolaridan biridir. Shu sababli ushbu tadqiqotda sut bezi saratoni natijasida o'pka to'qimasida yuzaga keladigan morfologik o'zgarishlar o'rganildi va me'yoriy ko'rsatkichlar bilan taqqoslandi.

Kalit so'zlar: o'pka, sut bezi saratoni, morfologiya, morfometriya.

МОРФОЛОГИЧЕСКИЕ И МОРФОМЕТРИЧЕСКИЕ ИЗМЕНЕНИЯ ЛЁГКИХ У 4- И 7-МЕСЯЧНЫХ БЕЛЫХ БЕСПОРОДНЫХ КРЫС ПОСЛЕ ИНДУЦИРОВАННОГО РАКА МОЛОЧНОЙ ЖЕЛЕЗЫ

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✓ ***Резюме***

По статистическим данным, рак молочной железы занимает первое место среди злокачественных заболеваний у женщин. Химиотерапия представляет собой метод лечения с использованием химических препаратов, обладающих способностью воздействовать на злокачественные опухоли. Однако препараты, применяемые в химиотерапии, могут вызывать различные изменения в лёгких. Поражение лёгких в результате рака молочной железы является одной из актуальных проблем в онкологии. В связи с этим в данном исследовании изучены морфологические изменения в ткани лёгких, возникающие вследствие рака молочной железы, и проведено их сравнение с нормальными показателями.

Ключевые слова: лёгкие, рак молочной железы, морфология, морфометрия.

Relevance

The lungs' primary function is gas exchange—absorbing oxygen - rich air and expelling carbon dioxide-saturated air. This process is facilitated by the active movements of the thoracic cage and diaphragm, as well as the lungs' contractility. However, the lungs also perform several other vital functions. They play an active role in maintaining the body's acid-base balance by regulating ion concentrations, and they are capable of eliminating various substances, including aromatic compounds and ethers. These functions can be disrupted by numerous factors.

Breast cancer can lead to various changes in the lungs. In chemotherapy, lung damage is one of the most pressing issues in oncology. Anti-cancer treatments should be accompanied by appropriate assessment and management, even in patients with lung insufficiency due to cancer. Timely and effective prevention and treatment of lung pathologies associated with tumors aim to preserve lung structure and function, thereby enhancing the quality of vital processes.

The purpose of the study: study of morphological and morphometric changes in the lungs of 4- and 7-month-old white rats following induced mammary gland cancer

Materials and methods

Morphological and morphometric examinations were conducted in the laboratory of Bukhara State Medical Institute, adhering to established normative and methodological documents. The research complied with the requirements of the national guidelines for the care and use of laboratory animals, as well as the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (ETS No. 123, Strasbourg, 1986). These standards are reflected in the legal and methodological documents of our republic.

The rats were divided into two main groups (n=30):

1. **Control Group**: Healthy experimental animals maintained under standard vivarium conditions—white non-pedigree rats (n=10).
2. **Experimental Group**: Rats in which mammary gland cancer was induced by administering the carcinogen 7,12-dimethylbenz[a]anthracene (DMBA) (n=10).

In our experiment, we utilized 7,12-dimethylbenz[a]anthracene (DMBA), a polycyclic aromatic hydrocarbon with oncogenic properties ($C_{20}H_{16}$), to induce cancer. DMBA is a colorless crystalline substance with a yellowish hue, highly soluble in oils but nearly insoluble in water. It does not occur naturally.

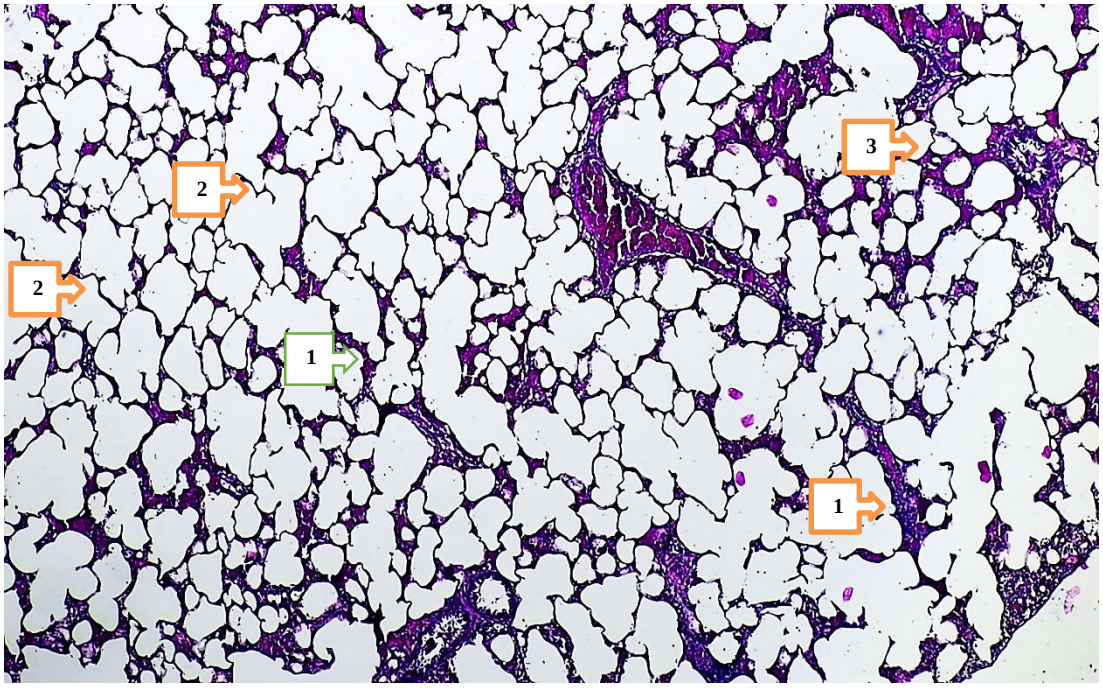
A single subcutaneous injection of 0.1 mg of DMBA into the mammary region of white non-pedigree rats in the experimental group stimulated the development of sarcomas. Topical application of DMBA led to the formation of papillomas and skin cancers in rats. Compared to other substances in this group, DMBA more frequently induced both localized and distant tumors.

Result and discussions

During histological examination of the lungs in 4- and 7-month-old white non-pedigree rats from the control group, the presence of the pulmonary artery (PA), pulmonary vein (PV), and main bronchus (MB) was observed in the lung hilum region. The lungs were externally enveloped by soft connective tissue composed of a flat mesothelium, with mesothelial height ranging from 3.54 to 3.9 μm in 4-month-old rats and from 3.94 to 4.32 μm in 7-month-old rats. The overall thickness of the

connective serous layer was 16.3–18.27 μm in 4-month-old rats and 18.1–20.3 μm in 7-month-old rats.

The main portion of the lung parenchyma was occupied by alveoli, interspersed with bronchi of various calibers. Alveoli were lined with flat alveolar epithelium containing round or elongated nuclei. Alveoli were separated by thin septa traversed by capillaries, with septal thickness measuring 8.3–9.2 μm peripherally and 7.4–8.2 μm centrally in 4-month-old rats, and 9.26–10.24 μm peripherally and 8.3–9.16 μm centrally in 7-month-old rats.



pic1. Microscopic Appearance of Lung Tissue in a 4-Month-Old Albino Rat (Control Group): 1. Terminal Bronchiole 2. Alveoli 3. Small Caliber Bronchus

In the intramural triangle, located between the parenchyma and the adventitia of the bronchus, adipose tissue inclusions were observed. In this region, lipid-associated lymphoid clusters (LALCs) were identified, appearing as circular structures composed of numerous lymphocytes. In 40% of 4- and 7-month-old rats in the control group, LALCs were present. In 4-month-old rats, their diameters ranged from 15.47 to 22.28 μm, with an area of 392.56 μm², while in 7-month-old rats, diameters ranged from 23.8 to 26.2 μm, with an area of 539.57 μm².

The PA was located medially, the MB centrally, and the PV laterally. Other bronchi also exhibited a well-defined adventitial layer. In histological sections of the caudal region, medium-sized bronchi had diameters ranging from 586.43 to 680.15 μm in 4-month-old rats and from 651.78 to 756.14 μm in 7-month-old rats. The thickness of the muscular layer in these bronchi was 35.6–39.41 μm in 4-month-old rats and 39.65–43.71 μm in 7-month-old rats.

Bronchi of all calibers were accompanied by blood vessels. Arteries exhibited well-developed smooth muscle elements, whereas veins, especially smaller ones, had fewer smooth muscle components, making them difficult to distinguish from alveoli. In front of the medium-sized bronchi, medium-sized arteries with diameters ranging from 13.8 to 19.32 μm in 4-month-old rats and from 15.33 to 21.47 μm in 7-month-old rats were observed penetrating the lung parenchyma.

In terminal bronchioles, the mucosal layer stained with hematoxylin, sparse smooth muscle tissue, and bronchial secretions were noted.

Histological Analysis of Lung Tissue in Albino Rats Following Induction of Breast Cancer with 7,12-Dimethylbenz(a)anthracene (DMBA)

In albino rats aged 4 and 7 months, after induction of breast cancer using 7,12-dimethylbenz(a)anthracene (DMBA), histological examination revealed several reactive and dystrophic changes in lung tissue. These alterations were characterized by:

Mesothelial Changes: A reduction in the height of mesothelial cells lining the connective tissue around the pulmonary artery (PA), pulmonary vein (PV), and main bronchus (MB) was observed, accompanied by cytoplasmic vacuolization and nuclear hyperchromatism.

Serous Layer Thickness: The overall thickness of the serous layer decreased, with measurements ranging from 14.2–16.1 μm in 4-month-old rats and 15.3–17.2 μm in 7-month-old rats.

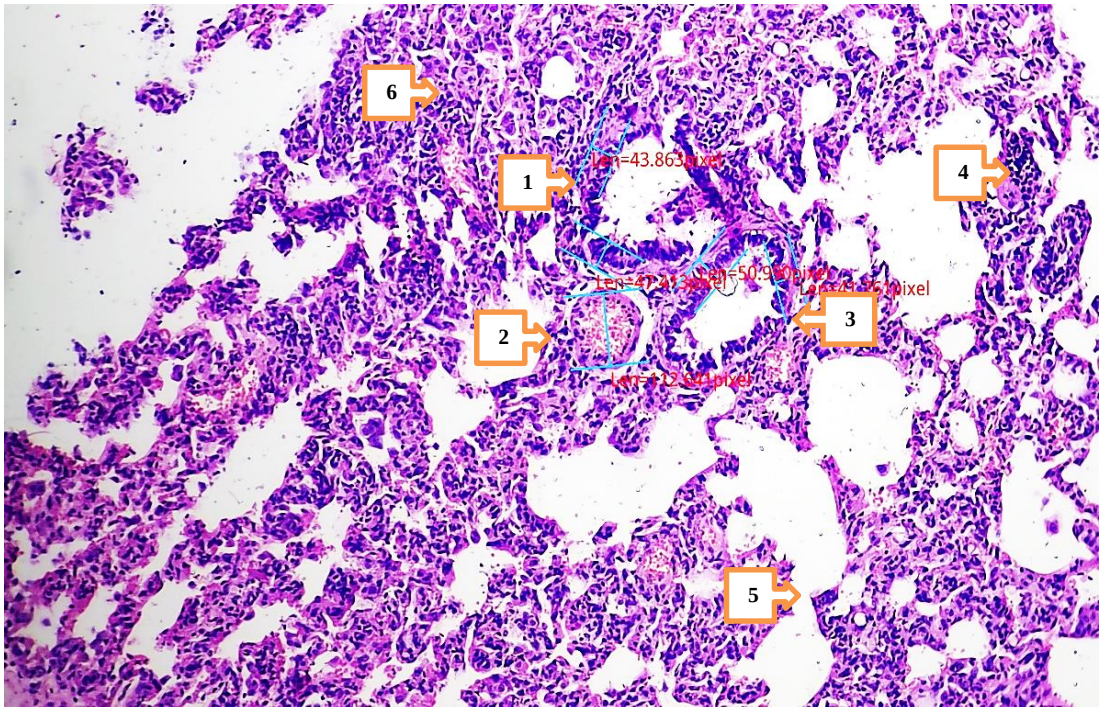
Alveolar Structural Changes: The alveolar walls exhibited partial loss, deformation, and fusion, leading to emphysematous alveoli. In some cases, interstitial inflammation with cellular infiltration was noted.

Alveolar Septal Thickness: The thickness of alveolar septa increased, with measurements of 10.1–11.2 μm at the periphery and 9.0–9.9 μm centrally in 4-month-old rats, and 11.5–12.7 μm peripherally and 10.2–11.5 μm centrally in 7-month-old rats.

Alveolar Collapse: Areas of atelectasis were observed, indicating regions of collapsed alveoli.

Lipid Infiltration and Lymphoid Clusters: Increased lipid infiltration in the intramural triangle region was noted, with lipid-associated lymphoid clusters (LALCs) present in 38% of 4-month-old rats and 45% of 7-month-old rats. The diameters of these clusters ranged from 17.53–24.34 μm in 4-month-olds and 25.71–28.33 μm in 7-month-olds, occupying areas of 464.4 μm² and 621.5 μm², respectively.

Bronchial Changes: The diameter of medium-caliber bronchi increased to 592.6–701.2 μm in 4-month-old rats and 664.8–722.9 μm in 7-month-old rats. The thickness of the muscle layer was 41.4–45.2 μm in 4-month-olds and 45.6–51.8 μm in 7-month-olds.



Pic 2. Microscopic Appearance of Lung Tissue in 4-Month-Old Albino Rats After Induction of

Experimental Breast Cancer

Stained with Hematoxylin-Eosin. Magnification: 20×10 objective lens.

1. **Alveoli**
2. **Small-Caliber Bronchus**
3. **Terminal Bronchiole**
4. **Alveoli**
5. **Small-Caliber Bronchus**

Vascular Changes: Perivascular infiltrates were observed around blood vessels, particularly in venous walls, with mild thickening of the intima.

Terminal Bronchiolar Changes: In terminal bronchioles, there was an increase in the number of epithelial cells, slight thickening of the epithelium, and a reduction in smooth muscle tissue and serous secretion. Some areas exhibited irregularities in the basal membrane and an increase in lymphocyte numbers.

These findings suggest that DMBA induces significant histopathological alterations in the lung tissue of albino rats, which may contribute to the understanding of pulmonary changes associated with breast cancer induction.

Summary

Following the induction of mammary carcinoma using 7,12-dimethylbenz(a)anthracene (DMBA) in 4- and 7-month-old albino rats, a series of pathological morphological and morphometric changes were observed in the lung tissue. The height of the mesothelium decreased, measuring 3.01–3.35 μm in 4-month-old rats and 3.18–3.52 μm in 7-month-old rats.Mesothelial cells exhibited vacuolization and nuclear hyperchromatosis.

The thickness of the serous layer also reduced: 14.2–16.1 μm in 4-month-olds and 15.3–17.2 μm in 7-month-olds, indicating atrophic processes and reduced trophism in the tissue. The thickness of the alveolar septa increased: 10.1–11.2 μm at the periphery and 9.0–9.9 μm centrally in 4-month-old rats; 11.5–12.7 μm peripherally and 10.2–11.5 μm centrally in 7-month-old rats.

These septa became thicker, deformed, and in some cases, collapsed, leading to atelectasis.

Lipid-Associated Lymphoid Clusters (LALC):

LALCs were present in 38% of 4-month-old rats and 45% of 7-month-old rats.

Their diameters ranged from 17.53 to 24.34 μm in 4-month-olds and 25.71 to 28.33 μm in 7-month-olds.

The areas occupied by LALCs were 464.4 μm² and 621.5 μm², respectively.

Peripherally, lymphohistiocytic infiltrations were noted.

Bronchial Changes:

The diameters of medium-sized bronchi were 592.6–701.2 μm in 4-month-old rats and 664.8–722.9 μm in 7-month-olds.

The thickness of the muscular layer ranged from 41.4 to 45.2 μm in 4-month-olds and 45.6 to 51.8 μm in 7-month-olds.

Perivascular infiltrations and thickening of the intima were observed in venous vessels.

Terminal Bronchiolar Changes:

In terminal bronchioles, there was an increase in epithelial cell numbers, irregularities in the basal membrane, and lymphocytic infiltrations.

These alterations suggest that DMBA exposure leads to inflammation, dystrophy, lipid infiltration, and activation of immune responses, resulting in the disruption of tissue structures in the lung. Notably, pathological changes were more pronounced and evident in 7-month-old rats compared to 4-month-olds.

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