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ULTRASTRUCTURAL AND MORPHOMETRIC CHANGES OF THE ENDOTHELIAL LAYER OF THE PULMONARY VASCULAR SYSTEM IN AN EXPERIMENTAL DIABETES MODEL

Dildora R. Sobirova [1], Abdulaziz A. Ahrorov [2]

1 Associate Professor, PhD, Department of Histology and Medical Biology, Tashkent Medical Academy, Tashkent, Uzbekistan

2 Student, Faculty of Treatment, Tashkent Medical Academy, Tashkent, Uzbekistan

ABSTRACT

Diabetes mellitus, compared to other chronic and non-communicable diseases, causes significant damage to the vascular endothelium, potentially leading to severe and even fatal complications. Among elderly patients with diabetes and vascular complications, mortality rates range from 60% to 85%. The primary factor contributing to these complications is microangiopathy, a condition characterized by damage to small blood vessels.

Key words: alloxan, diabetic rats, experimental diabetes, endothelium, blood vessels.

INTRODUCTION

Diabetes mellitus is one of the most prevalent diseases worldwide, making its prevention and treatment a critical public health concern. This chronic condition continues to spread rapidly, with a significant increase in diagnosed cases over the past decades. Approximately 25 years ago, the number of individuals with diabetes worldwide was below 130 million. Today, the number has surged to over 463 million, with every second adult being diagnosed with the disease. In Uzbekistan alone, there are 257,457 registered cases of diabetes, including 3,263 children and adolescents under the age of 18.

World Diabetes Day, established in 1991 by the International Diabetes Federation (IDF) and the World Health Organization (WHO), is observed annually on November 14. By 2040, the global number of diabetes cases is projected to rise to 642 million. The medical and social significance of diabetes is underscored by its severe complications, high disability rates, and increased mortality.

Endothelial cells, which play a crucial role in vascular homeostasis, are metabolically active and contribute to endocrine and immune protection. The endothelium regulates blood vessel integrity, permeability, angiogenesis, and hemostasis. Additionally, it balances vasodilation and vasoconstriction, modulates smooth muscle cell migration and proliferation, and plays a key role in fibrinolysis, thrombosis, and platelet adhesion and aggregation.

Histological changes: Researchers can examine lung tissue under a microscope to look for any structural changes, such as inflammation, fibrosis, or damage to the alveoli and bronchioles. It measures various aspects of lung function, including lung capacity, airflow, and the efficiency of gas exchange. Alloxan diabetes can potentially impair these functions, which has been shown to lead to respiratory problems.

Purpose of the study. Morphological and morphometric assessment of changes in the vascular endothelium as a result of inducing an experimental model of diabetes in animals using alloxan tetrahydrate.

Materials and methods. This study was conducted using laboratory-bred white rats weighing between 170 and 185 grams. Experimental diabetes was induced by administering a single intraperitoneal injection of alloxan acetate buffer at a dose of 11 mg% per 100 g of body weight. Following the injection, the animals exhibited characteristic diabetic symptoms, including reduced mobility, lethargy, polyuria, weight loss, shallow and rapid breathing, and excessive water intake.

After a 30-day experimental period, the rats were sacrificed, and lung tissues along with associated blood vessels were collected for further examination. To assess morphological and morphometric changes due to diabetes, micropreparations were obtained from 116 tissue samples. These samples were analyzed for structural boundaries, cellular components, blood vessel diameter, wall thickness, and changes in wall composition, including cell count and volume.

To visualize the obtained data, samples were scanned at 200x magnification using a NanoZoomer (HAMAMATSU PHOTONICS, Japan). The measurements and correlations were computed using specialized software to minimize human influence.

Research results. In experimental conditions, no significant morphological changes were detected in the lung and vascular tissue of decapitated rats for 30 days. Most of the changes were detected in the peribronchi around the vascular wall and around the root of the lung, as well as in the processes that occurred around the intermediate tumors around the small-caliber blood vessels. The essence of the morphometric examination method is that the perimeter of the cells

detected in the tissues at 200x, 400x magnification is delimited in color, and the number, level and volume are determined simultaneously. In the program used to delimit the cells by the perimeter, cells with a nucleus were automatically included in the inset.

In experimental conditions, rats induced with alloxan diabetes mellitus developed persistent hyperglycemia in the blood for 30 days. Then, after the rats were decapitated, tissues were removed from the lungs and blood vessels and micropreparations were prepared from them. The micropreparations were studied under a light microscope. The morphological changes in the obtained results were as follows: uneven moderate perfusion in the visceral membrane of the lung tissue, the membrane was of uniform thickness, the subpleural alveolar walls were of almost the same size, weakly formed interstitial edema was detected in the alveolar walls, and weakly formed plasmatic edema was detected in the intramural components of the lung tissue. Signs of slight pink edema were detected in the stromal fibers of the interalveolar wall.

The capillary vessel walls were of the same thickness, and at 400x and 800x magnification, signs of developing edema and plasmatic edema were detected in the capillary basement membrane. The trajectory of pericytes around the capillaries is clear, the foci of proliferation are poorly formed, perivascular edema is almost not detected. The boundaries of the basement membrane are almost preserved, and areas of fibrous structures with focal plasmatic infiltration are detected.

No sharp changes are detected in the blood vessels of the acinar arteries. Of the main morphological substrates: in the intima of the vessels, endothelial cells are high, in a swollen form, focal endotheliosis is detected. In the subendothelial layers, plasmatic infiltration and edematous foci are poorly formed. These changes are characteristic of specific morphological changes in diabetes mellitus and are also detected in other types of diseases. In the muscle layer, the arrangement of myocytes in an orderly trajectory is unchanged, the muscle layer is relatively hypertrophic, and edematous changes developing in the interval are detected. In the adventitia layer, there are sharp changes, around which there are traces of poorly formed plasmatic congestion and perivascular edema. In the areas of the arterioles located close to the bronchioles, weakly formed local lymphocytic infiltration foci and a small number of macrophages and histiocytes are detected. Around the vessels, weakly formed fibroblast proliferation and perivascular fibrosis foci are detected. Weakly formed peribronchial edema and signs of venous congestion are detected.

In parallel with the above changes, segmental blood vessels also retain an average fullness, the intima endothelium has a relatively flat appearance, edema

and plasmatic congestion are very poorly formed in the subendothelial areas, and a weakly formed appearance of intermediate edema is detected between the fibrous structures. It is determined that the vessel undergoes a weakly developed hypertrophy in the muscular layer. The adventitious layer is unchanged, and foci of local proliferation of fibroblasts are developed to varying degrees around the vessel. Between the segments, the fullness of venous blood vessels is average, and mostly uniform. Sharp changes in the histioarchitectonics of the lobular primary, secondary and tertiary pulmonary arteries, atherosclerotic changes in the intima, and deposits resembling lipid spots are detected. In these areas, the location of endothelial cells in the subendothelial layers is determined. Endotheliocytes forming the intima surface were flat, and no sharp morphological changes were detected. Plasmatic congestion developed between the muscle layer and fibrous structures, and hypertrophy of myocytes, as a result, an increase in the rheological properties of blood in persistent hyperglycemia leads to hemodynamic disorders, an increase in blood plasma viscosity and a slowdown in blood movement, and in order to ensure blood movement in the muscular-elastic type arteries, a compensatory adaptation mechanism is determined due to an increase in the contractility of the muscle layer of the vascular wall.

Conclusion. No significant proliferation of hypercellular structures was observed. The structure and cytoarchitecture of primary and secondary alveolocytes lining the inner alveolar wall remained largely unchanged. Most alveolocytes maintained a uniform size, with nuclei exhibiting moderate staining. The cytoplasm appeared homogeneously pink, and the majority of alveolar spaces were clear, with no pathological fluid accumulation detected. Capillaries within the alveolar walls displayed moderate fullness, and there was no evidence of erythrocyte adhesion. These findings suggest that despite persistent hyperglycemia in diabetic conditions, no drastic alterations were observed in alveolar cell integrity. However, subtle vascular changes, including mild endothelial swelling and minimal perivascular edema, indicate early-stage endothelial dysfunction.

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