CONTEMPORARY THEORIES ON THE ROLE OF THE THYMUS IN IMMUNE SYSTEM DEVELOPMENT

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Abstract: The thymus is the central organ of T-lymphocytopoiesis, where the formation of T-lymphocyte progenitor cells occurs alongside the synthesis of a number of thymic hormones. This gland plays a pivotal role in establishing and maintaining immune homeostasis. Under the influence of environmental factors, particularly fluctuations in temperature, the thymus undergoes pronounced structural and functional rearrangements. These changes demonstrate a cyclic character, within which three main phases can be distinguished: an initial or early response, a peak stage, and a late or distant phase. Each stage exhibits specific ultrastructural features, reflecting the adaptive potential of stromal and lymphoid elements. Early changes are generally manifested by activation of the secretory and synthetic machinery of stromal cells, while peak changes involve intensified cellular interactions, apoptotic processes, and remodeling of the thymic microenvironment. The distant stage is characterized by stabilization or compensatory modifications that ensure continuity of T-cell maturation. Such cyclic patterns of thymic adaptation highlight its sensitivity to temperature stress and underline its critical role in orchestrating immune responses.

Key words: Thymus, T-lymphocyte, B-lymphocyte, macrophage.

Introduction: The thymus is the central organ of T–lymphocytopoiesis, in which antigen-independent differentiation into T-lymphocytes occurs from bone marrow precursors of T-lymphocytes, effector cells of which carry out the reaction of cellular immunity and regulate humoral immunity. A more intensive study of the thymus began with the classical experiments of Y.Miller (I961), who proved its dominant place in the formation of the immune system and in immune reactions and with the development of electron microscopy.

The human thymus is located in the anterior mediastinum, behind the sternum. The organ with the anterior surface is in contact with the sternum and behind the aortic arch. The capsule of the organ consists of loose connective tissue with numerous hemocapillaries. The capsule of the organ is covered with fatty tissue from above in places. Lymph nodes are localized in the surface of the thymus capsule. It should be noted that the elements of the thymus capsule not only restrict it from nearby structures, but also participates in the fixation of the organ to the bone skeleton of the sternum and blood vessels.

It has been established that the thymus as an organ is first detected in cartilaginous fish, they also show a reaction of T-lymphocytes to mitogens. In shark fish, the thymus has lobules and cortical and cerebral zones are well expressed in them. The thymus is more perfect in birds, in which it, together with the Fabricius bag, provides immune reactivity. Foci of myeloid hematopoiesis are also found in the embryonic thymus. Later, at 8-9 weeks, stroma epithelial cells differentiate into interdigitating reticular cells responsible for creating a microenvironment for differentiating lymphocytes.

Material and methods of research. The experiments were carried out on white sexually mature mongrel male rats with an initial weight of 150-170 grams, who were on a normal laboratory diet. All experimental animals were obtained from the same vivarium, the age of the animals, their weight and other indicators were in the same conditions.

The following methods of morphological analysis were used in the experiment:

- method of light-optical morphology;
- radioautographic method;
-morphometric method

For light-optical studies, the materials were fixed in 12% formalin, in Buena liquid. Pieces of organs were poured into paraffin after appropriate treatment. Dewaxed sections 5-7 microns thick were stained with hematoxylin-eosin according to the generally accepted method. Cell composition was calculated in 3 structural zones of thymic lobules-cortical, cortical-medullary and medullary zones.

Research results and their discussion. The capsule consists of a dense network of reticular and collagen fibers. Each lobule of the gland consists of three separate layers that provide the necessary microenvironment for the maturation and formation of lymphocytes. It is known that the cortical zone has two layers: the outer subcapsular and the inner cortical. Primitive dividing cells (lymphoblasts) are found in the outer subcapsular layer. It is generally believed that they are formed from stem cells of the red bone marrow under the influence of the hormone thymosin[1,2].

The capsule of the thymus and the connective tissue of the interlobular septa contain blood, lymphatic vessels, nerve fibers. From the connective tissue, blood vessels enter the thymus lobule. In the cortical zone, capillaries form loops, go to the cortical-medullary zones and gather into venules. The cortico-medullary zone is the richest in blood vessels. Then the corticomedullary venules, together with the medullary venules, leave the thymus. Hemocapillaries of the cortical zone of the thymus lobes are surrounded by relatively densely located epithelial cells, the latter themselves are involved in the formation of a hematothymic barrier that protects differentiating thymocytes of this zone from various antigens traveling through the bloodstream [2,3].

Lymphoid cells of the outer part of the cortical zone are mainly represented by densely located lymphoblasts. Their diameter is about 7-8 microns, they contain a rounded nucleus with nucleoli. Quite often, cells are detected at various stages of mitotic division.In the inner part of the cortical zone, lymphocytes are located less frequently compared to the outer part[3,4,5,6]. Lymphocytes of this zone are smaller in diameter, contain a small number of intracellular organelles-free ribosomes, mitochondria, tubules of the granular endoplasmic network [7,8].

The cortical zone of the thymus under normal physiological conditions has a smaller number of macrophages. Macrophages are more common in the corticomedullary zone. Their shape is irregular, which is associated with a large number of protrusions and depressions of the plasmolemma. The cytoplasm of cells is filled with numerous lysosomes and large phagosomes. In the phagosomes of macrophages, the decay products of differentiating lymphocytes are often found.In individual cells , their cytoplasm is filled with lysosomes at various stages of decay [2,3,4].

Epithelial cells of various structural and functional zones of the thymus are heterogeneous in their morphological features. Cortical epithelial cells are mainly stellate in shape. Their intracellular organelles are represented by numerous free ribosomes, polysomes, evenly distributed, and a moderate number of mitochondria.

In the brain area, epithelial cells significantly differ in shape and number. The work of Hwang et al., (1974) found that the number of epithelial cells in the brain zone significantly increases with age in rats. So, if in the outer cortical zone of the thymus of adult rats lymphoblasts make up 62%, lymphocytes-26%, epithelial cells-12%, in the cerebral zone the proportion of epithelial cells is 7 times greater (86.3%) [1,2,3].

It was found that the epithelial tissue stroma of the thymus is represented by cells of various shapes and submicroscopic organization, "Interdigitating" reticular cells (IDCs) are one of the mandatory components of immune reactions. Cells similar in structure are also found in T-dependent zones of peripheral organs of the immune system. One of the obligatory ultrastructural signs of them is the presence of special Birbeck granules in them. IDCs are especially more common in the cortical-medullary and cerebral zones of the thymus. Unlike typical macrophages, they exhibit low phagocytic activity. There are Ia antigens and receptors on the surface of the IDC. Duijvestijn et al. (1983), isolating from the suspension of the thymus, distinguish three types of IDCs, differing in their ultrastructural and immunocytochemical parameters:

– Type I cells are characterized by the content of acid phosphatase in small granules, the plasmolemma gives a positive reaction to the Ia-antigen;

– Type II IDCs have large sizes, light cytoplasm with an abundant number of Birbeck granules. Granules with acid phosphatase activity of these cells are mainly localized near the nucleus.

– Type III cells have acid phosphatase and endogenous peroxidase activity, contain numerous vacuoles and phagosomes. They lack Ia-antigens. Cells of this type are similar in their properties to cortical macrophages [9,10].

One of the specific markers of interdigitating cells is protein-100.

Due to the presence of this protein, they differ sharply from the macrophages of the thymus.

Thanks to recent studies, the genesis of interdigitating thymus cells has been established. It turned out that the interdigitating cells are descendants of the monocyte line of the bone marrow stem cell and belong to the system of phagocytic mononuclears.

In addition to epithelial cells, macrophages and IDUs, the cells of the thymus microenvironment include mast cells, granulocytes and plasma cells. These cells under normal physiological conditions are localized in the connective tissue of the organ capsule, in the interlobular septa and perivascular spaces of the cortical zone.

Mast cells are of particular importance in immunogenesis among these cells. A huge number of studies and publications are devoted to them. A common type of cellular elements of the thymus are mast cells. They are located mainly in the connective tissue stroma, are often found near blood vessels, and are also diffusely scattered in the capsule and interlobular septa. Among the mast cells identified by many researchers in the thymus stroma, there are both degranulating and non-degranulating forms. Non-granulating cells are visualized as large, with a high density of granules masking the nucleus. Among the degranulating mast cells, cells with a weak (I degree) degree of degranulation predominate. Mast cells are multifunctional connective tissue cells. The variety of their granules make them participants in many physiological and pathological processes occurring in the body [11,12]. These are immunogenesis, formation and differentiation of connective tissue, carcinogenesis, allergic conditions and other conditions.

Thus, the thymus, having in its composition lymphoid elements and cells of the thymic microenvironment, having morphological features and, apparently, have functional differences, which together create conditions for the differentiation of T-lymphocytes, providing the functions of cellular immunity and the regulation of humoral immunity.

Conclusions:

1. The thymus of control white rats has a lobular structure, the specific weight of connective tissue in the thymus is not large-3%. The most acceptable is the difference in the chemical lobules of the cortical, cortical-medullary and medullary zones, where T-lymphocytopoiesis and stroma cells have certain specific features.

2. In the cortical zones, lymphoblasts, large and medium lymphocytes, dendritic cells are more concentrated, in medullary – interdigitating cells, small lymphocytes. The cellular composition of the cortico-medullary zone has an intermediate position. Macrophages and monocyte-like cells are mainly a cellular component of the cortical and corticomedullary zones of the thymus.

Literature:

1. Kvaratskhelia A. G., Klochkova S. V., Nikityuk D. B., Alekseeva N. T. Morphological characteristics of the thymus and spleen under the influence of factors of various origins // *Journal of Anatomy and Histopathology*. – 2016. – Vol. 5, № 3. – P. 79–83.
2. Kharibova E., Davronov R., D. Sh. Ultrastructural features of the white thymus stromal cells // *The Scientific Heritage*. – 2021. – № 79–2. – P. 29–30.
3. Akhmatova G.R. Efficiency of PDT in severe cervical dysplasia // *ACADEMICIA: An International Multidisciplinary Research Journal*. – 2021. – Vol. 11, № 3. – P. 2566–2568.
4. Davronov R. D., Davronova S. R. Modern views on the participation of the thymus in the processes of immunogenesis // *Scientific Progress*. – 2022. – No. 1. – P. 45–49.
5. Trufakin V. A., Shurlygina A. V. Problems of histophysiology of the immune system // *Immunology*. – 2002. – № 1. – P. 4–8.
6. Khaitov R. M., Pinegin B. V. Immunomodulators: mechanism of action and clinical application // *Immunology*. – 2003. – № 4. – P. 196–202.
7. Zufarov K. A., Tukhtaev K. R., Davronov R. A. Ultrastructural changes in the cells of the white pulp of the spleen in experimental salmonella infection // *Arkhiv anatomii*. – 1986. – Vol. 91, № 12. – P. 69–71.
8. Abdurakhmanov M. M., Inoyatov A. S. Avicenna: The revival of medicine and science // *Abu Ali ibn Sina (Avicenna) and modern medicine*. – Tashkent, 2019. – P. 7–10.

9. Davronov R. D., Davronova S. R. Structural and functional features of adaptive changes in the organs of the immune system under antigenic influence // *Morphology*. – 2008. – Vol. 133, № 2. – P. 38c–38c.
10. Davronova S. R., Davronov R. D., Bakhronov J. B. Structural and functional features of immune system cells in the dynamics of experimental temperature exposure // *BIO Web of Conferences*. – 2024. – Vol. 121. – Art. 03017.
11. Dubossarskaya Z. M., Dubossarskaya Yu. A. The main issues of reproduction immunology // *Medical aspects of women's health*. – 2010. – Vol. 31, № 4. – P. 15–21.
12. Oripova N. A. Immunological function of intestinal microflora, morphological features, its disorders and correction possibilities // *Scholastic: Journal of Natural and Medical Education*. – 2023. – Vol. 2, № 2. – P. 132–140.