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MORPHOMETRIC CHANGES IN AGE-SPECIFIC FEATURES IN THE THYMUS

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✓ ***Resume***

The thymus is a major secret in medicine (primarily immunology) and especially pediatrics. In the twentieth century, scientists developed a relationship to the organ as a generator and regulator of immune reactions, a participant in the production of large populations of immunocompetent cells.

The thymus is an important organ of the immune system in children. It consists of two segments located at the top of the chest and joined at the front of the trachea. The gland grows until the child reaches puberty, weighs 30-40 grams, then gradually undergoes atrophy (reverse development).

The thymus is a major component of the immune system and in many ways a central organ. Infectious diseases, systemic autoimmune diseases, oncology, the problem of tissue incompatibility determine a person's life, and therefore there is a growing scientific interest in the study of the immune system and its central organ - the function of the pancreas. The complexity of the study lies in the numerous integral interactions with other components of the immune system of the pancreas, neuroendocrine, hematopoietic and connective tissue, organs that provide barrier function, and others.

The interest of pediatricians in this area is related to a certain understanding of human ontogenesis from birth to old age, where the thymus plays a major role in the prenatal and postnatal periods. The purpose of this review is to draw some conclusions and recognition of the ambiguous evaluation of the functions associated with the cell membrane of the adrenal gland, its derivatives, and the cell membrane.

Key words: thymus; children; evolution of the pituitary gland; thymus morphology

МОРФОМЕТРИЧЕСКИЕ ИЗМЕНЕНИЯ ВОЗРАСТНЫХ ПРИЗНАКОВ ТИМУСА

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✓ ***Резюме***

Тимус - главный секрет медицины (в первую очередь иммунологии) и особенно педиатрии. В двадцатом веке отношение ученых к органу сложилось как генератор и регулятор иммунных реакций, участник производства больших популяций иммунокомпетентных клеток.

Тимус - главный компонент иммунной системы и во многих отношениях центральный орган. Инфекционные заболевания, системные аутоиммунные заболевания, онкология, проблема несовместимости тканей определяют жизнь человека, в связи с чем растет научный интерес к изучению иммунной системы и ее центрального органа - функции поджелудочной железы. Сложность исследования заключается в большом количестве интегральных связей с другими компонентами иммунной системы поджелудочной железы, нейроэндокринной, кроветворной и соединительной ткани, органов, обеспечивающих барьерную функцию, и др.

Интерес педиатров к этой области связан с определенным пониманием онтогенеза человека от рождения до старости, где вилочковая железа играет важную роль в пренатальном и послеродовом периоде. Цель этого обзора - привлечь внимание к некоторым результатам неточной оценки функций, связанных с диафрагмой, ее производными и клеточной мембраной.

Ключевые слова: вилочковая железа; дети; эволюция гипофиза; морфология тимуса

TIMUS BEZINING YOSH BELGILARIDAGI MORFOMETRIK O'ZGARISHLARI

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✓ ***Rezyume***

Timus tibbiyotning (birinchi navbatda immunologiya) va ayniqsa pediatriyaning asosiy siri hisoblanadi. Yigirmanchi asrda olimlarning tanaga bo'lgan munosabati immunitet reaktsiyalarining generatori va regulyatori, immunokompetent hujayralarning katta populyatsiyasini ishlab chiqarish ishtirokchisi sifatida rivojlandi.

Timus immunitet tizimining asosiy komponenti va ko'p jihatdan markaziy organ hisoblanadi. Yuqumli kasalliklar, tizimli otoimmün kasalliklar, onkologiya, to'qimalarning mos kelmasligi muammosi inson hayotini belgilaydi va shuning uchun immunitet tizimi va uning markaziy organi - oshqozon osti bezi funktsiyasini o'rganishga ilmiy qiziqish ortib bormoqda. Tadqiqotning murakkabligi oshqozon osti bezi, neyroendokrin, gematopoetik va biriktiruvchi to'qimalarning immun tizimining boshqa tarkibiy qismlari, to'siq funktsiyasini ta'minlaydigan organlar va boshqalar bilan ko'p sonli integral aloqalardadir.

Pediatrlarning ushbu sohaga bo'lgan qiziqishi tug'ilishdan qarilikgacha bo'lgan inson ontogenezini ma'lum bir tushunish bilan bog'liq bo'lib, bu erda timus bezi tug'ruqdan oldingi va tug'ruqdan keyingi davrda muhim rol o'ynaydi. Ushbu sharhning maqsadi diafragma, uning hosilalari va hujayra membranasi bilan bog'liq funktsiyalarni noto'g'ri baholashning ba'zi natijalariga e'tiborni qaratishdir.

Kalit so'zlar: timus bezi; bolalar; gipofiz bezining evolyutsiyasi; timus morfologiyasi

Relevance

Modern views suggest that the thymus is primarily the central organ of the immune system that determines central and humoral immunity. Living factors are involved in the differentiation of thymocytes, which in turn select antiviral, antifungal, antitumor, antitransplant, anti-tuberculosis and other types of immunity. The strong interaction of thymocytes with B-lymphocytes through T-cell-messengers provides adequate humoral immunity. Large population of lymphocytes The entire large population of lymphocytes interacts with the histocompany system and microbiome, phagocytic mononuclear cells and complements, cellular forms of barrier organs (skin, mucous membranes, etc.), endocrine and interacts (via receptors, cytokines). And the nervous systems, ultimately, function organically, providing control over the stability of the internal environment and creating a strong continuum called the body’s immune system. Deficiency or disruption of one of the main joints of the immune system (including the thymus) should affect the functioning of the entire continuum (large or small) and this should be primarily manifested by weak protection against infection, systemic, oncological diseases, tuberculosis, etc. there is a risk.

In addition to being a key member of the immune system, the thymus is involved in the development of the endocrine system and the formation of the hypothalamus, endocrine and lymphoid organs.

Although the term "thymus" has been known since ancient medical times, the history of the organ dates back to about 400 years. Its structure and functional properties have not been adequately studied at different ages [1].

Several variants of the origin of the organ name are described in the literature that can be studied. The fork-shaped anatomical shape of the iris gave it the name "thymus gland." Perhaps the name of the organ may also be related to the Greek words “thymos” - soul [1, 2].

One of the major immunological functions of the thymus gland was discovered in 1961 by immunologist Jacques F.A.P. Miller points out that thymectomy performed on mice after birth makes them very susceptible to various infections and leads to their early death. He also observed significant lymphopenia in the blood, spleen, and lymph nodes of these mice. These animals also could not refuse foreign skin transplantation, which was an important feature of the immune response at the time. Miller concluded that thymus-dependent (T) lymphocytes are the organ responsible for the development of immunocompetent cells that make up a particular cellular population.

To date, many publications have been published on the morphology of the thymus and its role in the immune response, but as before, in 2016, Zygmunt Zdrojevic, Evelina Pachura emphasized the regulatory role of the thymus in the immune system and harmonizes the body’s entire immune system. Bone marrow is a major cell donor for the lymphatic system, just as it is a donor for, for example, hematopoietic, cardiovascular, and other systems. Progenitor cells are formed in the thymus, which then divide into mature T cells [3].

In the same year, Rita Rennazi, Lorenzo Nardo, Gaia Favero, Anderson MS, Lio SV reaffirmed the concept that the thymus is the primary lymphoid organ responsible for the production of immunocompetent T cells; the thymus and its specific microenvironment (stroma) play a key role in many developmental processes leading to the formation of functionally mature T cells [4]. Nevertheless, the morphological appearance of the organ, its stability, and its multifaceted interaction with other organs and systems (including the mother-plantenta-fetal system) remain a major problem in the study of the direct functions of this gland. The thymus has a unique role in the fight against infection in humans and especially in children.

To date, embryogenesis and anatomical location of the thymus have been studied to some extent. By the end of the first month of intrauterine development, the thymus is placed in pairs III and IV of the band pockets. By the time the baby is born, it is the largest and only fully systemically and functionally formed lymphoid organ in the body. Thymus morphogenesis is approaching its final stage by 17 weeks of intrauterine development; By 21 weeks the thymus is clearly visible by sonography [6] and finally by 24 weeks the thymopoietic function is complete. From the 21st to the 36th week of pregnancy, the thymus gland enlarges 1.7-1.9 times; From week 37 onwards, its growth rate slows (growth does not exceed 1.3 times). It should be noted that in healthy newborns, the thymus is fully formed, works well, and is fully active, regardless of the activity of this organ of the mother [7]. The pancreas of a newborn makes up 0.5 percent of body weight (that is 10-15 grams), the spleen 11 grams, the heart 24 grams.

It is thought that the weight of the gland in newborns can range from 3.2 g to 20.0 g [5].

The authors of the publication devoted to the post-mortem examination of the pancreas note that the mass of the pancreas of the newborn averaged 4.8 g, at 1 month - 5.9 g, at 2 months - 7.9 g, at 6 months - 9.4 g. At the age of 1 year - 10.8 g, at the age of 2 years - 9.9 g [2]. According to some morphological researchers, the fastest growth of the pituitary gland is observed in the first year of a child's life, and the maximum body weight relative to body weight is recorded at the age of 2-4 years. The absolute maximum mass of the pituitary gland (25.0-40.0 g) is observed during puberty, after which the organ gradually undergoes atrophy, and the glandular tissue of the pituitary gland is replaced by adipose tissue [1, 2].

The size and weight of the iris are not constant, vary greatly in the same age group, and undergo age-related changes [6, 9]. The shape of the iris can be leaf-like (68.8%), cylindrical (9.6%), pyramidal (conical) (7.2%), and in rare cases, oval or indistinct [8]. In a number of cases, the authors suggest that there is a link between high blood fluid form and pathology; for example, the cylindrical form is observed in adults or children in chronic diseases, sepsis, purulent pleurisy, grade 2-3 malnutrition. It is assumed that the uneven rate of vascular growth, the changing direction creates the necessary conditions for the variability of growth of the thymus parenchyma, which is based on its morphological features in different children in the population [9].

The highest production of T lymphocytes lasts up to two years of a child's life. It is in these years that primary interactions with infectious factors occur and long-lived T-cells are formed that live and reproduce for more than 20 years. In the future, the influx of new pathogens will become a rare occurrence, so it will be impossible for the whole thymus to be held by the body, and the thymus will undergo age-related involution from the true thymus by ~ 3% per year. A pool of mature peripheral T-lymphocytes created with high energy expenditure (which then migrates from the thymus to the tissue) contains relatively long-lived cells that can respond with clonal expansion (proliferation) to meet the antigen. Therefore, age-related involution of the thymus does not lead to a catastrophic decline in immunity. In addition, the thymus has some compensatory abilities that replace certain functions of T lymphocytes that are lacking in the immune system [11].

According to modern concepts, the lobules of the thymus parenchyma are divided into 4 structural and functional zones [10]:

1. Subcapsular zone, in which there is a possibility of finding pre-T-lymphocytes, which is a non-lymphoid element of the thymus, as well as the proliferation of T-lymphocytes and the first stage of their maturation.

2. Using the first and second class antigens of the HLA system, as well as under the influence of thymus hormones and interleukins, the inner cortical zone, which is in direct contact with macrophages and epithelium, affects the latter. The maturation stage of T cells.

3. The medullary zone, which contains mainly mature T-lymphocytes, and probably their antigen-independent development occurs in contact with interdigitating and epithelial cells, as well as under the influence of thymus hormones and interleukins. It is from this zone that mature T cells migrate from the organ to the periphery.

4. Intralobular perivascular cavities in which T-cells move, and in cortical matter, these cavities are also part of the blood-thymic barrier, which includes the basement membrane, pericytes, and vascular endothelial epithelial cells [2].

Age-related involution is a characteristic feature of the thymus. Age-related involution results in an increase in infectious and autoimmune diseases, as well as a decrease in vaccine efficacy in old age. Age dependence is an irreversible and normal physiological process like the aging process. With involution, the amount of fat and collagen increases, the percentage of water decreases. The size of the organ decreases due to atrophy [13].

The size of the thymus reaches a maximum by the age of 1 year of life of the child compared to other organs. And if we talk about the absolute maximum weight, it is observed at the age of 12-14 years, then its change is observed. This is probably related to puberty because sex hormones have been found to cause organ atrophy. The effect of hormones on the thymus is due to the presence of estrogen receptors on the surface of stromal and lymphoid cells. Clear immunomodulatory properties, particularly the onset of thymic atrophy, are characteristic of B-estradiol [12]. General steroid hormones, and especially glucocorticoid hormones, affect lymphoid tissues, and the type of effect depends on the dose of the hormone and the stage of cell differentiation. At different doses, the same hormone can cause both apoptosis and an increase in thymocytes. At the end of puberty, thymus mass decreases by about 3% annually [13]. Adipose tissue mainly replaces the lymphoid tissue in the area of the connective capsule and septa.

Accidental involution of the thymus (AI), which many authors believe may indicate morphological rearrangement of the organ in response to any stressful effect, is of great interest for research.

For example, Pershin S.B. and others [14] link the stereotypical response of the pancreas to various negative, overpowering influences in the body (diseases, injuries, intoxication, starvation, frostbite, etc.) with random involution (AI) [14].

The reasons for the development of random involution can be very diverse. In addition to the above, these are also malignant tumors, metabolic diseases in the body [15]. Cases of accidental involution of the pituitary gland after splenectomy have also been reported [16]. The importance of cold solidification and hypoxia has also been identified. For example, in newborns with acute oxygen deficiency, accidental involution (TI) of the pituitary gland (AB) has been observed.

The process of alteration of the pituitary gland (AB) in children is also associated with learning loads that indicate age-related dynamics of development of physiological systems, creating important conditions for the body's adaptation, usually acting in a unilateral pressure regime.

Accidental involution of the thyroid gland (AB) is often observed in childhood in infectious diseases, especially in the gastrointestinal tract, severe pneumonia, meningoencephalitis, sepsis, local purulent processes (phlegmon, osteomyelitis), malignant tumors, cachexia of various origins [2].

In the monograph “Thymus Pathology in Children” [2], the complexity of the morphological examination of this organ led to a distinction between concepts such as thymus dysplasia and hypoplasia, dyscronism (maturity), and atrophy. So far, the reaction of the pancreas to psycho-emotional and other stresses remains a mystery. Why in different situations (e.g., during spaceflights [18] or under the influence of immunotoxicants [17]) this can only be manifested by a decrease in thymus cell proliferation and reflection on a non-stereotypical response to stress. However, the development of atrophy cannot be ruled out.

Speaking of thymic atrophy, Haley et al. (2005), Elmor [20] suggests the loss of thymus cells, a physiological phenomenon and is well known in old age. They do not talk about accidental evolution, but believe that in many cases thymic atrophy occurs, for example, after treatment for psycho-emotional stress, malnutrition, infections, and cancer. Thymus atrophy can result from thymocyte apoptosis, deterioration of the thymus structure, loss of ETR current to the thymus, or a combination of the above. According to the authors, these manifestations may occur as a result of direct (e.g., effects of HIV infection on thymocytes) and indirect (e.g., increased stress-related glucocorticoids) in the thymus. In the first case, as in the next case, nothing is said about a random revolution. For example, there are several experimental models and studies in some humans in which infection with pathogens leads to thymus atrophy. A recent study showed that providers are the most susceptible, while SD8 + SP T cells are the most resistant type of thymus during Salmonella Tyhi murium infection in mice. Furthermore, this study identified the role of infection-induced IFN-g production in slowing the maturation of CD4 + and CD8 + SP thymocytes [19]. Why, in cases of acute death in young children, thymomegaly is detected at autopsy, in others - a sharp decrease in the mass and volume of this organ? Even if this death occurred in both cases before (and often caused) a bacterial infection, i.e., there is one cause (infection + stress), but the result is different.

Conclusion

The conclusion is that the morphological structure (and function) of this organ initially (qualitatively) differed qualitatively, although evolutionarily, before the child was born, there should be criteria for its morphological specificity and maturity.

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