MORPHOLOGICAL PARAMETERS OF THE THYMUS GLAND IN CHILDREN

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ANNOTATION

Objective: to determine the degree of study of scientific literary sources on the morphology of thymus in children.

Methods: More than 30 scientific sources have been analyzed in the literature review of thymus morphology in children.

Results: in the process of studying scientific sources on the morphological aspects of the thymus gland in children, little has been studied; mainly a lot of information has been obtained on morphology by the older age of the thymus in humans.

Conclusions. Our study results consist in a huge number of integral connections of the thymus gland with other components of the immune system, neuroendocrine, hematopoietic and connective tissue, organs (and cells) providing barrier function, etc.

Keywords: thymus; children; involution of the thymus gland; thymus morphology.

Relevance. There are publications on the use of magnetic resonance imaging (MRI). This method is not invasive, allows obtaining a three-dimensional image nature, does not give radiation load; therefore, it can be repeatedly used in dynamic observation. Imaging in MRI allows you to obtain an almost anatomical image of the VV, with a well-differentiated tissue of the VV and surrounding fiber. The researchers note that MRI data are more reliable than in CT [14, 15]. A detailed characteristic of VF according to MRI data was developed in normal and in various pathological conditions, including in children [14-16]. The only limitation of widespread use in children's practice is the need to use anesthesia to stop the child's motor activity at the time of the procedure.

The disadvantage of CT is the presence of a high radiation load, which limits its use in pediatric practice [3-5]. CT devotes a number of publications to the diagnosis of VV volumetric formations: thymus [6-8], thymolip [9. 10], VV cyst [5. 11], aberrant thymus [10. 12]. In addition, this method, according to the authors, is the leading in the diagnosis of the listed variants of thymus pathology [13]. Doctors based on the results

of chest X-ray quite often diagnosed an increase in the thymus gland (VV) in children, and the degree of this increase was diagnosed by calculating the cardiotymic-thoracic index (CTTI). CTTI by J. Gewolb et al. is the ratio of the width of the cardiothymic shadow at the site of tracheal bifurcation to the transverse diameter of the chest at the level of the diaphragm dome [1]. The CTTI of 0.23-0.26 corresponded to normal BL dimensions; 0.33-0.37 - grade I timomegaly (TM); 0.37-0.42 - grade II timomegaly; CTTI greater than 0.42 - grade III timomegaly [2]. However, this method of assessing the morphometric parameters of VF did not quite suit the doctors due to the radiation load, the lack of a three-dimensional measurement of the organ, the lack of the ability to monitor the dynamics of the organ longitude. The literature contains information on the detection of hyperplasia (thymomegaly) of the thymus gland during computed tomography (CT) of the mediastinum [3].

In the literature of recent years, there are quite a few reports on the use of ultrasound of the thymus gland in pediatric practice, the authors of which, as advantages of this method, note its high effectiveness, safety for the patient, the absence of contraindications for the study, the possibility of dynamic monitoring of the structure and size of the thymus, including in newborns [17, 18]. Echographic criteria for assessing the thymus gland are linear parameters (length, width, anteroposterior size), based on which it is possible to calculate the mass, volume of the organ, and after birth the thymus index [19]. A great advantage of sonography over radiography is the ability to determine in a patient "decrease" in thymus size, which may correspond to hypoplasia and atrophic changes of the organ in the IV-V stages of the so-called accidental involution [20, 21].

The national guide for the radiation diagnostics of the chest organs (including the thymus gland) defines the indications for ultrasound examination: unclear allergic manifestations; preparation for operations or vaccinations; the atypically high weight of the child; severe diseases suffered and/or their atypical course; radiologically detected dilation of the mediastinal shadow; cases of sudden death syndrome in childhood among relatives of the child [22].
There are few publications in the domestic and foreign literature devoted to the problem of normative parameters of ultrasound assessment of the state of thymus in children [9, 13, 21, 23, 24]. The existing difference in sonometric parameters of the thymus in different regions, but similar in age groups, most likely arises due to territorial, ethnic, and environmental characteristics, variability of bacterial and viral flora, living conditions and other factors affecting the child's body. Nevertheless, currently, some works give an idea of the regional regulatory size of VF, taking into account age [21, 25, 26]. However, the generally accepted reference population values for the above parameters of the thymus (mass, volume) in children have not been established, which greatly complicates the process of designating TM, hypoplasia,

atrophy as phenomena beyond the norm. Probably, for this reason, at the moment, ultrasound examination of VL is not included in the standard of examination of healthy children [27].

Purpose of the study. Analysis of the literature volume of thymus gland enlargement (VV) in children based on the results of chest X-ray, and the degree of this increase - by calculating the cardiotimic-thoracic index (CTTI). CTTI by J. Gewolb et al. is the ratio of the width of the cardiothymic shadow at the site of tracheal bifurcation to the transverse diameter of the chest at the level of the diaphragm dome.

Literary scientific analysis. The interest of researchers and practitioners (pediatricians, endocrinologists, immunologists, and pulmonologists) is primarily due to the significant prevalence of thymomegaly syndrome (TM) in the pediatric population and its connection with excess respiratory morbidity. Mainly due to the high variability in the size of VF, in the works of domestic and foreign researchers there is no unambiguous assessment of its bipolar transformations. There is a certain problem in terminology. The following definitions are used to indicate an increase in VV in children in the medical literature: thymomegaly (TM), thymus hyperplasia, true thymus hyperplasia, thymus ricochet hyperplasia, thymus hypertrophy, persistent thymomegaly, accidental involution (AI), thymus gland enlargement syndrome (VVS), lymphatic-hypopysitic In some sources, the use of such definitions as: "large thymus," "small thymus" and "medium-sized thymus" is found, along with the concepts of "thymomegaly" and "thymus hypoplasia" [13, 27]. In the domestic literature of recent years, the term "timomegaly," "accidental involution" is more often used, in English - the concept of "thymus hyperplasia," "acute thymus involution," "thymus atrophy" is more common [26, 14, 8-16].

The term "timomegaly," by which morphologists mean an increase in the volume and mass of the thymus above the limit age values with the preservation of normal histoarchitectonics of the organ, was proposed in 1970 by prof. I.E. Ivanovo [11, 12]. Beginning in 1970, the term became widely used by both morphologists and clinicians. Often, the authors point out that TM is accompanied by a decrease in the function of VL, which determines the unfavorable quality of life of these children [1, 27, 24, 25]. Timomegaly was divided into congenital (primary) and acquired (secondary) [52]. The detection of TM in stillbirths and in children of the first months of life suggested the existing congenital nature of the process [26, 27]. Various adverse prenatal effects were noted as etiological factors affecting such Tm transformation, both in the first trimester of pregnancy and during fetogenesis [13, 22, 28]. A great importance was assigned to the factor of intrauterine infection [20, 24, 30]. It was noted that the alleged congenital TM is accompanied by a decrease in hormone secretion against the background of neuro-endocrine system dysfunction, lymphoid tissue hyperplasia, metabolic disorders in combination with congenital abnormalities in the development of various organs and

systems [20, 22, 24]. Kuzmenko L.G. considers congenital TM as a variant of fetodysplasia, malformation [20]. Loginova N.P. also describes the close relationship of congenital heart defects with morphological changes in the thymus and its reduced activity in relation to the production of thymulin and T-lymphocytes with CD3 + differentiation clusters. The author also notes a direct correlation relationship between the complexity of the defect, the level of thymopoiesis and the increment of thymulin, which are significantly lower than in healthy children [25].

A number of published works suggest the hereditary nature of timomegaly [2, 3]. There are analytical data [10, 15, 16-18] from outpatient charts, case histories that describe some features of the history and constitution of children with congenital SUVH and TM, as well as factors and markers of the risk of their intrauterine formation, for example, such as: aggravated family history of autoimmune and oncological diseases, the presence of chronic nasopharyngeal pathology in blood relatives [20, 29]; birth by caesarean section [10, 19]; high level of diseases in mothers, such as anemia (62.4%), pyelonephritis (28.2%), obesity (34%), iodine deficiency conditions (37%), TORCH syndrome (46%) [18, 20]; presence of chronic hypoxia in the fetus in the antenatal period, birth trauma [10, 20, 29].

According to T.V. Matkovskaya, there is a direct relationship between the age of parents and the development of TM in their children [24, 27].

It is believed that the acquired TM is based on primary or secondary hypocorticism, which develops under the influence of various pathological conditions and diseases (addisone disease, injuries, inflammatory lesions of the adrenal cortex or its destruction in massive hemorrhages and tumor process, hypothalamic syndromes in vasculitis, progressive, often occlusive hydrocephalus, brain tumors, etc.). At the same time, immunodeficiency syndrome is noted, similar to that of congenital TM [22].

The question of whether the increase in VL is a variant of the norm for young children or is a pathology is still being discussed [17, 22, 29].

Krasnoperova K.E. [13] considered the increase in Thymus in young children under various non-infectious influences as a manifestation of an adaptation syndrome with changes in metabolic processes and dysfunction of the immunogenesis system. Other authors also considered the increase in VV physiological, in the process of the same active adaptation of the child's body, but now to non-sterile conditions of the outside world [12. 14. 15]. Brum EB considers radiologically detectable Thymus enlargement in young children also as a normal physiological state due to the peculiarities of the structure of VF [16].

There is also a directly opposite opinion that TM is a pathological condition accompanied by immunodeficiency and impaired function of the neuro-endocrine system [14, 17-22]. At the same time, TM was attributed to the number of heterogeneous states in which the increase in VV could be both the result of accidental

involution (direct violation of TM function) and the result of secondary changes in this organ associated with other diseases (for example, thymus cyst) [23]. Separate sources discussed the reasons for the increase in VV and its stage (for example, I-III) within the framework of accidental involution, which was considered from the standpoint of G. Selye's theory. [8, 9, 10].

Erofeeva L.M. believes that an increase in VL occurs in cases where the mass of the organ exceeds the age norm: in the absence of viral-bacterial infection - by 50% or more; on the first day of viral and bacterial diseases - by 100% or more; in infectious and inflammatory diseases with a prolonged course, after resuscitation or steroid treatment - by 5% or more [83].

It should be noted that information on the prevalence of timomegaly in childhood is quite contradictory. In chest radiographs of children, thymomegaly was detected with a frequency of 8.1% [3] to 80-85% [18, 19]. According to sectional data, the frequency of increased VF was recorded among stillborn fetuses 28-42 weeks in 36% of cases, and in 16% among children who died in the first year of life; in those who died between the ages of 1 and 5, this percentage is significantly reduced to 0.2% [12, 17, 20]. According to A.V. Tyazhkaya, TM occurs in 12.8% of young children [22]; data of Yu.P. Tkachenko - in 29.9%); Sh.G. Huseynov - 37.1% [21]. In the work of Z.I. Esmurzieva et al. it was shown that according to the results of thymus ultrasound, the incidence of thymomegaly of varying severity in full-term newborns reaches 21.5%. The incidence of grade III timomegaly in the population, according to the author, does not exceed 4%, and grade III HV hypoplasia does not exceed 2% [28].

In boys, timomegaly is 2-2.5 times more common than in girls [11, 13, 18]. There are data on spontaneous regression of VL sizes by 3-5 years of age in 98% of children [23].

There is evidence of the influence of adverse environmental factors on thymus transformation and the nature of feeding the child [22-24].

Many authors note that children with TM are characterized by certain constitutional features: delicate pale skin, pastiness, abundant hair growth on the head, good development of the subcutaneous fat layer, weak muscle development, decreased tissue turgor, increased transverse body size, flattening of the facial skull and bridge, shortening of the neck and chest, elongation of the lower legs, forearms and feet [11. 15. 16. 30]. According to L.G. Kuzmenko et al., signs of various degrees of dysembryogenesis are observed in 90% of children with thymomegaly [15, 20]. Other authors note that these children have higher growth and weight indicators [15, 22, 28, 29], the presence of microanomalia and malformations with a frequency of 23.1% to 80.9% [5, 6, 7, 8]. Among the stigmas, the most common are diastasis of the rectus muscles of the abdomen, Gothic palate, dysplasia of the hip joints, umbilical and inguinal-scrotal hernias [8], among malformations - congenital defects of the heart and

main vessels [10, 17, 19, 20], malformations of the endocrine system, multiple non-chromosomal abnormalities, biochemical defects [17, 18, 21, 22].

Children with TM may develop symptoms of compression of the mediastinal organs in the form of dry cough, noisy breathing, swelling of the cervical veins [24]; hyperplasia of the lymphoid apparatus [24, 27, 28, 30], an increase in the number of white blood cells and lymphocytes in the peripheral blood [21, 23, 24, 25, 35], impaired adrenal function and the hypothalamic-pituitary-adrenal system [3, 4, 7, 8, 10, 12, 16, 34]. There are works in the domestic literature, the authors of which statistically significantly more often identify signs of secondary adrenal insufficiency with a decrease in the level of ACTH, 11-OKS and cortisol in children with TM [4, 8, 10, 17, 34]. There is evidence that this category of children has more frequent cases of hypoplasia and atrophy of the adrenal cortex [4, 17], signs of thyroid hypofunction [4, 7, 9, 10, 18] and genital glands [14, 19]. Work was presented with registration of the decrease in the level of thymic hormones in the serum of children with TM and impaired endocrine organ function [14, 15, 18, 19, 20-23]. All the above facts did not rule out the development to one degree or another of polyglandular insufficiency syndrome in children with a similar transformation of VV [17. 18. 19. 20].

The reviewed literature pays attention to the peculiarities of the neuropsychiatric development of children with TM, which are characterized by inactivity, delayed reactions, high tendon reflexes, rapid fatigue, and a decrease in internal inhibition processes [10, 18, 23, 27, 28]. So, for example, in the work of L.G. Kuzmenko et al. [30], when studying neuropsychiatric features in young children with thymomegaly (n = 90), it was found that schizoids (51%) and hyperexposure (33%) predominate among them. The proportion of hyperthymics is 10%, and healthy children - 6%.

The national pediatric literature is dominated by the view that TM is an immunodeficiency syndrome with a predominant T-cell link disorder [27, 29, 30], in which there is a decrease in the level of functional activity of T-lymphocytes, a low level of thymic serum activity and functional activity of the B-cell link of the immune system [1-9, 13-15]. Despite the high or normal content of B-lymphocytes, a decrease in the number of immunoglobulins of classes G and A was noted in serum in TM [3-8, 11-16]. The level of immunoglobulins of class M can be both increased [19] and normal [118]. There was an increase in the absorption capacity of neutrophils and macrophages with a decrease in their digestion capacity [7, 8]. It is noticed that at children of early age with a timomegaliya all indicators of T-cellular immunity are significantly reduced: the maintenance of T-cages (CD3+), T-helperov (CD4+ of T-cages), cytotoxic T-lymphocytes (CD8+ of T-cages), regulatory T-cages (CD4+CD25hi) and also the activated T-lymphocytes (CD4+CD25lo and CD3+HLA-DR+). An increase in the severity of these changes was observed as the degree of thymomegaly progressed, and T lymphopenia is associated with a weakening of the emigration of T

cells from the thymus to the peripheral part of the immune system. Such changes, according to the authors, cause a functional deficiency of the T-cell link of the immune system and can contribute to the manifestation of its failure, especially in conditions of increased load with pathogens [12].

Donetsk A.D. et al. [13] interpreted the revealed decrease in TREC in thymomegaly in children as evidence of a decrease in thymic T-lymphopoietic function. Such attenuation of T-lymphocyte emigration due to thymopoiesis disturbance resulted in compensatory enhancement of homeostatic proliferation, which in turn distorted the population structure of peripheral T-lymphocytes, which could lead to the development of autoimmune diseases in the long term. In old age, the ability of thymus tissue to generate new naive T cells and fight new threats is practically absent, which makes a person open to infectious diseases, and vaccination is less effective [12, 13]. Timomegaly and often and/or a long-term sick child. Lymphatic diathesis. The problem of an often ill child and the reactivity of his immune system requires a certain emphasis. This problem is far from unambiguous, it is more often based on socio-economic, environmental, biological and other factors. Traditionally, in the Russian Federation, an increased respiratory incidence is associated with a relatively insufficient immune protection of a child in a certain age period (from 1 month to 5 years). This applies more to organized childhood, where the problem lies in excess infection.

At the same time, Kuzmenko's proposal L.G. et al. [27-36] denote thymus transformations by terms: megalotimus, microtimus, emphasizing, in a certain part, the functional nature of these changes (voltage - overvoltage - exhaustion) and the complexity of predicting the further morphological evolution of the organ. But, since the morphology and functioning of any organ is dialectically inseparable, all these states (polar transformations) should negatively affect the sending of functions by the iron by definition. This is often the case. It all depends on the depth and level of assessment of the morphological substrate and the functional state of the organ (integral or its individual functions). And, naturally, there will come a time when a more accurate morphological assessment of organometric transformations of VF (electron microscopy, immunohistochemistry, etc.) and a more accurate assessment of its specialized functions (identification of various biomarkers) will be given [23-32].

Currently, we consider it advisable to designate the stages (degrees) of increasing or decreasing the morphometric parameters of VL, since these additions make it possible to longitudinal observation, study, and, if necessary, correct pathological conditions associated with VL depending on the depth (degree) of its transformation.

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