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FEATURES OF DISEASE INCIDENCE IN CHILDREN WITH LYMPHATIC-HYPOPLASTIC DIATHESIS

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Abstract In the article, the authors disclosed the latest modern data on the analysis of the literature on the structure and disease incidence of children with lymphatic-hypoplastic diathesis. It has been shown that recently the frequency of occurrence of children with lymphatic diathesis and thymomegaly has increased. The article analyzes the immune aspect and the disease incidence of children with lymphatic diathesis. In children lymphatic diathesis is accompanied by immunodeficiency and there is a predisposition to diseases of the bronchopulmonary system, tuberculosis, onco- and autoimmune diseases.

A detailed study of the problem of the immune and cytokine status of children with lymphatic diathesis will make it possible to develop possible approaches to treatment and prevention.

Keywords: Disease incidence, immunodeficiency, lymphatic-hypoplasty diathesis, thymomegaly.

Lymphatic-hypoplastic diathesis as a constitutional anomaly was first introduced in 1889-1890 by Viennese pediatrician T.Escherich and pathologist R. Paltauf.

The prevalence of LGD is lower than exudative-catarrhal and makes 10-12% [3,12].

In the last decade, there has been a steady increase in lymphatic diathesis, accounting for 27.8±2.6% among the child population [11].

The maximum frequency of LGD is observed at preschool age, amounting to 3,2-6,8% according to M.S. Maslov (1926), according to Veltishchev Yu.E. (1985) and 12.5-24% of children according to Bazhenova L.K. (1994).

Galinskaya T.P. and Sannikova N.E. [5] believe that signs of LGD can be revealed in 10-13% of young children. According to Vozgoment O.V. [5], LGD is formed by 2–3 years of age and usually ends by puberty.

Kuzmenko L.G. [10] indicates that in children with LGD at the age of 3-5 years the manifestations of lymphadenopathy quite often disappear, the size of the thymus normalizes, respiratory morbidity decreases to the population level, and the "immune profile" of the blood is restored. In her opinion, the thymus, "ripens" qualitatively, later in time reaches a "plateau" of optimal functioning, and then undergoes age-related involution.

With LGD, according to Moshchich A.P. [11], thymomegaly is found in about 70% of cases.

According to Kurbanova T.G. et al. [29], among children with acute and prolonged diseases of the bronchopulmonary apparatus, the detection of thymomegaly, as the main pathogenetic marker of LGD, is 30-32%.

Voropaeva Ya.V. [6], reveals thymomegaly in 10-50% of children. Most often, this condition is recorded in children of the first year of life in 40% of boys and 30% of girls. Data of Tyazhkoy A.V. [16] shows that thymomegaly occurs in 12.8% of young children and, according to Huseynov Sh.G. in 37.1% [7].

According to Veltishchev Yu.E. [5] and in the work of Fedorova M.Yu. [5] it was shown that lymphatic diathesis and its pathogenetic varieties are characterized by a polygenic type of inheritance with a predominant susceptibility to males. Having a polygenic basis, lymphocytosis and a decrease in the glucocorticoid activity of the adrenal cortex are considered to be pathogenetic markers in LGD [21].

It is known that the condition of the immune system plays an important role in the pathogenesis of acute inflammation, its relapses and chronicity [17].

It is known from the literature data that immunodeficiency, which is accompanied by pathology of the respiratory organs, in certain cases is associated with an increase in the thymus [4,19].

Thymus is the central organ of immuno- and lymphocytopoiesis [4,19].

As it is known, the synthesis of biologically active substances which are both secreted into the blood and act locally occurs in the thymus, [8]. In addition, thymosin peptides induce the maturation of T-lymphocytes, increase their mitotic activity, and increase the reactivity of T-helpers [8].

The available data in the literature, on the immune aspect accompanying lymphatic diathesis, are heterogeneous in thymomegaly. Many authors point to the hypofunction of the T-cell link of the immune system: a decrease in the number of T-lymphocytes and change in their subpopulation composition [3,4,9]. Studying T cell immunity in children with thymomegaly Vaganov P.D. et al. [4] define that T-lymphopenia affected both CD4 and CD8 cells, and these changes increased in parallel with the increase in the degree of thymomegaly.

A number of researchers paid attention to thymomegaly [4,36], as a prognostic marker indicator of the course of infectious processes in young children A number of authors have found that in somatic pathology associated with lymphatic diathesis, there is an increase in the level of CD8+ and IgM [8]. At the same time, in the course of other studies, opposite results were obtained [8,20].

Research results of Smiyan A.I. et al. [18] in young children with acute obstructive bronchitis against the background of thymomegaly revealed a more significant decrease in the content of lymphocytes, CD3+, CD4+, CD8+ and an increase in subpopulations of B-lymphocytes, as well as a decrease in the concentration of IgM, IgA and an increase in the level of IgG compared to patients without thymomegaly. In acute pathology of the respiratory organs in young children Kholmatova B.T. [20] revealedfound increases in CD8, CD16, and CD20 levels, with inconclusive decreases in IgA, IgM, and IgG levels.

There are home and foreign literary data that directly indicate the relationship of high respiratory morbidity with the syndrome of an enlarged thymus gland and thymomegaly [24,27,14,25,38].

Lukashevich M.G. and Surazakova T.N. [14] also noted a high disease incidence in children with increased life expectancy.

Kuzmenko L.G. et al. [10] established a relationship between high respiratory morbidity with LGD, which is accompanied by a low level of lymphocytes with the phenotype CD3, CD4, CD8.

According to Rovda Yu.I. et al. [15] one of the main signs of LGD is a high disease incidence of acute respiratory viral infections, bronchitis, tracheitis, otitis, conjunctivitis, blepharitis which are mainly of viral origin.

A number of researchers [13.15] showed that acute respiratory infections in children with thymomegaly are more severe than in children without thymomegaly, with this it was most clearly observed in children with grade III thymomegaly. In the same work, the authors associate the frequency of occurrence of mollionic forms of meningococcal infection with the degree of thymus enlargement: at stag degree I. 4.8% of the total, with stage II and III degree. 85.2%, respectively. Also Ivanov S.K. [2] established the features of the course of acute diseases in children with lymphatic diathesis, which are manifested by a high frequency of complicated and prolonged forms.

Sorokman T.V. et al. [37], analyzing the data on the relationship between the size of the thymus and respiratory morbidity, present the following statistics: more often thymomegaly occurs in obstructive variants of the respiratory tractdamage, namely, in stenosing laryngotracheitis and obstructive bronchitis, an increase in VL to stage III, which occurred in 75% of children, respectively, and in 23.5% up to stage I. A different trend was noted in non-obstructive variants of bronchial lesions: the thymus was increased to stage I in 62.5%, up to stage III Art. in 37.5% of patients [37].

Research by Bakhodirova A.N. et al.[1] showed that the degree of severity of respiratory failure in children, in addition to the general toxic manifestation of a respiratory disease, was also influenced by the presence of a burdened premorbid background, in particular, the presence of lymphatic-hypoplastic diathesis (12%).

According to the literature, a significant number of cases of sudden death syndrome are associated with thymic-lymphatic conditions that are similar in etiopathogenesis to LGD [www.eurolab.ua/encyclopedia/352/2675/].

When performing a post-mortem examination of the case histories of children who died suddenly from acute respiratory viral infections and pneumonia, pathoanatomical examination in most cases revealed signs of lymphatic-hypoplastic diathesis, which was accompanied by insufficiency of the lymphatic system, dysfunction of the adrenal glands [5]. The research carried out by Rovda Yu.I. et al. [15] also proves that in children with LD, the addition of pneumonia leads to the rapid development of signs of infectious toxicosis, respiratory and cardiovascular failure.

And also, in addition to the excessive level of respiratory morbidity in LGD and high frequency of bacterial complications, a number of authors note a higher mortality rate in this category of children [2,29].

Studying the influence of constitutional anomalies on tuberculosis infection in children, Yarovaya Yu. A. et al. [22] showed a more marked pronounced intoxication syndrome in children with LGD than in children with NAD and AD. In addition, unfavorable forms were noted in children with LGD, such as subacute disseminated tuberculosis, infiltrative pulmonary tuberculosis, which were not observed in groups of children with other types of diathesis.

In children with LGD, intercurrent infections are rare, but more often than in the general population, tend to be generalized, fulminant, or recurrent course with prolonged low-grade fever[13].

Chkhartishvili E. [23] associates the presence of thymomegaly with recurrent episodes of various conditions, such as rash, dermatitis, infections of the upper and lower respiratory tract, sinusitis, chronic cough, hypertrophy of the adenoids and tonsils.

Pneumonia in patients with thymomegaly is characterized by a more pprolonged and severe course; these are more often complicated forms with manifestations of II-III degree respiratory failure, neurotoxicosis and pulmonary edema [16, 30].

Kellogg C [28] suggest that measuring thymus function using (T-receptor excision rings – TRER) quantification can help to assess the risk of developing of comorbid conditions in patients, severe COVID-19 and other opportunistic infections, and can also predict patient response to vaccination.

It is possible that there are certain reasons for such a temporary delay in the development of the morphofunctional status of the HP, for example, fetal or genetic ones.

There are observations that oncological diseases and diffuse diseases of the connective tissue [10.15] occur more often in future in the children and adults (so-called "lymphatics" in the past) and tuberculosis develops more often.

It is known from the literature that any variant of lymphatic diathesis is a risk factor for leukemia [16], autoimmune and neoplastic processes [10], the development of secondary insufficiency of the adaptive and constitutional defense systems of the body, which causes a torpid, complicated course of infectious processes [9,29].

Based on current data on the pathogenesis of respiratory damages to children, genes for pro- and anti-inflammatory cytokines are candidate genes and are closely associated with the development and clinical course of these diseases [31,32].

As it is known, IL-1β is of particular importance in immune reactions and inflammatory processes, which induces the synthesis of other “anti-inflammatory” cytokines, such as TNF-α and IL-6,[33] low-molecular inflammatory mediators. IL-1β is also involved in the regulation of the immune response, which is of key importance in the development of infectious and inflammatory diseases [34].

Despite the numerous studies on pro- and anti-inflammatory cytokines, their contribution to the formation of lymphatic diathesis in children remains unclear.

Reviewing the literatry data, we revealed that children with LGD in children is accompanied by immunodeficiency and have a predisposition to diseases of the bronchopulmonary system, tuberculosis, onco- and autoimmune diseases. However, the literatry data extremely poorly reflect the problem of the immune status of children with lymphatic diathesis, in addition, the available data are contradictory and the literature practically does not describe the condition of immunity and cytokine status in RD against the background of lymphatic diathesis, which allows to develop possible approaches to treatment and prevention.

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