

## Morphofunctional State of Thymus Gland among Children of Early Age with Thymomegalia

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### Abstract

*The morphometric characteristics in children of early age with thymomegalia were studied. In this case was found the increase of the area of lobule of thymus due to the predominance of the cerebral cortex and a significant increase in the ratio of thymocytes / epithelial reticular cells because of the increase of the absolute number of thymocytes. The differences in area and diameter of the Hassall's corpuscles in the two compared groups were not revealed, however, was found a slight tendency to the decrease of these indicators in case of hyperplasia of thymus gland. These changes indicate the Morphofunctional inferiority of the thymus among children of early age with thymomegalia.*

**Key words:** *thymus, thymomegalia, epithelial reticular cells, thymocytes, Hassall's corpuscles.*

### INTRODUCTION

The thymus gland (thymus) is one of the central organs of the immune and endocrine system, responsible for the differentiation of T-lymphocytes. Children with impaired thymus function have an immunological, predominantly T-cell defect, and both decrease and hyperplasia of the thymus can be observed, which is an attempt to compensate for the impaired immune function [4, 5]. At the same time, the latter often remains unsatisfactory, as a result of which children with an enlarged thymus gland typically have a severe course of a number of infectious processes, especially meningococcal infection (MI), and frequent recurrent respiratory diseases [6, 10]. Severe immunodeficiency, along with adrenal insufficiency, also underlies most cases of sudden infant death syndrome (SIDS), for which significant thymomegalia is extremely typical [7, 12]. Immune disorders in the peripheral blood in children with thymomegalia have been repeatedly described earlier [2, 10]. At the same time, the interpretations of such data present significant difficulties, since patients, as a rule, was examined at the time of a serious infectious disease or were in a short period of remission between several repeated infectious processes. As a result, the revealed changes could be the result of not a true deficit, but only a targeted redistribution of immunocompetent cells. Much more informative for establishing the nature and mechanism of the immune defect is a direct study of the hyperplastic thymus, however, such studies are still very few in number, and the conclusions drawn on their basis

are contradictory [3]. In this regard, the aim of this work was to study the Morphofunctional state of the thymus gland in young children with thymomegalia.

### Material and methods

We studied 10 hyperplastic thymuses with a weight significantly exceeding the norm (on average -  $45.5 \pm 3.4$  g): 5 samples from children aged 1.5 - 8 months who died from fulminant meningococemia, 5 - from patients aged 2– 5 months who died from SIDS. In both groups there were 4 boys and 1 girl. The comparison was carried out with 5 normal weight thymuses (on average  $10.6 \pm 0.4$  g) from children aged 1 day to 3 months, including 2 boys and 3 girls who died from newborn asphyxia, multiple congenital malformations, congenital bilateral purulent pneumonia with aspiration of amniotic fluid. The degree of enlargement of the thymus gland was assessed on the basis of calculating the value of the thymus index (TI) according to the formula:  $TI = \text{thymus weight (g)} / \text{child's body weight (g)} \times 100\%$  [5]. Thymus samples were fixed in 10% neutral formalin for 48 hours, then processed according to the generally accepted method [13]. Sections 4–5  $\mu\text{m}$  thick were made from paraffin blocks and stained with hematoxylin and eosin [9]. The study of slides and the production of micrographs were carried out using a Leica DMLS microscope with LeicaQWin software (Germany). During the morphometric study of histological preparations of thymus along the entire perimeter of each preparation, the area of the cortical (Sq) and medulla (Smv), the ratio of Smv / Sqw (5 lobules in each observation), the area of the thymus lobule (SD), the area and diameter Hassall's little bodies (TG) - thymus bodies (STG and dTG, respectively). At a magnification of 1000, using the Bioscan program, the total number of thymocytes (T), reticuloepithelial cells (REC) was counted, their ratio T / REC was determined (3 lobules, 5 fields of view). The data were processed statistically using the Statistica 6.0 and SPSS 17.0 software. Significance was assessed using the nonparametric Mann-Whitney U test. The confidence interval was calculated for the mean values of the samples with a probability of 95%.

### Research results.

When assessing the degree of enlargement of the thymus gland among the examined, we obtained the following results: the value of TI in children with MI was -  $0.58 \pm 0.07$  (95% CI 0.38 - 0.78), with SIDS -  $0.96 \pm 0$ , 14 (95% CI 0.58 - 1.34), in the comparison group -  $0.28 \pm 0.04$  (95% CI 0.18 - 0.38). Thus, the TI indices in the groups with fulminant MI and SIDS significantly ( $P < 0.01$ ) exceeded the indicated indicator in the comparison group. Microscopic examination revealed that all studied thymuses are represented by lobules of various sizes, separated by connective tissue layers. In most cases, the lobules are well formed, the hyperchromic cortical and lighter medulla, epithelial and stromal-vascular components are clearly defined. The cortical zone of the thymus gland is represented by REC, lymphoblast's and lymphocytes (thymocytes) at different stages of differentiation, macrophages, eosinophil's and basophils are found. The most abundant population of the medullary zone is loosely located lymphocytes (Fig. 1). In the histological preparations of the thymus of the comparison group, signs of organ involution with untimely appearance of areas of adipose tissue in the interlobular spaces were revealed; among thymocytes of the cortical substance, multiple RECs, thymus bodies at different stages of development are light-optically clearly distinguishable. The cavity of large Morphofunctional mature TGs is filled with decay products,

phagocytosed lymphocytes, macrophages, nuclear detritus, some thymus bodies merge into large formations, which may include several small ones, or bridges are formed between them, single cystic expanded bodies are observed. With thymomegalia in the cortical zone of the thymus against the background of fulminant meningococemia and SIDS, there are signs of reactive morphological changes similar to the accidental transformation of the first phase, the presence of macrophages with extensive cytoplasm, in some cases containing phagocytosed cells, is found focal clusters consisting of a small number of lymphocytes, REK, with SIDS thymus bodies were few, often at a regressive stage of development (the contents are homogeneous, subjected to calcification). The main morphometric characteristics of the hyperplastic thymus gland differed significantly from the usual parameters. Thus, the area of the thymus lobule did not increase evenly, but almost exclusively due to the cortical part ( $P < 0.01$ ). As a result, the  $Smv / Skv$  ratio also changed significantly ( $P < 0.05$ ). At the same time, the expected parallel increase in the morphometric parameters characterizing Hassal's little bodies did not occur against the background of an increase in the thymus mass. Moreover, both STH and dTG in thymomegalia even tended to decrease. These patterns were typical for both children with MI and SIDS. There were no significant differences in the morphometric characteristics of the thymus in the groups of patients with MI and SIDS ( $P > 0.05$ ). Morphometric parameters of thymocytes and REC of the thymus gland in children with thymomegalia are presented in our work, morphometric parameters of thymocytes and REC of the thymus gland in children with thymomegalia significantly differed from the data in the comparison group. Thus, the absolute number of the former in thymomegalia was significantly higher ( $P < 0.01$ ), while the number of RECs in the hyperplastic thymus, on the contrary, was less ( $P < 0.05$ ;  $P < 0.01$ ). Accordingly, the ratio of T to REC in thymomegalia significantly exceeded this value in the comparison group ( $P < 0.01$ ). The revealed changes were typical for both patients with MI and children with SIDS. There were no significant differences in the morphometric parameters of thymocytes and REC of the thymus gland in the studied groups with MI and SIDS ( $P > 0.05$ ).

### **The discussion of the results**

As can be seen from the presented data, the thymus gland in young children with thymomegalia is not at all simply an enlarged full-fledged organ with a normal structure. On the contrary, this is a thymus with altered morphological characteristics, indicating a violation of its natural functioning. Among the morphological features of the hyperplastic thymus, an increase in the area of the cortex and a noticeable predominance of the cortex over the cerebral cortex were revealed, especially in patients with SIDS. The increase in thymus mass due to the cortical substance probably reflects the massive influx of immature thymocytes into this zone of the thymus gland, where the main stages of their differentiation take place [2,17]. On the other hand, the predominance of the cortical substance over the brain is an indirect sign of the presence of glucocorticoid insufficiency [11,16]. However, to what extent glucocorticosteroid insufficiency is primary, and to what extent it is due to the need for vital compensation of the thymus against the background of immunological insufficiency, remains unclear. It is known that with hypocorticism there is a change in the architectonics of the thymus with the replacement of the functioning parenchyma with adipose tissue, the formation of lymphoid follicle lobules with light centers in the center [8,13]. In cases with thymomegalia, no such changes were found. An increase in the absolute number of thymocytes and a

significant increase in the T / REC ratio is the second significant change in the histostructure of the thymus gland in thymomegalia. RECs are involved in the maturation of thymocytes, produce thymus hormones, interleukins, and other growth factors [2, 14]. In conditions of a relative deficit of REC against the background of an increase in the absolute number of immature thymocytes entering the cortex of the thymus gland, the process of full maturation of lymphocytes in the thymus can be significantly impaired. The role and function of thymus bodies is not fully understood. However, there is evidence of morphological changes in triglycerides against the background of immunodeficiency states [1,18]. As a result of our studies, no differences in the area and diameter of thymus bodies were found in the compared groups. However, there was a slight tendency towards a decrease in these indicators of thymus bodies in thymomegalia, which may be an indirect sign of suppression of normal apoptosis.

### Conclusion

Thus, the revealed structural changes in the thymus in the syndrome of an enlarged thymus gland in young children indicate it's not only morphological, but also Morphofunctional defects.

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