PEDIATRICS

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Ultrasound and morphological parallels in assessing the state of the immune system organs in children with immune deficiency

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The diagnosis of immune disorders is still a very difficult task. This study was performed to determine of the diagnostic ultrasound possibilities in identifying the signs of immune deficiency in children. According to the results, an increase in the spleen mass coefficient occurs with the growth in the number and size of lymphoid follicles. This is confirmed by both morphological and ultrasound data. An increase of the spleen mass coefficient in children with chronic immune-endocrine insufficiency is a reflection of system changes, which, for the most part, are manifested by hyperplastic (in few cases — involutive) processes in lymphoid organs and tissues. The technique of ultrasound examination of the spleen and neck and abdomen lymph nodes can be a non-invasive method for identifying children with immune deficiency and those risky for the development of fatal complications.

Keywords: spleen, ultrasonography, lymphoid organs, immune deficiency.

Introduction

In recent years, the world has seen a progressive increase in prevalence of immune disorders: autoimmune, allergic, immune defiicient and oncohematological diseases, both among adults and among children [1].

The immune system condition (ISC) determines the course and outcome of any disease [2]. An objective assessment of ISC is based on a combination of clinical and laboratory data. However, the immunobiological parameters depend on mosaic of many factors and characterize the ISC only in a certain period of time because of the short duration of active period of cells and half-life time of mediators of the immune response — from several days to several minutes. Thus, the diagnosis of immune disorders is still a very difficult task. Important data about the status of patient's lymphoid organs and tissue (spleen, lymph nodes, thymus, palate tonsils) can be obtaines by their in vivo visualization by means of ultrasound examination (USE) — the most relevant imaging methods in pediatrics [3; 4]. This required performing the present research.

Aim

Determination of the diagnostic ultrasound possibilities in identifying the signs of immune deficiency in children.

Methods and materials

The results of complex clinical and laboratory investigation and USE of 393 children aged 2 to 7 years, conducted at the outpatient clinic of the Federal Scientific Center for Medical and preventive health Risk management Technologies in the city of Perm, are summarized.

The inclusion criteria: children 2–7 years old (this age is characterized by the maturation of the immune system with maximum content of lymphoid follicles in the lymphoid organs and mucosa-associated lymphoid tissue).

The exclusion criteria: presence of the cardiovascular or liver diseases that cause changes in portal hemodynamics, as well as existence of hematological, lymphoproliferative, oncological, congenital, hereditary diseases, and chronic somatic illnesses.

All children were divided into 2 groups, depending on the number of diseases experienced per year and the severity of their course. The observation group (G1) included 89 children who were ill more than 4 times a year with protracted course (more than 10 days) of acute diseases and inflammatory complications (purulent otitis, sinusitis, bronchitis, pneumonia). The comparison group (G2) contained patients who were ill no more than 4 times a year without any inflammatory complications (304 children).

According to the clinical-laboratory data, children of the G1 were attributed as "immune-compromised" with clinical manifestations of secondary immune deficiency (SID).

USE was performed on the TOSHIBA APLIO XG diagnostic unit SSA-790A (Japan) using multi-frequency convex (3–6 MHz) and linear (10–14 MHz) transducers. The spleen lymphoid follicles status was analyzed and the spleen mass coefficient (SMC) was calculated using the following formula [5]:

$$SMC = (0{,}34\ l^2 h \times 1000) / m,$$

where "l" — spleen length (cm), "h" — spleen thickness (cm), "m" — child's body weight (g).

Neck and abdomen lymph nodes (LN) (as the regions with the highest antigenic stimulation) were studied by standard technique of USE.

In Perm Regional Bureau of Forensic-Medical Expertise the morphohistological study was performed involving the central and peripheral immune system organs (thymus, spleen, lymph nodes, tonsils, Peyer's plaques, respiratory system lymphoid tissue and parotid glands) as well as the adrenal glands in 20 children 2–7 years old died after acute trauma.

At autopsy the SMC(a) was calculated: SMC(a) = Ms x 1000 / Mt, where "Ms" — spleen mass (g), "Mt" — body weight (g).

According to the results of this study, all dead children were divided into 2 groups: group-1 — with chronic immune-endocrine insufficiency (CIEI): systemic hyperplasia or reduction of lymphoid follicles, degenerative changes in the thymus, hypoplasia of the adrenal cortex (6 children); and group-2 — without signs of CIEI (14 children).

Results

A comparative analysis of the average SMC values showed a significant ($p < 0.05$) increase in the G1: SMC = 4.64 ± 0.26; while in the G2 SMC = 1.69 ± 0.13. In 80.9 % of children of the G1, the SMC was above normal, in 12.36 % — within normal limits, and in 6.74 % of G1 children — less than normal (Table 1).

Table 1. **The SMC average group values in the observation group**

SMC value	n	M	S	m
Low SMC (< 2)	6 (6.74 %)	1.62	0.33	0.34
Normal SMC (2–4)	11 (12.36 %)	3.86	0.26	0.22
High SMC (> 4)	72 (80.90 %)	4.90	0.80	0.18

In children of the G1 with high SMC, the lymphoid follicular hyperplasia (LFH) was revealed by USE in 100 % of cases (72 children) (Fig. 1). In all these children, the reactive cervical and mesenteric LNs were determined (Fig. 2). In 7 (63.6 %) children of the G1 with normal SMC the ultrasound signs of spleen LFH were revealed; in 11 children (100 %) the reactive neck LNs and in 9 children (81 %) reactive mesenteric LNs were revealed.

In all children of the G1 with low SMC, USE didn't reveal any signs of spleen LFH. Neck and mesenteric LNs had no signs of high activity (all parameters were significantly lower than in children with high SMC).

The autopsy study showed the SMC(a) average group value in G1 = 4.8 ± 2.3, which is significantly ($p \leq 0.05$) more in comparison with the value of the SMC(a) in G2 (3.4 ± 0.7).

In one child with severe perinatal organic lesions of the central nervous system who died as a result of acute respiratory viral infections complicated by severe destructive pneumonia, SMC(a) was significantly lower than normal (1.62). The histological preparations of this child revealed the lymphoid follicles reduction not only in spleen, but in LNs and other lymphoid structures.

In one child, SMC(a) was within normal limits (3.18); in four children SMC(a) was more than 4 and histological preparations of lymphoid organs showed the expressed macrophage reaction and enlargement of the lymphoid follicles reactive centers.

The condition of the thymus and adrenal glands fit into the general group picture: depletion of the adrenal cortex with the atrophy and involutive processes in the thymus.

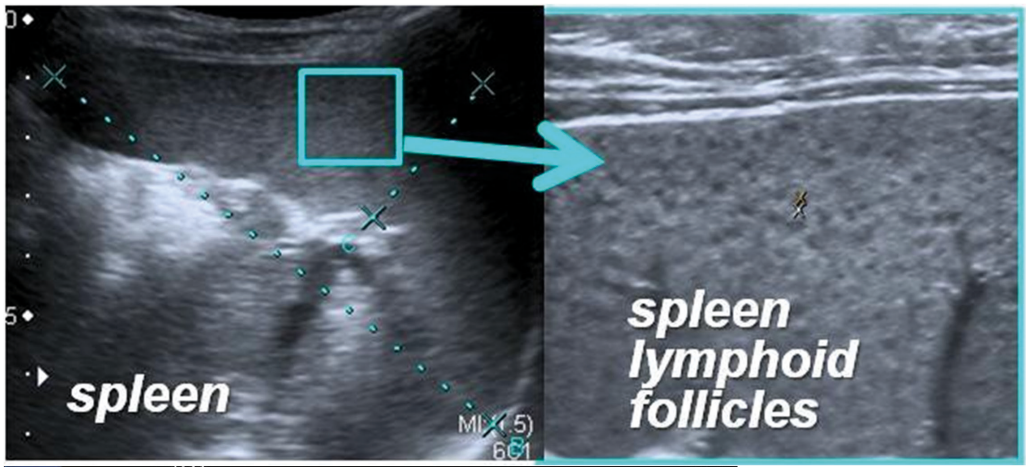

Fig. 1. Hyperplasia of the spleen lymphoid follicles (SMC = 5.5)

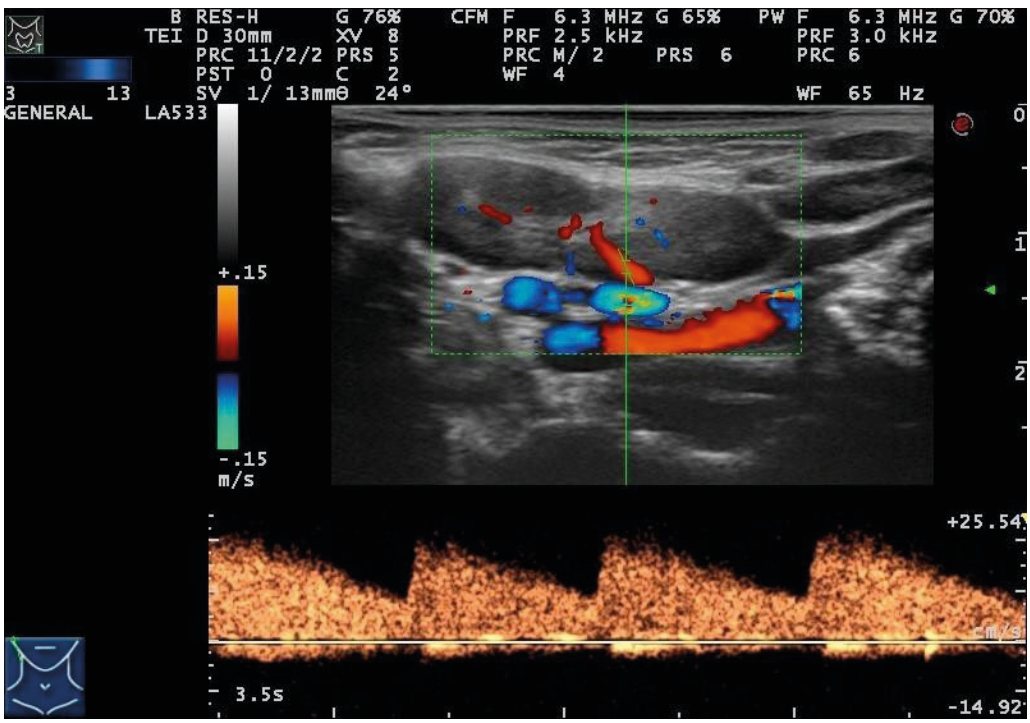

Fig. 2. LN with cortical layer thickening with the clear cortico-medullary differentiation, significantly large linear dimensions, normal angio-architectonics with an increase in the linear velocity of blood flow in the portal LN artery

Morphometric parameters of lymphoid follicles reliably correlated with SMC(a) value (Table 2).

Table 2. **Correlation analysis of the SMC(a) value, spleen and mesenteric lymph nodes' follicles area**

SMC value	Spleen follicles area	r	p	Mesenteric lymph nodes follicles area	r	p
1.62	12756	0.95	0.03	11659	0.92	0.09
3.18	15207			14955		
4.29	16203			15836		
5.76	23752			19242		
6.38	30457			29541		
7.59	34627			33627		

Note: r — the correlation coefficient; p — correlation significance

Conclusion

With the growth in the number and size of lymphoid follicles, an increase in the SMC occurs. This is confirmed by both morphological and ultrasound data.

An increase of the SMC in children with chronic immune-endocrine insufficiency is a reflection of system changes, which, for the most part, are manifested by hyperplastic (in few cases — involutive) processes in lymphoid organs and tissues.

The technique of USE of the spleen and neck and abdomen lymph nodes can be a non-invasive method for identifying children with immune deficiency and those risky for the development of fatal complications.

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