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SPECIFIC PATHOMORPHOLOGICAL CHANGES IN CHILDHOOD LYMPHOCYTIC LEUKEMIA

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Summary: The main objective of this article is to identify the specific pathomorphological changes characteristic of lymphocytic leukemia in young children. From a pathomorphological perspective, childhood lymphocytic leukemia is manifested by focal leukemic infiltration in the bone marrow and almost all lymphoid organs at the early stages of the disease. Depending on whether the lymphocytic leukemia develops from T or B lymphocytes, leukemic infiltration appears in specific areas of the lymphoid organs. In lymphocytic leukemia, pathomorphological changes initially occur in the stromal-vascular structures of the organs and subsequently spread to the parenchyma.
The aim of this study was to examine the pathomorphological changes associated with childhood lymphocytic leukemia. In children, lymphocytic leukemia is manifested by the appearance of focal leukemic infiltrates in the bone marrow and in all lymphoid organs. Depending on whether the leukemia originates from T or B lymphocytes, the leukemic infiltrates are localized in the corresponding T- or B-cell zones. Initially, leukemic cells appear in the stroma of the organs and subsequently infiltrate the parenchyma.

Keywords: children, leukemia, lymphocytic leukemia, bone marrow, thymus, spleen, lymph node, liver, leukemic infiltration

Acute lymphoblastic leukemia (ALL) in children is considered the most common oncological disease among children aged 2–5 years. Its main clinical and morphological feature is the excessive production of lymphocytic cells in the bone marrow. The disease progresses very severely and often ends in death. Therefore, identifying and recognizing the early primary signs of the disease is of great importance. Every year, 50 out of one million children are diagnosed with this disease (1,2).

Tumors of the blood and lymphatic tissue account for half of all malignant tumors, and 38–40% of them are leukemias. Among children under 15 years of age, acute lymphocytic leukemia occurs in 4.1 ± 0.4 cases per 100,000 children, with a male-to-female ratio of 1.3:1, reaching its highest incidence between the ages of 2 and 5.
Modern diagnosis of acute lymphoblastic leukemia is based on the FAB classification, whose main criterion is the confirmation of blood cell blasts through morphological and cytological methods (3,4,5). A diagnosis of acute leukemia is made when 25–30% blasts are present in a bone marrow sample, and three types of cells are identified: L1, L2, and L3. In acute lymphoblastic leukemia, L1 lymphoblasts account for 85% of cases, L2 for 14%, and L3 for 1% (6,7).
The main diagnostic method is the cytomorphological method. A trephine biopsy should be taken from the iliac bone marrow, and the diagnosis is confirmed by the presence of poorly differentiated blast cells in the histological specimen.
Objective of the Study.

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Taking these discussions into account, the main objective of this article was to identify the specific pathomorphological changes characteristic of lymphocytic leukemia in young children.

Materials and Methods.

To achieve this goal, autopsy materials of children who died from lymphocytic leukemia over the past 10 years (2009–2018) at the Republican Scientific Research Institute of Hematology and Blood Transfusion were comprehensively examined. During this period, a total of 2,568 children with lymphocytic leukemia were treated at the institute's clinic, of whom 84 died. Among them, 37 were girls and 47 were boys. By age group: 12 children died before the age of 2, 28 before the age of 4, 26 before the age of 6, and 18 before the age of 10.

The medical histories of the deceased, their laboratory test results, and autopsy reports were analyzed. Tissue samples taken from internal organs and their histological preparations were studied under a microscope, with the necessary areas photographed and described in detail.

Results of the Study.

Examination of the trephine biopsy material, specifically the bone marrow, revealed that depending on the stage of leukemia development, leukemic blast cells in mild cases accumulated in focal clusters, whereas in severe cases they occupied almost the entire bone marrow and infiltrated it diffusely. Hemorrhagic foci, necrosis, and hypoplasia of other bone marrow cells were frequently observed.

Thymus.

A specific feature of childhood lymphocytic leukemia is that in almost all cases the thymus was enlarged to varying degrees, with its weight reaching up to 30 grams in some instances. Externally, the lobules were almost uniformly enlarged, soft, and grayish-white in color; in some cases, the lobules had fused with one another, and small hemorrhagic spots appeared on the surface.

Microscopic examination showed that the thymic lobules varied in size, the interstitial tissue was expanded, and leukemic cells had accumulated around the blood vessels. Leukemic infiltration of the thymic parenchyma was observed only in T-lymphocytic leukemia. In this case, the cortical layer of the lobules was slightly expanded and showed diffuse penetration by leukemic cells (Figure 1). In the medullary layer, leukemic cells were found only around the blood vessels, while the Hassall's corpuscles were enlarged with an increased amount of necrotic material inside them.

Spleen.

In most cases, the weight of the spleen was 2–3 times higher than normal, and in some patients it reached up to 750 grams. The organ became more rounded in shape, its capsule thickened, its color became pale and dense, and on section, the tissue appeared firm with no clear distinction between the white and red pulp.

Microscopic examination revealed that leukemic cells initially accumulated in the marginal zone of the white pulp. They then occupied the lymphocytic mantle zone of the lymphoid follicles and even infiltrated the germinal centers. Another important finding was that leukemic cells infiltrated the periarteriolar T-cell zone only in certain cases. Thus, it can be concluded that involvement of this area occurs only when the leukemia originates from T lymphocytes (Figure 2), whereas in B-lymphocytic leukemia, leukemic cells accumulate mainly in the lymphoid follicle regions. In most cases, diffuse infiltration of leukemic cells was also observed in the soft cords of the red pulp.

Lymph Nodes.

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Another characteristic feature of childhood lymphocytic leukemia is that lymph nodes do not always become enlarged. In most cases, the lymph nodes remained anatomically close to normal size. Only in a few cases was enlargement of lymph nodes in specific anatomical regions observed.

Lymph nodes, despite being enlarged, retained their softness and were not fused together; their tissue appeared pale pink.

Microscopic examination revealed that leukemic cells initially accumulated around the peripheral sinuses of the node, and later appeared within the medullary sinusoids and the interstitial tissue. It was also found that when leukemia originated from T lymphocytes, the paracortical zone became significantly enlarged due to diffuse infiltration by leukemic cells (Figure 3). Only in a few cases did infiltration of the cortical lymphoid follicles by leukemic cells lead to deformation and disruption of their morphofunctional structures.

Liver.

The liver was slightly enlarged, light brown in color, soft, and contained whitish-gray foci and streaks within the tissue.

Microscopic examination showed that leukemic cells accumulated mainly in the Disse space, that is, along and around the sinusoidal walls (Figure 4), and in some cases around the central vein as well. As a result, hepatocytes exhibited mild disruption of their trabecular architecture, with proteinaceous deposits in the cytoplasm, and in some areas vacuolar changes or hyaline–granular dystrophy developed.

Discussion.

In childhood lymphocytic leukemia, the pathomorphological features are present not only in the bone marrow but also in the thymus, spleen, lymph nodes, and even the liver (1,4,7). In the bone marrow, the disease is most often manifested by focal leukemic infiltration, which distinguishes it from other types of leukemia.

In the thymus, the findings are more specific: in T-lymphocytic leukemia, leukemic infiltration begins in the interstitial tissue and subsequently spreads into the parenchyma, often replacing the cortical layer.

The characteristic pathomorphological changes in the spleen depend on the type of lymphocytic leukemia. In T-lymphocytic leukemia, the marginal zone and periarteriolar region are primarily affected by leukemic infiltration, whereas in B-lymphocytic leukemia the changes begin in the marginal zone and later completely involve the lymphoid follicle

In the lymph nodes, similar patterns are observed depending on the type of leukemia: in T-lymphocytic leukemia, leukemic infiltration predominates in the paracortical zone, whereas in B-lymphocytic leukemia, the medullary region is completely infiltrated and the lymphoid follicles of the cortical layer are covered by leukemic cells.

In the liver, both types of lymphocytic leukemia exhibit almost identical changes, namely leukemic infiltration primarily affecting the perisinusoidal Disse space and the area around the central vein.

Conclusions:

1.In childhood lymphocytic leukemia, from a pathomorphological standpoint, the disease is manifested at the early stages by focal leukemic infiltration in the bone marrow and almost all lymphoid organs.

2. Lymphocytic leukemia is characterized by leukemic infiltration in specific regions of the lymphoid organs, depending on whether it originates from T or B lymphocytes.

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3. In lymphocytic leukemia, pathomorphological changes first appear in the stromal–vascular structures of the organs and subsequently spread into the parenchyma.

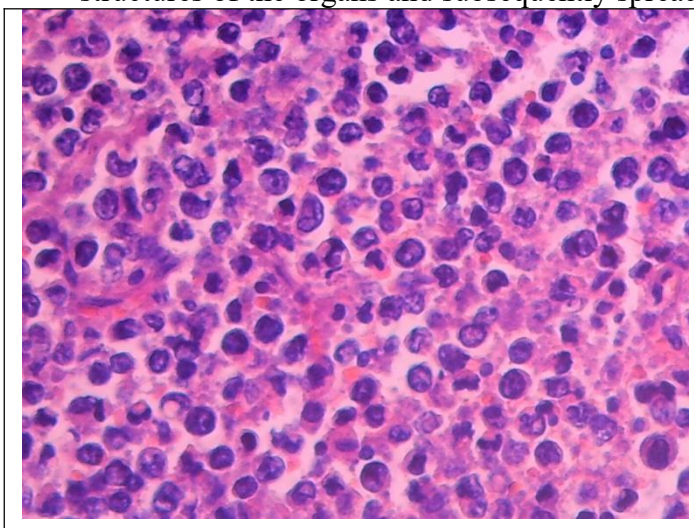

Figure 1. Thymus. Lymphoblastic leukemic infiltration. Stain: H&E. Magnification: 10×40

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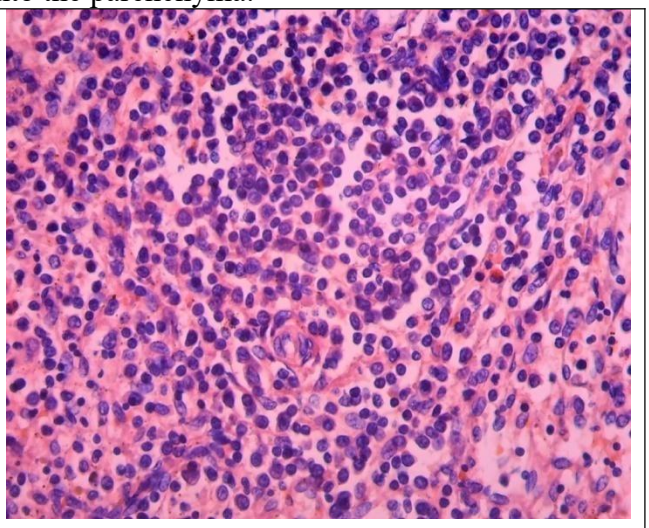

Figure 2. Leukemic infiltration in the periarterial area. Окр: Г-Э. Х: 10 x 20

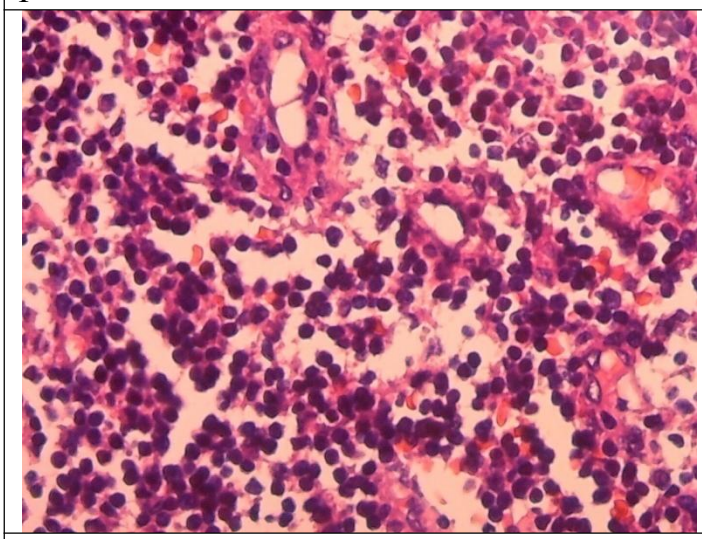

Figure 3. Lymph node. Leukemic infiltration of the paracortical area.Окр: Г-Э. Х: 10 x 40

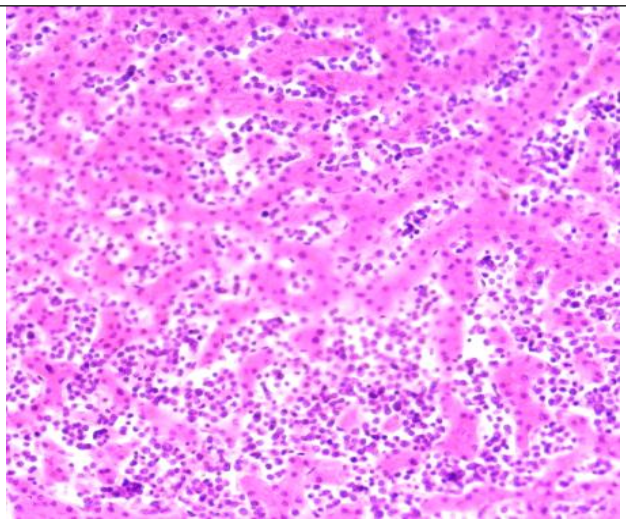

Figure 4. Liver. Leukemic infiltration of the Disse space. Окр: Г-Э. Х: 10 x 20

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