UDC 616-053.2+616.9+616:579.61.

CLINICAL-ANAMNESTIC AND IMMUNOPHENOTYPING ANALYSIS OF CHILDREN'S LYMPHOCYTIC LEUKEMIA

Salaeva Z.Sh.

Urgench branch of Tashkent Medical Academy, Urgench, Uzbekistan

✓ ***Resume***

Our studies have shown that in order to conduct a clinical and anamnestic analysis of lymphocytic leukemia in children, the following examination plan is drawn up. It will be necessary to conduct a general blood analysis, a puncture of the sternum, an immunophenotyping method to determine the subpopulation of B and T lymphocytes, and an immunohistochemical examination to detect blast lymphocytes.

In this scientific study, immunophenotyping was conducted in 22 patients with acute lymphoblastic leukemia, diagnosed at the Republican Hematology Center. According to the results of the investigation, the leukemic blasts of acute lymphoblastic leukemia (ALL), consisting of V-lymphocyte precursors, were found to have a large number of immunophenotypic aberrations. The changes in the bone marrow and lymphoid organs, which morphologically determine the acute and chronic forms of lymphocytic leukemia in children, serve as a fundamental basis in the scientific and practical activities of clinical doctors.

Key words: Children, leukemia, lymphoid leukemia, bone marrow, spleen, lymph node

КЛИНИКО-АНАМНЕСТИЧЕСКИЙ И ИММУНОФЕНОТИПИЧЕСКИЙ АНАЛИЗ ЛИМФОЛЕЙКОЗА ДЕТСКОГО ВОЗРАСТА

Салаева З.Ш.

Ургенчский филиал Ташкентской медицинской академии г. Ургенч, Узбекистан

✓ ***Резюме***

С целю проведения клинико-анамнестического анализа лимфоцитарного лейкоза у детей, что показывают исследования у больных составляется следующий план. Потребуются общий анализ крови, пункция грудина, иммунофенотипирование для определения субпопуляций В-Т лимфоцитов иммуногистохимическое исследование для выявления бластных лимфоцитов. В данном научном исследовании проведено иммунофенотипирование 22 больных острым лимфобластным лейкозом, диагностированным в Республиканском гематологическом центре.

По результатам обследования у лейкемических бластов острой лимфобластного лейкоза, состоящих из предшественников В-лимфоцитов выявлено большое количество иммунофенотипических аберраций. Изменения в костном мозге и лимфоидных органах морфологически определяющие острой и хронической формы лимфолейкоза у детей, служат фундаментальной основной в научной и практической деятельности врачей клиницистов.

Ключевые слова: детей, лимфолейкоза, грудина, селезенка, лимфатический узел, костный мозг

БОЛАЛАР ЛИМФОЦИТАР ЛЕЙКОЗИНИНГ КЛИНИК-АНАМНЕСТИК ВА ИММУНОФЕНОТИПЛАШ ТАҲЛИЛИ

Салаева З.Ш.

Тошкент тиббиёт академияси Урганч филиали, Урганч, Узбекистон

✓ ***Резюме***

Тадқиқотлар шуни кўрсатдики, болаларда лимфоцитар лейкоз касаллигининг клиник-анамнестик таҳлил ўтказиш учун касалларда қуйидагича текширув режаси тузилади. Қоннинг умумий таҳлили, тўш суягини пункция қилиш, В ва Т лимфоцитлар субпопуляциясини аниқлаш бўйича иммунофенотиплаш усулини ўтказиш, бласт лимфоцитларни аниқлаш учун иммуногистокимё текшируви ўтказиш керак бўлади.

Ушбу илмий тадқиқот ишда Республика гематология марказида диагнози аниқланган, В-лимфоцитлар ўтмишдошларидан ривожланган ўткир лимфобластли лейкоз билан касалланган 22 та пациентларда иммунофенотиплаш текшируви ўтказилган. Текширув натижалари кўрсатишича, В-лимфоцитлар ўтмишдошларидан иборат ўткир лимфобластли лейкознинг (ЎЛЛ) лейкемик бластлари кўп сонли иммунофенотипик аберрацияли эканлиги аниқланди.

Болаларда лимфоцитар лейкознинг ўткир ва сурункали шаклларини морфологик жиҳатдан белгилайдиган ҳар бирига хос суяк кўмиги ва лимфоид аъзолардаги ўзгаришлар клиник шифокорлар илмий-амалий фаолиятида фундаментал асос бўлиб хизмат қилади.

Калит сўзлар: болалар, лейкоз, лимфолейкоз, суяк кўмиги, талоқ, лимфа тугун

Relevance

Children's acute lymphoblastic leukemia is the most common oncological disease in children aged 2-5 years, accounting for 80% of all leukemias**.** The main clinical and morphological sign is the high production of lymphocytic cells from the bone marrow. The disease is very severe, often ending in death. Therefore, it is important to identify and know the initial primary symptoms of the disease. Every year, 50 out of a million children are affected by this disease [6,7.10]

Tumors of the tissues of the blood and lymphatic system make up half of all malignant tumors, and 38-40 percent of them are leukemias. Acute lymphoblastic leukemia occurs in 4.1 ± 0.4 per 100,000 children under 15 years of age, with a ratio of 1.3:1 in boys and girls, with a peak between 2 and 5 years of age.

Modern diagnosis of acute lymphocytic leukemia is determined based on the FAB-classification, the main criterion of which is confirmation of blood cell blasts by morphological and cytological methods [3,4,5].

Acute leukemia is diagnosed if there are 25-30% blasts in the bone marrow sample, and 3 types of cells are identified: The results of immunophenotyping test show that among children's lymphocytic leukemia, the high incidence of V-lymphocyte form and its various markers leads to proper planning of its prevention and treatment.

The molecular pathogenesis of lymphocytic leukemia primarily depends on the multistage replication process of V-lymphocytes. In this disease, lymphocytosis and various degrees of aberration are detected by high-precision immunofermentation method. The mechanism of the formation of tumor cells depends on the mutation of a number of genes, their activation under the influence of antigens, the response to signals from the surrounding tissues, and ultimately, cytogenetic disorders. [3,10,11].

Clinical and morphological symptoms of acute lymphoblastic leukemia develop very quickly. When the disease is detected, the relative weight of lymphoblasts in the body is 3-4% of the body weight [5,8,13].

In order to conduct a clinical and anamnestic analysis of such diseases, the following examination plan is drawn up for patients: general blood analysis, chest bone puncture, immunophenotyping to determine the subpopulation of V and T lymphocytes, and immunohistochemistry to determine blast lymphocytes..

Purpose of the study. Study of immunophenotypic specificity, aberrant expression of acute lymphoblastic leukemia developed from V-lymphocyte progenitors and comparison with literature data.

Materials and methods

In our research, we studied the autopsy materials and medical documents of 58 children who died from complications of lymphocytic leukemia and were treated at the Republican Specialized

Hematology Scientific and Practical Medical Center in 2019-2021. Autopsy examination was carried out at the Republican Center for Pathological Anatomy of the UzR SSV.

Result and discussion

In this scientific study, the diagnosis was made at the Republican Hematology Center, Immunophenotyping was performed in 22 patients with acute lymphoblastic leukemia developed from B-lymphocyte progenitors.

According to the results of the investigation, the leukemic blasts of acute lymphoblastic leukemia (ALL), consisting of V-lymphocyte precursors, were found to have a large number of immunophenotypic aberrations. In 50% of tumor cells, asynchronous expression of cell differentiation antigens, and in most cases aberrant expression of myeloid markers, markers of T-lymphocyte line was observed. 85% of childhood acute lymphoblastic leukemia is B-lymphocyte, 15% T-lymphocyte, NK cell leukemia is very rare. Risk factors for OLL in children include: young age, 2-5 years of age, exposure to X-rays, genetic diseases, obesity, type 1 neurofibromatosis. As a pathogenesis, high accumulation of lymphoblasts with a low level of differentiation in the bone marrow and disruption of the apoptosis process take place.

The first cell of the V-lymphocyte lineage is the pro-B-cell. IL-7 and stromal cells are important in the proper differentiation of B-lymphocytes. CD45 is expressed on the pro-V cell, and CD22, CD34, and CD38 are produced from it by transferaseAt the next stage of B-cell differentiation, CD10, CD34, CD79a, CD38 are expressed and they are called Pro-BI cells. It is at this stage that immunoglobulin genes are recombined. At the next stage, pre-B II cells appear, in which CD20 is expressed. Immature V lymphocytes express a number of immunoenzymatic markers, namely CD20, CD45, CD10, CD38, and in rare cases express CD21, CD5, CD81. Mature V lymphocytes mainly express IgD IgMs.

Table 1

Immunophenotypic classification of B- and T-lymphocytic leukemias (according to the classification of the European Group for Immunodiagnosis of Leukemia, 1995)

B-cell lymphocytic leukemia	
Two or fewer of the 3 B-cell markers expressed, such as CD19+ or CD79a+ or SD22cyt. Mostly TdT+ and HLA-DR+, expressed B- O'LL and mostly expressed TdT- Mostly TdT+ and HLA-DR+, expressed V- OLL and mostly expressed TdT.	
Pro-B-OLL (BI)	No other marker was expressed
«Common»-OLL (BII)	$CD10^+$
Pre-B-OLL (BIII)	Cytoplasmic IgM^+
Done -B-OLL (BIV)	Cytoplasmic chains
T-cell lymphocytic leukemiya	
Cytoplasmic or membranous CD3+, often:TdT^+, HLA-DR^-, $CD34^-$, expressed, but these markers are of little importance for diagnosis.	
Pro-T-OLL (TI)	$CD7^+$
Pre-T-OLL (TII)	$CD2^+$ or $CD5^+$ or$CD8^+$
Cortical T-OLL (TIII)	$CD1a^+$
Done T-OLL (TIV)	$CD3mem^+$, CD1a-
Alpha/beta $^+$ T-OLL (a)	
Gamma/delta $^+$ T-OLL (b)	

It is known that acute lymphoblastic leukemia, developed from V-lymphocyte precursors, is the most common tumor in children, and is morphologically manifested by the proliferation of cells that are not characteristic of the V-line. Differentiated antigens of lymphocyte precursors are expressed on the surface membrane of malignant tumor cells of leukemia. Here, the common-B variant is 80%, pre-V – 14%, pro-B 6%.

Currently, to identify this tumor, a method of immunophenotyping with a clear result, that is, flow cytofluorimetry, is used. This technique requires highly selective monoclonal antibodies.

Immunophenotypes of leukemic cells in peripheral blood are determined by flow cytometry. The expression of normal cell antigens in the blood is taken as an internal standard. In the diagnosis of hematological diseases, selective gating on the panleukocyte marker CD45 is carried out, and this method is convenient, blast cells are better compared to healthy cells.

Immunophenotyping in B-cell lymphocytic leukemia confirmed that CD19+ or CD79a+ or SD22cyt markers were detected in the majority of V-line lymphocyte clones (see Table 1).

As shown in the table, it was found that markers were expressed at a low level from pro-V lymphocyte clones, and cytoplasmic immunoglobulin M was expressed in pre-B lymphocytes. A number of cytoplasmic chains were observed to be expressed from mature B lymphocytes. It was observed that CD3mem+, CD1a- markers were expressed.

Thus, in our study, it was confirmed that B-lymphocytic leukemia was significantly more common than T-lymphocytic leukemia. When T lymphocyte clones were examined by immunophenotypic method, mainly CD3+, most often: TdT+, HLA-DR-, CD34 markers were detected. Of these, it was observed that CD7 was expressed by pro-T lymphocytes, CD2+ or CD5+ or CD8+ markers by pre-T lymphocytes, CD3mem+, CD1a- markers were expressed by T-lymphocytes.

Conclusions

1. It has been confirmed that lymphocytic leukemia in children occurs mostly in boys, at the age of 3-4 years.

2. L.A. in differentiating acute and chronic forms of lymphocytic leukemia in children. Makhonov, 1986. according to the table, it was proved that there is a big difference in clinical-morphological predictive signs.

3. According to the results of blood analysis and immunophenotyping, it was found that V-lymphocytic form is more common among children's lymphocytic leukemia.

LIST OF REFERENCES:

1. Alekseev N.A., Vorontsov I.M. Leukosis u detey L.: Medicine. -1989- 247 p.
2. Vladimirskaya E.B., Rumyantsev A. G. Differentsirovochnye potentsii stvolovyx hemopoieticheskikh kletok. // Voprosy hematology/oncology and immunology and pediatrics. 2002. - M. — T. 1, No. 1. - S. 7-11.
3. Vladimirskaya E.B. Torubarova N.A. Ostrye leukozy i hypoplasia krovetvoreniya u detey. / M.: Medicine. - 1985. - 209 p.
4. Vladimirskaya E.B. Rostovye faktori v regulyatsii krovetvoreniya. V kn.: Biological basic protivoopukholevoy therapy. Vladimirskaya E.B., Moscow, 2001, S. 33-58.
5. Karachunsky A.I. Strategy therapy ostrogo lymphoblastnogo leukoza Autoreferat dissertatsii doktor meditsinskikh nauk. - 1999. - 54 p.
6. Makhonova L.A., Mayakova S.A., Peterson I.S., Tupitsin N.N. Diagnostics and treatment of leukaemia, diagnosis and treatment // Pediatrics. -1991.-No. 11.-S. 54-58.
7. Makhonova L.A., Gavrilova I.E., Mayakova S.A. i dr. Modificatory biological reactions in the program lecheniya ostryx leukozov i zlokachestvennyx lymphoma u detey. // Children's oncology. 1995. — No. 2-3. - S. 27-30.
8. Methodicheskaya razrabotka dlya studentsov V kursa pediatriceskogo fakultata po razdelu "Hematology", theme zanyatiya: "Acute leukozy u detey. Aplasticheskie anemii» Prepared by: associate professor of the department Stremenkova I.A. associate professor department Dushko S.A. Stavropol, 2015g.-15 p.
9. Axel E.M. Zlokachestvennye novoobrazovaniya u detey. Statistics / Oncopediatrics. 2015. 2. 2: 154-157.
10. Buechner J., Caruana I., Künkele A., Rives S., Vettenranta K., Bader P., Peters C., Baruchel A., Calkoen F.G. Front Pediatr. 2022 Jan 25; 9: 784024. doi: 10.3389/fped.2021.784024. eCollection 2021.
11. Borowitz M.J., Devidas M., Hunger S.P. et al. Clinical significance of minimal residual disease in children acute lymphoblastic leukemia and its relationship to the prognostic factors: a Children's Oncology Group study. Blood. 2018;111(12):5477-85. doi: 10.1182/blood-2008-01-132837.
12. Keating A.K., Gossai N., Phillips C.L., Maloney K., Campbell K., Doan A. et al. Reducing minimal residual disease with blinatumomab prior to HCT for pediatric patients with acute lymphoblastic leukemia. // Blood Adv. (2019) 3:1926–9. 10.1182/bloodadvances.
13. Jiménez-Morales S., Aranda-Uribe I.S., Pérez-Amado C.J., Ramírez-Bello J., Hidalgo-Miranda A. Mechanisms of Immunosuppressive Tumor Evasion: Focus on Acute Lymphoblastic Leukemia. Front Immunol. 2021 Nov 18;12:737340. doi:10.3389/fimmu.2021.737340. eCollection 2021.
14. Truong T.H., Jinca C., Mann G., Arghirescu S., Buechner J., Merli P., Whitlock J.A. Front Pediatr. 2021 Dec 23;9:782785. doi: 10.3389/fped.2021.782785.e Collection 2021.

Entered 09.09.2022