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A CASE OF ACUTE LYMPHOBLASTIC LEUKEMIA WITH TRANSLOCATION t(1;7) (q41,p22) t(4;12)(q34;q23), +mar.

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Abstract. To date, a lot of data has been accumulated proving that chromosome changes in patients with acute lymphoblastic leukemia are of great clinical and prognostic significance. Due to the widespread introduction of the method of differential staining of chromosomes into practice, it became possible to study the karyotype in patients not only at the onset of the disease, but also at different stages of its development. It has been shown that individual chromosomal aberrations are specific for certain types of acute leukemia. A number of chromosomal markers are associated with a favorable prognosis (for example, hyperdiploidy - more than 50 chromosomes in acute lymphoblastic leukemia). Other karyotype disorders, such as, for example, the "Philadelphia" chromosome in acute lymphoblastic leukemia, loss and deletion of chromosomes 5 and 7 in acute non-lymphoblastic leukemia, are prognostically unfavorable aberrations. Of great interest are rare variants of non-random chromosomal disorders, the role of which in the pathogenesis of leukemia is still not clear.
Keywords: acute lymphoblastic leukemia, cytogenetics, unique translocation.

Acute lymphoblastic leukemia (ALL) is the most common malignant neoplasm of the hematopoietic system in children: ALL accounts for approximately 30% of all childhood neoplasms [2,14]. In adults, ALL is less common, accounting for approximately 20% of adult leukemia cases. Diagnosis and assessment of the risk of progression of acute lymphoblastic leukemia is currently based on the results of morphological and immunological studies, as well as data from cytogenetic and molecular genetic analysis [10,11]. There is a small percentage of biclonal leukemias - lymphoblastic with the expression of myeloid markers or myeloid with the expression of lymphoblastic markers [1,5,8].

In accordance with the revised classification of the World Health Organization, two main subtypes of ALL are distinguished: B-lymphoblastic leukemia, traditionally called B-cell progenitor ALL (B-ALL) and T-lymphoblastic leukemia (T-ALL) [3,6]. These subtypes are characterized by tumor growth of lymphoid progenitor cells within B- or T-hematopoietic lines, respectively, which can occur at any stage of lymphoid cell differentiation and lead to significant disease heterogeneity [4,7,9]. Currently, among B-ALL and T-ALL, several subtypes of the disease are distinguished, characterized by specific genetic abnormalities, morphology of leukemic blast phenotypes and, thus, having a different prognosis. The contribution

of the clonal evolution of the karyotype observed under the conditions of cytostatic therapy of ALL to the prognosis of the course of the disease is beyond doubt. Despite intensive cytogenetic and molecular biological studies of leukemia, there are still many unresolved problems in this area of oncohematology. In this regard, today the search for new non-random chromosomal rearrangements in acute leukemia and the identification of their relationships with the course and prognosis of the disease, as well as with the effectiveness of the therapy, is relevant [12,13].

PURPOSE OF THE STUDY. The study of chromosomal disorders in acute leukemia.

MATERIAL AND METHODS. The object of the study was the bone marrow and peripheral blood of patient M., born in 1996, who in June 2020. Republican specialized scientific - practical medical center of hematology of the Ministry of Health of the Republic of Uzbekistan. (Tashkent) was diagnosed with acute leukemia. Prior to contacting a specialized medical institution, the individual symptoms of the disease were felt by the patient for several months. Upon admission to the Republican Specialized Scientific - Practical Medical Center of Hematology of the Ministry of Health of the Republic of Uzbekistan, hemogram studies were performed (Hb - 91 g / l, erythrocytes - 2.8×10^{12} / l, color index - 1.0, platelets - 1.0×10^{9}/l, leukocytes - 39×10^{9}/l, blasts - 76%, segmental/nuclear neutrophils - 15%, lymphocytes - 8%, monocytes - 1%, ESR - 45 mm/h), myelograms (hypercellularity, total blastosis (92 %) of bone marrow punctate), cytochemical study (peroxidase negative, glycogen positive, fine and coarse granular), biochemical blood test (total protein - 48.2 g / l, total bilirubin - 28.5 μmol / l, direct - abs, ALT - 0.07 mmol/l, AST - 0.1 mmol/l), hemostasis study (PTI - 60%, fibrinogen - 5.0 g/l, fibrinolysis - 240 min).

Based on clinical and laboratory data, patient M. was diagnosed with acute lymphoblastic leukemia. According to the protocol for the management of ALL, a prephase was started with prednisolone 60 mg/mkv, the hemostatic goal was hemoxane - 10.0 intravenously drip, taking into account fever against the background of secondary immunodeficiency of mycoses, detoxification therapy, prevention of hyperuremia, substitution therapy - TA transfusions.

As part of the examination of Patient M., a study of the karyotype of leukemic cells was performed using the method of standard cytogenetic analysis.

Chromosome analysis was performed by standard cytogenetic study (SCI) (GTG-banding, 400 segments per karyotype). Cultivation was performed without stimulation of nuclear cells of the bone marrow and peripheral blood in a short-term culture (24 h) at a temperature of 37□C on a nutrient medium containing RPMI-1640 with glutamine, 20% fetal calf serum. Cell division at the metaphase stage was stopped with colcemid, which was added to the medium in an amount of 80 μl upon planting. Hypotonicization of cells with a solution of potassium chloride (0.55%) was carried out for 20 minutes at a temperature of 37°C. The cells were fixed three times through a fixative cooled to -4□C (ethanol/glacial acetic acid, 2.5:1). Chromosome preparations were prepared by dropping a suspension of nuclear cell fragments onto wet, cooled glass slides. The resulting preparations were dried at room temperature,

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stained according to the Romanovsky-Giemsa method with pre-treatment with 0.25% trypsin solution, and microscoped (Leica Germany). Search for metaphases was carried out at x200 magnification (objective HCXPLFLUOTAR 20x/0/50 ∞/0.17/D), analysis of metaphase plates at x1000 magnification (objective Plancheomat HI 100x/1.30 ∞/0A). A total of 30 metaphase plates were analyzed. Chromosomes were identified in accordance with the international system of cytogenetic nomenclature ISCN 2009.

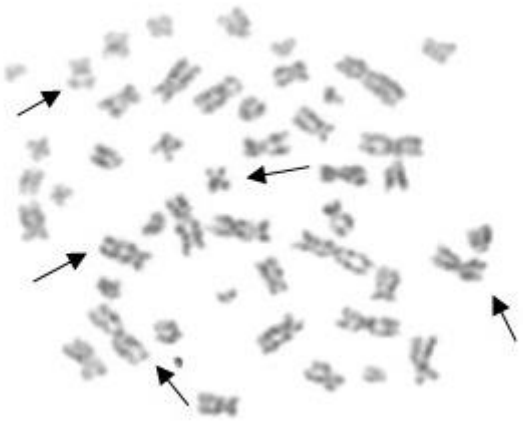

Fig.1. Metaphase plate of a patient with ALL
Karyotype 47,XY, t(1;7)(q41;p22), t(4;12)(q34;q23), +mar.
Arrows on the left 7, on the right (from top to bottom) 12,4,1- chromosomes

When examining the karyotype of bone marrow cells and peripheral blood of patient M., 60% of complex complex translocations and 40% of normal metaphase plates were identified.

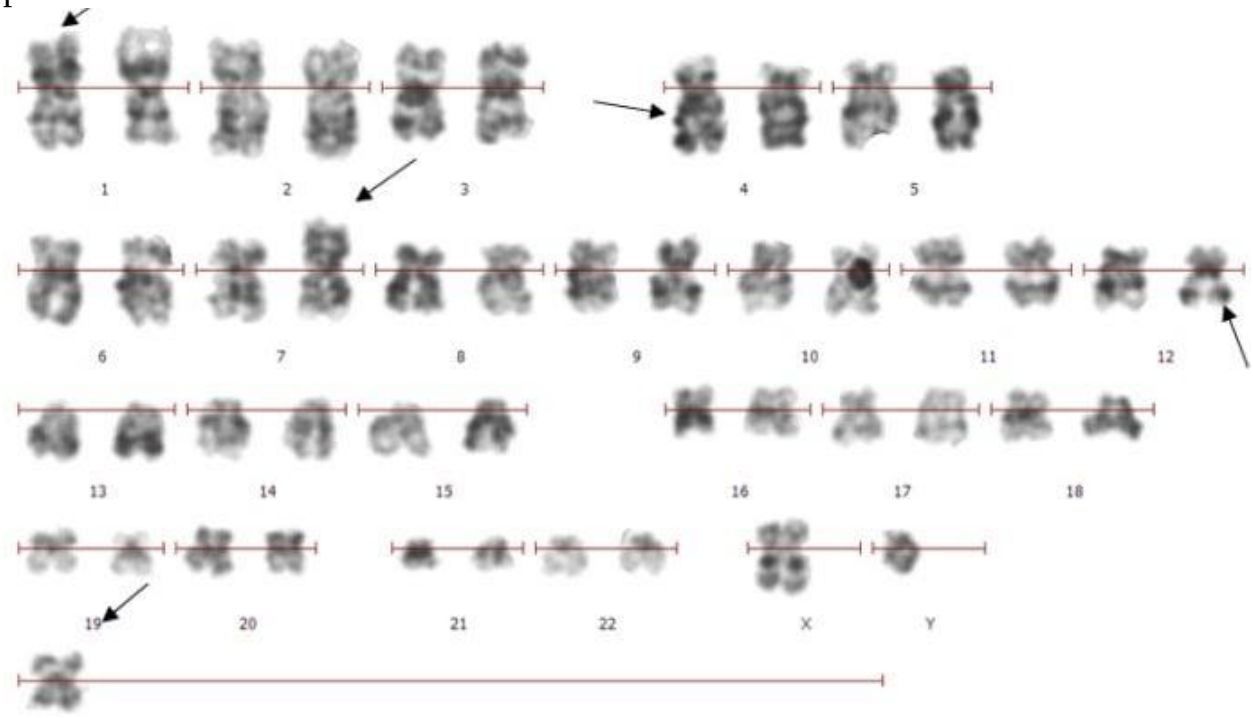

Fig. 2. Analysis of the metaphase plate using the VideoTest-Karyo 3.1 program.
Karyotype 47XY, t(1;7)(q41;p22), t(4;12)(q34;q23), +mar.
Arrows indicate derivatives of chromosome 1,4,7,12 and an additional chromosome.

In the study of metaphase plates, a cytogenetically visualized derivative of chromosomes 1 (der1), 4 (der4), 7 (der7), 12 (der12) was found. The relative size of the lengths of 1q41, 7p22 and 4q34, 12q23 chromosomes, thanks to differential staining, made it possible to identify breaks in chromosome regions. The site of breakdown of derivative chromosomes was identified using the ISCN 2013 system.

Analysis of metaphase plates was performed using the VideoTest-Karyo 3.1 program and confirmed the presence of cytogenetic rearrangement involving the 1st and 7th, 4th and 12th chromosomes. In addition, an additional chromosome of unknown origin was found in the karyotype.

Thus, karyotyping of bone marrow and peripheral blood cells by SCRI in a patient with acute lymphoblastic leukemia made it possible to identify structural rearrangements of the karyotype, indicating a translocation t(1;7) (q41,p22) t(4;12)(q34;q23), +mar. Analysis of clinical and laboratory data and the lack of response to therapy, which determine the primary resistant course of the disease, may indicate a possible prognostically unfavorable value of the restructuring that we identified in acute lymphoblastic leukemia.

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