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SIGNIFICANCE OF STANDARD CYTOGENETIC ANALYSIS IN THE DIAGNOSIS OF ACUTE LEUKEMIA

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Resume. A study of significant genetic aberrations in a group of oncohematological patients in the city of Tashkent (Uzbekistan) was carried out using a standard cytogenetic study and an assessment of their role in the prognosis of the disease. The data obtained were compared with the effectiveness of polychemotherapy and prognostic groups were formed. In the group of poor prognosis, multiple genetic aberrations were more common, in contrast to the group of patients with a favorable prognosis of the disease, who predominantly had single genetic aberrations. A standard cytogenetic study allows you to simultaneously identify a wide range of genetic abnormalities to determine the prognosispatients with acute leukemia.

Keywords: acute leukemia, chromosomal translocations, prognosis, cytogenetics

The incidence of hemoblastoses averages 10 per 100 thousand of the population per year and occupies the 6th–8th place among neoplasms, accounting for 6–7% of them [5,6]. According to the Republican Specialized Scientific and Practical Medical Center for Hematology of the Republic of Uzbekistan, in 2021, in the overall structure of the incidence of malignant neoplasms in Uzbekistan, hemoblastoses accounted for 3.2% [2,13]. According to the World Health Organization (WHO), diseases of the hematopoietic and lymphoid tissues account for about 1% of all causes of death in the population. They account for 6 to 10% of all deaths from malignant neoplasms, and among patients under the age of 30 years - 50% [2,13]. Standard cytogenetic research (SCR) is now increasingly used in various fields of practical medicine. So, in oncohematology, this method allows one-stage detection of a wide range of clinically significant genetic anomalies to determine the prognosis and treatment tactics for patients with hematological malignancies [7,8]. The most well-known and widespread method of cytogenetic research is G-differential staining of chromosomes, which makes it possible to fully describe the karyotype and detect marker and variant rearrangements of the genome.

Purpose of the study: Using a standard cytogenetic study, determine chromosomal abnormalities in patients with acute leukemia and evaluate their role in the prognosis of the disease.

Material and methods. The study included 88 patients with acute leukemia who underwent diagnostic examination and received treatment at the Republican Specialized Scientific and Practical Medical Center for Hematology of the Republic

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of Uzbekistan. Verification of the diagnosis is based on: complaints made by patients, anamnesis data, physical and instrumental examinations, as well as clinical and laboratory tests. Of them:50 men and 38 women. Acute myeloid leukemia (AML) was verified in 46 patients, acute lymphoblastic leukemia in 42.The age of the patients ranged fromfrom 18 to 68 years (median 42.2 ± 2.1 years), median of age in AML - 42.3, with ALL - 32.1 years. In this study, we formed prognosis groups based on independent prognostic factors [10]. The object of the study was the conclusions with the result of a standard cytogenetic study (GTG-banding) performed in patients with hemoblastoses. Bone marrow aspirate (sternal puncture) of patients, taken into sterile tubes with heparin, was used as a biological material for SIC. Chromosomes were analyzed using stored digital images. The number of chromosomes in each metaphase plate was counted, the structure of metaphase chromosomes was analyzed by comparing homologues, assessing the relative sizes of chromosomes within each metaphase plate, the sizes of the short (p) and long (q) arms of each chromosome, centromere location and correspondence of G-positive bands in homologous chromosomes. Chromosomes were identified according to the ISCN classification system, and in the absence of GTG banding, according to the Denver classification. For each patient, 20 metaphases were analyzed.

Result and discussion. During the study, 62 (70.5%) of 88 patients had a normal karyotype (among them AML-35, ALL-27) and 26 (29.5%) patients had cytogenetic aberrations (in 15 patients with ALL, in 11 - AML).

Table number 1.

Proportion and spectrum of structural changes in karyotype in patients with AL

Chromosomal disorder	AL			
	AML n=46		ALL n=42	
	n	%	n	%
Total	6	13.0	eleven	26.1
t(15,17)(q22;q21)	3	6.5	-	-
t(9,22)(q34;q11.2)	-	-	3	7.1
t(8,21)(q22;q22)	1	2.1	-	-
der(?)	2	4.3	2	4.7
del 8q?	-	-	1	2.3
t(1,7)(q41;p22)	-	-	1	2.3
t(10,19)(q22;q13.3)	-	-	1	2.3

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The criteria for evaluating the prognosis were the speed of onset of clinical and hematological remission, the presence or absence of cytogenetic remission, the presence of relapse, and the duration of the overall survival of patients. The prognosis was considered favorable in the case of a rapid onset of clinical and hematological remission during the first courses of chemotherapy, the presence of cytogenetic remission and patient survival for more than 3 years, and the absence of relapse. The prognosis was regarded as unfavorable in case of death within a year or a rapid onset of relapse, extremely unfavorable in case of death before the start of treatment or during the first course of therapy. The intermediate prognosis corresponds to survival within 1-3 years, the presence of clinical and hematological remission in the absence of a pronounced cytogenetic response.

Table number 2.

Proportion and spectrum of quantitative changes in karyotype in patients with AL

Chromosomal disorder	AML n=46		ALL n=42	
	n	%	n	%
TsGNK	31	67.3	22	52.3
hypodiploidy (2n>46)	3	6.5	2	4.7
Hyperdiploidy (2n<46)	1	2.7	2	4.7
Total	4		3	

The group of AML patients with a favorable prognosis includes 3 balanced chromosomal anomalies: translocation t(15;17) (q22;q21), characteristic of acute promyelocytic leukemia (APL) (chimeric oncogene PML-RARA), as well as translocation t(8;21)(q22;q22)/RUNX1-RUNX1T1 and inv(16) (p13.1;q22)/CBFB-MYH11 inversion, which are characteristic of the so-called CBF-leukemias (core binding factor leukemias) [6]. In our case, t(15,17) (q22; q21) type translocation was observed in 3 patients and t(8,21) (q22; q22) in one patient with AML. In this group, translocations t(8;21), t(15;17), as well as inversion ipv(16), which corresponds to the literature data [12].

Table number 3.

Detectable chromosomal translocations and their prognostic significance

Chromosomal translocations	**Genetic aberrations**	**Prognosis for AL**	**Existing approaches in treatment**
t(9;22),	p190 and p210	Adverse	Specific therapy with

Philadelphia chromosome	BCR/ABL		tyrosine kinase inhibitors
t(8;21)	AML/ETO	Favorable	Program polychemotherapy
t(15;17)	PML/RARa	Favorable	Full treatment transretinoic acid (ATRA)
t(1;7)	E2A/PBX	Intermediate	Possible intensification of courses polychemotherapy or allogeneic bone marrow transplantation.
t(10,19)	CBFB/MYH11	Adverse	Possible intensification of courses polychemotherapy or allogeneic bone marrow transplantation.

In most cases of monosomy (with the exception of monosomy Y), an unfavorable prognosis was noted, as was the case with karyotype ploidy disorders, whiletrisomy (+13, +21) were characterized by an intermediate prognosis. Quantitative changes in the karyotype in our observations, as mentioned above, were found in 9 (10.2%) cases. At the same time, 4 (4.5%) of them were patients with AML and 5 (5.7%) - with ALL. According to the literature, in AML from this risk group, the frequency of complete remissions is also 90%, and the 5-year overall survival is 55–85% [7, 8]. In the group of acute lymphoblastic leukemias, a favorable prognosis was characteristic of cases of a hyperdiploid set of chromosomes. Acute lymphoblastic leukemias developed in an extremely unfavorable way with the presence of translocation of the type t(9.22) (q34; q11.2), t(1.7) (q41; p22) and t(10.19) (q22; q13.3) was found only in patients with ALL. This group had the highest recurrence rate. Monosomic karyotype is of great importance in AML as a factor of unfavorable prognosis.

Conclusions. In patients with acute leukemia with an unfavorable course of the disease and refractoriness to ongoing therapy, multiple (2 or more) genetic aberrations occur with the most frequent profile of abnormal genes: MLL, AML / ETO, BCR / ABL and MLL, AML/ETO and TEL/AML, in contrast to patients in the group with a favorable prognosis of the disease, who had only single genetic aberrations. In international practice, risk groups for patients with acute leukemia are currently formed on the basis of detected cytogenetic and molecular genetic disorders (recommendations of the American Society of Clinical Oncologists and the European Cooperative Group Leukemia Net, IEP (International Expert Panel)). The use of a standard cytogenetic study makes it possible to simultaneously detect a wide range of clinically significant genetic anomalies, including complex karyotype disorders, to determine the prognosis and treatment tactics for patients with acute leukemia.

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