Spectrum Journal of Innovation, Reforms and Development
Volume 07, Sep., 2022 | ISSN (E): 2751-1731
Website: www.sjird.journalspark.org

PROGNOSTIC SIGNIFICANCE OF TP53 GENE MUTATIONS WITH ACUTE LEUKOSIS

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Abstract
Acute leukemia is a malignant tumor of the hematopoietic system. It has a poor prognosis due to a number of complex features1. Based on the rate of development and cytogenetic analysis, leukemia has been classified into four main types 2: acute lymphocytic leukemia (ALL), acute myeloid leukemia (AML). Although research on leukemogenesis has been carried out for many years. The mechanisms underlying the development of this hematologic malignancy remain unclear. Multiple risk factors considered implicated in leukemia, and genetic factors such as constitutional genetic variation in components of DNA damage response pathways have become the subject of research. The TP53 protein functions by regulating cell cycle arrest, DNA repair, apoptosis and gene transcription to provide cellular responses to DNA damage. Frequent mutations and differential expression of TP53 in various types of cancer highlight the important role of p53. in carcinogenesis and tumor progression. Functional single nucleotide polymorphism (SNP) at codon 72 It was shown that the TP53 gene (rs1042522), encoding the transversion of G to C (Arg to Pro), is associated with interindividual differences in TP53 expression in malignant tumors, including leukemia. In addition, he has it was reported that the Arg72 variant induces apoptosis markedly better than the Pro72 variant. In addition, he has it was reported that the Arg72 variant induces apoptosis markedly better than the Pro72 variant. Thus, this genetic polymorphism holds promise as a potential biomarker for leukemia. To date, numerous studies have investigated the relationship between the Arg72Pro TP53 polymorphism and susceptibility to leukemia, but the effect of the Arg72Pro TP53 polymorphism on leukemia was still controversial.

Keywords: acute leukemia, mutation, TP53 gene.

Introduction

The TP53 gene encoding a tumor suppressor is located on the short arm of the 17th chromosome (region 17p13.1), consists of 11 exons and has a length of 19144 nucleotide pairs [8,9]. The p53 protein is a transcription factor and induces tumor suppression through the regulation of gene expression, leading either to stop cell cycle at checkpoints G1/S and S/G2, or to programmed cell death (apoptosis) [1-7]. Mutations of the TP53 gene are associated with more than 50% of malignant neoplasms, including leukemias and lymphomas.

Purpose of the Study

To determine the frequency, structural features and prognostic value of TP53 gene mutations in acute leukemia.

Materials and Methods

Bone marrow and peripheral blood samples from patients with acute leukemia (n =88) were studied. Of all the examined patients, 46 were diagnosed with acute myeloid leukemia (AML), 42 with acute lymphoblastic leukemia (ALL). Average the age of patients with AML was 42,3±2,1 years, with ALL — 32,1±1,7 years. AL was diagnosed in accordance with the WHO recommendations based on the clinical picture and analysis of blood and bone marrow, as well as on the basis of a cytochemical study of blast cells. The morphological variant of AML was determined according to the Franco-American-British (FAB) classification. The M3 variant according to the FAB classification was detected in 8 patients, M4 — in 1, in 37 patients the AML variant was not differentiated. In the study group, all patients underwent cytogenetic and molecular genetic testing (polymerase chain reaction - PCR).

Results. It was established that functionally significant, that is, leading to a decrease in the activity of the encoded protein, mutations of the TP53 gene in acute myeloid and lymphoblastic leukemias were detected with a frequency of 9,7% (with 95% CI from 4,3 to 19,2%) and 21.1 % (at 95% CI from 8,1 to 43.7%), respectively**.** In the case of AML, these mutations were detected at morphological variants of M3 (n = 4), with ALL - 6 mutations, which can be explained by the small size of the study sample. The effect of mutations in the TP53 gene on the prognosis of AML turned out to be extremely unfavorable. All patients with mutant p53 were resistant to program polychemotherapy, and there were no cases of achieving clinical and hematological remissions. The median overall life expectancy of patients did not exceed 6 months. In the comparison group (patients with AML without mutations in the TP53 gene) probabilistic survival was 28,8 ± 6,1%, median overall life expectancy was 6 months. The prognosis for ALL with the presence of mutations in the TP53 gene was unfavorable. In 3 cases, patients were resistant to program polychemotherapy. The median overall life expectancy of patients with ALL with mutations in the TP53 gene did not exceed 5 months. In the comparison group (patients with ALL without gene mutations TP53) one-year probabilistic survival was 43.2 ± 13.6%, median total life expectancy — 7 months.

CONCLUSIONS

Mutations of the TP53 gene with a high frequency (60%) were determined in AML with complex chromosomal aberrations and did not occur in the presence of other specific molecular lesions. The frequency of TP53 gene anomalies in ALL was 21,1%. The presence of mutations in the TP53 gene determined the unfavorable prognosis of program treatment in the examined group of AL patients. The median overall life expectancy of patients with mutant p53 did not exceed 3 months.

REFERENCES

1. Egamova S.K. Cytogenetics in acute leukemia. New day in medicine, ISSN- 2181-712X № 6 (38), 2021, P.244-249
2. Egamova S.K. Algoritm for the diagnosis of acute leukemia. British medical journal, №2, 2021, P.160-174.

3. Egamova S.K. Prognostic significance of genetic mutations in patients with acute leukemia. Neuroquantology, Vol 20, 2022, P. 1093-1097
4. Khamdamova M. T., Barotova M.M. Clinical aspects of the use of laser photodynamic therapy in cervical pathology. American Journal of Medicine and Medical Sciences 2021, 11(4): 353-355
5. Khamdamova M. T., Barotova M.M. Laser photodynamic therapy in the treatment of cervical pathology. Academicia: An International Multidisciplinary Research Journal https://saarj.com.ISSN: 2249-7137 Vol. 11, Issue 3, March 2021. P.2499-2504
6. Khamdamova M. T., Rabiev S. N. Features of the course of pregnancy in women of different somatotypes. Academicia: An International Multidisciplinary Research Journal.ISSN: 2249-7137,Vol.11, Issue 3, March 2021. P.2569-2572
7. Khamdamova M. T., F. Sh. Oripova, G.A. IKhtiyarova, K.Shukurlaev New Methods of Correction of Inflammatory Diseases of the Genitalia (Clinical and Experimental Study). Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 4, 2021, Received 05 March 2021; Accepted 01 April 2021. P. 1865 - 1872
8. Petitjean A., Mathe E., Kato S., Ishioka C., Tavtigian S. V Impact of mutant p53 functional properties on TP53 mutation patterns and tumor phenotype: lessons from recent developments in the IARC TP53 database /Hum. Mutat.-2007.-Vol. 28.- P. 622—629
9. Vinogradov A. V., Rezaikin A. V., Sergeev A. G. TP53 gene point mutation detection using sequencing techniques in acute and chronic leukemia patients // Cel. Ther. Transplantat. - 2010. -Vol. 3, N 9. -P.126.