

MOLECULAR-GENETIC FEATURES OF VASCULAR THROMBOSIS

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Annotation. During the study, in 107 patients with vascular thrombosis of various localization, the associative relationship of Leu33Pro in the integrin beta-3 (ITGB3) gene in the formation of pathology data was analyzed. In the studied groups, the actual distribution of C807T polymorphism genotypes corresponded to those expected at the Hardy-Weinberg equilibrium ($p < 0.05$).

Key words: ischemic stroke, myocardial infarction, deep vein thrombosis of the lower extremities, genetic polymorphism Leu33Pro ITGB3.

Relevance. In recent years, there has been an increase in the proportion of vascular thrombosis of various localizations among young people [4]. The incidence, according to various sources, varies from 3 to 23 per 100,000 people [2]. Hereditary thrombophilia can most often be considered as a provocateur in these situations, since some patients have occlusion of the cerebral and coronary arteries due to intravascular thrombosis during examination [1, 6]. Thrombophilia is defined as a violation of hemostasis and hemorheology, characterized by an increased tendency to develop thrombosis or intravascular coagulation, which is based on acquired and genetically modified blood clots. conditioned disorders in various parts of hemostasis and hemorheology [3]. Among the factors that increase the risk of thrombosis, platelet receptor genes are very important. In this case, a genetic marker of the platelet receptor gene for collagen (ITGA2 807C>T) and fibrinogen (ITGB31565T>C) is analyzed. With a defect in the collagen receptor gene, platelet adhesion to the vascular endothelium and to each other increases, which leads to increased thrombosis. When analyzing the genetic marker ITGB31565T>C, it is possible to identify the effectiveness or ineffectiveness of antiplatelet therapy with aspirin. Disorders caused by mutations in these genes increase the risk of thrombosis, myocardial infarction, and ischemic stroke [5].

Material and methods of research. During the genetic study, we examined 107 patients with vascular thrombosis of various localizations who were in the neurological, cardiological and surgical departments of the clinic of the Andijan State Medical Institute and the Andijan branch of the Republican Scientific Center for Emergency Medical Care, who formed the main group. Among them, patients with DVT $n=35$, with IS $n=35$, with MI $n=37$. The control group consisted of 103 conditionally "healthy" individuals without thromboembolic diseases (TES) at the moment and in the anamnesis. Diagnosis of these diseases was carried out in accordance with currently accepted clinical recommendations. Isolation of a DNA molecule from peripheral blood was performed using the Ampli Prime RIBO_prep kit. Genotyping of the Leu33Pro ITGB3 polymorphism was performed using the Tag Man probe method on a Rotor-Gene Q amplifier (Quagen, Germany), using a commercial test kit of Litech LLC (Russia).

Statistical processing of the results was performed using the standard OpenEpi V.9. 2 application software package. The deviation of the empirical genotype frequencies from the theoretically expected Hardy-Weinberg distribution was analyzed using the Statistica 6.0

software package. The frequencies of both alleles and Leu33Pro genotypes in the integrin beta-3 (ITGB3) gene are presented as absolute values, numbers and percentages. Accordingly, differences between groups were evaluated using the χ^2 criterion. Moreover, to quantify the effect of each variant on disease risk, univariate odds ratios (OR) were calculated with corresponding 95% confidence intervals (95% CI).

The aim of the study is to study the frequency of distribution and evaluate the relationship of the Leu33Pro polymorphism in the integrin beta-3 (ITGB3) gene in patients with vascular thrombosis of various localizations.

Results obtained and their discussion

In the study, the proportion of Leu and Pro alleles in patients with vascular thrombosis of various locations and in the control group Leu и Pro was 91.1% and 8.9% versus 95.6% and 4.4%, respectively. Statistical processing revealed a slight decrease in the frequency of the wild Leu allele ($\chi^2=3.4$; $P=0.06$; $OR=0.5$; $95\%CI:0.21-1.06$) and a tendency to increase the mutant Pro allele was found in patients with vascular thrombosis of various localizations compared to conditionally healthy donors. The calculated coefficient of the odds ratio showed that the chance of detecting a functional unfavorable Pro allele in the respondents of the main group increased 2.1 times compared to the representatives of the control group ($\chi^2=3.4$; $P=0.06$; $OR=2.1$; $95\%CI:0.94-4.83$).

As can be seen (Table 1), the frequency of the unfavorable Pro/Pro genotype among patients with vascular thrombosis of various localizations was slightly higher than in the control group (0.9% vs. 0.0%, respectively, with $\chi^2=1.0$; $P=0.3$).

Table-1.

Association between the Leu33Pro polymorphism in the integrin beta-3 (ITGB3) gene in patient and control groups

Study groups	Alleles and genotypes	Statistical difference in relation to the control group			
		Odds ratio		χ^2	p-value
		OR	95% CI:		
Main group (n=107)	Leu	0.5	0.21 – 1.06	3.4	0.06
	Pro	2.1	0.94 – 4.83		
	Leu/Leu	0.5	0.20 – 1.11	3.1	0.08
	Leu/Pro	2.0	0.85 – 4.71	2.6	0.1
	Pro/Pro	***	***	1.0	0.3

Also, the wild Leu/Leu genotype of the study group was found to be slightly lower compared to the control group ($\chi^2=3.1$; $P=0.08$; $OR=0.5$; $95\%CI:0.20-1.11$). This means that there is no association of these genotypes (Leu/Leu, Pro/Pro) with respect to the formation

of vascular thrombosis of various localizations, such as DVT, AI, MI. However, there is a tendency to increase the proportion of carriers of the unfavorable Leu/Pro genotype among patients compared to the control group (15.9% vs. 8.7%, respectively).. 1). According to the odds ratio, the risk of developing vascular thrombosis of various localizations in the presence of this genotype increases 2.0 times ($\chi^2=2.6$; $P=0.1$; $OR=2.0$; $95\%CI:0.85-4.71$). (Table 1).

Conclusion. Thus, the analyzed data of the study showed that, in patients with DVTNA, IS, and MI, the detection of the minor Pro allele and the associated unfavorable Leu/Pro genotype was associated with a low risk of developing and relapsing thrombogenic complications as a result of a moderate increase in platelet aggregation ability. Also, if the Pro /Pro mutant genotype was detectedPro in the main group, there was no risk of developing these pathologies.

List of literature.

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