GENETIC ASPECTS OF THE CLINICAL COURSE OF SYSTEMIC SCLERODERMA

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Systemic sclerosis (SSc) is a multifactorial autoimmune disease with high clinical heterogeneity. Mechanisms of chronic hypoxia and angiopathy play a particularly important role in the pathogenesis of the disease. The HIF1A gene (hypoxia-inducible factor 1-alpha) encodes the key transcription factor for adaptation to hypoxia, regulating angiogenesis, fibrosis, and inflammation. The Pro582Ser (rs11549465) polymorphism is associated with altered HIF-1α activity and may influence the clinical course of SSc.

Objective of the study. To evaluate the association of the Pro582Ser (rs11549465) polymorphism of the HIF1A gene with the clinical features of SSc in 60 patients.

Materials and methods. The study included 60 patients with a confirmed diagnosis of SSc (according to the American College of Rheumatology / European Alliance of Associations for Rheumatology criteria). Mean age was 49 ± 11 years; 85% were women. Genotyping of the rs11549465 polymorphism of the HIF1A gene was performed by PCR followed by restriction fragment length polymorphism analysis. Clinical assessment included skin score, evaluation of pulmonary, esophageal-gastric, and cardiovascular involvement, as well as immunological profile.

Results. Genotype distribution: CC - 58.3%, CT - 33.3%, TT - 8.4%. Carriage of the T allele was associated with more pronounced interstitial lung disease ($p < 0.05$) and a higher modified Rodnan skin score (mRSS) compared to CC carriers. The frequency of pulmonary hypertension among T allele carriers was 44.4% versus 26.5% in CC carriers. Esophageal involvement was observed in 55.6% of T-allele carriers and 36.4% of CC carriers. T-allele carriers more frequently experienced early (within 3 years of onset) development of visceral manifestations. No statistically significant differences in gender and age were found between the groups.

Conclusion. The Pro582Ser (rs11549465) polymorphism of the HIF1A gene is associated with a more severe and progressive course of systemic sclerosis, especially regarding pulmonary and esophageal-gastric involvement. The T allele can be considered a potential genetic marker of unfavorable disease course, which is important for risk stratification and personalization of therapy.