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TNF-A GENE POLYMORPHISM AS A RISK FACTOR FOR ACNE AND ATOPIC DERMATITIS

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Abstract: Skin diseases are a significant socio-economic problem, as their diagnosis and treatment in the United States alone costs $ 75 billion annually. About 900 million people worldwide suffer from them. In addition to the high cost of their treatment, they cause moral and physical discomfort to patients, impair their social activity, lead to disability, and even death. It should also be noted that this group of diseases is one of the most common in the world. In turn, the peak in prevalence in this cohort of pathologies is acne. This is a chronic inflammatory disease of the sebaceous glands of the skin, manifested by a rash formed by papules and pustules, after the regression of which may remain atrophic scars, which has a negative cosmetic effect. The main site of localization is the skin of the face, torso, and upper extremities.

Acne affects people between the ages of 12 and 24, due to hormonal changes in the body during puberty, but also occurs in people aged 30-40. It has also been observed that women get sick more often, but a more severe course is observed in men. Another important pathology is atopic dermatitis.

It is a chronic inflammatory skin disease that often relapses and is associated with other atopic manifestations such as asthma, food allergies, and allergic rhinitis.

It mainly affects children, about 15-20%, and 2-3% of the adult population worldwide. It should also be noted that the incidence of the disease over the past 50 years has increased 2-3 times in developed countries. Although the etiology and pathogenesis of these diseases are not related, several studies have found that polymorphism of the TNF-α gene can affect the predisposition to their development and severity.

Keywords: TNF-α, gene, polymorphism, acne, atopic dermatitis.

The TNF-α (tumor necrosis factor-alpha) gene is located on the short arm of the sixth chromosome in the III region of the main histocompatibility complex (6p21.3) [1]. Many mutations in this gene are located in its promoter zone and are associated with the development of autoimmune diseases. These polymorphisms include: -1031 (T / C), -863 (C / A), -857 (C / A), -851 (C / T), -419 (G / C), -376 (G / A), -308 (G / A), -238 (G / A), -162 (G / A) and -49 (G / A) [2]. In their work, most scientists studied polymorphism 308 (G / A), for which there are 3 genotypes: GG - homozygous normal, GA - heterozygous, and AA - homozygous mutant, where the letters G and A denote the replaced nitrogenous base in the DNA molecule: guanine (G) and adenine (A), respectively [1]. In humans, this gene is responsible for the formation of tumor necrosis factor, which is a potent proinflammatory cytokine produced by immune cells such as monocytes and macrophages, and plays a role in the transmission of intercellular signals in inflammation and can cause necrosis and apoptosis. TNF-α plays an important role in protecting the body from infectious agents and prevents the development of malignant tumors [3].

In turn, as mentioned above, the polymorphism of this gene may be responsible for the predisposition to acne and atopic dermatitis and the severity of their course. Kornélia Szabó and others in their study found that allele A was more common in patients with acne [4]. Another researcher found a similar result but noted that the GA genotype was more common in the group of patients, which may be a risk factor for the development of this pathology [1]. B. Wang conducted research on people of different nationalities. It was found that polymorphism 238 (G / A) was responsible

for the predisposition to acne in Asians, and polymorphism 308 (G / A) - in Asian and Turkish populations, but does not play a role in patients of the European group of peoples [5]. L. Li and co-authors in their meta-analysis also found that allele A is a predictor of acne and is responsible for the more severe course of the disease in men [6].

In contrast to the study of B. Wang, Jian-Kang Yang and the authors found that this polymorphism causes a predisposition to acne in patients of the European population [7]. Another study in patients from Pakistan showed that TNF-α gene polymorphisms 238 (G / A) and 308 (G / A) are responsible for the predisposition to acne and more severe course in carriers of mutant alleles [8].

Subsequent work on the study of genotype in the Uzbek population found that allele A is responsible for both the predisposition to acne and the more severe course of this nosology [9].

Another group of researchers found that polymorphism 308 (G / A) may be a factor that increases the likelihood of developing acne, but does not correlate with its severity [10]. In contrast, Gulsen Akoglu and others found that the 308 (G / A) polymorphism of this gene was not associated with the development of acne [11].

Concerning atopic dermatitis, a study of forty families with a combination of three atopic manifestations found that the frequency of allele A in the human genotype was more than 2 times compared with the control [12]. Other researchers have emphasized that the GA genotype is the most unfavorable and correlates with an increased risk of atopic dermatitis [13]. An interesting result is a group of scientists who claim that the GA genotype is associated with increased production of the cytokine TNF-α and is less common in patients with atopic dermatitis. However, the GG genotype, which they associate with reduced TNF-α production, in contrast, is characteristic of patients with this nosology [14].

Summarizing the above information, it can be assumed that the polymorphism of the TNF-α gene, especially 308 (G / A), is associated with the development of acne and atopic dermatitis and the severity of their course. This suggests the

involvement in the pathogenesis of both nosologies of the cytokine TNF-α because the polymorphism of this gene affects its production.

Thus, in the future, by influencing its formation by inhibition or stimulation, it will be possible to achieve a better therapeutic effect in the treatment of acne and atopic dermatitis.

However, these studies require in-depth study and work with a larger sample of patients to establish more accurate results.

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