EXAMINING GENETIC POLYMORPHISM IN INDIVIDUALS WITH VIRAL IMMUNITY

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Annotation: *In the world, the number of patients with this disease exceeds 1% of the total population. In 70% of cases, the disease begins at the age of 10-25 years, children under 10 years of age, including newborns and infants, account for approximately 25% of all patients with vitiligo. To analyze the genetic structure in patients with vitiligo and determine the activity of genes: DDS and GNB3, assessing their possible role in the pathogenesis of the disease clinic of skin and venereal diseases of the regional center of the city of Samarkand in the period from 2019 to 2021. To compare the results of laboratory studies, a group of 10 healthy donors was examined. Analysis of the clinical material was carried out on the basis of the history*

of life and disease, assessment of the general condition and local status of the patient. In each patient, the clinical form of the disease was determined according to the classification of vitiligo. As a result of our genotyping of patients with vitiligo, an association of haplotypes of the SCVZ gene encoding the beta subunit of the C-protein with vitiligo was revealed. Considering that the gs 5443 polymorphism modulates the immune response of T-lymphocytes and is associated with type II diabetes, this makes possible its involvement in the autoimmune component of the pathogenesis of vitiligo.

Keywords: *vitiligo, polymorphism*

Introduction: Vitiligo is characterized by the sudden appearance of depigmented spots due to a violation of the secretory function of melanocytes or their death, develops in individuals with a genetic predisposition, is accompanied by pronounced dysregulatory changes in cell-mediated reactions of the immune system, autonomic imbalance with a predominance of sympathetic tone and serious social maladjustment due to personal characteristics and external social factors. Vitiligo is a common dermatosis. In the world, the number of patients with this disease exceeds 1% of the total population. In 70% of cases, the disease begins at the age of 10–25 years; children under 10 years of age, including newborns and infants, account for approximately 25% of all patients with vitiligo [1]. Vitiligo can occur at any age, last indefinitely, spontaneous restoration of normal skin color is rare. The reasons for the appearance of depigmented lesions are not known. It is not clear enough as a result of what disorders melanin synthesis abruptly stops and melanocytes die. Various endogenous and exogenous factors can have a direct and indirect damaging effect on melanocytes. Among external factors, infectious and toxic agents, excessive ultraviolet radiation, and stress are of the greatest importance. For many decades, vitiligo has been associated with autoimmune thyroiditis, rheumatoid arthritis, lupus erythematosus, atopic dermatitis, liver diseases of infectious or toxic origin, helminthic invasion, and a number of congenital syndromes [2]. However, the incidence of vitiligo in these patients is not higher than in the general population. A number of authors [3, 4],

summing up the results of many years of research, believe that patients with vitiligo in most cases do not have any severe or chronic concomitant diseases, and the therapy of functional disorders of the digestive system, vegetovascular dystonia, identified in 28% of patients, did not affect the result of repigmentation. Many researchers believe [5, 6] that vitiligo is a serious cosmetic defect that occurs in individuals with a genetic predisposition and, in most cases, who have experienced emotional disorders. Only in 4-7% of patients vitiligo is combined with autoimmune thyroiditis. In modern genetic studies, the relationship between the occurrence of vitiligo and various aspects of inheritance has been demonstrated. Among sporadic cases of vitiligo in the European population, the average age of onset is 24.2 years, while in families with multiple cases of the disease, the average age is 21.5 years (statistically significant difference) [7]. Earlier onset of the disease in "family" cases and the risk of disease in distant relatives is a typical characteristic of polygenic disease. About 20% of patients with vitiligo have at least one blood relative with a similar disease. Formal genetic segregation analysis of vitiligo determines the existence of many loci, disorders in which form a predisposition to vitiligo. However, key genes responsible for the manifestation, progressive course or predisposition to this disease have not been found. In vitiligo, a decrease in the antioxidant potential was found, leading to an active damaging effect of free radicals on melanocytes and the accumulation of lipid peroxidation products [8, 9]. Later, it turned out that free radicals have a damaging effect on various cells involved in various types of inflammatory reactions, and antioxidant defense disorders are not the main mechanisms of depigmentation in vitiligo. The theory of violations of the immune mechanisms of regulation is the most reasonable. With a long course and a widespread pathological process, changes in the subpopulation composition of T-lymphocytes are observed. At the same time, especially at the initial stages of the disease, the levels of activation receptors of lymphocytes increase, reflecting the degree of activation of immunocompetent cells [10]. Currently, most researchers believe that the leading role in the development of autoimmune diseases belongs to cell-mediated reactions, in which there is a pronounced imbalance of cytokines. In vitiligo, a decrease

in the activity of regulatory T-lymphocytes is detected, which is confirmed by a decrease in the amount of transforming growth factor-β (TGF-β) and interleukin-10 (IL-10) in the blood serum of patients [11]. Treatment of vitiligo is a difficult task. Since the causes of its occurrence are unknown, in most cases the disease develops against the background of complete physical well-being. It is proposed to use mainly topical steroids and/or immunomodulators with a lesion area of up to 20%, as well as long-term phototherapy [12, 13]. Complex therapy includes enzyme preparations, hepatoprotectors, vitamins and microelements (zinc, copper) [14, 15]. A number of recommendations contain information on the use of sedatives and antidepressants. The aim of this study was to study the clinical features of the course of vitiligo and the effectiveness of complex therapy, including the immunomodulatory component thymogen and externally 1% pimecrolimus, and the correction of affective disorders in patients with various forms of vitiligo using the antidepressant drug agomelatine.

Aim: To analyze the genetic structure in patients with vitiligo and determine the activity of genes: DDS and GNB3, assessing their possible role in the pathogenesis of the disease.

Materials and Methods: This study included 53 patients with various forms and stages of vitiligo aged 12 to 59 years, who were on outpatient treatment at the clinic for skin and venereal diseases of the regional center of the city of Samarkand in the period from 2019 to 2021. To compare the results of laboratory studies, a group of 10 healthy donors was examined. Analysis of the clinical material was carried out on the basis of the history of life and disease, assessment of the general condition and local status of the patient. In each patient, the clinical form of the disease was determined according to the classification of vitiligo. The clinical examination included a general examination of the patient's skin, an examination using a fluorescent lamp, and measuring the area of depigmented lesions using a ruler. The areas of each lesion were summarized and evaluated as a percentage relative to the body surface area. All patients underwent a clinical examination, including examination using a fluorescent lamp,

history taking, determination of the area of lesions. Laboratory and instrumental studies included:

- Clinical blood test;

- Genotyping of single nucleotide polymorphisms (8MP genotyping) by pyrosequencing.

Two genes were included as “candidate” genes in the study:

- OBC and SKVS;

- Determination of the content of natural auto-antibodies to various organs and tissues in the blood serum;

- Study of the subpopulation composition of T- and B-lymphocytes, analysis of the functional activity of T- and B-lymphocytes, as well as NK cells.

Results and discussion: Clinical characteristics of the examined patients with vitiligo. The average age of patients seeking medical help ranged from 12 to 59 years, among which the number of women was significantly higher than that of men.

Of the clinical forms of the disease, the vulgar form: multiple, randomly or (mostly) symmetrically located spots on the skin of the trunk, limbs and face was observed in 58 (76.3%) patients. Acrofacial: damage to the hands, feet, face in the periorbital and perioral areas - in 11 (14.4%). Focal: one or more spots in one area - in 5 (6.7%). Segmental: spot along the nerve or plexus - in 2 (2.6%) patients. The combination of vitiligo and Setton’s nevus - depigmentation surrounding the birthmark was detected in 6 patients with the vulgar form of the disease. 2 patients had depigmentation of the scalp hair (leukotrichia).

When comparing the genotypes of 69 patients with vitiligo and 20 healthy donors (control group), for the 008 and CMDD genes with known functions, and comparing the obtained data with the phenotypic characteristics of the patients, we found a new association of a single single nucleotide polymorphism with vitiligo. Thus, a general analysis demonstrated an association of haplotypes of the CMVS gene encoding the beta subunit of the C protein with vitiligo, compared with healthy donors (Fig. 1). According to the literature, the rz 5443 polymorphism modulates the immune response

of T-lymphocytes and is associated with type II diabetes [Baton M., 2008], which makes it possible to participate in the autoimmune component of the pathogenesis of vitiligo. Figure 1. Results of the analysis of polymorphism of the SMVS gene.

Conclusions: As a result of our genotyping of patients with vitiligo, an association of haplotypes of the SCVZ gene encoding the beta subunit of the C-protein with vitiligo was revealed. Considering that the gs 5443 polymorphism modulates the immune response of T-lymphocytes and is associated with type II diabetes, this makes possible its involvement in the autoimmune component of the pathogenesis of vitiligo.

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