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Comparative analysis of immunogenetic determinants of HLA system A, B, C loci in the indigenous residents of the Khabarovsk territory, donors and psoriatic patients

The paper gives the data of a study of HLA-antigens in 31 aborigines (the Ulch) of the Khabarovsk Territory, 1600 donors, 85 patients with psoriasis. In aborigines low frequency of HLA antigen A1 and tendency for increase of HLA B13 were found. Indices of HLA B-17 were the same as in the control group. In patients with psoriasis high frequency of antigens HLA A-1, HLA B-13, HLA B-17 and low frequency of antigens HLA A-28, B-7, Cw-3, Cw-4 was determined. This can point out the absence of genetic susceptibility for psoriasis in the Ulch.

Keywords: psoriasis, genetic susceptibility, HLA-antigens.

Introduction

According to modern concepts, psoriasis is an erythematous-squamous dermatosis of a multifactorial nature, having the genetic factors as the main reason in its development. It is characterized by hyperproliferation of epidermal cells and processes of keratinization, inflammatory reaction in the dermis, the changes in the various organs and systems. The prevalence of psoriasis in the population is about 0.1 to 3% [4]. Psoriasis occurs with equal frequency in men and women in different age periods.

There are hypotheses about the role of bacterial and viral factors in the etiology of psoriasis and possible changes under the influence of the genetic apparatus. It is believed that psoriasis is a slow-moving lymphotropic retrovirus infection [3].

Immune disorders play an important role in the pathogenesis of psoriasis. Skin lesions are accompanied by the influx of activated T-lymphocytes. Increased synthesis of interleukin-1 (IL-1) by activated macrophages and keratinocytes induces T-cells to the production of IL-2, which in its turn is a potent stimulator of T-lymphocyte proliferation. Activation of T-helper cells is pathogenetically associated with proliferation of epidermal cells [6, 7, 8].

The cause of psoriasis is not evident, but a significant part is assigned to hereditary factors. Segregation analysis indicates a multifactorial inheritance with a share of the genetic component equal to 60–70%, environmental – 30–40%. There is evidence to link the various genetic markers, race, nationality and type of psoriasis. Hereditarily determined psoriasis is observed in most patients and is manifested in childhood and adolescence, with no family history of the disease, the risk of a child is 8%, the risk of both parents is 41%.

Clinical observations show that the indigenous people (Ulchi) rarely take medical advice of a dermatologist concerning psoriasis. Among patients with psoriasis in the Ulchi region only 0.03% are Ulchi. In this regard, we consider the data on the frequency of histocompatibility antigens HLA loci A, B and C in patients with psoriasis and frequency of histocompatibility antigens HLA loci A, B, C in indigenous peoples.

The purpose of the study was to investigate the HLA-antigens and analyze the data (residents of the Ulchi District, donors Khabarovsk and psoriasis residents of the Khabarovsk Territory), and to clarify, whether there was a predisposition to psoriasis in the indigenous

inhabitants of the Khabarovsk Territory.

Materials and methods

In a comprehensive study of different groups of patients in the “HLA and disease” program in the Khabarovsk Territory a group of residents of the Ulchi District was surveyed (31 people were Ulchi). Immunogenetic indicators in indigenous people were compared with the same parameters in patients with psoriasis (85 "caucasoids").

Histocompatibility antigens were defined. The studies were conducted in the zonal center of immunological tissue typing "Hemotransfusion Station" (Head of Laboratory is G.B. Kalatushkina). Peripheral blood lymphocytes were investigated by means of the reaction of "complement - dependent cytotoxicity" using microtechnology of P. Terasaki [9]. - Control group of 1600 donors.

To determine the association between histocompatibility antigens and disease criterion relative risk was calculated [1, 2]:

$$RR = \frac{fn(1-fk)}{fk(1-fn)}$$

Formula 1. The calculation of the relative risk criterion association between histocompatibility antigens and disease

Blood group was determined using standard sera system AB0, Rh identity – using standard antirezus sera.

Results

Table 1 shows that the frequency of histocompatibility antigens HLA loci A, B and C in patients with psoriasis in the Khabarovsk region is represented by the following genetic determinants: HLA A-1, HLA B-13 and HLA-17 ($p < 0.001$) [5].

Carriage of certain HLA-antigens in humans is much too high for some diseases, indicating that predisposition to human affection with some form of the disease is genetically determined.

Table 1

Distribution of antigens HLA loci A, B, C in the indigenous population, donors and patients with psoriasis

HLA antigens (loci A, B, C)		Donors in Khabarovsk (n = 1600) antigen frequency, %	Population of the Ulchi District of the Khabarovsk Territory (n = 31), antigen frequency, %	patients with psoriasis (n=85), antigen frequency, %	Relative risks (RR)
HLA-A					
A_1		20.80±1.015	7.50±1.25**	37.50±5.25***	2.31
A_2		47.25±1.248	50.0±8.8	56.50±5.37	1.44
A_3		24.00±1.068	30.0±5.29	15.30±3.90	0.59
A23	A_9	24.80±1.068	52.5±9.34*	18.8±4.24	0.75
A24			5.0±0.80*		
A25	A_{10}	23.50±0.120	15.0±2.6	16.50±4.03	1.07

A26		15.0±2.6		
A_{11}	14.50±0.880	10.0±1.7	14.10±3.77	1.00
A_{19}	15.80±0.910	7.5±1.25	10.60±3.34	0.66
A_{28}	5.40±0.570	10.0±1.7	1.18±1.17***	0.12
A33		7.5±1.25		
HLA-B				
B_5	12.50±0.830	10.5±1.79	16.50±4.03	1.42
B_7	21.50±1.030	17.5±3.05	8.24±2.98**	0.35
B_8	12.00±0.810	10.5±1.79	7.06±2.78	0.60
B_{12}	17.00±0.930	10.5±1.79	12.90±3.64	0.75
B_{13}	11.75±0.810	17.5±3.05	48.20±5.42***	7.00
B_{14}	5.00±0.650	-	4.71±2.30	1.04
B_{15}	9.00±0.720	20.0±3.5*	2.35±1.64	0.30
B_{16}	12.00±0.810		8.24±2.98	0.70
B_{17}	8.80±0.710	7.0±1.16	25.90±4.75***	3.65
B_{18}	10.70±0.770	7.0±1.16	7.06±2.78	0.68
B_{21}	3.40±0.450	2.5±0.35	4.71±2.30	1.57
B_{22}	4.40±0.510	2.5±0.35	-	-
B_{27}	9.80±0.740	12.5±2.15	10.60±3.34	1.12
B_{35}	23.20±0.110	15.0±2.6*	14.10±3.77	0.56
B_{37}				
B_{40}	12.00±0.810		12.90±3.64	1.13
B_{41}			1.18±1.17	-
HLA-C				
C_{W1}	4.70±0.530	10.0±1.7*	5.88±2.55	1.38
C_{W2}	18.20±0.960	15.0±2.6	9.41±3.17	0.49
C_{W3}	23.40±1.060	35.0±5.83	10.60±3.34**	0.41
C_{W4}	12.70±8.320	7.50±1.25	2.35±1.64**	0.205
C_{W5}	0.86±0.230	-	-	-
C_{W6}	15.90±0.910	5.0±0.80**	18.80±4.24	1.26
C_{W7}	-	5.0±0.80	1.18±1.17	-
***p<0.001; ** p<0.01				

Identification of a specific antigen by tissue typing in clinically healthy people indicates the likelihood of the disease. Genetic determinism of many pathological processes is implemented through concrete systems: structural features, levels of biochemical and enzymatic indicators.

The frequency of HLA-antigens depends on ethnicity and geographic area. Knowledge of the characteristics of distribution of HLA-antigens specific to different ethnic groups is necessary for studying the association to the HLA-antigens with diseases.

Histocompatibility antigens are defined in 31 native inhabitants of the Khabarovsk Territory. Immunogenetic indicators of the HLA loci A, B, and C are analyzed (Fig. 1). It was found that:

• antigen HLA A1 is 7.5 ± 1.25% vs 20.80 ± 1.015% of donors, and 37.50 ± 5.25% *** in patients with psoriasis;

• HLA B13 antigen was 17.5 ± 3.05% against 11.75 ± 0.81% in donors Khabarovsk and 48.20 ± 5.42% *** in patients with psoriasis.

• antigen HLA B17 is 7.0 ± 1.16% against 8.80 ± 0.71% in donors Khabarovsk and 25.90 ± 4.75% *** in patients with psoriasis.

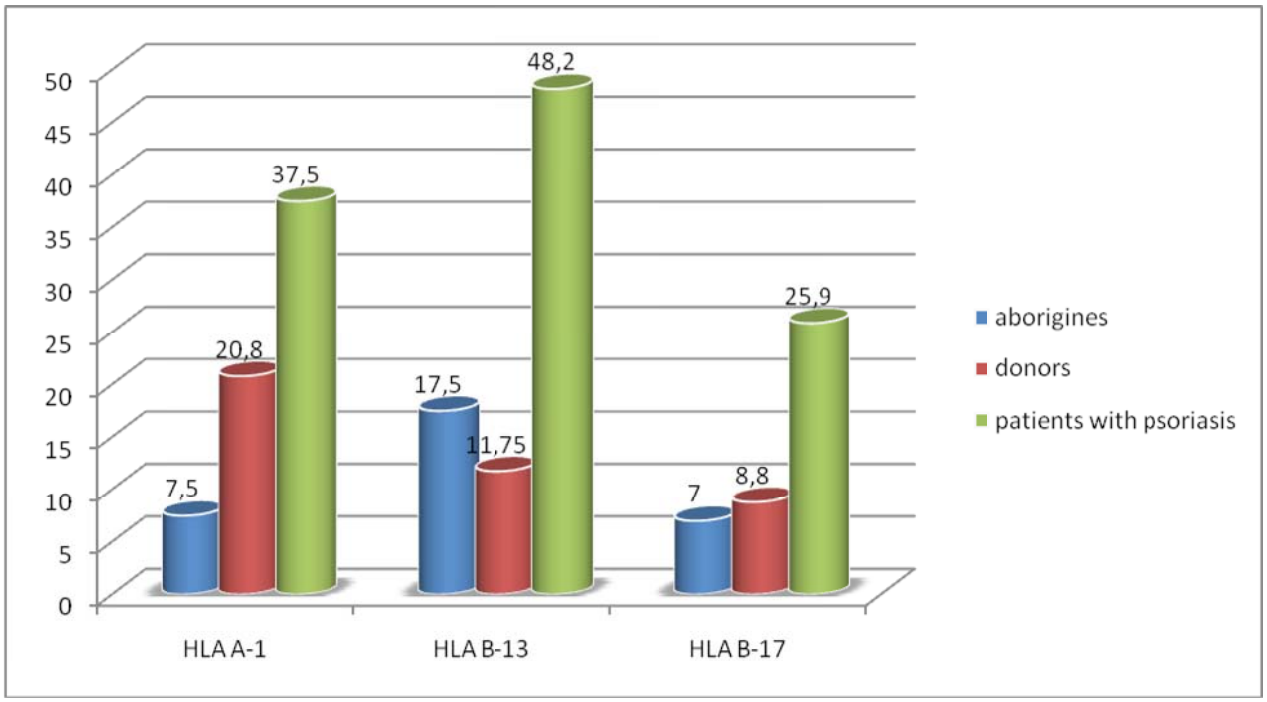

Fig. 1. Immunogenetic determinants of HLA loci A, B, C in the indigenous inhabitants of the Ulchi District of the Khabarovsk Territory

As seen in Figure 1: there is a decrease of antigen HLA A1 frequency: 7.5 ± 1.25% ($p < 0.01$); there was a trend to an increase in HLA B13: 17.5 ± 3.05% ($p > 0.05$) ; indicators HLA B17 7.0 ± 1,16% ($p > 0.05$) did not differ from the control group.

Discussion of the results

Genes encoding the major histocompatibility antigens are multifunctional. The clinical significance of leukocyte antigens is associated with susceptibility to certain diseases. In terms of histocompatibility antigens HLA loci A, B, and C in a group of residents Ulchi District a slight increase in the content of the antigen HLA B13 ($p > 0.05$) was revealed in comparison with donors.

Some increase in the incidence of HLA B13 indicates that in this case the phenotypic characteristics have the most value. Therefore, under adverse conditions, trigger factors may contribute to the disease. This corresponds to the literature data, as the antigen HLA B17 is responsible for genetic predisposition, and the antigen HLA B13 - for environmental factors. As it was mentioned earlier, the proportion of environmental components in the multifactorial inheritance is about 30 - 40%, while the genetic component makes 60 - 70%.

The data show that the genetic determinants in the indigenous population of the Khabarovsk Territory have no predisposition to psoriasis. When analyzing the possible triggering environmental factors in the development of psoriasis in people of the Ulch district, one should pay the most attention to climate, stress, and nutrition as the most important factors for this population.

Adverse environmental factors in the first place should include climatic conditions. Climate of the Khabarovsk Territory is monsoon. It is created under the influence of the Asian continent and the Pacific Ocean. Climatic conditions of the individual parts of the territory vary considerably from north to south, and depending on the proximity of the sea, as well as the characteristics of the terrain. The variety of terrain distorts main flow directions, but the monsoon climate remains generally in all areas.

The second factor is stress. In modern life a man constantly is required to solve problems that naturally arise in the course of evolution. Therefore stress occurs in everyday life and we should give great importance to the adaptation.

Thirdly, attention should be drawn to the nutrition in the region. And if the first two factors (monsoon climate and stress) are the negative ones, the third is positive. Indigenous people in their way of life, especially in ethnic cuisine, found a cure. Eating fish (chum salmon) is useful. Biological resources of the Amur River (fish) contain omega-3 fatty acids, which have a protective effect in the treatment and prevention of psoriasis.

Conclusions

1. Histocompatibility antigens were defined in the native inhabitants of the Khabarovsk Territory (31 people). The authors analyzed immunogenetic indicators of HLA. Decrease frequency of antigen HLA A1 ($p < 0.01$), a tendency to increase HLA B13 ($p > 0.05$) were revealed, while figures of HLA B17 ($p > 0.05$) did not differ from the control group.

2. Indigenous genetic determinants have no predisposition to psoriasis in the Khabarovsk Territory. Some increase in the incidence of HLA B13 shows that not only genotypic features, but phenotypic ones play role.

3. Under adverse conditions, trigger factors may contribute to the disease. The most vulnerable are the patients with HLA B13 antigen, since the antigen is the most affected one by environmental factors.

4. It is very important for patients with psoriasis to have foods containing omega-3. This is pathogenetically justified and useful. Prevention of psoriasis is a balanced diet. Balanced nutrition allows patients to increase an interrelapsing period, to stay healthy longer.

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