GENERAL PATHOLOGY AND PATHOLOGICAL PHYSIOLOGY

Informative Value of Monitoring of Immune Status and Genome Expression in Blood Leukocytes in Psoriatic Patients

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Comparative analysis of association with psoriasis before and after treatment of 53K/H2A and 43K/H2A leukocyte protein markers and parameters of leukocyte population (18 indexes) including concentration of peripheral blood lymphocyte subpopulations as markers of the immune status revealed advantages of the former method of patient monitoring for the evaluation of treatment efficacy. The method showed 100% sensitivity and correlation with the dynamics of clinical symptoms. A significant correlation of 53K/H2A parameter with blood content of $CD3^+$, $CD4^+$, $CD8^+$, and $CD72^+$ lymphocytes was established.

Key Words: *psoriasis; leukocytes; proteins; immunity; monitoring*

The success in the treatment of chronic recurrent diseases including psoriasis depends on recognition and practical application of the idea on the existence of asymptomatic pre- and postclinical periods in the course of all diseases [8,9]. To this end, in addition to clinical symptoms, some laboratory markers of the body state at the cellular level as minimum autonomous structural body units should be used for early diagnosis of the disease (for prophylaxis of severe clinical consequences) and objective evaluation of treatment efficacy (for prevention of relapses). At present, evaluation of the immune status of patients, in particular, blood lymphocyte populations is widely used for the analysis of clinically masked pathology [10-12].

Here we compared informative values of immune status parameters (analysis of lymphocyte populations and differential leukocyte count) and the content of 53 and 43 kDa proteins (53K and 43K) in blood leukocytes [2-7] in the monitoring of psoriatic patient.

MATERIALS AND METHODS

Protein content in leukocytes was evaluated by one-dimensional electrophoresis in polyacrylamide gel as described elsewhere [7]. Leukocyte composition in children and adults was determined at the Institute of Dermatology and Venerology and Institute of Immunology, respectively. Lymphocyte populations were identified using monoclonal antibodies against differentiation antigens: $CD3^+$ (T-lymphocytes), $CD4^+$ (T-helper-inducers), $CD8^+$ (T-supressor-killers), and $CD72^+$ (B-lymphocytes). Identification of lymphocyte populations was performed on a FACS Calibur laser flow cytometer (Becton Dickinson; Institute of Immunology) and on an EPICS cytometer (Institute of Dermatology and Venerology). Twelve children aged 6-14 mainly (8 children) with exudative psoriasis and erup-

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tion spreading from 5 to 65% receiving selective phototherapy were examined before and after treatment. A group of adults (n=9, 23-63-year-old) included 4 and 3 patients with generalized and exudative psoriasis, respectively, and 2 patients with arthropathy. In children, differential leukocyte count was determined.

RESULTS

In children, only two parameters of leukocyte population, the relative content of neutrophils and absolute B-lymphocyte count, were decreased before treatment (Table 1). In adults the content of B-lymphocytes was increased before treatment. The mean and individual content of 53K/H2A proteins in leukocytes was increased (in children and adults) before treatment.

Analysis of the correlation between abnormal parameters and patient's state (sensitivity of the given parameters to the pathology) in children revealed the most close correlation of psoriasis with relative contents of neutrophils and B lymphocytes, which suggest insufficient sensitivity of these parameters for monitoring of the pathological process. On the contrary, changes in 53K/H2A were found in 100% children. Abnormal changes in relative B-, T-, $CD4^+$, and $CD8^+$ lymphocyte content were observed in 78, 56, 50, and 50% adult patients, respectively, while abnormal 53K/H2A and 43K/H2A protein parameters — in 100 and 72% patients, respectively. Examination of a larger group of psoriatic patients (n=108) revealed abnormal 53K/H2A and 43K/H2A parameters in 80 and 42% patients, respectively. However, each patient had at least one abnormal protein parameter, which was a necessary precondition for reliable monitoring.

Psoriatic patients also showed changes in 1 to 10 of 18 parameters of leukocyte populations, however, individual (gene-specific) type of distribution of abnormal parameters and, especially, individual dynamics of these parameters during treatment make patient monitoring very difficult.

After treatment, the mean values of all 18 parameters of leukocyte populations were normal (Table 1), which corresponded to attenuation of clinical skin manifestations of psoriasis. The mean content of leu-

TABLE 1. Laboratory Parameters of Venous Blood (10^6/liter) in Psoriatic Patients Before and After Treatment ($M\pm s$)

Parameter		Standard	Children with psoriasis (6-14 years)		Adults with psoriasis (23-63 years)
			before treatment	after treatment	
Leukocytes		4000-9000	5800±1350 (8)	6300±1000 (0)	—
Lymphocytes	abs.	1200-3000	2600±600 (33)	2560±600 (20)	—
	%	25-48	45±7 (33)	42±11 (50)	34±12 (29)
Neutrophils	abs.	2000-5500	2700±1000 (33)	3200±1100 (0)	—
	%	50-70	46±8 (67)	51±11 (56)	—
Monocytes	abs.	90-600	280±240 (25)	340±220 (10)	—
	%	3-11	5±4 (42)	5±3 (10)	—
Eosinophils	abs.	20-300	220±250 (42)	300±390 (20)	—
	%	0-5	4±5 (25)	4±5 (20)	—
Lymphocytes					
$CD3^+$	abs.	1000-2000	1700±400 (25)	1970±460 (75)	—
	%	40-80	70±5 (0)	75±7 (38)	58±16 (56)
$CD4^+$	abs.	500-1300	1000±300 (25)	1200±400 (25)	—
	%	20-60	40±6 (0)	45±11 (12)	42±11 (50)
$CD8^+$	abs.	200-700	620±340 (25)	600±120 (38)	—
	%	10-40	25±7 (0)	24±4 (0)	32±10 (50)
$CD72^+$	abs.	200-500	130±100 (38)	220±60 (50)	—
	%	5-19	5±2 (50)	8±2 (0)	22±13 (78)
$CD4^+/CD8^+$		1.0-2.5	1.80±0.6 (12)	2.00±0.60 (12)	1.4±0.7 (50)
Leukocyte proteins	abs.				
53K/H2A		≤0.25	0.43±0.10 (100)	0.35±0.12 (90)	0.37±0.09 (100)
43K/H2A		>1.6	2.97±0.66 (0)	2.40±0.49 (10)	1.83±1.29 (72)

Note. In parentheses: % patients with abnormal values of the parameter.

kocyte proteins also decreased (Table 1). After treatment, abnormal 53K/H2A and 43K/H2A parameters were registered in 90 and 10% children, respectively, which was paralleled by an increase in the number of patients with absolute abnormal $CD3^+$ and B-lymphocyte and relative neutrophil contents (Table 1).

The increased number of children with abnormal values of some leukocyte composition parameters after treatment associated with positive clinical dynamics does not allow to use these parameters for patient monitoring, because of the possibility of compensatory character of these abnormalies. However, 3 children, 13- and 12-year-old girls and in 14-year-old boy, showed an increase in leukocyte 53K/H2A content from 0.35 to 0.37, from 0.3 to 0.42, and from 0.33 to 0.6, respectively. Since both girls and the boy suffered from psoriasis for 3, 3 and 4 years, respectively (mean duration of the disease in the group — 2.2 years), the impairment of 53K/H2A parameter in these children is probably connected with enhanced torpidity and pathological changes of other systems and organs due to attenuated homeostasis induced by prolonged treatment and chronic pathology. The number of changed parameters of leukocyte composition in these children comprised 4, 5, and 6 corresponding to 53K/H2A increase.

The fact that 70% examined children showed improved 53K/H2A parameter, but in all children as least 1 leukocyte parameter became abnormal after treatment is important for the comparison between informative values of both methods of patient monitoring. Changes in leukocyte composition can present an individual compensatory reaction, which does not correspond to positive clinical dynamics and masks monitoring. This confirms that, in contrast to leukocyte population composition, their protein parameters can be used for clinical monitoring of treatment efficacy and individual reactivity of the patients.

The following dynamics of leukocyte protein parameters was registered in a patient hospitalized at the Institute of Dermatology and Venerology twice over a year. By the moment of the first hospitalization 53K/H2A and 43K/H2A parameters were 0.55 and 4.72, respectively, they decreased to 0.42 and 2.54 after routine methotrexate treatment (+liniment and phytotherapy) and were 0.45 and 2.99 by the time of discharge from the hospital. One month later and against the background of treatment with polyvitamins and trace elements, these parameters were 0.38 and 2.55, during exacerbation of chronic gastritis, colitis and viral infection they were 0.4 and 2.4, by second hospitalization, after prostatitis treatment at the urological department — 0.34 and 2.34, by the moment of discharge (treatment with essentiale, cytostatics, corticosteroids, laser and magnitotherapy, and vitamins) — 0.5 and 2.95. Thus, the examined parameters never reached the normal (<0.25 and >1.6 for 53K/H2A and 43K/H2A, respectively), which suggests that therapy is insufficient and new or more prolonged (in case of positive dynamics) treatment is required for patient recovery.

Normalization of protein parameters associated with skin recovery was achieved only in one child. However, multiple mechanisms of regulation of gene expression [1] suggest that complete clinical recovery can be achieved only after long-term maintenance of normal leukocyte protein parameters provided by stable compensatory state of the genome due to topological changes in DNA.

In conclusion, it is necessary to note that a significant correlation was found between 53K/H2A parameter before treatment and relative content of $CD3^+$, $CD4^+$, $CD8^+$, and $CD72^+$ lymphocyte subpopulations. Pierson correlation quotients were -0.66 ($p<0.05$), -0.72 ($p<0.01$), -0.58 ($p<0.05$), and -0.65 ($p<0.05$), respectively.

The examined of cell immunity parameters for monitoring of psoriatic patients has some disadvantages, however, other parameters can be more acceptable for monitoring of a particular or general pathology. In any case, evaluation of the immune status can help to select treatment strategy, which can be monitored by 53K/H2A and 43K/H2A leukocyte protein parameters.

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