GENETICS

Abnormalities of Human Genetic Apparatus Manifested in Leukocyte Proteins in Psoriasis

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The content of 53K/H2A and 43K/H2A proteins in leukocytes of patients with psoriasis, newborns, and healthy donors was studied. In all patients one or both parameters differed from normal. Mean values and distribution of 53K/H2A in healthy siblings of psoriatic proband significantly differed from those in newborns and donors. It was concluded that 53K/H2A is a marker of pathological changes in the genome responsible for predisposition to psoriasis. This marker can be revealed in peripheral blood leukocytes before skin manifestations of the disease.

Key Words: *psoriasis; leukocytes; protein markers of pathology*

Psoriasis is highly heritable (inheritance coefficient from 64-72% [2] to 91% [4]), widespread, chronic, relapsing, polygenic, and multifactor disease associated with hyperproliferation of skin cells. It was hypothesized that only predisposition to this disease is inherited [7]. The triggering factor of this pathology is poorly understood. It was recently hypothesized that disturbances in differentiation of peripheral blood lymphocytes (PBL) play a role in the pathogenesis of psoriasis. PBL can transform keratinocytes, infiltrate the skin, and release growth factors and/or immunomodulators [8-11].

Here we analyzed genetic aspects of the pathogenesis of psoriasis and predisposition to this disease by examining abnormalities in human genetic apparatus at the level of protein products of genes in PBL.

MATERIALS AND METHODS

Peripheral blood from patients and donors (3 ml) was stabilized with heparin (25 U/ml). Leukocytes were isolated as described previously [3]. Leukocyte proteins were analyzed by electrophoresis in polyacrylamide gel [6]. The content of 53 and 43 kDa proteins in PBL was measured by the amplitude of the corresponding densitogram regions after staining with Coomasse R-250 on a Jilford densitometer at 570 nm and standardized by the content of H2A histone.

Patients (n=108) from Central Skin Venerologic Institute with various forms of psoriasis aged from 6 to 69 years (mean age 30 years) were examined. By the moment of investigation the duration of the disease varied from several months to 44 years (more than 10 years in 59% patients). In 57% patients psoriasis was provoked by stresses and psychic trauma and in 22% by inflammatory and infectious diseases.

Control group consisted of 19 donors (Central Hemotransfusion Station, mean age 23 years). Histogram intervals were determined by the formula:

$$i=X_{max}-X_{min}/k,$$

where k=1+3.321lg$n$, X_{max}, X_{min} are extreme values for given sample, k is the number of classes determined by Sterdgers formula [1], n is the number of measurements. The limits for normal were set at the maximum and minimum in the modal classes of both distribu-

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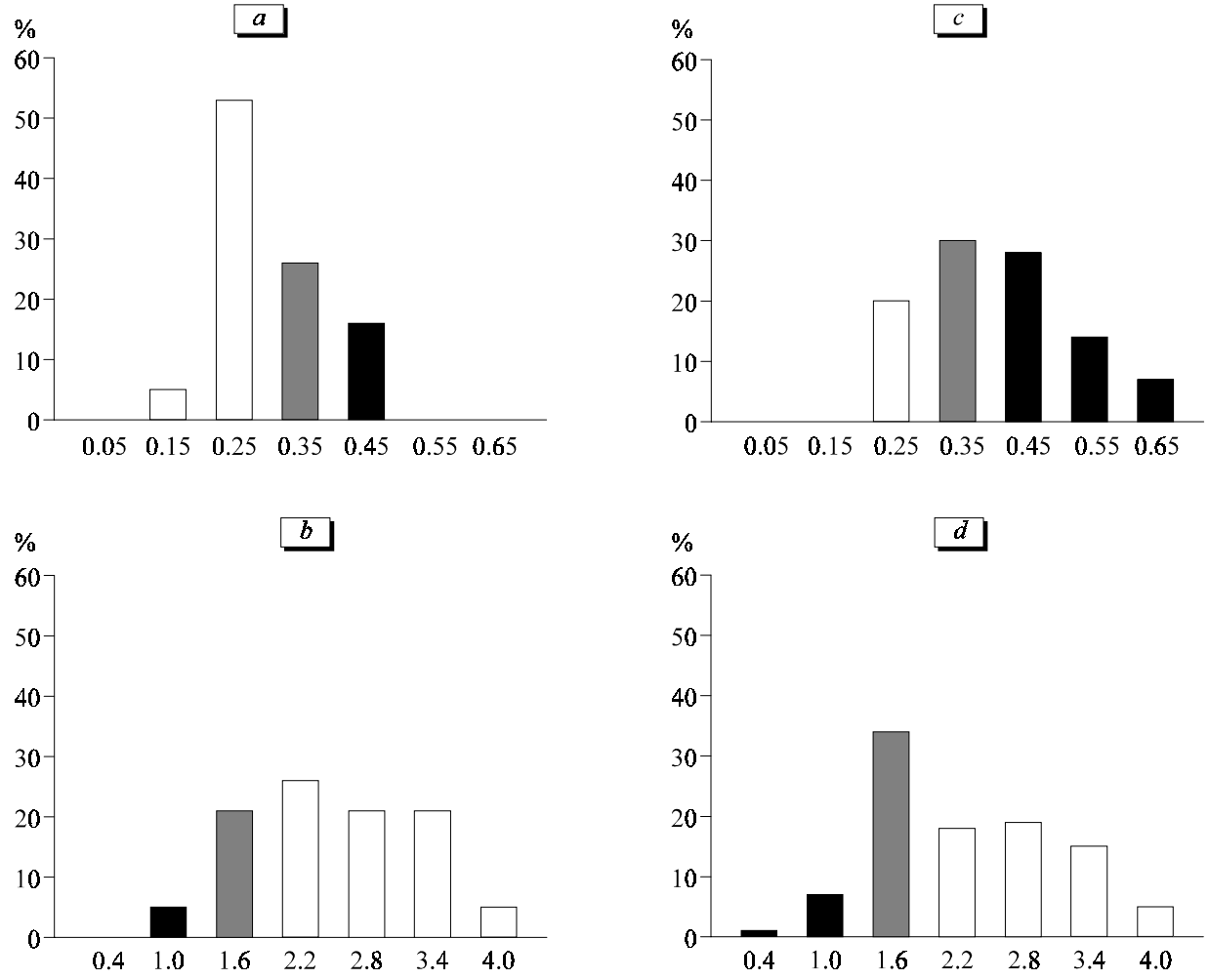

Fig. 1. Distribution of donors (*a, b*) and psoriatic patients (*c, d*) according to the content of 53K/H2A (*a, c*) and 43K/H2A (*b, d*) in the peripheral blood leukocytes. Open bars: normal; hatched bars: risk group; dark bars: maximum risk group.

tions (53K/H2A<0.25 and 43K/H2A>1.6, respectively). Risk groups (0.25<53K/H2A≤0.35 and 1.0<43K/H2A≤1.6) and maximum risk groups (53K/H2A>0.35 and 43K/H2A≤1.0) were specified.

The data were processed statistically using Student's *t* test.

RESULTS

In 80% psoriatic patients the ratio 53K/H2A in PBL was increased (>0.25) and the ratio 43K/H2A decreased (<1.6) in 42% patients (Fig. 1). Abnormal content of one or both proteins was found in all psoriatic patients.

Before treatment the 53K/H2A ratio in psoriatic patients differed significantly ($p<0.001$) from that in healthy donors (Table 1). These differences persisted after PUVA therapy ($p<0.05$) and disappeared after selective phototherapy (SPT) and drug therapy (DT). Thus, the efficiency of SPT and DT is similar and exceeds that of PUVA therapy. It can be assumed that UV sensitizers used during PUVA therapy can produce a negative effect.

Analysis of the relationship between index of normal and age showed that no siblings (mean age 10 years) could be included in the normal group (45%). It can be assumed that they differ from donors of the corresponding age though have no clinical manifestations of psoriasis.

When comparing the distribution of donors, newborns, and healthy siblings of psoriatic probands in groups corresponding to normal, risk, and maximum risk (basing on 53K/H2A parameter) we found that siblings differed significantly (χ^2 test) from newborns (8.15; $p<0.025$) and older donors (7.18; $p<0.05$). Student's *t* test also showed that siblings significantly differ from donors ($p<0.05$) and newborns ($p<0.025$) by the 53K/H2A ratio.

Thus, the relative content of 53K and H2A in blood leukocytes indicates genetic changes in siblings of psoriatic probands responsible for inherited predisposition to psoriasis. This confirms that psoriasis can-

TABLE 1. Relative Content of 53K/H2A and 43K/H2A Proteins in Leukocytes of Donors and Psoriatic Patients (*M*±*m*)

Protein	Donors (*n*=19)	Psoriatic patients (*n*=62)			
		before treatment	after treatment		
			PUVA (*n*=25)	SPT (*n*=25)	DT (*n*=12)
53K/H2A	0.25±0.07	0.36±0.12*	0.37±0.09**	0.31±0.10	0.32±0.11
43K/H2A	2.16±0.86	2.03±0.88	1.64±0.81	2.35±0.64	2.05±1.07

Note. *P<0.001, *p<0.05 compared to the donors.

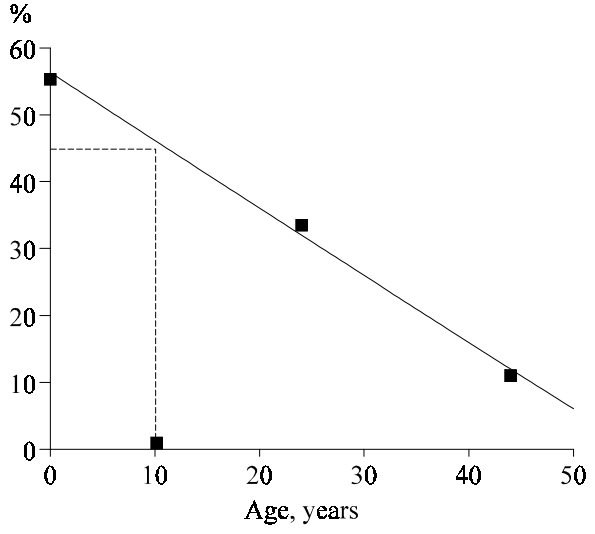

Fig. 2. Index of norm (% subjects with 53K/H2A<0.25) as a function of patient age for the group of newborns (*n*=2147), two donor groups (*n*=19, *n*=25), and siblings (*n*=6) of psoriatic probands.

not be regarded as skin pathology which agrees with conclusions of other authors [7-10].

The parameter 53K/H2A can be used for early diagnosis of genetic pathology in siblings of psoriatic probands, for psoriasis prophylaxis in families burdened with this disease, and for selection of therapeutic methods.

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