

INCREASED SERUM LEVELS OF THE PREGNANCY ZONE PROTEIN IN PSORIASIS

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Abstract. On the basis of immunological studies on psoriasis in recent years, it seems probable that immunological mechanisms are of importance and that psoriasis could be regarded as an immunogenetic disease. In this study, increased serum levels of an immunosuppressive factor, the pregnancy zone protein (PZ), were found in psoriatic patients. Patients with elevated levels (>2 S.D. units) of PZ showed a positive association with continuous symptoms and a negative association with blood groups A and Fy(a+b-). Thus, induction of PZ occurs mainly in psoriatic patients who have a particular genetic constitution. The results support the hypothesis that PZ is not only an immunosuppressive but also an immunoreactive protein.

Key words: Psoriasis; Pregnancy zone protein; Immunology

During the last few years new data have been published which indicate that immunologic mechanisms are involved in the etiology of psoriasis. Thus the levels of IgA (12), secretory IgA (18) and to some extent also IgE (13) have been found to be elevated among psoriatics. Anti-IgG has been detected both in serum (15) and in skin (16). This antibody (19), as well as antinuclear factor (14), has been detected on the surface of peripheral lymphocytes. Auto-antibodies directed against the stratum corneum have been found (17). The number of T-cells and the response to pokeweed mitogen and concanavalin A in the lymphocyte transformation test has been found to be reduced (14). The association between certain HLA antigens and psoriasis has attracted wide attention (24) and this association indicates an immunogenetic etiology of psoriasis.

PZ is an α_2 -globulin with a molecular weight of about 360 000 and a carbohydrate content of about 10% (21). PZ has been found in the sera of pregnant women (23), women taking oral contraceptives

(1) and males treated with estrogen for prostatic cancer (2). The serum level of PZ rises during pregnancy, but is low in spontaneous abortion compared with normal pregnancy of comparable gestation length (3). About 10% of all individuals seem to be low inducers of PZ, viz. they show only a small increase during pregnancy or treatment with oral contraceptives (4, 9, 22).

PZ has been shown to have immunosuppressive properties in vitro (8, 20). Furthermore, an increased serum level of PZ has been found to be associated with genetic incompatibility between mother and fetus (5). This observation indicates that PZ might be an immunoreactive protein. Consequently an elevated level of PZ could be expected in diseases with an immunogenetic background, such as psoriasis.

In this report we present data on the PZ level in a series of psoriatic patients from northern Sweden. This material has previously been studied with respect to associations with HLA antigens, blood groups, serum groups and red cell enzyme types (6) and with clinical parameters such as age at onset, and continuity of symptoms (7). In these studies, a fairly close relationship was found between psoriasis *per se* and certain phenotypes in the HLA, MNSs, and Lewis systems. Furthermore, in patients with continuous psoriatic symptoms the blood group factor A and the blood group Fy (a+b-) were overrepresented.

MATERIAL AND METHODS

In the serum samples of the psoriatic patients, the concentration of PZ ($\mu\text{g/ml}$) was measured by radioimmunoassay (10). These values were compared with those in a

Table I. Serum levels of PZ ($\mu\text{g/ml}$) in psoriatic patients and controls of different sex and age groups

Age group	Patients						Controls					
	Males			Females			Males			Females		
	M	S.D.	n	M	S.D.	n	M	S.D.	n	M	S.D.	n
15-24	11.6	12.5	7	43.5	59.6	13	7.8	8.3	58	9.9	10.6	49
25-34	21.2	21.3	6	171.6	271.7	9	4.8	5.0	40	23.2	22.9	33
35-44	17.2	20.0	11	70.5	14.6	5	14.6	15.1	26	48.7	57.8	29
45-54	33.9	35.3	11	113.1	125.2	8	18.6	18.7	35	48.8	71.8	47
55-64	694.2	301.0	12	74.7	51.7	9	16.0	16.8	36	93.1	57.1	53
65-	29.0	21.2	7	109.8	57.3	9	23.8	23.2	11	43.4	26.3	34

control material of apparently healthy women (11) and men (this investigation). Association with genetic markers (HLA antigen, the blood groups ABO, Rhesus, MNSs, Kell, Lewis and Duffy, the serum groups haptoglobin, Gc and third component of complement and the red cell enzymes PGM₁, 6-PGD and AK) and clinical parameters were also studied. In these studies, psoriatic patients with a PZ level higher than 2 standard deviation units above the normal level (considering age group and sex) were designated "high"; the others were called "low".

RESULTS

The PZ concentration was measured in the sera of 111 psoriatic patients, 55 males and 56 females. In Table I quantitative measurements are shown for

Table II. Relationship between PZ level and ABO groups, Duffy groups, and continuity of symptoms in psoriatic patients

Trait	PZ level			n
	Low	High	% high	
ABO groups				
A	46	9	16.4 ^a	55
B	9	2	18.2	11
AB	5	3	37.5	8
O	23	13	36.1 ^a	36
Total	83	27	24.5	110
Duffy groups				
Fy(a+b-)	23	1	4.2 ^b	24
Fy(a+b+)	38	13	25.5	51
Fy(a-b+)	22	12	35.3	34
Total	83	26	23.9	109
Symptoms				
Continuous	39	20	33.9 ^c	59
Intermittent	39	5	11.4	44
Total	78	25	24.3	103

^a $P < 0.05$. ^b $P < 0.025$. ^c $P < 0.01$.

107 patients and controls. Four patients were below 15 years of age and control material was lacking for these. Of the patients, 28 individuals had values higher than 2 standard deviation units above normal values, which is significantly higher than expected ($P < 0.001$). Due to the large standard deviations and the small numbers, none of the comparisons (considering sex and age group) in Table I is statistically significant. In eleven out of twelve trials, however, the mean PZ level was higher in the psoriatic patients than in the controls ($P < 0.01$). One male patient in the age group 55-64 had a very high PZ level, due to estrogen treatment for prostatic cancer. This patient was excluded from subsequent studies. Even without this patient the mean PZ level for the age group 55-64 was higher in the patients than in the controls. The relationship between high (> 2 S.D.) PZ level and genetic markers was studied. No significant associations were found between high PZ and markers, which are associated with psoriasis *per se* (HLA, MNSs, and Lewis). However, a relationship was found with continuity of psoriatic symptoms and with the ABO and Duffy blood groups (Table II). The frequency of patients with a high PZ level was lower in blood group A ($P < 0.05$), higher in blood group O ($P < 0.05$), lower in the Fy(a+b-) blood group ($P < 0.025$) and higher in patients with continuous symptoms ($P < 0.01$).

DISCUSSION

The results show that the PZ level is elevated in psoriatic patients and that this increase is associated with continuity of symptoms and with two genetic marker systems, ABO and Duffy.

The situation is further complicated by the fact that we have shown earlier (7) that continuity of symptoms is positively associated with blood

Table III. Combined effect of continuity of symptoms and ABO and Duffy blood groups on the PZ level in psoriatic patients

Symptoms	Blood group	High PZ level		No. examined
		n	%	
Continuous	A	7	20.6	34
Continuous	'Not A'	13	52.0 ^a	25
Intermittent	A	1	5.6	18
Intermittent	'Not A'	4	15.4	26
Continuous	Fy(a+b-)	1	5.3	19
Continuous	'Not Fy(a+b-)'	19	47.5 ^a	40
Intermittent	Fy(a+b-)	0	0.0	3
Intermittent	'Not Fy(a+b-)'	5	12.2	41

^a $P < 0.001$.

groups A and Fy(a+b-). These complex relationships are illustrated in Table III, which shows the combined effect of blood groups and continuity of psoriatic symptoms. The frequency of individuals having a high PZ level showed a highly significant increase in the combinations "continuous, not A" ($\chi^2 = 13.79$, 1 D.F., $P < 0.001$) and "continuous, not Fy(a+b-)" ($\chi^2 = 19.18$, 1 D.F., $P < 0.001$). In these combinations about 50% of the patients had a high PZ level. Furthermore, in 17 patients with continuous symptoms and lacking both A and Fy(a+b-), 12 (71%) had a high PZ level. These results can be given the following alternative interpretations:

1. The etiology of psoriasis includes certain immunological, possibly autoimmune, episodes, which in their turn trigger the induction of the "immunoreactive protein" PZ in individuals having a certain genetic constitution.

2. The induction of PZ is caused by the treatment given to psoriatic patients, but is dependent on the genetic constitution.

Since the patients have not been subject to an exhaustive investigation concerning all previous medication, it is not possible at present to distinguish with certainty between these two alternatives. The association with continuous symptoms is consistent with both explanations. Patients with constant symptoms may have a genetic constitution which renders them more likely to produce PZ, but on the other hand patients with constant symptoms are likely to have received more medication than those with intermittent symptoms. Many psoriatic patients receive topical treatment with corticosteroids, but there is no evidence so far that corticos-

teroids are inducers of PZ. Patients with sarcoidosis, frequently treated with corticosteroids, have been found to have normal serum levels of PZ (unpublished observation). Estrogen, which is the only known steroid inducer of PZ, is not likely to have caused the increase in PZ, since there was no significant difference between males and females (cf. Table I), and the only male who was treated with estrogen was excluded from the analysis.

To sum up: The PZ level is elevated in psoriatic patients. This increase is associated with certain genetic factors and with continuity of symptoms. The increase may be caused either by the treatment or by the disease itself, most likely the latter.

The results lend some support to the hypothesis (5) that immunological reactions may stimulate the production of PZ and thus that PZ is not only an immunosuppressive but also an immunoreactive protein. To further substantiate this hypothesis it would be of interest to examine the PZ level in diseases with a well-defined immunogenetic and preferably autoimmune etiology.

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