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HEMATOLOGICAL CHANGES IN PSORIASIS

Secondary Anemia, XVIII

Lars Molin and Peter Reizenstein

From the Departments of Dermatology and Internal Medicine, Karolinska sjukhuset, Stockholm, Sweden

Abstract. Hematological changes were studied in psoriasis. Although these changes are so mild that the psoriatics, as a group, have no significant anemia, the individual hemoglobin and serum iron concentrations are nevertheless significantly correlated to the severity of the psoriatic lesions, to each other, and to the serum albumin concentration. Serum albumin values are significantly lower in severe than in mild psoriasis. The reticuloendothelial (RE) activity was estimated by measuring the blood clearance of colloidal radiogold and of ^{51}Cr-labelled, heat-sensitized erythrocytes. The results of the two tests were closely correlated. The RE-uptake of ^{51}Cr-labelled erythrocytes was significantly more rapid in psoriatics than in controls. While, in psoriasis, hematologic changes per se are not particularly relevant, the investigation shows that even mild psoriasis in a relatively inactive phase causes changes in iron, albumin, and erythrocyte turnover.

Anemia is a well known complication of inflammatory and malignant diseases (2, 3, 8, 9). Its pathogenesis is, however, only partly understood. In cases of malignant tumour, increased consumption or iron and folates has been proposed because of increased cellular proliferation. In patients with inflammatory diseases a decreased intestinal iron absorption has been proposed (4, 10). Previous results suggest that increased uptake in reticuloendothelial (RE) cells of both iron and red cells could explain the secondary anemia (9).

Psoriasis is a condition of considerable interest because the inflammatory changes, such as the epidermal Munroe microabscesses and a mild dermal inflammatory cell infiltrate, are quite small, and because the increased proliferation of epidermal cells is of a non-neoplastic nature. Our purpose therefore was to investigate the pathogenesis of anemia in psoriasis.

MATERIAL

The present investigation consisted of a retrospective part, a follow-up part, and a special hematological part. In the *retrospective part* all patients hospitalized for treatment of psoriasis at the Department of Dermatology, Karolinska Sjukhuset, Stockholm, during the four-year period 1966–69 were included. This series comprised 417 patients who had been treated on 543 occasions. If a patient had been treated for psoriasis on several occasions, only the first occasion in each year was taken into consideration.

The follow-up part comprised 300 psoriatics earlier hospitalized because of psoriasis more than 5 years previously at any of the three departments of dermatology in the region of Stockholm (Karolinska sjukhuset, St. Görans sjukhus, Södersjukhuset). This series has been described in detail elsewhere (6). With some exceptions all the psoriatics were in employment and could thus not be considered as real patients as they had not themselves sought medical care but were invited to the follow-up investigation. Some individuals were included in both the retrospective and the follow-up series, though on different occasions.

Special hematological part comprised 18 of the psoriatics in the follow-up series. They were included because they had neither any history of hematological, gastro-intestinal, kidney, or liver disease, nor any other complicating disease such as joint involvement clinically or roentgenologically, present or recent infections, or increased alcohol consumption.

As controls in the special hematological part of the investigation 23 healthy volunteers (14 males and 9 females) were used who had no history of abnormal bleeding, anemia, or iron therapy. None of them had been a blood donor. None had received medical treatment during the year prior to investigation, and all of them were working. None of the female controls had been pregnant during the last year.

METHODS

In the *retrospective part* information was taken from the case records concerning age at onset of psoriasis, severity and duration of the disease at admission, and the occurrence

Table I. *Severity of psoriasis in the psoriatics investigated*

The extent is given in per cent of body surface

	Males	Females
Extent of psoriasis		
Retrospective series		
Less than 30 %	199	166
More than 30 %	108	70
Follow-up series		
Less than 30 %	104	166
More than 30 %	23	7
Special hematological series		
Less than 30 %	9	5
More than 30 %	2	2
Intensity of psoriasis		
Follow-up series		
Minimal or mild	64	138
Moderate or severe	63	35
Special hematological series		
Minimal or mild	5	6
Moderate or severe	6	1

and types of joint complaint and of concomitant other disease. The severity of the psoriasis was graded regarding the percentage involvement of the body surface (extent) and the intensity of the lesions, on a four-graded scale based mainly on the palpable infiltration (Table I). The grading system has been described in detail (6). The following laboratory variables were studied on admission to the hospital: hemoglobin concentration (Hb), red and white blood cell counts (RBC, WBC), differential cell count (neutr, eos, bas, lymph, mono) serum iron concentration (SeFe), total iron binding capacity (TIBC), erythrocyte sedimentation rate in one hour (ESR) and serum protein electrophoresis (alb, alfa-1, alfa-2, beta, gamma).

In the *follow-up part* all psoriatics were personally examined regarding the extent and intensity of the psoriatic lesions, and the joint involvement. The laboratory investigations mentioned above were performed at the time of examination together with investigations concerning liver (transaminases S-GOT, S-GPT, bilirubin and alkaline phosphatase concentrations) and kidney (serum creatinine concentration, osmolarity of the urine) function. Customary methods in the Central Clinical Laboratory at the Karolinska sjukhuset were used for the laboratory investigations mentioned.

The psoriatics included in the *special hematological part* were studied in detail concerning liver function (intravenous bromsulfthalein and galactose tests, fine needle biopsy) and concerning the plasma iron and plasma folic acid clearance and the function of the reticuloendothelial system.

The method of folate bio assay and of estimating the serum folate clearance rate after an intravenous dose of 15 μg folates per kg body weight has been described (2) as has the method of studying the ^{59}Fe-clearance rate from the plasma (9, 14).

After an intravenous injection, about 95 % of a colloidal ^{198}Au dose is taken up by the RE cells, and we attempted to use the clearance rate of ^{198}Au to estimate RE-function. When a tracer dose of gold is used, hepatic circulation may influence the results. For this reason, 7 mg carrier colloidal gold was given in the present study, together with the ^{198}Au. The method has been described (14).

An alternative method to estimate the RE-uptake is to inject the patient's own, ^{51}Cr-labelled, heat-sensitized erythrocytes. Ten ml of blood, sensitized at 49,5°C for 20 minutes, are incubated with 50 μCi ^{51}Cr in sterile ACD-solution for 30 minutes, and 100 mg sterile ascorbic acid is added. Ten ml of the mixture is reinjected intravenously, and blood samples taken after 5, 10, 15, 20, 30, and 45 minutes. To evaluate the effect of heat sensitization, the fraction of deformed erythrocytes is counted in a smear of the heated blood. The fraction of heat-sensitized, deformed cells thus counted was closely correlated with the fraction obtained with a kinetic method as described below.

In some cases the ^{198}Au clearance curves were single exponential functions, and here the slope of this function is given. In other cases, these curves described multiple exponential functions, and here the slope is given for the first of the exponential functions, which was obtained by the graphic subtraction method previously described (7).

^{51}Cr-curves were always corrected for the fraction of erythrocytes which were not adequately sensitized during the sensitization procedure and which would thus not be cleared from the circulation, but would have a "normal" red cell life span. This fraction was calculated by letting a computer subtract different constants from the values in the clearance curve until a maximum value for the coefficients of correlation between the radioactivity and the time was obtained. The ^{51}Cr slope given, Cr Ic, is the one corresponding to the function giving this maximum correlation coefficient. It was thus assumed that, within the family of curves studied, the maximum correlation coefficient denotes the minimum spread around a single exponential function.

The slopes or "k-values" given are defined as the fractional decrease per minute in the serum concentration of ^{51}Cr, ^{198}Au, ^{51}Fe or folate. Thus $k = 0.693/(T\ 1/2)$.

Conventional statistical methods were used. Differences

Table II. *Hemoglobin and serum iron concentration in psoriatics*

	n	Mean	S.E. of mean	S.D.
Hemoglobin (g/100 ml)				
Retrospective series				
Men	307	14.2	0.07	1.31
Women	236	13.1	0.07	1.12
Follow-up series				
Men	124	14.4	0.09	0.97
Women	172	13.1	0.07	0.94
Serum iron (μg/100 ml)				
Retrospective series				
Men	55	76.4	7.7	57.3
Women	53	79.6	7.2	52.7
Follow-up series				
Men	126	112.5	3.7	41.5
Women	169	111.1	3.3	43.4

Table III. *Differences in hematological variables in psoriatics with mild (=minimal or mild) and severe (moderate or severe) forms or psoriasis*

Retrospective series

Hematological variable	Severity of psoriasis	No. of patients	Mean	Statistical significance of difference between mild and severe
Hemoglobin concentration (g/100 ml)				
Men	Mild	199	14.57	***
	Severe	108	13.46	
Women	Mild	166	13.23	***
	Severe	70	12.58	
Serum iron concentration (μg/100 ml)				
Men	Mild	16	137.6	***
	Severe	39	51.3	
Women	Mild	25	110.0	***
	Severe	28	52.4	
Total iron binding capacity (μg/100 ml)				
Men	Mild	7	348.1	—
	Severe	25	284.8	
Women	Mild	12	315.4	—
	Severe	20	288.0	
ESR (mm/hr)				
Men	Mild	198	16.7	***
	Severe	108	38.1	
Women	Mild	163	16.6	***
	Severe	69	34.8	
White blood cells (hundreds/mm³)				
Men	Mild	198	74.26	***
	Severe	108	89.89	
Women	Mild	166	74.56	*
	Severe	66	83.01	

* $0.05 > p > 0.01$; ** $0.01 > p > 0.001$; *** $p > 0.001$.

between mean values were tested with Student's *t*-test. The relationship between quantitative and semi-quantitative variables was tested by correlation analysis.

RESULTS

Table II shows that the psoriatic persons had statistically significant anemia neither while in the hospital (retrospective series) nor during follow-up. The mean serum iron values were significantly lowered when the patients were ill and admitted to hospital (retrospective series) though not later, during follow-up. Although the mean hemoglobin values were not lowered, individual values were significantly correlated to the extent of the psoriatic lesions ($r = -0.149$, $p < 0.001$). So also were the serum iron concentrations ($r = -0.479$, $p < 0.001$), though not the total iron-binding capacities.

Table IV. *Differences in albumin and alfa-2 globulin concentration in psoriatics with mild and severe forms of psoriasis*

Retrospective series

Serum protein fraction	Severity of psoriasis	No. of patients	Means	Statistical significance of difference between mild and severe
Albumin				
Men	Mild	33	45.91	***
	Severe	37	41.11	
Women	Mild	19	44.37	**
	Severe	21	39.43	
Alpha-2 glob.				
Men	Mild	33	0.53	**
	Severe	37	0.64	
Women	Mild	19	0.56	*
	Severe	21	0.68	

There were statistically highly significantly lowered hemoglobin values and serum iron values, as well as higher erythrocyte sedimentation rates, in the patients who were admitted for more severe forms of psoriasis, than in those with milder forms of the disease (Table III). The same relationship was found between the severity of psoriasis and the hematological values studied in psoriatics with and without joint involvement.

Serum proteins were essentially normal during the follow-up, when the psoriasis persons were well. When the patients were ill and admitted to hospital (retrospective series) there were changes correlated to the severity of the skin lesions. Those with more severe psoriasis had significantly lower serum albumin and higher alfa-2-globulin values than those with milder psoriasis (Table IV).

The anemia was significantly correlated both to the severity of the skin disease, and to the serum iron, ESR, and serum albumin. The more pathologic the latter were, the more anemic were the patients (Fig. 1). In principle, a similar correlation pattern was found for the serum iron (Fig. 2).

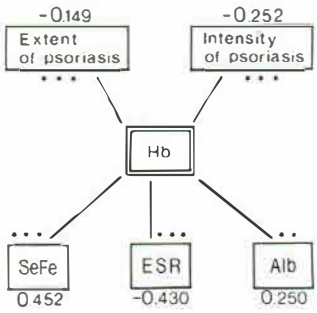

Fig. 1. Significant correlations of anemia to severity of psoriasis, and to other hematological variables. Retrospective series. Figures indicate correlation coefficients. *** = $p < 0.001$; ** = $0.01 > p > 0.001$.

There was a statistically significantly ($0.01 < p < 0.001$) more rapid RE uptake of ^{51}Cr-labelled erythrocytes in psoriatics than in controls, even though this was examined during follow-up, when the disease was relatively inactive. Numerically speaking, the plasma iron clearance was also more rapid in psoriasis than in controls, but these differences were not statistically significant (Table V).

The results of the two methods of measuring the RE uptake were significantly correlated to each other, and also to the folate clearance rate ($r = +0.726$, $0.05 > p > 0.01$).

Table V. *Reticuloendothelial (RE) uptake and radioiron clearances (fraction/minute)*

Variables	Psoriasis *n*	Psoriasis Mean±S.D.	Controls *n*	Controls Mean±S.D.
RE uptake				
CrIc	10	0.15±0.10	23	0.075±0.029
AuKI	13	0.14±0.08	12	0.165±0.055
Iron clearance rate (FeK)	13	0.009±0.004	8	0.007±0.002
Folate clearance (FAK)	13	0.06±0.02	6	0.10±0.07

DISCUSSION

Two facts seem clear. The first is that hematological changes in psoriasis are very mild, so mild in fact that several previous studies could hardly detect them at all (1, 5, 11), although some anemia (12) and hypoferremia (13) have been described.

The second is that although they are so mild, the hematological changes are clearly correlated, not only to the severity of the psoriatic lesions, but also to each other.

The correlation pattern found suggests that it is the patients with the lowest serum albumin and serum iron who are the most anemic. This pattern has also been found in anemias secondary to rheumatoid arthritis (3, 8), cancer (2, 9), and trauma (14). It is suggested that these forms of secondary or symptomatic anemia may have a common pathogenesis. The present investigation of anemia in psoriasis is relevant not because of the clinical symptoms of anemia—clearly these would be negligible in most psoriatic cases—but because of the fundamental, possibly common pathophysiologic mechanism which causes hypoalbuminemia, hypoferremia and anemia in patients with so seemingly diverse diseases as rheumatoid arthritis, cancer, and psoriasis.

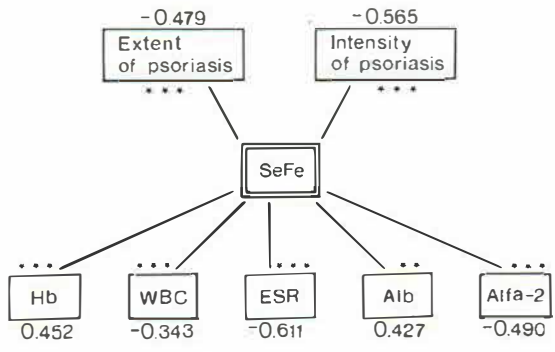

Fig. 2. Significant correlations of serum iron concentration to clinical and other hematological variables. Retrospective series. Figures indicate correlation coefficients. *** = $p < 0.001$; ** = $0.01 > p > 0.001$.

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L. Molin. M.D
Department of Dermatology
Regionsjukhuset
S-581 85 Linköping
Sweden