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HL-A ANTIGENS (17, 27, UPS) IN PSORIASIS WITH SPECIAL REFERENCE TO PATIENTS WITH ARTHRITIC LESIONS

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Abstract. Fifty patients with longstanding and severe psoriasis vulgaris have been tissue-typed. HL-A 17 and 27 from second sublocus and UPS from third sublocus have been found to occur in increased frequency. HL-A 27 was found to be more prevalent among those with arthritic lesions. The lack of significantly increased frequency of HL-A 13 is discussed.

Key words: Psoriasis; Psoriatic arthritis; Histocompatibility antigens; Sacro-iliac joints

The possible immunological and biological significance of the correlation between the presence of certain specific HL-A antigens and specific disease states has been widely studied and discussed in recent years (12).

A statistically significant association between the presence of HL-A antigens 13 and 17 and psoriasis has been observed by different research groups (8, 13, 15, 17, 18). Patients who have HL-A 17 seem to have a more severe form of psoriasis than those with HL-A 13 (9). However, this finding has been debated by others (18).

In the original description of the correlation between HL-A antigens 13 and 17 and psoriasis, neither of these particular HL-A specificities was found to be particularly prevalent in patients with arthritic lesions (18). In two recently published reports (4, 20) HL-A 27 was found in a high proportion of psoriatic patients with peripheral arthropathy, sacro-iliitis and spondylitis. Many other diseases, which are either characterized by arthritis, sacro-iliitis and spondylitis as a primary symptom, or as a secondary phenomenon, have been described as being associated with a high frequency of HL-A 27 (1, 3, 4, 6, 14, 19).

In the present study we have investigated the presence of HL-A antigens, mostly among inpatients with psoriasis vulgaris treated at the Department of Dermatology, Karolinska sjukhuset.

This selection of patients means that they represent more severe and longstanding cases of psoriasis, half of them also with arthritis.

In our study we have also included HL-A antigens belonging to the third sublocus.

MATERIAL AND METHODS

Fifty Swedish unrelated patients with psoriasis vulgaris, 31 men and 19 women, were included in the present study. The average age of the men was 47.5 years (±14.7 standard deviation (S.D.)) and women 50.3 years (±24.6 S.D.). The mean duration of their psoriasis was, for the men, 16.5 years (±12.4 S.D.) and for the women, 15.2 years (±10.6 S.D.). 47 of these patients were hospitalized; 3 were outpatients at the time of the study.

48 patients were X-rayed for changes in their sacro-iliac joints. Two projections were used: 1) antero-posterior projection, 2) postero-anterior projection. The roentgenograms were read on two different occasions by a radiologist (Associate Professor Nils Lindvall, Radiological Department, Karolinska sjukhuset, Stockholm). The radiological criteria for sacro-iliitis were used according to L. Diethelm's handbook of medical radiology (5). Only those patients with unequivocal signs of sacro-iliitis were included.

47 of these patients were evaluated for the presence of arthritic lesions in peripheral joints, either by physical examination (42 patients) by one of us (J. M.) or by studying the case reports (5 patients). Those classified as positive fulfilled the criteria formulated by Moll & Wright (10) with the exception that no patient with solely arthralgias or stiffness of the joints was included. X-ray examinations of peripheral joints were performed in only 5 patients, when a differential diagnosis between primary osteoarthrosis and arthritis of the distal interphalangeal joints of the fingers could not be settled by physical examination.

No grading of the severity of arthritic lesions was performed.

Serological examination (Rose-Waaler test) as described by Svartz (16) was performed for the presence of rheumatoid

Table I. *Frequency of HL-A specificities in 50 psoriasis vulgaris patients, 25 of whom with concomitant arthritis.*

	50 psoriasis patients	25 patients with arthritis	100 controls
First HL-A locus			
HL-A 1	15 ns[a]	10 ns	20
HL-A 2	33 ns	15 ns	55
HL-A 3	15 ns	7 ns	23
HL-A 9	9 ns	4 ns	26
HL-A 10	4 ns	4 ns	8
HL-A 11	4 ns	1 ns	15
HL-A 28	3 ns	1 ns	9
W 19	3 ns	2 ns	12
W 32	2 ns	1 ns	6
Second HL-A locus			
HL-A 5	4 ns	—	11
HL-A 7	7 ns	3 ns	29
HL-A 8	9 ns	5 ns	16
HL-A 12	7 ns	3 ns	15
HL-A 13	2 ns	—	2
HL-A 14	—	—	5
HL-A 17	11 $p<0.01$	5 ns	5
HL-A 27	17 $p<0.01$	12 $p<0.001$	14
W 5	4 ns	1 ns	16
W 10	6 ns	3 ns	18
W 15	14 ns	8 ns	26
W 16	4 ns	3 ns	5
W 18	2 ns	2 ns	5
W 21	1 ns	—	3
W 22	1 ns	—	11
TT	1 ns	—	1
SL	1 ns	—	1
Sabell	1 ns	1 ns	0
TY	3 ns	3 ns	3
Third HL-A locus			
W 20	5 ns	3 ns	9
UPS	16 $p<0.01$	10 $p<0.01$	12

[a] ns = not significant.

factor in all patients with peripheral joint involvement. According to the norm of the laboratory, a titre of 1/64 was considered weakly positive and 1/128 and higher as positive.

Tissue typing

Cells were tissue typed by the method described by Kissmeyer-Nielsen & Kjerbye (7). Determinations of the following HL-A specificities were performed:

First locus: HL-A 1, 2, 3, 9, 10, 11, 28, W19, W32.

Second locus: HL-A 5, 7, 8, 12, 13, 14, 17, 27, W5, W10, W15, W16, W18, W21, W22, TT, SL, Sabell, TY.

Third locus: W20, UPS.

Most sera used for tissue typing were obtained by the Scandiatransplant organization.

The controls consisted of 100 healthy unrelated blood donors.

Statistical methods

Standard χ^2-test and Fisher's exact test were used, the latter method when one or more of the expected numbers in the 2×2 table were less than five. Significance was assigned to frequency differences when p values were less than 0.01.

RESULTS

No significant differences in antigen frequencies were obtained for alleles of the first HL-A locus (Table I). A significant difference could be shown in the second sublocus for HL-A 17 and HL-A 27 (Table I). Thus HL-A 17 occurred in 22% of the patients, compared with 5% in the control group, and HL-A 27 in 34% compared with 14%. Within the third locus alleles, antigen UPS was found in 32% of patients, compared with 12% in controls. All these differences are significant ($p < 0.01$). No significant decreases in antigen frequencies were recorded.

25 of the studied patients had arthritic lesions (Tables I, II). 12 patients (48%) had HL-A 27 ($p < 0.001$ when compared with the control group). 10 (40%) had the antigen UPS from the third sublocus ($p < 0.01$). HL-A 17 was present in 5 cases (20%). However, this difference was not significant, compared with the control group. Even in the joint group there were no significant differences within the first sublocus.

In Table II we have listed all the patients with involvement of the joints. HL-A 27 occurs in 3 out of 11 patients with sacro-iliitis only, in 7 out of 11 patients with both sacro-iliitis and peripheral joint involvement and 2 out of 3 patients with peripheral arthritic lesions only. Two patients had a positive Rose-Waaler test (titre $\geq$ 1/128) and both patients were positive for HL-A 27. Extra reactions with two antisera, with known specificities of HL-A 9 in one case and HL-A 9, 14, W16, W18 in the other, occurred with cells from 19 of the patients in this study.

DISCUSSION

In earlier reports, an increased frequency of HL-A 13 as well as of HL-A 17 has been demonstrated among psoriatic patients (8, 13, 15, 17, 18). In our study only HL-A 17 and 27 from second sublocus occurred at a significantly higher frequency. This difference in results between the present patient material and earlier reported ones could possibly be due to our selection of patients. Thus most of our patients had such a degree of disease that hospital treatment was indicated. In an American study (9) it was found that patients positive for HL-A 17 had a more severe form of disease than those that were HL-A 13 positive.

It has been demonstrated earlier that a correlation exists between the degree of severity of psoriatic disease and the presence of arthritic lesions (11).

Table II. *25 patients with arthritic lesions; clinical, radiological and laboratory findings*

Patient	Age	Sex	Duration of psoriasis (years)	Duration of joint involvement (years)	Rose-Waaler titre	Sacro-iliitis	Peripheral arthritis	Phenotype
A. B.	63	♀	7	14	1/32	+	+	9, W32, W5, 27, W20
R. B.	43	♂	22	10	1/16	+	+	1, 2, 8, W10, (UPS)
G. G.	80	♀	17	17	Neg.	+	+	2, 10, 7, W18
B. J.	45	♂	10	10	1/128	+	+	2, 3, 27, W15
S. K.	40	♂	11	3	1/8	+	+	1, 11, 27, W18
W. K.	57	♂	12	2	Neg.	+	+	1, 10, 8, W16
G. L.	41	♂	21	1	Neg.	+	+	1, 2, 27, TY, (UPS)
I. N.	65	♀	7	34	Neg.	+	+	1, 8, TY
K. Å.	10	♀	5	1	1/16	+	+	2, 10, 27, W15, (UPS)
B. L.	35	♀	20	6	Neg.	+	+	3, 9, 27
N. S.	70	♂	13	16	Neg.	+	+	1, 3, 8, 27
H. A.	63	♀	30	–	–	+	–	2, 9, W15, W16, (UPS)
L. G.	48	♂	33	–	–	+	–	1, 2, 12, 17
E. H.	52	♂	29	–	–	+	–	2, W19, 12, 17
H. L.	32	♂	7	–	–	+	–	2, 10, W10, TY, (UPS)
G. L.	17	♀	2	–	–	+	–	1, 3, 7, 17
B. S.	71	♂	4	–	–	+	–	2, W15, 27, (UPS)
U. S.	20	♀	6	–	–	+	–	2, 17, 27, W20
P. O.	69	♂	26	–	–	+	–	1, 3, 7, W15
T. B.	62	♂	17	–	–	+	–	2, 3, W16, (Sabell), (UPS)
P. M.	59	♂	29	–	–	+	–	2, 9, W15, W10, (UPS)
M. S.	29	♂	14	–	–	+	–	3, W15, 27, (UPS)
G. N.	46	♂	8	1	Neg.	–	+	2, W19, 27, W15, (UPS)
B. L.	43	♂	35	8	1/128	–	+	2, 12, 27, W20
E. B.	59	♀	42	2	1/8	–	+	1, 28, 8, 17

In our group of patients a very high proportion showed joint involvement and a strong association to HL-A 27. Zachariae et al. reached the same conclusion (20).

These results thus indicate that tissue typing could be of value for a prognostic evaluation of disease. Interestingly, an increased frequency of HL-A 27 has been found in many diseases involving arthritis (1, 3, 4, 14, 19). The significance of these findings is quite clear, thus individuals positive for HL-A 27 have a higher relative risk of developing arthritis than those who lack this antigen (12).

In this report we have not made the usual distinction between sero-positive and -negative arthritis and excluded those who where seropositive. The finding that 2 of our patients had seropositive arthritis as well as HL-A 27 might indicate that the concept of psoriatic arthritis should be re-evaluated on the basis of the HL-A system.

The significance of the increased frequency of UPS is difficult to evaluate as it has never been reported before. It might be accidental. We have no explanation for the extra reactions with the two antisera (containing anti HL-A 9 in one case and anti HL-A 9, 14, W16, W18 in the other) in 19 of our patients.

The finding of an association between certain HL-A specificities and psoriasis implies a genetic predisposition to disease in certain individuals. In order to assess what possible gene(s) is (are) involved, further analysis of families with an increased incidence of psoriasis will be necessary. Since psoriasis also occurs in patients who lack either antigens (17), the gene(s) involved is (are) probably not identical with the gene for either HL-A antigen. Thus this makes the alternative of cross-reactions less possible between hypothetical causative agents and the gene products of HL-A 13 and/or 17 on cell surface, as has been suggested (2). The more likely mechanism underlying susceptibility to disease would be the presence or absence of specific gene(s) close to the HL-A-locus, which is believed to be carried by the autosomal chromosome no. 6 (12). Associations between HL-A antigens and disease would then be revealed because of genetic linkage disequilibrium in this region. Other markers, such as the MLC genes, are present in this chromosome, which might be most useful in the further analysis of the mapping

of gene(s) responsible for increased risk of developing psoriasis.

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