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THE RELATION OF HL-A ANTIGENS TO LIVER HISTOLOGY IN METHOTREXATE-TREATED PSORIATICS

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Abstract. A total of 45 patients with severe psoriasis vulgaris treated with Methylaminopterin NFN (Methotrexate Lederle) were HL-A typed in order to seek a possible correlation between HL-A antigens and the histological abnormalities in post-Methotrexate (MTX) liver biopsies. Highly significantly increased frequencies of w17 and TY ($p<0.0001$) were found, while HL-A13 was only slightly increased. No statistically significant correlations were found between HL-A antigens and liver histology. HL-A typing does not seem to be of any predictive value in the pre-MTX screening of psoriatics in order to rule out patients with a high risk of liver damage during long-term MTX therapy.

Key words: HL-A antigens; Psoriasis; Methotrexate; Liver histology

It has become increasingly obvious (4, 9, 10) that the prolonged use of MTX is often hepatotoxic even in the small doses given for psoriasis.

Extensive pre-MTX screening of psoriatics becomes mandatory to prevent high-risk patients from being exposed to MTX therapy. This screening has hitherto included a clinical history, liver function tests and liver biopsy. As elevated levels of certain HL-A histocompatibility antigens have been found in patients having long-lasting liver disease with the histological picture of chronic aggressive hepatitis (1, 2, 7), it is possible that HL-A typing might also be of predictive value.

The purpose of this study was to seek a possible correlation between HL-A antigens and the histological liver abnormalities in 45 MTX-treated psoriatics.

MATERIAL AND METHODS

A total of 45 patients with severe psoriasis vulgaris (8) had been treated with Methotrexate in weekly, single, oral doses of 25 mg (maximum). Before the patients underwent a control liver biopsy between February and April 1974 at the Finsen Institute, they were HL-A typed (6). In 43 of these cases, a suitable liver biopsy was obtained and evaluated as described elsewhere (8, 9, 10). Fisher's exact test (13) was used for an inter-patient comparison of the antigen frequencies and between the patients and 424-1967 healthy unrelated controls (14). All patients were investigated for all antigens listed in Tables II and III, and most of these antigens (including HL-A 13 and w17) were studied in all controls, but the TY antigen was studied in only 424 controls.

RESULTS

There were 17 male and 28 female patients. The average age was 53 years (range 28–75 years). In 9 males and 24 females, psoriasis had started before the age of 30. The average total dose of MTX was 3516 mg (range 175–8355 mg). In addition to psoriasis vulgaris, 6 patients had psoriatic arthropathy (8) while none had pustular psoriasis.

Table I gives the frequencies in all patients of the HL-A13, w17, and TY antigens which have previously (11, 15, 16) been found to be associated with psoriasis vulgaris. It is evident that there were highly statistically significantly ($p<0.0001$) increased frequencies of w17 and TY as compared with our normal material (12, 14). However, HL-A13 was only insignificantly increased.

The relationship between HL-A antigens and the results of our histological investigation is shown in Tables II and III for the LA (1st) and FOUR (2nd) series, respectively.

The main histological diagnoses were: 2 cirrhoses, 6 possible cirrhoses, 6 fibroses, 9 mixed changes, 6 non-specific reactive hepatitis, 3 fatty changes, and 11 normals.

There was no chronic aggressive hepatitis (3).

Table I. *Frequencies (per cent) of HL-A13, w17, and TY in 45 psoriatics and in controls*

HL-A antigen	Frequency in 45 patients	Controls: No. investigated	Controls: Frequency	Fisher's *p*
HL-A13	6.7	1 967	4.3	0.31
W17	28.9	1 967	7.7	3×10^{-5}
TY	15.6	424	1.4	3×10^{-5}

No statistically significant associations were found between any HL-A antigens and liver histology. In particular HL-A8 was decreased in the group with pathological liver histology, although not significantly. The HL-A1 antigen level isequally increased in both groups of patients (63 and 64 % vs. 31 % in controls).

DISCUSSION AND CONCLUSION

It did not prove possible to disclose any statistically significant correlation between liver pathology and HL-A antigens. In particular, we did not find any significant tendency to react with hepatitis in patients with HL-A8, as did several authors (1, 2, 7) in chronic aggressive hepatitis. Thus the HL-A typing does not seem to have any predictive value in the pre-MTX screening of psoriatics. As previously reported (16) we found w17 significantly increased in the entire group of patients, while HL-A13 was only slightly increased.

The increase in HL-A1 is most likely due to the increase in w17 and TY, as these two antigens are associated with HL-A1 in the random population (14). There was no significant association between w17, TY, or HL-A13 and age of onset in this rather small material. However, (5) the observation of Tiilikainen (17) of an increased frequency of the TY antigen is strongly supported by this study.

One of our 6 patients with psoriatic arthropathy had HL-A type 27 (17 % vs. 8 % in controls) which is in agreement with Zachariae et al. (18) who found HL-A type 27 in 18 % of their 34 patients with psoriasis vulgaris and psoriatic arthropathy.

As shown in a previous article (8), evaluation with regard to possible liver disease against the background of a clinical and biochemical examination of the patient is inadequate. Liver biopsy is the current method having sufficient accuracy for assessing abnormalities of the liver parenchyma.

A pre-MTX liver biopsy is mandatory as patients with pathological liver histology worsened more often during MTX therapy than those with a normal pre-MTX liver histology, as shown in a blind study (9).

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Table II. *LA antigens in relation to liver histology*

LA antigens	Histology: Pathological: Cirrhosis, possible cirrh., fibrosis (14 pats.)	Others (18 pats.)	Sum (32 pats.)	Normal (11 pats.)
HL-A1	10	10	20	7
HL-A2	4	6	10	3
HL-A3	4	3	7	5
HL-A9	3	6	9	3
HL-A10	0	1	1	0
HL-A11	4	1	5	0
w19	1	5	6	2
w25	0	1	1	0
w28	1	0	1	0
w29	0	2	2	1
w32	1	3	4	0

Table III. *FOUR locus antigens in relation to liver histology*

	Histology			
	Pathological			
FOUR locus antigens	Cirrhosis, possible cirrh., fibrosis (14 pats.)	Others (18 pats.)	Sum (32 pats.)	Normal (11 pats.)
HL-A5	4	1	5	1
HL-A7	1	0	1	0
HL-A8	3	2	5	3
HL-A12	5	4	9	1
HL-A13	1	1	2	1
w5	3	2	5	0
w10	2	1	3	2
w14	0	1	1	0
w15	2	3	5	1
w16	0	1	1	0
w17	3	6	9	4
w21	1	3	4	1
w22	1	0	1	0
w27	1	5	6	3
TY	1	3	4	2
MK	0	0	0	1
4A2	0	1	1	2

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