Arch Dermatol Res (1996) 288 : 363–365

ORIGINAL PAPER

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HLA risk haplotype Cw6,DR7,DQA1*0201 and HLA-Cw6 with reference to the clinical picture of psoriasis vulgaris

Received: 24 May 1995

Abstract **Psoriasis vulgaris has HLA associations. We have previously defined HLA-Cw6,DR7,DQA1*0201 as the central element of the risk haplotypes for psoriasis. On the other hand, Cw6 as a single gene has the strongest association with psoriasis. The aim of this study was to determine whether the risk haplotype and Cw6 correlate with the clinical parameters of the disease. The series consisted of 64 patients and the clinical parameters were age at onset, family history of psoriasis, arthritis and the frequency of inpatient treatment. The HLA risk haplotype Cw6,DR7,DQA1*0201 had previously been found in 30% and Cw6 alone in 54% of the patients. The presence of Cw6 correlated with early age at onset (P_c = 0.01). The presence of the risk haplotype correlated with a positive family history of psoriasis among the first-degree relatives (P_c = 0.02) and an overall positive family history (P_c = 0.04), but Cw6 had a stronger correlation with an overall positive family history (P_c = 0.01). There were no positive correlations with arthritis or the number of inpatient treatment periods. Only type I psoriasis was associated with Cw6 (P_c = 0.0006). In conclusion, Cw6 and the haplotype Cw6,DR7,DQA1*0201 are important in the heredity of psoriasis vulgaris, but the presence of Cw6 alone is sufficient to indicate a clinically significant risk for psoriasis.**

Key words Psoriasis vulgaris · HLA risk haplotypes

Introduction

The genes in the HLA region contribute to susceptibility to psoriasis vulgaris, the most important alleles common to psoriasis patients from different ethnic groups being Cw6, DR7 and DQA1*0201 [2–4, 8, 10, 11, 13, 14, 16]. In addition, specific sequences of the HLA-C molecule confer a significant risk for developing psoriasis [1, 7, 12].

We have previously defined certain HLA risk haplotypes among Finnish psoriasis patients [8]. The haplotypes associated with the greatest risk for psoriasis carry the alleles mentioned above, that is Cw6, DR7 and DQA1*0201 ($P = 7{,}5 \times 10^{-7}$, RR = 24,4, EF = 0.29).

The aim of this study was to determine whether the simultaneous presence of all these risk alleles correlates with some clinical parameters of psoriasis. The clinical parameters were also correlated with the presence of Cw6 alone irrespective of the other alleles present, because Cw6 shows the strongest individual association with psoriasis.

Patients and methods

The HLA types of 64 random patients (aged 20–69 years) had previously been determined [8]. The cinical parameters defined were age at onset, family history of psoriasis, type of psoriasis (guttate, chronic stationary or erythrodermic), arthritis (fulfilling clinical and radiological criteria) and number of hospital admissions during 1990–1991. A group of 26 patients with a positive family history and an onset not later than age 25 years were classified as type I psoriasis, and a group of 9 patients with a negative family history and an onset later than age 35 years were classified as type II psoriasis.

Results

The HLA haplotype Cw6,DR7,DQA1*0201 correlated with a positive family history for psoriasis among the first-degree relatives (P_c = 0.02) and any positive family history (P_c = 0.04; Table 1). Age at onset showed a correlation with Cw6 (20 vs. 29 years, P_c = 0.01) and with an overall positive family history for psoriasis (P_c = 0.01). The presence of the risk haplotype or Cw6 did not correlate with arthritis, the number of hospital admissions or the clinical type of psoriasis (Table 1), as all but two of

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Table 1 HLA risk haplotype and HLA-Cw6 correlated with the clinical picture of psoriasis vulgaris

Marker	Age at onset (years)	Positive family history (first degree relative)	Arthritis	Number of hospital admissions during 1990–1991	Type of psoriasis[a]		Positive family history (all)
					I (n = 26)	II (n = 9)	
Cw6,DR7,DQA1*0201							
Positive (n = 19) (all markers present)	19 ± 10	12 (63%)	1 (5%)	2.5	9	0	14 (74%)
Negative (n = 45) (some markers or none)	26 ± 13	13 (29%)	8 (18%)	3.3	17	9	19 (42%)
P uncorrected	0.03	0.01	NS	NS	0.04		0.02
P corrected	NS	0.02			NS		0.04
Test	t-test	Fisher			Fisher		Fisher
Cw6							
Positive (n = 33)	20 ± 10	17 (52%)	3 (9%)	2.7	18	0	23 (70%)
Negative (n = 31)	29 ± 14	9 (29%)	6 (19%)	3.5	8	9	11 (35%)
P uncorrected	0.005	NS	NS	NS	0.0003		0.006
P corrected	0.01				0.0006		0.01
Test	t-test				Fisher		Fisher

[a] 29 patients could not be definitely classified

the patients had the plaque form, the two exceptions being erythrodermic.

The patient group was unselected. Not all the patients could be definitely classified into class I or II. If only the classifiable cases were included, the presence of Cw6 showed a correlation with type I (P_c = 0.0006; Table 1). No significant differences were found if haplotype-positive and Cw6-positive groups were compared with each other. If the patients without any HLA risk allele for psoriasis were included, the results showed that type II was not associated with the haplotype Cw6,DR7,DQA1*0201 (P_c = 0.03, Fisher's test; data not shown).

Discussion

There are two types of psoriasis, type I with early age at onset and a positive family history of psoriasis, and type II manifested at a later age and with no relatives with psoriasis [6]. Type I has HLA associations and is heritable [6, 13], which means that the two types differ in their immunogenetic background. This was confirmed in the present study: none of the patients with type II carried the HLA risk haplotype or Cw6. However, the classification always leaves out many patients in the "grey zone" between types I and II.

In the present study we had an unselected group of patients whose HLA haplotypes were known. The correlation between the HLA risk haplotypes and the clinical parameters was studied. To our knowledge, no such investigation has been reported before.

The age at onset was earlier in the patients carrying the haplotype Cw6,DR7,DQA1*0201 (19 vs. 26 years), and the difference reached significance when correlated with the presence of Cw6 alone (20 vs. 29 years, P_c = 0.01). However, these HLA associations did not correlate with the typical bimodal distribution for age at onset in psoriasis types I and II, but the HLA risk haplotype and Cw6 precipitate a slightly earlier onset of psoriasis. The results are in accordance with earlier reports on the relationship between HLA and age at onset [2, 6, 9].

The presence of the risk haplotype correlated with a positive family history among the first-degree relatives and any positive family history, but the presence of Cw6 correlated better with any positive family history of psoriasis. Thus, the HLA risk haplotype and Cw6 especially are associated with an increased incidence of the disease in a family.

The HLA risk haplotype and Cw6 did not show any positive correlation with arthritis, and thus we could not confirm the result of an Italian study [15] in which an association was found with HLA-B39 and Cw6. The clinical type of psoriasis also did not correlate, since all but two of the patients had plaque-type psoriasis, the two exceptions being eryhtrodermic.

There have been studies that show that patients with severe disease have an onset of psoriasis earlier in life than patients with mild disease [5, 6]. The overall course of the disease (clinical relapses, typical nail changes) was not recorded here because of the wide age distribution of the patients, which could have resulted in misleading findings. If the number of hospital admissions was taken as a measure of the overall severity of the disease, there was no correlation with the risk haplotypes or Cw6. It seems that there are other factors affecting the clinical picture which might be more important than HLA.

It seems that Cw6 and the HLA risk haplotype Cw6,DR7,DQA1*0201 are important in the heredity of psoriasis vulgaris, but the presence of Cw6 alone is sufficient to indicate a clinically significant risk for psoriasis.

This is of interest because Cw6 is the most important allele common to psoriasis patients in different ethnic groups.

Acknowledgements This study was supported by grants from the Finnish Academy of Sciences and the Paulo Foundation (to I.I.).

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