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HLA CLASS I IN IRANIAN PSORIATIC PATIENTS

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ABSTRACT

The association of HLA and disease varies in different populations. We have studied the association of HLA class I in Iranian psoriatic patients, in order to compare this association with other reports. Fifty-one Iranian patients with psoriasis were HLA typed. The frequency of HLA antigens in patients and patient subgroups, based on clinical patterns, age of onset, family history and provocative factors, were compared with each other and with normal controls. The results indicate that the disease is strongly associated with HLA-Cw6 (chi-square, corrected P-value (Pc) ≤ 0.0009), and negatively associated with Cw3 (Pc ≤ 0.00009 and Pc ≤ 0.03, respectively). Psoriatic patients with early onset disease and non-pustular psoriasis (NPP) showed a more significant association with HLA-Cw6 (Pc ≤ 0.0004 and Pc ≤ 0.0003, respectively). There was no statistically significant relationship between the presence of a positive family history and early onset of disease.

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INTRODUCTION

Psoriasis is a common, genetically determined, inflammatory and proliferative disease of the skin. Population surveys, twin and other family analyses and HLA studies all confirm the genetic basis of psoriasis.[3] The earliest studies revealed an association with HLA-B13 and HLA-B17.[2,12,13,17,18] B13 and B17 appear to be linked to HLA-Cw6,[11,16] which was first shown by Batchelor and Morris[1] to be the HLA phenotype most strongly associated with psoriasis. The strong association of Cw6 with psoriasis was subsequently confirmed by others.[10,16] One study indicated that non-pustular psoriasis exists in two distinct patterns, one of which is of early onset, hereditary and HLA-Cw6 associated, and the other which is of late onset and non-inheritable.[6] Others, however, found that psoriasis occurred independently of age of onset in first-degree relatives of probands.[8] This discrepancy may be a result of different analytical methods and patient selection, as well as of population differences. In this regard, some investigators[7] have stressed that the results of analysis on one population may not necessarily be extrapolated to another population.

The association of HLA antigens and psoriasis has not been investigated in Iran, and the degree of the association is not known, if any. In the present research we have investigated the HLA phenotype of psoriatic patients in Iran, and searched for any possible subdivisions in patient populations, based on clinical parameters and HLA phenotypes.

Table I. Subject data

Total number (F - M)	51 (26 - 25)	
Age at onset (years)	range: 2-62; mean: 23	
	Number	Total Percent
Presence of family history[A, B]	10	19.6
Clinical status[C, D]		
Plaque type	47	92.2
involving < 50% of body surface	25	49
involving ≥ 50% of body surface	9	17.6
guttate	1	2
napkin	0	0
flexoral	8	15.7
palmoplantar pustular	2	3.9
plaque with pustule	3	5.9
generalized pustular	4	7.8
erythrodermic	13	25.5
unstable	2	3.9
non-pustular	43	84
severe psoriasis[E]	24	47
nail involvement	33	64
presence of Kobner's phenomenon	24	47
presence of arthropathy	5	9.8

A- Based on physical examination of relatives or reliable history.
B- Parent: 3; sibling: 3; child: 0; other relatives: 4.
C- The classification of patients to subgroups was performed in order to find any relationship between subgroups and HLA antigens.
D- Clinical information was based on past medical status as well as present illness.
E- Severe psoriasis: this subgroup comprises patients with any of the following patterns throughout their life: generalized pustular psoriasis, erythrodermic psoriasis, unstable psoriasis, or plaques involving ≥ 50% of body surface.

PATIENTS AND METHODS

Patients

A total of 51 unrelated, Iranian caucasian psoriatic patients were studied. A definitive clinical diagnosis of psoriasis was established by at least two dermatologists in Razi hospital, a dermatologic center in Tehran, Iran. Skin biopsies were performed on 14 patients, and the diagnosis of psoriasis was histologically confirmed. Information concerning relatives was obtained through physical examination of relatives or reliable history. The HLA phenotypes of 100 Iranian caucasians were used as controls (using previously published data).[9] The patients' clinical data are presented in Table I.

Methods

HLA typing was done using the standard microlymphocytotoxicity technique.[15] The frequency of 44 well-known class one human leukocyte antigens was studied using well characterized anti-HLA antisera from Behring-Hoechst, Marburg, FRG, and biotest AG, Frankfurt, W. Germany.

Statistical methods

The chi-square method and, when conditions for this test were not met, the Fisher exact test was used. For the final evaluation of the level of significance we have corrected the exact P-value with the number of alleles tested (corrected P-value = Pc).[14]

RESULTS

HLA antigens in psoriatic patients

The frequency of HLA antigens in psoriatic patients and in normal controls are presented in Table II. As depicted, concerning the A locus antigens of class one, we did not find any statistically significant association between psoriatic patients and any HLA antigens as compared with normal controls. Regarding the B locus antigens of class one, although we have an increase of B13, there is no significant association between any antigens of the B locus and psoriasis as compared to normal controls.

As for C locus antigens, we have found a significant

Table II. Frequencies of HLA-A, -B and -C antigens in psoriatic patients and in normal controls.

Antigens	Normal controls with Ag		Patients with Ag		Pc*
	total panel	freq.	total panel	freq.	
A1	30:100	30%	12:51	23.5%	NS**
A2	35:100	35%	21:51	41.2%	NS
A3	21:100	21%	8:51	15.7%	NS
A11	32:100	32%	7:51	13.7%	NS
A24	18:85	21%	10:51	19.6%	NS
A10	30:100	30%	7:51	13.7%	NS
A25	1:100	1%	0:51	0%	NS
A26	24:100	24%	7:51	13.7%	NS
Aw34	11.97	11%	0:51	0%	NS
Aw66	0:2	0%	0:51	0%	NS
A28	17:100	17%	3:51	5.9%	NS
Aw68	0:0	0%	1:51	1.9%	NS
A29	3:99	3%	3:51	5.9%	NS
A30	1:98	1%	4:51	7.8%	NS
A31	1:98	1%	1:51	1.9%	NS
A32	1:97	1%	4:51	7.8%	NS
B5	41:100	41%	18:51	33%	NS
B51	29:99	29%	8:51	15%	NS
Bw25	18:99	18%	9:51	18%	NS
B7	6:100	6%	4:51	8%	NS
B8	10:100	10%	2:51	4%	NS
B12	11:100	11%	1:51	2%	NS
B44	11:100	11%	1:51	2%	NS
B13	6:100	6%	10:51	20%	NS
B14	15:99	15%	2:51	4%	NS
B15	25:99	25%	5:51	8%	NS
Bw62	5:100	5%	3:51	6%	NS
Bw63	15:99	15%	0:51	0%	NS
B17	10:100	10%	3:51	6%	NS
B18	6:99	6%	2:51	4%	NS
B21	16:100	16%	7:51	14%	NS
Bw55	7:100	7%	0:51	0%	NS
B27	6:100	6%	0:51	0%	NS
B35	35:100	35%	13:51	25%	NS
B40	18:100	18%	1:51	2%	NS
Bw60	6:100	6%	0:51	0%	NS
Bw42	5:90	5%	0:51	0%	NS
Bw53	14:99	14%	0:51	0%	NS
Cw2	11:98	11%	0:51	0%	NS
Cw3	38:100	38%	1:51	2%	≤0.00009
Cw4	37:100	37%	8:51	16%	NS
Cw5	4:98	4%	3:51	6%	NS
Cw6	13:98	13%	23:51	45%	≤0.0009
Cw7	20:100	20%	0:51	0%	≤0.03

* Pc = corrected P-value (chi-square, or Fisher exact test)

** N.S. = Not significant

association between Cw6 and psoriasis as compared to normal controls (Pc ≤ 0.0009). We have also found a significant negative association between each of the Cw3 and Cw7 antigens and psoriasis as compared to normal controls (Pc ≤ 0.00009 and Pc ≤ 0.03, respectively).

HLA antigens in subgroups of psoriatic patients

Family history

Ten out of 51 psoriatic patients (19.6%) had at least one relative affected with psoriasis. Comparison of frequencies of any HLA antigens in patients with positive family histories versus patients with negative

Table III. Frequency of HLA-Cw6 antigen in different groups of psoriatic patients compared with one another.

Patient group	Relative freq. of Cw6	Level of significance*
positive family history patients	40%	N.S.**
negative family history patients	37%	
patients with age of onset < 30 years	48%	N.S.
patients with age of onset ≥ 30 years	37%	

* chi-square test
** N.S. = Not significant

family histories did not show any significant difference (Table III; only data regarding Cw6 is presented).

Age at onset

Thirty-seven patients had early onset disease (age of onset below 30 years), while age of onset in the remaining 14 patients was equal to or greater than 30 years (late onset disease). Frequencies of HLA antigens were not significantly different in these two subgroups of psoriatic patients (Table III; only data related to Cw6 is presented). However, it is noteworthy that early onset psoriatic patients were associated with HLA-Cw6 with a significance level of Pc ≤ 0.0004 as compared to normal controls.

Non-pustular psoriasis (NPP)

Frequencies of HLA antigens in patients with NPP did not differ significantly from those of normal controls, except for the frequency of Cw6 (Pc ≤ 0.0003).

Family history versus age of onset

Nine out of 37 patients with early onset disease had positive family histories, while only one out of 14 patients with late-onset disease had a positive family history. Although the percentage of having positive family histories was higher in patients with early onset disease, the difference was not statistically significant.

Kobner's phenomenon versus age of onset

Kobner's phenomenon was present in 16 psoriatic patients, 10 of which had early onset and 6 late onset disease. Nevertheless, there was no statistically significant relationship between age of onset and the presence of Kobner's phenomenon.

DISCUSSION

In this study 19.6% of patients had positive family histories. According to Farber et al,[4] 36% of relatives of psoriatic patients were reported to be affected. A study by Hellgren[5] on 40000 individuals in parts of Sweden showed that 6.4% of relatives of patients with psoriasis were affected. Regarding these two reports, our results are different. This difference may be related to the difference in populations.

The present study did not show any strong association between psoriasis and HLA-A and -B antigens, as reported by others. Surprisingly, we observed a significant association between Cw6 and psoriasis in our patients, which confirms earlier findings. Concerning patient subgroups, patients with NPP and patients with early onset disease showed a greater statistically significant association with Cw6 (Pc ≤ 0.0003 and Pc ≤ 0.0004, respectively) as compared to normal controls. The negative associations of Cw3 and Cw7 with psoriasis were significant statistically, and show that these antigens may have protective roles regarding psoriasis; however, the negative association of Cw7 is not very strong and may need further investigation in order to be completely approved.

The relatively weak association of B13 with psoriasis is probably due to linkage disequilibrium of B13 to Cw6. Other investigators mentioned linkage of B13 with Cw6.[11,16] The frequency of B13 and Cw6 in our patients is 19.60% and 45.09%, respectively; therefore 8.83% of patients are expected to have both B13 and Cw6. Surprisingly, 19.60% (10 out of 51) of our patients had both antigens (Δ = 10.77). It is not known, however, whether this linkage is secondary to psoriasis or not.

Regarding the relationship between family history and age of onset, it is worth mentioning that although the percent of early onset disease was higher in patients with positive family histories, we could not confirm its significance statistically. Thus our results cannot confirm previous reports.[6] Concerning the presence of two distinct patterns of non-pustular psoriasis (NPP) (one of which is of early onset, hereditary, and HLA-Cw6 associated, and the other which is of late onset and non-inheritable), when we divided NPP patients to two subgroups based on age of onset, although the frequency of HLA-Cw6 was higher in NPP early onset patients, the difference between subgroups was not statistically significant. These results may indicate that

the two mentioned patterns are not universally correct, again probably due to the difference in populations.

Finally, our study confirms a genetic predisposition for psoriatic patients, as people with Cw6 are at higher risk for developing psoriasis.

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