Association of Psoriasis With Human Leukocyte Antigens in Turkish Population

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The aim of this study was to compare the frequency of HLA alleles in patients with psoriasis to that in controls and whether the risky alleles correlated with the clinical parameters of the disease.
Sixty-five psoriatic patients and 170 organ transplant donors as controls were studied. The clinical parameters were age at onset (below 40 years of age), family history of psoriasis and arthritis. HLA-A, B, DR and DQ antigens were tested by microlymphocytotoxicity assay.
HLA-B38 showed the strongest association with psoriasis. The frequencies of A2, B22, DR14 and DR4 were also significantly increased. There was no significant association of any particular HLA gene with the age of onset, the presence of arthritis or the presence of the disease in family members.
This study demonstrates the differential association of HLA according to the clinical parameters and identifies high-risk alleles in Turkish psoriatic patients.
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Psoriasis has polygenic, multifactorial characteristics of inheritance with variable age at onset, variable familial occurrence and aggravation by a number of environmental factors[1]. The aim of this study was to compare the frequency of HLA alleles in Turkish patients with psoriasis to that in controls.

MATERIAL AND METHODS

Sixty-five psoriatic patients were studied, of whom 35 were female and 30 male. A clinical diagnosis of definite psoriasis vulgaris was established in all of the patients. Patients with erythrodermic or pustular psoriasis were not included in the study. All patients had currently active disease. Age at onset varied from one-month to 70 years of age, with 49 (75.4%) of the patients noting evidence of psoriasis before the age of 40 years. Out of the 65 patients, 23 (35.4%) had psoriatic arthritis and 19 (29.2%) had a psoriatic first or second degree relative. Control HLA phenotypes were determined in 170 unrelated organ transplant donors. The donors were examined for the presence of psoriasis. HLA-A, B, DR and DQ antigens were tested by microlymphocytotoxicity assay[2]. Pearson's c test and Fisher's exact test were used in the statistical analysis.

RESULTS

In comparing 111 different HLA specificities, one would expect to find, by

chance alone, at least one significantly extreme value. Multiplying the normal significance level by the number of comparisons (111 in this case) may compensate for this type of error. When this was done, HLA-B38 showed the strongest association with psoriasis (odds ratio=58, corrected p<0.001). The frequencies of A2 (odds ratio=3.7, corrected p <0.001), B22 (odds ratio=8.4, corrected p=0.01), DR14 (odds ratio=11.9, corrected p <0.0001) and DR4 (odds ratio=3.1, corrected p=0.03) were also significantly increased (Table 1). The statistically insignificant results are not shown. No "protective" allele was detected after P-values were corrected for the number of comparisons made. When the subgroup of patients with psoriatic arthritis was evaluated separately, an increase was noted in HLA-B38 and DR18 but it was not significant when corrected (odds ratio=5.6, p=0.026, corrected p>0.05 and odds ratio=11.3, p=0.038, corrected p >0.05 respectively). There was no significant association of any particular HLA gene with the age of onset or the presence of the disease in family members (Table 2).

Table 1. Frequency of statistically significant HLA antigens in psoriatic patients.

ANTIGENS	PERCENTAGE POSITIVE		p VALUE IN 65	ODDS RATIO
	PATIENTS	CONTROLS	PATIENTS[a]	
HLA A2	66.2	34.1	<0.001	3.7
HLA B22	16.9	2.3	0.01	8.4
HLA B38	15.4	0	<0.001	58
HLA DR14	33.8	4.1	<0.0001	11.9
HLA DR4	33.8	14.1	0.03	3.1

[a]p values are corrected values for the number of comparisons made (n=111).

Table 2. Clinical parameters subdivided by HLA type.

ANTIGENS		PATIENTS WITH FAMILY HISTORY		PATIENTS WITH EARLY ONSET DISEASE[a]		PATIENTS WITH PSORIATIC ARTHRITIS	
	N[b]	N[b] (%)	p VALUE	N[b] (%)	p VALUE	N[b] (%)	p VALUE
HLA A2	43	16 (37,2)	0,04c	31 (72)	0,38	15 (34,8)	0,90
HLA B22	11	3 (27,2)	1	9 (81,8)	0,71	2 (18,1)	0,30
HLA B38	10	3 (30)	1	6 (60)	0,24	7 (70)	0,026c
HLA DR14	22	8 (36,3)	0,36	15 (68,1)	0,33	4 (18,1)	0,038c
HLA DR18	6	2 (33,3)	1	6 (100)	0,32	5 (88,3)	0,018c
HLA DR4	22	6 (27,2)	0,80	17 (77,2)	0,80	10 (45,4)	0,22
TOTAL	65	19 (29,2)		49 (75,4)		23 (35,4)	

[a] Disease onset before 40 years of age.

[b] Number of patients

[c] p values <0.05, corrected p values >0.05.

DISCUSSION

Psoriasis is one of the HLA-associated conditions in which disease susceptibility appears to be heritable. However the mode of inheritance has been difficult to define in simple Mendelian terms. Numerous studies of HLA association have been carried out, of which the results differ in many populations (Table III). A previous study in Turkey revealed increased association of psoriasis with HLA A1, A11, B13, B17, B35 and DR4[3]. As a clinical parameter, only psoriatic arthropathy was investigated and a high frequency of alleles HLA DR 4 and Bw6 was found.

Most of the previous studies agree that 75-90% of patients experience disease onset before the age of 40 years[13]. Henseler et al. have distinguished two types of nonpustular psoriasis on the basis of age of onset[13]. Patients with type I psoriasis (disease onset before the age of 40 years) are much more likely than patients with type II (onset after the age of 40 years) to have affected first-degree relatives, to express known susceptibility alleles for psoriasis at the HLA locus and to experience severe and recurrent disease[13]. In our group of patients, we did not find any association of any particular HLA gene with the age of onset or the presence of the disease in family members. In some studies, the early onset disease is considered to be below the age of 30 years[5]. In our study, when the data were reevaluated for the age of onset below 30 years, there was no significant association with neither the HLA subtypes nor the clinical features (data not shown). To summarize, this study demonstrates the differential association of HLA according to the clinical parameters and identifies high-risk alleles in Turkish psoriatic patients.

Table III. HLA associations in different populations.

Author, Year (reference)	Country	n[a]	Type of psoriasis	HLA alleles
Current study, 2000	Turkey	65	Mixed	A2, B22, B38, DR14, DR4
Satar et al, 1994[3]	Turkey	51	Mixed	DR2
Azizlerli et al, 1988[4]	Turkey	40	Mixed	A1, A11, B13, B17, B38, DR4
Kim et al, 2000[5]	Korea	84	Early onset	A30-B13-Cw6-DrB1*07-DQA1*02-DQB1*02b
Vejbaesya et al, 19986	Thailand	67	Early onset	A2, B46, B57, DQB1*0303
Schmitt-Egenolf et al, 1996[7]	Germany	60	Early onset	Cw6-B57-DRB1*0701-DQA1*0201-DQB1*0303b
O'Donnell et al, 1993[8]	Ireland	93	Mixed	B13, B17, B27
Ikaheimo et al, 1996[9]	Finland	70	Mixed	Cw6, DR7, DQA1*0201
Szczerkowska-Dobosz et al, 1996[10]	Poland	115	Early onset	B13, B17, Cw6
White et al, 1972[11]	USA	156	Early onset	A13, w17
Russell et al, 1972[12]	USA	66	Early onset	A13, w17

[a]number of patients

[b]extended haplotype

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