Clinical and Genetic Aspects of Psoriatic Arthritis "Sine Psoriasis"

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ABSTRACT. ***Objective.*** To characterize the clinical pattern of psoriatic arthritis (PsA) sine psoriasis.

Methods. Fifty-seven patients (31 men, 26 women, mean age 46.32 ± 14.12 yrs) with undifferentiated spondyloarthropathy (SpA) were studied. Two subsets were defined: (1) 21 patients with familial psoriasis (12 men, 9 women, mean age 49.29 ± 14.17 yrs); (2) 36 patients without familial psoriasis (19 men, 17 women, mean age 44.58 ± 14.00 yrs). The prevalence of the following clinical variables was evaluated: low back pain, enthesopathy, dactylitis, distal interphalangeal (DIP) arthritis, spinal involvement, and discitis. In all patients the following HLA haplotypes were tested: B7, B13, B17, B18, B27, B38, Cw6, and DR7.

Results. Dactylitis and DIP arthritis were markedly present in the articular subset with familial psoriasis ($p < 0.0001$) that also showed a high frequency rate of HLA-Cw6 ($p < 0.0001$ vs controls and patients without familial psoriasis). HLA-B27 was markedly frequent in patients without familial psoriasis ($p < 0.0001$ vs controls and $p = 0.019$ vs patients with familial psoriasis). In addition, in patients with familial psoriasis the log-linear model showed that the presence of HLA-Cw6 was related to the presence of DIP arthritis as well as dactylitis (likelihood ratio chi-square change of 5.891 and $p = 0.015$).

Conclusion. A subset of patients with PsA "sine psoriasis" is identified by the occurrence of a SpA with dactylitis and/or DIP arthritis, presence of HLA-Cw6, and familial psoriasis in first or second-degree relatives. (J Rheumatol 2003;30:2638–40)

Key Indexing Terms:
PSORIATIC ARTHRITIS "SINE PSORIASIS" PSORIATIC ARTHRITIS PSORIASIS

In about 20% of patients with psoriatic arthritis (PsA), articular involvement may precede the onset of rash[1]. In these cases diagnosis remains unclear until the classical changes of skin and/or nails suddenly appear. A family history positive for psoriasis could be a helpful clue in clinically unconfirmed cases. We wished to characterize this articular pattern, which might be considered peculiar to psoriatic arthritis "sine psoriasis."

MATERIALS AND METHODS

Fifty-seven patients with the undifferentiated pattern of spondyloarthropathy (SpA) defined according to the European Spondylarthropathy Study Group criteria[2] (31 men, 26 women, mean age 46.32, SD 14.12 yrs) attending the Rheumatology Unit from February 2001 to November 2001 were included in this study (Table 1).

On the basis of family history positive for the presence of psoriasis in first and/or second-degree relatives, confirmed by a dermatologist, we preliminarily defined 2 subsets of patients: (1) 21 patients with undifferentiated SpA and family history positive for psoriasis (12 men, 9 women, mean age 49.29, SD 14.17 yrs); and (2) 36 patients with undifferentiated SpA without family history positive for psoriasis (19 men, 17 women, mean age 44.58, SD 14.00 yrs) (Table 1).

All patients underwent clinical examination and blood tests. Hands, wrists, elbows, knees, ankles, feet, spine and sacroiliac joints were examined on radiographs.

In both groups we evaluated the prevalence of the following clinical variables: low back pain, enthesopathy, dactylitis, distal interphalangeal (DIP) arthritis, spinal involvement (on the basis of the radiographic evaluation of spine and/or sacroiliac joints), and discitis.

A microlymphocytotoxicity test[3] was used to type for HLA antigens. In particular, we analyzed the presence of haplotypes of B7, B13, B17, B18, B27, B38, Cw6, and DR7, which are usually related to psoriasis and/or peripheral or axial pattern of PsA.

Statistical analysis. Continuous variables are expressed as mean ± standard deviation (SD). Categorical variables were compared by chi-square analysis. In patients with a positive family history of psoriasis, we studied the relationships between the categorical variables that were significant in the univariate analysis. The variables were included in a hierarchical log-linear analysis procedure[4] to quantify the association between them. The model was built by the backward elimination method. A p value ≤ 0.05 was considered significant. The SPSS software package for Windows (release 11.0.1; SPSS Inc., Chicago, IL, USA) was used for statistical analysis.

RESULTS

In Table 2 we give the prevalence of different clinical variables tested in the 2 patient subsets.

The results show a statistically significant difference between these 2 groups of patients for the presence of

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Table 1. Characteristics of patients studied.

	Females		Males	
	N	Age ± SD, yrs	N	Age ± SD, yrs
Patients				
With familial psoriasis	9	40.33 ± 12.27	12	56.00 ± 11.87
Without familial psoriasis	17	43.71 ± 13.48	19	45.37 ± 14.77
Total	26	42.54 ± 12.93	31	49.48 ± 14.50

Table 2. Prevalence of clinical variables tested in 57 patients with undifferentiated SpA, 21 with family history positive for psoriasis and 36 without psoriasis.

Variable	Psoriasis, n (%)	No Psoriasis, n (%)
Low back pain	19 (90.5)	34 (94.4)
Enthesopathy	17 (81.0)	30 (83.3)
Dactylitis	13 (61.9)*	4 (11.1)
DIP arthritis	15 (71.4)*	5 (13.9)
Spinal involvement	20 (95.2)	34 (94.4)
Discitis	14 (66.7)	20 (55.6)

* $p < 0.0001$.

dactylitis ($p < 0.0001$) and DIP arthritis ($p < 0.0001$); both were markedly present in the articular subset of patients with family history positive for psoriasis.

Table 3 shows the distribution of HLA haplotypes in the general population of our geographic area and in the 2 groups of patients studied. Compared to controls, the distribution of HLA haplotypes in the subset without family history positive for psoriasis showed a higher frequency for HLA-B27 ($p = 0.019$), while in patients with family history positive for psoriasis we found an increased frequency of Cw6 ($p = 0.002$).

Variables found to be relevant in the univariate analysis (HLA-Cw6, DIP arthritis, and dactylitis) were included in the log-linear model. The procedure did not reject any variables and the final model consisted of their interaction (HLA-Cw6*DIP arthritis*dactylitis), with a likelihood ratio chi-square change of 5.891 and $p = 0.015$. This analysis showed that the presence of HLA-Cw6 is related to the presence of DIP arthritis as well as to dactylitis.

DISCUSSION

Psoriatic arthritis is a condition clinically recognized by the contemporary presence of skin and joint involvement. Moreover, considering that in 20% of cases articular involvement may precede the onset of rash, PsA "sine psoriasis" should not be a rare clinical finding. As speculated in the past[5,6] and recently reappraised[7,8], its existence has always been debated, because in the absence of the characteristic rash, its diagnostic setting is fairly difficult to establish. According to current classification criteria, patients with PsA "sine psoriasis" have to be included in the wide spectrum of the undifferentiated subset of SpA.

Our purpose in this study was detection of clinical clues for the appropriate diagnosis of this intriguing condition.

Table 3. Frequency (%) of HLA haplotypes in 1089 controls and in 57 patients with undifferentiated SpA, 21 with family history positive for psoriasis and 36 without psoriasis.

HLA Haplotype	Controls, n (%)	Psoriasis, n (%)	No Psoriasis, n (%)
B7	100 (9.18)	0 (0)	2 (5.60)
B13	91 (8.35)	4 (19.00)	6 (16.70)
B17	93 (8.60)	0 (0)	0 (0)
B18	230 (21.12)	3 (14.30)	9 (25.00)
B27	28 (2.57)	0 (0)	9 (25.00)**†
B38	57 (5.23)	2 (9.50)	7 (19.40)
Cw6	223 (20.47)	13 (61.90)*††	5 (13.90)
DR7	257 (23.61)	9 (42.90)	7 (19.40)
DR11	540 (49.61)	10 (47.60)	22 (61.10)

* $p < 0.0001$, psoriasis group vs controls (Fisher's exact test). ** $p < 0.0001$, no psoriasis group vs controls (Fisher's exact test). † $p = 0.019$, psoriasis group vs no psoriasis group (Fisher's exact test). †† $p < 0.0001$, psoriasis group vs no psoriasis group (chi-square test).

Because patients with psoriasis in first and/or second-degree relatives risk developing skin disease[9], we selected, from a group of patients with undifferentiated SpA, those with positive family history for psoriasis. Compared to patients with the undifferentiated disease pattern, patients with family history positive for psoriasis showed an increased prevalence of dactylitis and DIP arthritis, 2 characterizing features of classical PsA. In addition they also showed an increased prevalence for haplotype HLA-Cw6.

In contrast, in patients without a family history positive for psoriasis we observed no increased prevalence of dactylitis or DIP arthritis. In addition they were characterized by an increased prevalence of HLA-B27, the genetic marker of SpA.

Two distinct forms of psoriasis vulgaris are detectable[10]. The first is hereditary and has an early onset, between 15 and 25 years of age. The second is sporadic and occurs at a later age. Over 80% of patients with onset of disease at an early age had the presence of haplotype HLA-Cw6 and had first-degree family members with psoriasis.

In addition, previous reports describe that the frequency of HLA-Cw6 was higher among patients with early onset psoriasis, both the simple form[11] and also that complicated with arthritis[12]. Recently, a study by Rahman and coworkers[13] outlined that patients with PsA with early onset psoriasis have an increased frequency of HLA-Cw6 associated with a strong familial tendency and predilection for skin lesions occurring before arthritis. In our study, the increased frequency of HLA-Cw6 in patients with family history positive for psoriasis could be the expression of an inheritable susceptibility.

On the basis of our results, the subset of patients with PsA "sine psoriasis" is identified by the clinical features of a seronegative SpA with dactylitis and/or DIP arthritis, in the presence of HLA-Cw6 and a family history positive for psoriasis in a first or second-degree relative. In these patients, log-linear analysis confirms that presence of HLA-Cw6 is related to the presence of DIP arthritis and also dactylitis. These 3 clinical variables clearly describe the disease subset we investigated.

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