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Original article

Age at disease onset may help to further characterize the disease phenotype in psoriatic arthritis

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ABSTRACT

Objective: To evaluate whether the age of disease presentation helps to better characterize the disease phenotype in PsA.
Methods: Retrospective cohort study that included 205 consecutive patients fulfilling the CASPAR criteria for PsA. Study outcomes were assessed using univariate and multivariate analyses according to the age of onset of both skin and joint disease (cut off at 40 years).
Results: Early onset psoriasis (EOP) showed more extensive skin involvement (OR 2.3, $P=0.011$), axial pattern as disease onset (OR 4.6, $P=0.009$) and mixed pattern during evolution (OR 2.4, $P=0.019$), family history of both psoriasis (OR 3.1, $P=0.003$) and PsA (OR 4.0, $P=0.021$), higher prevalence of HLA-C*06 (OR 2.03, $P=0.03$) and HLA-B*27 (OR 2.7, $P=0.02$). Early onset arthritis (EOA) had more family history of PsA (OR 2.9, $P=0.007$), and HLA-B*27 positivity (OR 5.9, $P<0.0001$). Patients with late onset arthritis (LOA) were more likely to have DM (OR 4.0, $P=0.009$), hypertension (OR 2.5, $P=0.004$), dyslipidemia (OR 2.3, $P=0.011$), and obesity (OR 1.7, $P=0.012$). Late onset psoriasis (LOP) tended to have more obesity (OR 1.9, $P=0.035$), DM (OR 9.4, $P<0.0001$), hypertension (OR 4.1, $P<0.0001$), and ischemic heart disease during follow-up (OR 5.9, $P=0.021$). In multivariate analysis, LOP predicted DM development (OR 12.1, $P=0.006$). LOA was shown to be an independent risk factor for hypertension (OR 5.2, $P=0.039$).
Conclusion: Age at disease onset exerts a strong influence on several domains of disease phenotype in PsA. Therefore, this descriptor should be considered a good stratification option for epidemiological and genetic studies in PsA.

Psoriasis is a chronic inflammatory skin disease that affects 1%–3% of the general population, with the highest incidence and prevalence observed in white populations [1]. Psoriatic arthritis (PsA) is also a common feature of what is now called psoriatic disease [2]. At present, HLA-C*06 and B*27 are the most important genetic biomarkers in psoriatic disease since they establish marked traits that in turn allow phenotypic differentiations in both populations [2]. Since the seminal work by Henseler and Christophers, early onset psoriasis (EOP) or type I, refers to patients with onset before 40 years, more extensive skin disease, strong family aggregation and HLA-C*06 positivity. On the contrary, late onset psoriasis (LOP) or type II, refers to an onset at or after 40 years, being more sporadic and seldom family-inherited, and its genetic background is unclear at present [3]. Similarly, a split between early and late onset disease has been proposed in PsA [2,4].

Another interesting aspect in the study of psoriatic disease is the fact that cardiovascular (CV) comorbidity seem to be more frequent in subjects with age of onset over 40 years. In that sense, type 2 DM appeared to be related to the presence of arthritis and an onset age after 40 years in one psoriasis study [5]. Although psoriasis is associated with a higher prevalence of CV risk factors in adults, the relationship between the age of onset and its influence on the development of this kind of risk is not completely understood [5,6]. Recently, a French study showed that the age of onset of psoriasis did not seem to confer an additional risk for the development of CV and metabolic comorbidities during adulthood [7]. However, several studies in psoriasis and PsA do suggest this association [8–12].

Although currently the division of psoriasis into two major types (I and II) is a widely accepted descriptor of this condition, it is unclear whether this division can also be applied to patients with PsA. Nor do we know whether the stratification of psoriatic disease

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according to age at disease onset will be of help to better characterize the clinical and CV risk profile in these patients. The aim of this study was to find out whether the stratification of psoriatic disease according to the age of onset helps to better define the disease phenotype of these patients.

1. Methods

This was a retrospective cohort study including 205 consecutive patients treated at a single university hospital who fulfilled the CASPAR classification criteria for PsA [13]. These patients were attended according to a standard protocol in a monographic PsA clinic within our Rheumatology department. All demographic, clinical, laboratory, therapeutic and radiographic variables were collected in a standardized manner as depicted below. Patients were informed about the objectives of the study and consent informed sheets were signed by all participants. This study was conducted following the rules of good clinical practice (Helsinki Declaration). An institutional ethics committee of Hospital Universitario Central de Asturias approved the final version of this study.

1.1. Study population and study variables

The cohort was composed by 112 men and 93 women with a mean age of 52.9 ± 13 years. The description of joint patterns was made on the basis of the dominant pattern observed in the last 5 years of follow-up. Patients with 4 or less swollen joints were labelled as oligoarthritis category; those who presented 5 or more were tagged under the polyarthritis category. Patients who presented radiographic sacroiliitis with inflammatory back pain (IBP), irrespective of the presence of peripheral arthritis, conformed the axial pattern. For the purposes of this study, patients were stratified in early and late onset disease according to a cut off point of 40 years. This cut off was applied for onset ages in both skin and joint disease.

Family history of psoriasis and PsA was collected. Educational level was assessed and classified under three categories according to the achieved degree: primary, secondary (high-school), and university studies. Data regarding skin disease included the main type of psoriasis, location of lesions, nail disease and percentage of patients with involvement of three or more body areas. Psoriasis was confirmed by a dermatologist. In relation to the clinical features of arthritis, both the onset pattern of arthritis (oligoarticular, polyarticular, axial, mixed, distal interphalangeal (DIP) involvement, enthesitis, or dactilitis) depending on the dominant pattern over the first six months of disease, as well as the main pattern during follow-up were taken into account. Pelvic, lumbar and cervical lateral X-rays were included in the radiographic study to assess spinal involvement. X-rays of affected areas during follow-up were also obtained. Laboratory data included the following routine tests: blood and urine biochemistry, hemogram, ESR, HLA-B*27, HLA-C*06, RF and CRP.

Glucocorticoid, NSAID, conventional as well as biologic DMARD use was collected.

1.2. Definition of cardiovascular risk factors and cardiovascular outcomes

The following variables were also collected:

- diabetes mellitus (DM): defined by the analytical finding during monitoring of glucose elevation of more than 126 mg/dL on two fasting determinations, chronic treatment with antidiabetic or insulin, or diagnosis by medical specialist;
- high blood pressure (hypertension): defined as finding at least two determinations on different days of blood pressure greater than 140/90 mmHg during follow-up, chronic use of antihypertensive treatment or diagnosis by medical specialist;
- dyslipidemia: defined as the ongoing finding of cholesterol figures above 240 mg/dL or triglycerides figures above 200 mg/dL during follow-up, chronic treatment with lipid-lowering drugs, or diagnosis by medical specialist;
- obesity: defined as the presence of a body mass index (BMI) greater than 30 kg/m^2, whereas overweight involves a BMI between 25 and 29.9 kg/m^2;
- smoking habit: we consider as active smokers, all those smoker patients at the time of the study (irrespective of the number of cigarettes); on the other hand, those patients with past smoking habit (at least five years), but not being active smokers at the time of the study, are regarded as former smokers;
- ischemic heart disease: defined as at least one cardiac event such as acute myocardial infarction, stable or unstable angina, diagnosed by medical specialist;
- cerebrovascular disease: any transient or permanent event as a result of a disorder of cerebral circulation either ischemic or hemorrhagic diagnosed by medical specialist;
- peripheral vascular disease: defined as the presence of at least one episode of peripheral arterial ischemic disease diagnosed by medical specialist.

1.3. Statistical analysis

Descriptive statistics with mean and standard deviation for quantitative variables and percentages for qualitative variables were included. Differences between qualitative variables were analysed by using Chi^2 and Fisher's exact tests. Differences between quantitative variables were analysed by using Student's *t*-test. To determine the strength of the association of each variable depending on the age of onset of psoriasis and PsA, an odds ratio (OR) of each variable (univariate analysis) was estimated, with its corresponding confidence interval (CI) of 95%. To infer the value of each variable in the occurrence estimation of each cardiovascular risk factor depending of the age of onset, significant variables in the univariate analysis (including age) were introduced in a multivariate analysis with a backward stepwise approach. The statistical analysis software package used was SPSS v.19.0.

2. Results

We evaluated 205 patients, 112 (54.63%) males and 93 (45.37%) females. The mean age was 52.9 ± 13 years. The mean age at psoriasis onset was 30.5 ± 17.1 years and the mean age of onset of arthritis was 43.3 ± 14.2 years. The mean lag time between the onset of psoriasis and onset of arthritis was 14.6 ± 12.6 years.

Educational level was distributed as follow: 52.7% of patients had primary school education, 25.8% had secondary education and 21.6% had a university degree.

Baseline demographic, clinical and cardiovascular characteristics of patients are shown in Table 1. During follow-up, men showed more frequently nail disease [57.1% vs. 38.7; OR 2.1 (1.2–3.7) $P = 0.009$] and higher lipid levels [36.6% vs. 23.7%; OR 1.9 (1.1–3.4) $P = 0.045$].

In 139 patients, psoriasis debuted before the age of 40 with an average age of onset of disease of 20.7 ± 9.7 years, versus 66 patients with psoriasis after 40 years (average onset age 53.5 ± 7.6 years).

A higher latency between the onset of skin psoriasis and arthritis in patients with EOP was observed, specifically an average of 18 ± 7.6 years in patients with EOP versus 6.6 ± 5.6 years in patients with LOP ($P < 0.0001$).

Regarding the clinical features, EOP patients presented with more extensive skin disease ($P = 0.011$), greater family history of