Axial involvement according to ASAS criteria in an observational psoriatic arthritis cohort

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ABSTRACT

The definition of axial involvement in psoriatic arthritis (PsA) is still under debate. Currently, the axial spondyloarthritis (SpA) criteria defined by Assessment of Spondyloarthritis International Society (ASAS) may be the most adequate[1]. The aims of present study were to assess axial involvement according to ASAS criteria in an observational PsA cohort and define the clinical characteristics more associated with this kind of involvement.

Our study included consecutive patients who had a visit in a tertiary Rheumatology centre. All patients included fulfill ClASsification criteria for Psoriatic Arthritis (CASPAR) criteria for PsA and all of them had a recent radiographic assessment of sacroiliitis. Clinical and laboratorial data were taken into account to classify patients as fulfilling or not ASAS criteria for axial SpA. Clinical and demographic data were analyzed about their association with presence of ASAS criteria of axial SpA in a univariable logistic regression analysis. Variables with a p-value <0.05 were re-tested in a multivariable logistic regression. Those variables that maintained statistical significance were tested alone in another multivariable model. Analyses were performed with IBM SPSS Statistics (version 20.0).

Regarding the 233 patients included, only 42 patients (19.4%) fulfilled ASAS criteria for axial SpA. However, 22 patients had asymptomatic radiographic sacroiliitis according to modified New York criteria. The prevalence of asymptomatic sacroiliitis was 15.7% between patients without axial symptoms.

In multivariable analysis, inflammatory back pain (IBP) [OR=25.111; 95% confidence interval (CI) = 8.770, 71.900, p-value <0.001], presence of HLA-B27 [OR=9.072; 95% CI=2.756, 29.860; p-value <0.001] and male gender [OR=3.767; 95% CI=1.264, 11.232; p-value = 0.017] were associated to axial involvement according to ASAS criteria.

Axial SpA ASAS criteria are useful to identify axial involvement in PsA patients. This type of involvement is more common in males, in the presence of HLA-B27 and IBP. Axial disease should be systematically assessed in clinical practice, mainly in patients presenting with this clinical features.

Keywords: HLA-B27; ASAS criteria; Axial involvement; Psoriatic arthritis.

INTRODUCTION

Psoriatic arthritis (PsA) is a chronic inflammatory disease, which may present with a predominantly axial or peripheral involvement. The heterogeneity of its clinical manifestations is well known in clinical practice and it leads to several problems to define patient subsets. The understanding of these different forms of disease is of major importance because it can elucidate about different pathophysiologic pathways involved in this condition.

The ClASsification criteria for Psoriatic Arthritis (CASPAR) were validated and are widely used in the PsA management[2]. However, the definition of axial involvement in PsA is still under debate. Currently, the axial spondyloarthritis (SpA) criteria defined by Assessment of Spondyloarthritis International Society (ASAS) may be the most adequate[3]. Nevertheless, it seems to exist a large overlapping between these two criteria in clinical practice.

The definition for axial PsA vary from an isolated unilateral grade 2 sacroiliitis to those used for ankylosing spondylitis[4]. Some studies suggest that up to 50% of PsA have axial involvement with inflammation in the

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axial skeleton causing inflammatory symptoms and structural damage[5]. However, this prevalence may differ dramatically according to the study design. Thus, axial PsA may be present between 25% (early disease and studies based only on clinical assessments) and 75% of PsA patients (late disease and studies using sophisticated imaging)[6].

On the other hand, these patients with axial involvement seem to have different characteristics comparing to typical ankylosing spondylitis (AS), as they can have structural damage changes on radiographs with no or few axial symptoms[7]. Furthermore, it seems that prevalence of asymptomatic axial involvement is higher than previously expected. Williamson et al. performed magnetic resonance imaging (MRI) to 68 PsA patients and found features of axial involvement in 26/68 patients (38%). However, clinical features of sacroiliitis were present only in 10 of those 26 patients with abnormal scans (38%)[8].

Queiro *et al.* performed a cross-sectional study based on 70 patients, and found that 14 patients (20%) had axial radiographic involvement and no evidence of symptomatic spinal disease[9]. Therefore, these issues concerning axial PsA remain controversial and a consensual definition of this subgroup of patients is still under debate.

The aims of the purposed study were to assess axial involvement according to ASAS criteria in an observational PsA cohort and define the clinical characteristics more associated with this kind of involvement.

METHODS

POPULATION AND DATA COLLECTION

Our study included consecutive patients who had a visit in a tertiary Rheumatology centre in Spain, from October 2013 until December 2014. This centre has being following an observational PsA cohort since 1992. All patients included in this observational cohort fulfill CASPAR criteria for PsA[2]. An ethical approval from the local ethic committee was obtained.

All patients were evaluated using a standard protocol every 6–12 months. All patients were assessed by the same physician. Demographic data and disease characteristics, such as disease duration, age at psoriasis onset and familiar history were systematically assessed for all patients. Clinical assessments included a 68 tender/66 swollen joint count, Psoriasis Area and Severity Index (PASI)[10], axial symptoms and their characteristics, namely the presence of current or past history of chronic back pain, for more than 3 months duration that began before 45 years of age. Moderate-severe psoriasis was defined as a PASI more than 10 or current or past systemic treatment for psoriasis or current or past psoralen ultraviolet A (PUVA) phototherapy. Patients included in this transversal study were also systematically assessed for inflammatory back pain (according to ASAS criteria), arthritis, uveitis, enthesitis (heel), dactylitis, family history of SpA, psoriasis, intestinal inflammatory disease and good response to non-steroidal anti-inflammatory drugs (NSAIDs). Data on blood results, including erythrocyte sedimentation rate (ESR) and C reactive protein (CRP) were recorded at each visit. A patient was considered as having an elevated CRP if it had happen at least in one visit after excluding other causes of elevated CRP. The human leukocyte antigen (HLA) B27 status was evaluated for each patient. A new pelvic radiography was made if a recent sacroiliac evaluation (in the last 3 years) was not available. The evaluation of radiographic sacroiliitis according to modified New York criteria was performed in a blinded manner by a senior rheumatologist with more than 25 years of experience in handling SpA. The active patients of this cohort between October 2013 and December 2014 were classified as having or not axial SpA according to ASAS criteria, taking into account the available data in January 2015.

STATISTICAL ANALYSIS

Age, male gender, PsA symptoms duration, age at beginning of PsA symptoms, psoriasis disease duration, first degree relative with PsA, first degree relative with psoriasis, familiar history of AS, body mass index (kg/m^2), HLA-B27, inflammatory back pain, uveitis, dactylitis, enthesitis, moderate to severe psoriasis, Crohn disease/colitis and distal interphalangeal involvement were analyzed in an univariable logistic regression analysis, using ASAS criteria for axial SpA as the dependent variable. Variables with a p-value <0.05 were re-tested in a multivariable logistic regression. Those variables that maintained statistical significance were tested alone in another multivariable model. Analyses were performed with IBM SPSS Statistics (version 20.0).

RESULTS

PATIENT CHARACTERISTICS

A total of 233 patients were included in this study, from

October 2013 until December 2014. The demographic and clinical characteristics of the study population are presented in Table I.

Concerning all patients included, 83 (37.2%) had current or past history of chronic back pain, for more than 3 months duration that began before 45 years of age. However, only 42 (19.4%) fulfill ASAS criteria for axial SpA (16.5% according to image arm and 8.5% according to clinical arm). In our study, 22 patients had radiographic sacroiliitis according to modified New York criteria, without axial symptoms. Considering that there were 140 patients without history of back pain defined as above, then the prevalence of asymptomatic sacroiliitis was 15.7% between patients without axial symptoms.

TABLE I. BASELINE DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF THE STUDY POPULATION (N=233 PATIENTS)

Demographic variables (n=211 to 233)	
Male gender, n (%)	126 (54.1)
Age, mean (S.D.), years	57.9 (12.8)
First degree relative with psoriasis, n (%)	103 (46.4)
First degree relative with PsA, n (%)	23 (10.6)
Familiar history of AS, n (%)	10 (4.7)
Age at psoriasis onset, mean (S.D.), years	32.2 (15.2)
Age at PsA onset, mean (S.D.), years	40.3 (13.8)
BMI, mean (S.D.)	27.6 (4.6)
Disease characteristics (n=211 to 233)	
Psoriasis duration, mean (S.D.), years	26.9 (13.0)
PsA symptom duration, mean (S.D.), years	17.6 (11.9)
Presence of HLA-B27, n (%)	30 (13.4)
Moderate-severe psoriasis, n (%)	77 (34.5)
Back pain, >3 months duration, before 45 years of age, n (%)	83 (37.2)
Inflammatory back pain (ASAS definition), n (%)	61 (27.4)
Dactylitis, n (%)	103 (45.4)
Enthesitis (heel), n (%)	86 (38.6)
Uveitis, n (%)	8 (3.6)
DIP involvement, n (%)	77 (33.8)
Crohn disease/colitis, n (%)	5 (2.3)
Radiographic sacroiliitis (X-ray)*, n (%)	61 (26.2)
Axial SpA according to ASAS criteria, n (%)	42 (19.4)

*According to modified New York criteria; n: number; S.D.: standard deviation; PsA: Psoriatic arthritis; ASAS: Assessment of SpondyloArthritis international Society; DIP: distal interphalangeal; SpA: Spondyloarthritis; BMI: body mass index

UNIVARIABLE ANALYSIS

In univariable analysis, axial involvement according to ASAS criteria for axial SpAwas more probable in males, younger patients, longer duration of PsA symptoms, younger age at onset of PsA symptoms, familiar history of ankylosing spondylitis and first degree relative with PsA. The presence of HLA-B27, inflammatory back pain (IBP), history of uveitis and moderate to severe psoriasis were also associated with the presence of axial involvement according to these criteria (Table II).

MULTIVARIABLE ANALYSIS

In multivariable analysis, patients with IBP were more likely to attain axial involvement according to ASAS criteria [OR=25.111; 95% confidence interval (CI) = 8.770, 71.900, p-value <0.001]. Axial involvement was also more probable in the presence of HLA-B27 [OR=9.072; 95% CI=2.756, 29.860; p-value <0.001] and in males [OR=3.767; 95% CI=1.264, 11.232; p-value = 0.017].

DISCUSSION

In our population, 42 patients (19.4%) fulfilled CASPAR and ASAS criteria for axial SpA. Besides the prevalence of axial PsA has already been described, fewer studies addressed the overlap of this two classification criteria. In a small study, which enrolled 100 patients with psoriasis, 17 fulfilled CASPAR criteria. In those patients, 5 also fulfilled ASAS criteria for axial SpA (29.4%)[11]. Our results identified IBP (according to ASAS criteria), presence of HLA-B27 and male gender as factors associated with a higher probability of PsA patients being classified as having axial SpA according to ASAS criteria.

In this study, the prevalence of HLA-B27 was significantly different between two groups (51.5% of those fulfilling ASAS criteria; 8.9% of those not fulfilling ASAS criteria; p<0.001). Of course that care should be taken when interpreting these results because HLA-B27 is a major criterion in ASAS classification criteria. In general, the prevalence of HLA-B27 is higher in AS (85-90%) comparing to PsA patients (40-45%)[12]. This could be an important genetic marker of a subgroup of PsA patients as its prevalence in peripheral PsA is only a little higher than general population and increases in patients with axial involvement (not reaching the prevalence in ankylosing spondylitis)[12]. There are seve-

TABLE II. CLINICAL AND DEMOGRAPHIC FACTORS WHICH PREDICTED AXIAL INVOLVEMENT OF PSA PATIENTS ACCORDING TO ASAS CRITERIA

	Axial involvement according to ASAS criteria (n=42)	No axial involvement according to ASAS criteria (n=175)	Univariable logistic regression OR (CI 95%), p-value (n=200 to 217)	Multivariable logistic regression OR (CI 95%), p-value (n=183)	Multivariable logistic regression* OR (CI 95%), p-value (n=207)
	Clinical and demographic variables not included in ASAS criteria for axial SpA				
Male gender, n (%)	34 (81.0%)	83 (47.4%)	4.711 (2.064, 10.753), p<0.001	4.836 (1.177, 19,866), p=0.029	3.767 (1.264, 11.232), p=0.017
Age, mean (S.D.), years	54.0 (±11.4)	58.9 (±13.0)	0.970 (0.943, 0.997), p= 0.027	1.033 (0.976, 1.093), p=0.259	
PsA symptoms duration, mean (S.D.), years	20.9 (±13.2)	17.3 (±11.7)	1.024 (0.996, 1.052), p= 0.089		
Age at onset of PsA symptoms, mean (S.D.), years	32.6 (±11.5)	41.7 (±13.8)	0.947 (0.919, 0.976), p<0.001	0.952 (0.904, 1.001), p=0.055	
Psoriasis disease duration, mean (S.D.), years	26.3 (±12.9)	26.9 (±13.2)	0.996 (0.969, 1.024), p=0.785		
Body mass index, mean (S.D.), kg/m^2	27.6 (±5.0)	27.5 (±4.4)	1.005 (0.929, 1.086), p= 0.904		
Moderate to severe psoriasis, n (%)	18 (48.6%)	52 (30.2%)	2.186 (1.062, 4.501), p= 0.034	1.336 (0.368, 4.855), p=0.660	
DIP involvement, n (%)	11 (29.7%)	62 (35.4%)	0.771 (0.357, 1.665), p= 0.508		
	Variables included in ASAS criteria for axial SpA				
HLA-B27, n (%)	17 (43.6%)	12 (7.1%)	10.174 (4.292, 24.119),	8.447 (1.904, 37.469), p= 0.005	9.072 (2.756, 29.860), p<0.001
Inflammatory back pain, n (%)	34 (82.9%)	25 (14.5%)	28.754 (11.490, 71.956), p<0.001	15.737 (4.806, 51,535), p<0.001	25.111 (8.770, 71.900), p<0.001
Familiar history of AS, n (%)	6 (18.2%)	3 (1.8%)	12.148 (2.865, 51.502), p= 0.001	2.911 (0.224, 37.794), p=0.414	
First degree relative with PsA, n (%)	9 (27.3%)	14 (8.3%)	4.152 (1.620, 10.642), p=0.003	2.564 (0.413, 15.918), p= 0.312	
First degree relative with psoriasis, n (%)	19 (55.9%)	80 (46.2%)	1.472 (0.703, 3.086), p= 0.305		
Uveitis, n (%)	4 (11.1%)	3 (1.7%)	7.125 (1.522, 33.362), p= 0.013	1.356 (0.107, 17.269), p=0.814	

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TABLE II. CONTINUATION

	Axial involvement according to ASAS criteria (n=42)	No axial involvement according to ASAS criteria (n=175)	Univariable logistic regression OR (CI 95%), p-value (n=200 to 217)	Multivariable logistic regression OR (CI 95%), p-value (n=183)	Multivariable logistic regression* OR (CI 95%), p-value (n=207)
Dactylitis, n (%)	14 (37.8%)	80 (45.7%)	0.723 (0.349, 1.497), p=0.382		
Enthesitis (heel), n (%)	13 (36.1%)	67 (39.0%)	0.886 (0.420, 1.868), p=0.750		
Crohn disease / colitis, n (%)	3 (8.1%)	2 (1.2%)	7.324 (1.179, 45.510), p=0.033	10.802 (0.301, 388.030), p=0.193	

*Only statistical significant variables in the first model were selected; OR: Odds Ratio; CI: Confidence Interval; PsA: Psoriatic arthritis; AS: Ankylosing spondylitis; DIP: Distal interphalangeal; ASAS: Assessment of SpondyloArthritis international Society; SpA: Spondyloarthritis.

ral studies in agreement to this observation. Chandran *et al.* studied 206 PsA patients and found HLA-B27 positivity as a risk factor for axial involvement at first clinic visit [OR = 5.75, 95% CI (2.22, 14.90), p<0.001][12]. Similarly, a cross-sectional study performed in 70 PsA patients found correlation between HLA-B27 with bilateral sacroiliitis and with axial PsA (defined as the presence of radiographic sacroiliitis greater than or equal to grade 2, and/or any other typical radiological sign of spondylitis in patients with psoriasis)[9]. Furthermore, the axial radiographic phenotype between PsA seems to differ according to the presence of HLA-B27. Torre Alonso JC *et al.* reported a greater incidence of this genetic marker in bilateral sacroiliitis (85%) comparing to unilateral sacroiliitis (22%)[13]. Other more recent studies reinforced the association between HLA-B27 with specific patterns of involvement, such as, bilateral sacroiliitis[14] and also spondylitis[15]. In a recent review, it was stated that HLA-B27 in PsA would be associated with an AS-like phenotype and fulfillment of the diagnostic criteria for AS[16]. Male gender seems to be associated with axial PsA, however, according to literature, this association has less evidence than ankylosing spondylitis. Fewer studies addressed this issue, nevertheless, a study which performed MRI to 68 PsA patients show that MRI-diagnose sacroiliitis was more probable in males [18 of 37 males (49%)] comparing to females [8 of 31 (26%), p = 0.05][8]. Gladman *et al.* identified 82 women and 112 men followed at a dedicated PsA clinic. Results of a logistic regression analysis showed some evidence that male gender was associated to a more advanced axial involvement[17]. In another study, when a secondary outcome was analyzed, an association between gender and axial involvement was found. These authors redefined the criteria to axial involvement and based them only on the New York radiographic criteria. Male gender was a risk factor when this outcome was analyzed[12].

As described above, IBP may not be present in all PsA patients with axial involvement as there was a prevalence of 15.7% of asymptomatic sacroiliitis. However, when this feature is present, there is a high probability of an axial involvement, as demonstrated by an OR of 25.111. In those patients the suspicion of an axial PsA should be raised.

Other factors, as longer PsA duration[8], severe peripheral arthritis, elevated ESR[12], erythrodermic psoriasis[11] and lower onset ages of psoriasis and arthritis[18] were described as risk factors for axial involvement in PsA. On the other hand, Chandran *et al.* also described

that family history of PsA decreased the odds of axial involvement[12]. However, our study did no show these associations as statistically significant in the multivariable analysis.

The most important limitation of our study was that MRI assessment of sacroiliitis was performed only when clinically justified. This important factor could have led to an underdiagnosis of axial non-radiographic SpA. Patients with this condition may represent an early disease stage, which is important to identify. This patient subset may benefit from specific therapy; however, prevention of radiographic progression is a topic still in debate. Some SpA features, such as arthritis, psoriasis, good response to non-steroidal anti-inflammatory drugs and elevated CRP were not analyzed. However, we must take into consideration that all of these patients had psoriasis and arthritis. On the other hand, the classification of axial involvement was made in a clinical basis and the response to non-steroidal anti-inflammatory drugs and the CRP were considered in an individual patient basis.

The sacroiliac radiographs were assessed by an experienced rheumatologist in a blinded manner. This means that when he assessed the sacroiliac radiographs for this study, he had no information about any clinical or laboratorial data regarding the patient who he was accessing. It is known that there is an important inter- and intra-observer variability for this exam; however, this is a common bias present in the clinical practice that we should be aware of.

One of the strengths of our study was that all patients who had a visit during the enrolment period were included. So, the patients included in this study really represent a real world sample of PsA patients followed in a tertiary rheumatology centre.

To the best of our knowledge, the present study was the first to describe in a PsA cohort the prevalence of patients fulfilling ASAS criteria for axial SpA and the clinical characteristics associated with that fulfillment.

As HLA-B27 and IBP are already included in ASAS criteria, we highlight gender and other characteristics described in other studies as factors that should raise physician's suspicion of a possible axial involvement in a PsA patient.

In conclusion, ASAS criteria for axial SpA are useful to identify axial involvement in PsA patients. This type of involvement is more common in males, in the presence of HLA-B27 and IBP. Axial disease should be systematically assessed in clinical practice, mainly in patients presenting with this clinical features.

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