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Original Article

Psoriatic Arthritis: Differential Features at the Time of Clinical Presentation in a Large Cohort of Patients with Polyarthralgia

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Abstract

Objective: Most patients with psoriatic arthritis begin with cutaneous psoriasis, which is why all early detection strategies are based on screening in the dermatological consultation and referral to a rheumatologist. However, there are cases of patients who consult initially for musculoskeletal symptoms, mostly joint pain, regardless of family and/or personal history of psoriasis. This study aimed to estimate the frequency of psoriatic arthritis in a cohort of patients who consulted for polyarthralgia and to determine the differential features, at the time of clinical presentation, in relation to both patients with final diagnosis other than psoriatic arthritis and patients with diagnosis of rheumatoid arthritis.

Methods: Consecutive patients with polyarthralgia (including arthralgia of the hands) were included. Clinical examination, laboratory tests, ultrasound with power Doppler of both hands, and radiography of both hands and feet were performed at baseline. All patients were followed up and the definitive diagnosis of psoriatic arthritis was established.

Results: A total of 1055 were included, 88 (8.3%) ended with diagnosis of psoriatic arthritis. Diagnosis of psoriatic arthritis was positively associated with a family history of psoriasis (odds ratio = 4.14), psoriasis (odds ratio = 78.94), radiographic erosions (odds ratio = 5.74), and ultrasound with at least 1 joint with positive power Doppler (odds ratio = 7.11). In comparison with rheumatoid arthritis patients, diagnosis of psoriatic arthritis was positively associated with psoriasis (odds ratio = 433.42) and family history of psoriasis (odds ratio = 41.63). On the other hand, it was negatively associated with positivity, for both rheumatoid factor (odds ratio = 0.03) and anti-cyclic citrullinated peptide antibodies (odds ratio = 0.06).

Conclusion: The frequency of psoriatic arthritis was 8.3% and was associated with a personal and/or family history of psoriasis, radiographic erosions, and inflammatory involvement by Power Doppler Ultrasound (PDUS). In comparison with rheumatoid arthritis patients, psoriatic arthritis was associated with a personal and/or family history of psoriasis, while the presence of both rheumatoid factor and/or anti-cyclic citrullinated peptide antibodies was shown to be a protective factor for the diagnosis of psoriatic arthritis.

Keywords: Psoriatic arthritis, rheumatoid arthritis, rheumatoid factor, anti-cyclic citrullinated peptide antibodies, ultrasound, radiography

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Introduction

Psoriasis is a skin disease that can be related to multiple coexisting diseases. The most common coexisting condition is psoriatic arthritis (PsA), which can occur in up to 30% of patients with psoriasis. Psoriatic arthritis is a chronic inflammatory arthropathy that affects both the peripheral joints, the spine and the entheses and is characterized by various phenotypic subtypes with a variable clinical course, which generally leads to both late diagnosis and treatment.[1,2]

Psoriatic arthritis represents about 20% of referrals to early arthritis clinics and is a major challenge for its diagnosis and management. Its early diagnosis is very important in order not to cause long-term functional disability and to guarantee optimal management of arthritis and its comorbidities. To favor the early diagnosis of PsA, other conditions that can mimic the disease must be ruled out and, therefore, can delay an adequate therapeutic approach.[3,4]

Since many patients with PsA start with cutaneous psoriasis, most early detection strategies are based on detection in the dermatological setting and referral to rheumatologists.[5] However, there are cases of patients who consult initially for musculoskeletal symptoms, mostly joint pain, regardless of family and/or personal history of psoriasis.[6]

The aims of the present study were to estimate the frequency of PsA in a cohort of patients who consulted for polyarthralgia, including arthralgia of the hands, and to determine the differential features, at the time of clinical presentation, of these patients in relation to both patients with final diagnosis other than PsA and patients with final diagnosis of rheumatoid arthritis (RA).

Methods

A prospective longitudinal study including consecutive patients older than 18 years who were admitted for polyarthralgia, including arthralgia of the hands, to "Reuma-check"® evaluation program[7,8] was performed from August 2017 to March 2021. This baseline evaluation program includes clinical examination, laboratory tests, ultrasound with power Doppler (PD) of hands, and radiography (x-ray) of hands and feet. The different evaluating physicians (laboratory, imaging, and clinical) were unaware of the data from the other studies.

Baseline Clinical Assessment

All information to complete Clinical Disease Activity Index (CDAI)[9] and Disease Activity Index in 28 joints-erythrocyte sedimentation rate (DAS28-ESR)[10] was collected. Demographic characteristics were assessed. Clinical data (time of evolution of arthralgias, comorbidities) were collected. Musculoskeletal assessment was performed according to standard clinical procedures and included tender joint count (TJC 28), swollen joint count (SJC 28), visual analog scale with respect to patient global perception of disease activity (VAS patient global) and physician (VAS physician global). Function was evaluated by the Argentinean version of Health Assessment Questionnaire-Disability Index.[11]

Baseline Laboratory

Erythrosedimentation rate, C-reactive protein (CRP), rheumatoid factor (RF) by immunoturbidimetry, and anti-cyclic citrullinated peptide antibodies (ACPAs) by chemiluminescence were determined in all patients on the same day of the clinical evaluation.

Baseline Ultrasound Evaluation

All ultrasound (US) examinations were performed by a single rheumatologist with extensive experience in US, on the same day of the clinical evaluation. Patients were asked not to talk with the medical operator during the US examination. A MyLab 25 Gold (Esaote) machine with a multifrequency linear transducer (6-18 MHz) was used. A standardized scanning method recommended by European society (EULAR)[12] was used. The following joints were assessed bilaterally: wrist, second to fifth metacarpophalangeal, and second to fifth proximal interphalangeal, giving a total of 18 assessed joints per patient. Joint cavity widening, due to the presence of synovial fluid and/or synovial hypertrophy (grayscale synovitis) according to the "Outcomes measures in Rheumatology" definitions,[13] was evaluated at each joint. All joints were evaluated by PD technique to assess the presence of increased abnormal synovial vascularization. Intraarticular PD signal was scored on a semiquantitative scale 0-3 (grade 0 = no intraarticular PD signal; G1 = presence of a single PD signal; G2 = more than 2 confluent foci of PD signal but occupying less than 50% of intraarticular area; G3= PD signal in more than 50% of the intraarticular area). In order to maximize PD sensitivity and minimize the presence of artifacts, the settings of PD were adjusted as follows: low pulse frequency repetition (500 and 1000 Hz), dynamic range 20-40 dB, low wall filters,[2-3] and PD gain

Main Points

- This study adds to the classic findings of psoriatic arthritis (PsA), and the frequency of diagnosis from the arthralgia consultation was 8%.
- Personal and/or family history of psoriasis permits to differentiate PsA patients from other diagnosis.
- Radiography and ultrasound could differentiate PsA patients and patients with diagnosis other than PsA.

Table 1. Sociodemographic, Clinical, Laboratory, and Imaging Features of All Patients with Polyarthralgia, Including Hand Arthralgias

Feature	All patients, n = 1055
Age (years), mean (SD)	52.8 (14.2)
Female, %	76.1
Time between the onset of symptoms and the baseline visit (months), mean (SD)	28.7 (40.4)
Diabetes mellitus, %	10.6
Arterial hypertension, %	27.3
Dyslipidemia, %	17.5
Smoking, %	39
Family psoriasis, %	6.7
Cutaneous psoriasis, %	7.8
Patient global VAS (0-100), mean (SD)	50.7 (20.6)
Tender joints (28), mean (SD)	3.4 (3.5)
Swollen joints (28), mean (SD)	0.7 (1.6)
ESR, mean (SD)	20.1 (17.2)
CRP, mean (SD)	4.7 (13)
DAS28-ESR, mean (SD)	3.3 (1.1)
CDAI, mean (SD)	12.9 (7.2)
HAQ, mean (SD)	0.7 (2.5)
Rheumatoid factor, %	21.2
ACPAs, %	9.4
X-ray bone erosions, %	10.3
Ultrasound synovitis with positive power Doppler signal, % (hand and wrist)	7.7

SD, standard deviation; VAS, visual analog scale; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; DAS28-ERS, Disease Activity Index in 28 joints-erythrocyte sedimentation rate; CDAI, Clinical Disease Activity Index; HAQ-DI, Health Assessment Questionnaire-Disability Index; ACPAs, anticitrullinated protein antibodies.

below the level at which color noise appeared in the underlying bone.[14-17]

Baseline Radiography Assessment

X-ray of hands and feet was performed on the same day of the clinical evaluation. The presence or absence of erosions was determined by an experienced medical rheumatologist, at any joint included on the Sharp/van der Heijde.[18]

Follow-Up

Clinical, laboratory, and images data were uploaded to an electronic clinical system report. All patients were followed up after the first evaluation (baseline), only patients who completed at least 2 visits were included, by their treating rheumatologists, and the definitive diagnosis of PsA was established according to the Classification Criteria for Psoriatic Arthritis.[19] Also, a final diagnosis of RA was established according to the ACR/EULAR 2010 criteria.[20]

The study was conducted according to the Declaration of Helsinki and local law. Ethical approval for the study was obtained from the Italian Hospital from La Plata's Hospital's local ethics committee, and informed consent was obtained from all patients (number evaluation: 25326).

Statistical Analysis

Descriptive statistic was used to summarize patients' characteristics. Continuous variables were expressed as medians and interquartile range (IQR) or as means and standard deviation, and categorical variables were expressed as percentages with their corresponding 95% CI. Comparisons were performed using parametric and non-parametric tests for continuous variables and the Chi-squared test for categorical variables. A multivariate logistic regression analysis was performed. Dependent variable was: final diagnosis of PsA, and as independent variables those variables that in the bivariate analysis were significantly associated with the diagnosis of PsA, this applied for the comparison between patients with final diagnosis of PsA and patients with final diagnosis other than PsA, and for the comparison between patients with PsA and patients with RA.

Results

A total of 1055 patients with polyarthralgia, including hands arthralgia, were included (Table 1), of which 88 (8.3%, 95% CI: 6.8-10.1) had a final diagnosis of PsA. Median time between baseline assessment (clinical presentation) and diagnosis of PsA was 2 weeks (IQR = 0-2).

Comparison: PsA vs other diagnosis than PsA. Table 2 shows the sociodemographic, clinical evaluation, laboratory, and imaging features of patients with final diagnosis of PsA and their comparison with those patients with other diagnosis than PsA (n = 967).

Others diagnosis frequency includes arthralgias without diagnosis 20%, RA 17%, undifferentiated arthritis 5.8%, crystals arthritis 3.8%, systemic autoimmune diseases 9.1%, and osteoarthritis/soft tissue 36%.

No significant differences were found between patients with a final diagnosis of PsA and controls regarding the presence of diabetes mellitus, arterial hypertension, and dyslipidemia (10.2% vs. 15.4%, $P = .13$, 27% vs. 30.1%, $P = .55$ and 17.4% vs. 17.6%, $P = .97$, respectively), while there were significant differences regarding smoking, 52.4% of patients with PsA vs. 37.6% no PsA ($P = .008$).

In the multivariate logistic regression analysis, the diagnosis of PsA was positively associated with a family history of cutaneous psoriasis (odds ratio (OR)= 4.14, 95% CI: 1.12-15.34), personal history of cutaneous psoriasis (OR = 78.94, 95% CI: 30.43-204.78), x-ray erosions (OR = 5.74, 95% CI: 1.94-16.93), and US with at least 1 joint with positive PD signal (OR = 7.11, 95% CI: 1.88-26.88) (Table 3).

Comparison: PsA vs RA. Totally 190 (18%, 95% CI: 15.8-20.4) patients had a final diagnosis of RA. Median time between baseline assessment (clinical presentation) and diagnosis of RA was 2 weeks (IQR = 2-2). Table 2 shows

Table 2. Sociodemographic, clinical, laboratory, and imaging features of patients with final diagnosis of PsA and their comparison with both patients with diagnosis other than PsA and patients with final diagnosis of rheumatoid arthritis

	Psoriatic Arthritis, n = 88	Diagnosis Other Than Psoriatic Arthritis, n = 967	*P*	Rheumatoid Arthritis, n = 190	*P*
Age (years), mean (SD)	50.4 (12.6)	53 (14.4)	.09	56.1 (13.6)	.001
Female, %	56.8	77.9	<.0001	72.1	.01
Time between the onset of symptoms and the baseline visit (months), mean (SD)	55.2 (64.3)	26.2 (36.5)	<.0001	30.5 (47.6)	.0005
Family psoriasis, %	26.1	4.8	<.0001	4.4	<.0001
Cutaneous psoriasis, %	70.9	1.9	<.0001	1.6	<.0001
Patient global VAS (0-100), mean (SD)	56.8 (23.1)	50.2 (20.3)	.01	55.3 (20.7)	.64
Tender joints (28), mean (SD)	2.8 (2.6)	3.5 (3.6)	.11	5 (3.7)	<.0001
Swollen joints (28), mean (SD)	1.5 (2.1)	0.6 (1.5)	<.0001	1.7 (2.5)	.50
ESR, mean (SD)	21.3 (17.4)	20 (17.2)	.49	29.2 (24.8)	.008
CRP, mean (SD)	5.4 (6.6)	4.6 (13.4)	.59	10.7 (22.5)	.03
DAS28-ESR, mean (SD)	3.4 (1.2)	3.3 (1.1)	.67	4.1 (1.2)	.0001
CDAI, mean (SD)	14.1 (7.2)	12.8 (7.2)	.17	17.4 (8)	.003
HAQ, mean (SD)	0.7 (0.4)	0.7 (2.6)	.97	1.3 (5.8)	.31
Rheumatoid factor, %	11.4	21.9	.05	66.4	<.0001
ACPAs, %	2.2	9.9	.09	41.7	<.0001
X-ray bone erosions, %	39.2	7.7	<.0001	18.1	.0003
Ultrasound synovitis with positive power Doppler signal, %	33.7	5.2	<.0001	22.9	.06

SD, standard deviation; VAS, visual analog scale; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; DAS28-ERS, Disease Activity Index in 28 joints-erythrocyte sedimentation rate; CDAI, Clinical Disease Activity Index; HAQ-DI, Health Assessment Questionnaire-Disability Index; ACPAs, anticitrullinated protein antibodies.

Table 3. Multivariate logistic regression analysis for the comparison between patients with final diagnosis of psoriatic arthritis and patients with final diagnosis other than psoriatic arthritis

Features	Odds Ratio (95% CI)
Female	0.73 (0.27-1.99)
Time between the onset of symptoms and the baseline visit	1.01 (0.99-1.01)
Smoking	1.64 (0.64-4.17)
Family psoriasis	4.14 (1.12-15.34)
Cutaneous psoriasis	78.94 (30.43-204.78)
Patient global VAS (0-100)	1 (0.98-1.02)
Swollen joints (28)	1.02 (0.80-1.31)
ESR	0.98 (0.96-1.01)
X-ray bone erosions	5.74 (1.94-16.93)
Ultrasound synovitis with positive power Doppler signal	7.11 (1.88-26.88)

VAS, visual analog scale; ESR, erythrocyte sedimentation rate.

all features of patients with final diagnosis of PsA and their comparison with those patients with RA. No significant differences were found between patients with a final diagnosis of PsA and patients with RA regarding the presence of diabetes mellitus, arterial hypertension, and dyslipidemia (15.4% vs. 13.4%, $P = .65$, 30.1% vs. 33.8%, $P = .54$ and 17.6% vs. 22.9%, $P = .32$, respectively), as well as smoking, 52.4% of patients with PsA vs. 44% of patients with RA ($P = .20$).

In the multivariate binomial regression analysis, the final diagnosis of PsA was positively associated with the personal history of cutaneous psoriasis (OR = 433.42, 95% CI: 29.41-6378.25) and the family history of cutaneous psoriasis (OR = 41.63, 95% CI: 4.91-351.98). On the other hand, it was negatively associated with positivity, for both RF (OR = 0.03, 95% CI: 0-0.39) and ACPAs (OR = 0.06, 95% CI: 0-0.96) (Table 4).

Discussion

We have studied the differential features at the same time as the clinical presentation in patients with a final diagnosis of PsA in a large cohort of polyarthralgia, including hand arthralgias (n = 1055). The frequency of PsA in our cohort of patients was 8.3%.

When we compared the differential features between patients with PsA and the rest of patients with final diagnosis other than PsA, we found in the bivariate analysis that patients with PsA were more frequently male, had a long time between the onset of symptoms (arthralgia) and the baseline visit, there was a higher percentage of smoking, had a family and/or personal history of cutaneous psoriasis, a greater global VAS of the patient, a greater number of swollen joints, a greater percentage of patients with radiographic erosions, and a greater percentage of patients with inflammatory involvement by PDUS. However, when performing the multivariate binomial logistic regression analysis, the final diagnosis of PsA was positively associated with the family and/or personal history of cutaneous psoriasis, radiographic erosions, and inflammatory involvement by PDUS. Although some of the named features are part of the AP classification criteria that support this association, it is important to highlight the role of US as an important tool in view of the need for a timely and differential diagnosis.[21] Additionally, these patients could benefit from the assessment of enthesis by US for better characterization.[22-25] In our previously published cohort of PsA and axial SpA, we found a difference between the presence of clinical enthesitis and enthesitis by US at diagnosis, in PsA, 30% had clinical enthesitis and 45% by US and in axial spondyloarthritis (SpA), it was 42% and 69%, respectively.[8,26]

Table 4. Multivariate logistic regression analysis for the comparison between patients with final diagnosis of psoriatic arthritis and patients with final diagnosis of rheumatoid arthritis

Features	Odds Ratio (95% CI)
Age	0.88 (0.78-1.05)
Female	0.08 (0-5.93)
Time between the onset of symptoms and the baseline visit	1.01 (0.98-1.05)
Family psoriasis	41.63 (4.91-351.98)
Cutaneous psoriasis	433.42 (29.41-6378.25)
Tender joints (28)	0.47 (0.29-2.46)
ESR	1.02 (0.96-1.08)
CRP	0.99 (0.91-1.08)
DAS28-ESR	1.16 (0.23-5.91)
CDAI	1.25 (0.98-1.54)
Rheumatoid factor	0.03 (0-0.39)
ACPAs	0.06 (0-0.96)
X-ray bone erosions	1.86 (0.16-21.69)

ESR, erythrocyte sedimentation rate; CRP:,C-reactive protein; DAS28-ERS, Disease Activity Index in 28 joints-erythrocyte sedimentation rate; CDAI, Clinical Disease Activity Index; ACPAs, anticitrullinated protein antibodies.

When comparing the differential features between patients with PsA and patients with final diagnosis of RA, we found in the bivariate analysis that patients with PsA were younger, with a higher percentage of male, had a long time between the onset of symptoms (arthralgia) and the baseline visit, had a family and/or personal history of cutaneous psoriasis, fewer tender joints, higher ESR and CRP values, higher DAS28-ESR and CDAI values, lower percentages of positivity for both RF and ACPAs, and higher percentage of radiographic erosions. However, when performing the multivariate logistic regression analysis, the final diagnosis of PsA was positively associated with family and/or personal history of cutaneous psoriasis, while positivity for both RF and ACPAs was shown as a protective factor for the final diagnosis of PsA. In a previous study, we have shown in an extensive cohort of patients with arthralgia that both RF and ACPAs are important biomarkers for the development of RA, and also in the same study, the presence of synovitis by PDUS proven to be an associated factor for the development RA.[7] However, in the current study, synovitis detected by PDUS does not seem to be a tool to differentiate PsA from RA. It should be noted that there could

be some specific anatomical alterations that are specific to each disease according to the US study,[14,27] but we could believe that maybe in early stages of the disease, they are not evident.

Based on the above, we can affirm that the fact of having cutaneous psoriasis and/or a family history of psoriasis allowed us to distinguish patients with a final diagnosis of PsA, comparing both patients with a diagnosis other than PsA and patients with RA. We can also affirm that 2 accessible and low-cost imaging methods such as x-ray (radiographic erosions) and PDUS (inflammatory involvement at the level of the hands) can help to distinguish patients with a final diagnosis of PsA from those patients with a final diagnosis other than the PsA. Regarding the distinction between patients with a final diagnosis of PsA and patients with RA, a complementary method usually used such as the laboratory helped us to distinguish between these 2 diseases since the positivity for RF and/or ACPAs was shown as a protective factor for the development of PsA.

Although it was not maintained as a differential feature of patients with PsA in the multivariate logistic regression analysis, in the bivariate analysis, there were significant differences in favor of a long time between the onset of symptoms and the baseline visit in patients with PsA compared to both patients with final diagnosis other than PsA and patients with RA. On the other hand, radiological involvement (radiographic erosions) was greater in patients with PsA compared to both patients with final diagnosis other than PsA and patients with RA. Both features allow us to intuit a greater evolution of the disease in patients with PsA at the time of clinical presentation. We cannot explain this finding, but we can think that in PsA perhaps the symptoms are more overlapping and that patients prior to rheumatology consultation have consulted other medical specialties without reaching the diagnosis of PsA. On the other hand, it must be taken into account that most studies on the early diagnosis of PsA are based on referral from dermatological centers and that they use validated questionnaires.[28] Our findings are from patients who consulted for musculoskeletal symptoms spontaneously or were referred from primary care.

One of the main limitations of our study was that we neither use specific compound indices of PsA to assess disease activity nor use specific indices to assess the extent of skin involvement.

As a strength of our study and to the best of our knowledge, this is one of the first works evaluating the differential features of patients with PsA at the time of the first rheumatology consultation in the context of a large cohort of patients with musculoskeletal symptoms, which were evaluated in a comprehensive way (clinical, laboratory, and images) in the same center and under the same procedures.

In conclusion, the frequency of PsA in our polyarthralgia cohort, including hand arthralgias, was 8.3% and at the time of clinical presentation was associated with a personal or family history of cutaneous psoriasis, hand erosions (x-ray), and the presence of hand US with PD signal at joint level. The frequency of RA in our cohort of patients was 18%. In comparison with patients with RA, at the time of PsA clinical presentation, it was associated with a personal and/or family history of cutaneous psoriasis, while the presence of both RF and/or ACPAs was shown to be a protective factor for the final diagnosis of PsA.

Ethics Committee Approval: Ethical committee approval was received from the Local Ethics Committee of Hospital Italiano de La Plata (Approval No: 25326).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

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Declaration of Interests: The authors have no conflicts of interest to declare.

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