

# Early Psoriatic Arthritis: The Clinical Spectrum

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

*Methods.* We studied 47 consecutive patients: 29 had definite PsA and 18 had the “sine psoriasis” subset. Inclusion criteria were articular and/or enthesal involvement of  $\leq 12$  weeks’ duration and the exclusive use, before enrollment, of nonsteroidal antiinflammatory drugs to control articular symptoms. All patients underwent clinical examination, blood tests, total-body bone scintigraphy, articular ultrasonography, and radiography of clinically involved joints and/or entheses.

*Results.* On the basis of clinical examination, early PsA was an oligo-enthesoarthritis in over 75% of patients studied. In contrast, the number of joints and/or entheses showing increased tracer uptake on bone scintigraphy was 3 times greater, compared to the clinical evidence ( $p < 0.001$ ). Articular ultrasonography confirmed the inflammatory involvement of synovium and/or entheses in all articular sites active at time of bone scintigraphy, but silent at clinical examination. In addition, 7 patients showed the occurrence of joint and/or enthesal erosions on standard radiography.

*Conclusion.* Bone scintigraphy yields a more accurate evaluation of entheso-articular involvement and distribution in patients with early PsA. Our results suggest that clinical oligo-enthesoarthritic presentation of early PsA might represent in most cases a polyarticular condition that is at increased risk for clinical progression. These findings have a significant influence on the clinical decision-making process in patients with early PsA. (First Release Nov 15 2007; J Rheumatol 2008;35:137–41)

## Key Indexing Terms:

PSORIASIS

PSORIATIC ARTHRITIS

CLINICAL INVOLVEMENT

BONE SCINTIGRAPHY

DIAGNOSTIC IMAGING

In recent years, rapid therapeutic intervention before the onset of stable structural damage has become the primary goal in treatment of patients with rheumatoid arthritis. Indeed, optimal outcome may be obtained with an early diagnosis and rapid, effective therapy. In the case of psoriatic arthritis (PsA), it has been demonstrated that the severity of articular inflammation may be clinically underestimated<sup>1</sup>. In addition, it is still believed that PsA is a mild condition, characterized by fewer longterm sequelae and unlikely to progress to permanent joint damage. In the last 20 years, the potentially devastating joint destruction of PsA has been clearly recognized, and the need for rapid detection and quick therapeutic intervention has become mandatory in this condition as well<sup>2–4</sup>.

We describe our diagnostic experience in patients with PsA within weeks of onset of articular symptoms. In particular, we give detailed clinical characteristics of this syndrome, which could be defined as “early psoriatic arthritis.”

## MATERIALS AND METHODS

*Patients.* Forty-seven patients (25 women, 22 men, mean age  $26 \pm 6$  yrs) consecutively attending the rheumatology unit from September 2004 to April 2005 entered the study. General physicians and/or dermatologists referred the patients. Those referred by general physicians also had a dermatologic examination. Twenty-nine patients (17 women, 12 men, mean age  $28 \pm 6$  yrs) had established PsA according to the Moll and Wright criteria<sup>5</sup> and 18 (8 women, 10 men, mean age  $26 \pm 5$  yrs) had the “sine psoriasis” subset according to our previous investigation<sup>6</sup>.

*Inclusion criteria.* The inclusion criteria were: (1) articular and/or enthesal involvement of  $\leq 12$  weeks’ duration; and (2) the exclusive use, before enrollment, of nonsteroidal antiinflammatory drugs on demand to control articular symptoms.

*Clinical assessment.* After medical history was obtained, a detailed examination was performed by 2 expert rheumatologists (RS, ADP); this included determination of number of affected joints (tender and/or swollen) according to the American College of Rheumatology joint count<sup>7</sup>; and number of involved entheses assessed according to the MASES score<sup>8</sup>. Spinal involvement was determined using maneuvers for sacroiliac joints<sup>2</sup> and back movements<sup>9–11</sup>. All patients underwent standard radiography of joints and/or clinically involved entheses.

*Bone scintigraphy.* After clinical examination, all patients received a 740-MBq injection of  $Tc^{99m}$  methylene diphosphonate. Total-body delayed images of the anterior and posterior views, and spot views were acquired 3 h after administration of tracer. Images were acquired using a large field of view gamma camera (Millennium, GE Healthcare) with a high resolution col-

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limator connected to a computer. Images were displayed on hard-copy photographic film and were submitted for reporting with patient names removed. Scintigraphic images were classified using a 4-point scoring system, showing normal tracer uptake (score 0) and mild (score 1), moderate (score 2), or marked (score 3) increase of uptake. Images were independently scored by 2 nuclear medicine physicians (AC, EN) after they had examined a training set of 6 bone scans together to establish a common understanding of the classifications.

*Ultrasonography.* Within 3 days, all patients underwent articular ultrasonography on the joints and/or entheses showing increased tracer uptake at bone scintigraphy but not clinically involved; and on 2 standard control joints and/or entheses without clinical involvement and with normal tracer uptake, chosen randomly for each patient. Ultrasound studies were performed using a gray-scale and color Doppler technique by a single experienced reader (PG), who was blind to all other study findings. A Philips iU22 ultrasound machine was used according to the European League Against Rheumatism (EULAR) guidelines<sup>12</sup>. The presence and the location of synovitis and/or enthesitis were recorded with reference to the Outcome Measures in Rheumatology Clinical Trials (OMERACT/EULAR) definition of pathology<sup>13</sup>.

*Laboratory assessment.* Laboratory tests included hematology, serum chemistry, and urinalysis; erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), rheumatoid factor (RF), antinuclear antibodies (ANA), and complement fractions C3 and C4 were determined.

*Statistical analysis.* For categorical variables, statistical analysis was carried out using Fisher's exact test or chi-square test where appropriate. Continuous variables were reported as mean ± standard deviation or as median and interquartile range, depending on the Gaussian distribution of data. The difference for the paired variables was analyzed with the Wilcoxon signed-rank test. A p value < 0.05 was considered statistically significant. Data were analyzed with SPSS, release 14.0.2.

## RESULTS

*Clinical and scintigraphic findings.* At clinical examination, oligoarthritis was the most frequent disease subset, occurring in 35 patients, while polyarthritis and spondylitis were less common, occurring in 6 patients each. Tables 1 and 2 give the numbers of articular and enthesal sites, respectively, involved at clinical examination and bone scintigraphy in all patients. The proximal interphalangeal joints were the most frequently clinically involved articular sites, followed by distal interphalangeal and knees. Other sites (sacroiliac, ankle, and metatarsophalangeal) showed a lower prevalence of clinical involvement.

The total number of joints and/or enthesal sites showing

Table 1. Number of articular sites involved at clinical examination and bone scintigraphy in 47 patients with early PsA.

Site, n	Clinical Examination	Bone Scintigraphy
Proximal interphalangeal	20	26
Distal interphalangeal	18	26
Knee	14	29
Sacroiliac	10	28
Ankle	9	15
Sternoclavicular	3	34
Metatarsophalangeal	0	18
Metacarpophalangeal	0	10
Total	81	186

Table 2. Number of enthesal sites involved at clinical examination and bone scintigraphy in 47 patients with early PsA.

Site, n	Clinical Examination	Bone Scintigraphy
Calcaneal	14	38
Paravertebral	6	24
Iliac	4	13
Femur	0	4
Total	24	103

increased tracer uptake with bone scintigraphy was greater than that noted at the clinical examination (Tables 1 and 2). Mean uptake score was 2.3 ± 0.4 in the 186 articular sites and 2.4 ± 5.5 in the 103 enthesal sites involved at bone scintigraphy. In particular, enthesal involvement on bone scintigraphy reached a greater proportion of the total distribution (36% vs 23% documented by clinical examination). On the basis of tracer uptake on bone scintigraphy the profile of joint and/or enthesal distribution was markedly different. Indeed, an increase in the number of sternoclavicular, knee, and sacroiliac joints was observed. Enthesal sites (calcaneal and paravertebral) also showed a more relevant involvement upon scintigraphy as compared to the clinical evidence findings. In particular, femoral entheses and metacarpophalangeal joints showed evidence of increased tracer uptake in the absence of clinical involvement. In addition, the median number of joints and/or entheses showing increased tracer uptake on scintigraphy was significantly greater (p < 0.001) than the median number of joints and/or entheses that were clinically involved (Table 3). This result is confirmed upon categorizing patients according to the clinical disease subsets (Table 3).

*Ultrasonographic findings.* Articular ultrasound showed the presence of synovial fluid effusion and signs of synovitis and/or enthesitis in all the articular and/or enthesal sites with an increased tracer uptake on bone scintigraphy, even in cases that were not clinically involved (representative examples shown in Figures 1 and 2). A significant vascular spot was detected on color Doppler images in 71% of the clinically involved sites and in none of the sites not clinically involved. Only 2 of the 94 control sites tested showed the presence of some degree of joint involvement (synovial and/or enthesal).

Table 3. Median number (interquartile range) of articular and/or enthesal sites involved at clinical examination and bone scintigraphy in all patients with early PsA (n = 47) and in the oligoarthritic (n = 35), polyarthritic (n = 6), and spondylitic (n = 6) subsets.

Subset	Clinical Examination	Bone Scintigraphy	p
All early PsA patients	2 (2)	6 (3)	< 0.001
Oligoarthritic subset	2 (1)	6 (3)	< 0.001
Polyarthritic subset	5 (2)	12 (6)	< 0.05
Spondylitic subset	2 (1)	6 (1)	< 0.05

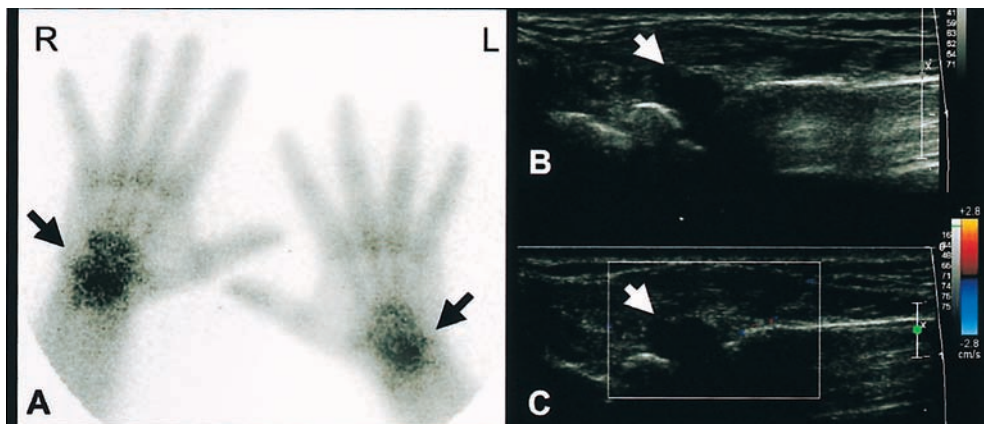


Figure 1. 28-year-old male patient: clinical assessment showed an oligoarthritic form, while total-body bone scintigraphy demonstrated a polyarticular pattern. In particular, on bone scintigraphy (A) the wrists showed increased uptake (arrows) in the absence of symptoms or signs of clinical involvement. B-mode ultrasonography (B) of the left radio-carpal joint demonstrated gray-scale changes of synovial hypertrophy (arrow); on the echo-color Doppler scan (C) note the absence of hyperemia (arrow).

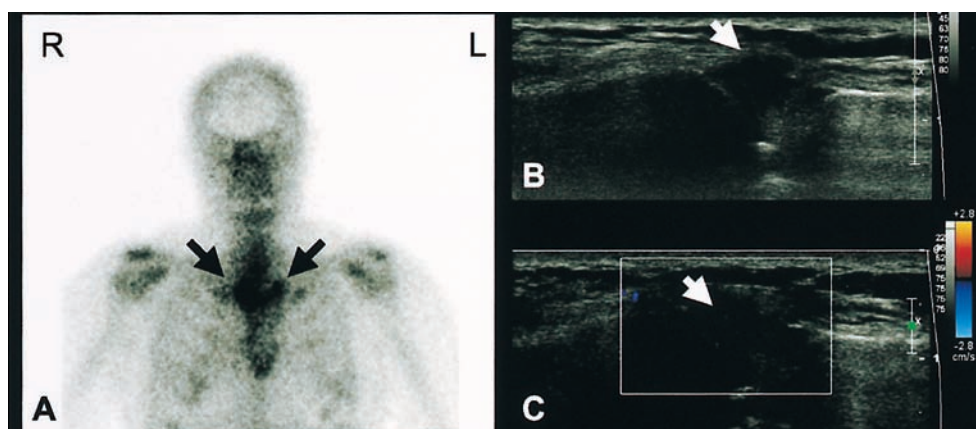


Figure 2. 45-year-old female patient: clinical assessment showed a polyarticular form with 5 joints involved, while total-body bone scintigraphy demonstrated involvement of other articular sites. In particular, on bone scintigraphy (A) there was increased tracer uptake at sternoclavicular joints (arrows) in the absence of symptoms or signs of clinical involvement. B-mode ultrasonography (B) of the right sternoclavicular joint demonstrated gray-scale changes of synovial hypertrophy (arrow); on the echo-color Doppler scan (C) note the absence of hyperemia (arrow).

**Radiographic findings.** In 7 patients (15%) radiography showed the occurrence of articular erosions: calcaneal in 4 patients, and metacarpophalangeal, wrist, and metatarsophalangeal in 1 patient each.

**Laboratory findings.** ESR was increased in 47% of the total patients and CRP in 89%. No significant levels of ANA were found, and C3 and C4 complement fractions were normal in 68% of the patients and increased in 32%.

## DISCUSSION

The severity of articular inflammation in psoriatic patients may be clinically underestimated and the clinical pattern of the condition worsens over time<sup>1</sup>. Jones, *et al* demonstrated that 64% of patients starting with mono- or oligoarthritis developed polyarthritis during followup<sup>14</sup>. The significantly

greater disease duration of the polyarthritic group suggested that the number of joints involved was a function of disease duration. When compared to subjects with oligoarthritis, psoriatic patients with polyarthritis had been more frequently treated with disease modifying antirheumatic drugs (DMARD; 9% vs 51%, respectively). The study by Jones, *et al*<sup>14</sup> is a useful starting point for analysis of our results. Indeed, it suggests that PsA is not a mild condition, it has several longterm sequelae and frequently progresses to permanent joint damage; and that delaying the treatment with DMARD may lead to an unfavorable outcome. The results of our investigation show that erosions are not rare even in the early phases of the disease.

Our findings reveal a marked discrepancy between clinical and imaging results. The clinical presentation of early PsA

seems to be mainly an oligo-enthesoarthritis. In contrast, total-body bone scintigraphy in early PsA has shown evidence of sites of articular involvement that were not apparent at the clinical examination. Patients with oligo-enthesoarthritis on bone scintigraphy revealed articular involvement with a median value of 6 articular sites (a 3-fold increase as compared to the clinical evidence). It has been reported that scintigraphic articular uptake may reflect an increased risk of progression of articular damage<sup>15,16</sup>. In addition, our results show a strong correlation between scintigraphic uptake and ultrasonographic evidence of inflammatory involvement. It is well known that the detection of articular involvement by physical examination, apart from having suboptimal reproducibility, has low sensitivity<sup>17</sup>. Bone scintigraphy could represent a better way to determine entheso-articular involvement and to identify sites not yet evident from a clinical viewpoint. It could provide an opportunity for a staging of the disease that is more representative of the actual distribution.

Our results are also in agreement with those of Offidani, *et al*<sup>18</sup>, who showed that in psoriatic patients free from arthritic symptoms the use of magnetic resonance imaging allows clear and adequate evaluation of cartilage, bone, and soft tissue, and is diagnostically superior to radiographs in revealing clinically silent and radiologically invisible articular lesions<sup>18</sup>. Availability of more accurate evaluation of entheso-articular involvement in patients with early PsA using bone scintigraphy could also illustrate the clinical change over time, as reported above. Knowledge of the number of biologically involved sites may enable choice of the most appropriate treatment. However, this issue can only be addressed by specifically designed followup studies.

On the basis of these points, it should be considered that features of PsA observed in the early stages might be clinically underestimated. Moreover, clinical measures that are widely used in established PsA fail to quantify the activity of skin and/or articular elements. Indeed, the Psoriasis Activity and Severity Index (PASI) is not appropriate because PsA in the early stages also includes patients without rash<sup>19</sup>. On the other hand, the Psoriatic Arthritis Response Criteria instrument (PsARC) also is not appropriate because it is unable to measure enthesal involvement, which appears to be the most characterizing aspect of this syndrome<sup>20</sup>. Finally, another point that may be potentially misleading for rapid recognition of this syndrome is the routine use of indices such as ESR or CRP that are normal in nearly half of the cases observed.

Our results suggest the following conclusions: (1) Early PsA is an entheso-articular syndrome with a consistent risk of clinical progression. (2) Its marked enthesal involvement is a distinctive clinical aspect that helps to discriminate it from other conditions observed at their onset, such as rheumatoid arthritis; in particular, this shows the need for an appropriate distinction between "early rheumatoid" and "early psoriatic" arthritis. (3) Adequate clinical or biological indices are still needed to monitor this condition. The PASI and/or PsARC

and measurements of ESR and CRP are not completely appropriate to measure its outcome.

The primary goal in the management of all forms of arthritides is rapid therapeutic intervention before the onset of stable structural damage. However, in early PsA a therapeutic approach with a traditional DMARD would be insufficient in controlling the progression over time. This observation is based on the fact that DMARD are usually ineffective in the control of enthesal involvement of spondyloarthropathies<sup>21,22</sup>. A more detailed diagnostic approach, such as total-body bone scintigraphy, would be the best contribution to an appropriate therapeutic program.

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