

## CONCISE REPORT

## A polyarticular onset predicts erosive and deforming disease in psoriatic arthritis

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**Objectives:** To analyse the factors predicting erosive-deforming arthropathy in patients with psoriatic arthritis (PsA).

**Methods:** A prospective cohort study was undertaken with 71 patients diagnosed as having PsA (44 men and 27 women, mean age 47 (SD 12) years). At the recruitment period patients had disease without evidence of radiological damage. Patients were studied and followed up according to a standard protocol from January 1991 to June 2001. Erosive and deforming disease was defined by the presence of erosions, joint space narrowing, subluxation, and/or ankylosis of peripheral joints. Univariate and multivariate analyses were performed to evaluate factors predicting erosive and deforming disease.

**Results:** At the end of the study 32 of 71 (45%) patients had developed erosive and deforming disease. Among them, 18 of 32 (56%) had a polyarticular onset, two of 32 (6%) showed a distal interphalangeal joint disease onset, six of 32 (19%) presented with oligoarthritis, and six of 32 (19%) presented with axial disease as the form of disease onset ( $p=0.001$ ). Mean time to detect erosions or joint space narrowing was 20 (SD 4) months. Men showed fewer erosions than women ( $p=0.05$ ). Patients who carried the HLA-B27 antigen showed less erosive disease than patients who lacked it ( $p=0.05$ ). Patients with erosive and deforming disease had poorer functional performance than those without it as measured with the Health Assessment Questionnaire (HAQ) and the American College of Rheumatology (ACR) criteria ( $p<0.05$  with both measurements). In multivariate analysis, only a polyarticular onset remained as an indicator of erosive and deforming disease (odds ratio (OR) 37, 95% confidence interval (95% CI) 3.6 to 88,  $p=0.025$ ).

**Conclusions:** A polyarticular onset (five or more swollen joints) of PsA was the unique independent risk factor which predicted the appearance of erosive and deforming disease over time. These data may be useful for clinicians treating patients with PsA, as it may guide treatment towards a more aggressive and earlier intervention.

Psoriatic arthritis (PsA) is a form of pleomorphic arthropathy which, until recently, was considered a benign arthritis.<sup>1</sup> Despite the fact that arthritis mutilans has been recognised as a distinct pattern of PsA, its presence was described in only 5% of patients.<sup>1,2</sup> However, joint deformity and destruction, as well as disability, are common among patients with PsA, thus challenging the concept that this arthropathy is benign.<sup>1</sup>

There are few reports describing the factors in PsA associated with disease progression and radiological damage. Gladman *et al* showed that patients who presented with five or more swollen joints were at increased risk for progression of joint deformities, as were patients who had been given high

doses of drugs.<sup>3</sup> The same group of investigators showed that some HLA antigens were predictive of progression of deformities.<sup>4</sup> Therefore, it would be very useful for clinicians treating patients with PsA to identify those who are destined to develop severe disease, so that treatment can be started as soon as possible.

In the present report we analysed patients with PsA with erosive and deforming joint disease to define their clinical features and to identify which clinical factors predicted its appearance.

## PATIENTS AND METHODS

This prospective cohort study comprised 71 patients with PsA (44 men and 27 women, mean age 47 (SD 12) years) defined according to the definition given by Moll and Wright.<sup>2</sup> Patients were recruited consecutively at one university hospital from January to June 1991 and were followed up in accordance with a standard protocol every six months until June 2001, when data were finally collected and analysed. At their first visit, patients presented with disease of 12 (SD 8) months in duration without erosions or any other type of anatomical damage on radiographic examination. Demographic and epidemiological data, clinical history, physical examination, laboratory data, radiographs, and functional evaluations were obtained for all patients. At the first six monthly visit patients were classified according to the system of Moll and Wright,<sup>2</sup> but at the end of the study the final classification was made according to the system proposed by Torre-Alonso *et al*.<sup>5</sup> Oligoarthritis was diagnosed when four or less swollen joints were present on physical examination, polyarthritis if there were five or more, and axial disease was diagnosed on the basis of inflammatory back pain and radiological sacroiliitis (bilateral grade two or more) irrespective of the presence of peripheral disease. Functional assessment was made using the Health Assessment Questionnaire (HAQ) general version,<sup>6</sup> and with the classification of global functional status given by the American College of Rheumatology (ACR).<sup>7</sup>

Complementary means of confirmation included a complete blood count, erythrocyte sedimentation rate, C reactive protein level, rheumatoid factor, antinuclear antibody test, hepatic and renal function testing, complement proteins C3 and C4 levels and serum immunoglobulins. We performed HLA-B27 testing by serological methods and HLA-Cw typing by polymerase chain reaction with sequence specific primers (PCR-SSP) in the whole cohort and in 177 healthy blood donors of the same racial origin. Radiographic evaluation included anteroposterior and lateral views of the hands, feet, and cervical, dorsal, and lumbar column. We also obtained a

**Abbreviations:** ACR, American College of Rheumatology; 95% CI, 95% confidence interval; DMARDs, disease modifying antirheumatic drugs, HAQ, Health Assessment Questionnaire; PsA, psoriatic arthritis; OR, odds ratio; RR, relative risk

**Table 1** Characteristics of patients with and without erosive and deforming disease

Variables	Erosive disease n=32	Non-erosive disease n=39	p Value
Age (years (SD))	48 (11)	46 (12)	NS
Age at psoriasis onset (years (SD))	28 (10)	26 (11)	NS
Age at arthritis onset (years (SD))	36 (9)	38 (10)	NS
Psoriasis duration (years (SD))	18 (11)	19 (10)	NS
Arthritis duration (months (SD))	8 (7)	10 (6)	NS
Family history (%)	19	23	NS
Psoriasis first (%)	72	77	NS
Male to female ratio	1	2.5	0.05
Polyarthritis (%)	73	27	0.0001
Axial disease (%)	43	57	NS
Oligoarthritis (%)	43	57	NS
DIP disease (%)	62	36	0.048
Onychopathy (%)	62	49	NS
HLA-B27 (%)	22	46	0.05
HLA-Cw*0602 (%)	50	56	NS
HAQ (mean (SD))	1.2 (0.3)	0.6 (0.4)	0.012
ACR class III and IV (%)	19	8	0.036
DMARD use (%)	69	64	NS
Corticosteroid use (%)	47	44	NS

DIP, distal interphalangeal joint; HAQ, Health Assessment Questionnaire; DMARDs, disease modifying antirheumatic drugs.

**Table 2** Radiological features of patients with erosive and deforming disease

n=32	(%)	Type of lesion	Anatomical site affected
14	44	Erosions+joint space narrowing (I)	Hands, feet, elbows, knees
5	16	Erosions	Hands, feet
6	19	I+ankylosis	Hands, feet, elbow
7	22	I+subluxations	Hands, feet

modified Ferguson view of the sacroiliac joints,<sup>8</sup> which were graded on the following basis: 0=normal, 1=possible, 2=minimal, 3=moderate, 4=ankylosis. All symptomatic joints were also radiographed. At least two senior rheumatologists read all radiographs, and there was agreement, except in five cases, which were resolved with a radiological atlas.

Erosive and deforming arthritis was defined by the presence of erosions, joint space narrowing, subluxations, and/or ankylosis of appendicular joints. At the end of the study the erosive disease was recorded as a categorical variable, and therefore we analysed these data for number of affected patients instead of the number of deformed and eroded joints for each patient.

Data on the use of disease modifying antirheumatic drugs (DMARDs) and corticosteroids were also collected.

All variables were compared between patients with and without erosive and deforming disease. Categorical data were compared by Pearson's  $\chi^2$  and Fisher's exact tests, whereas continuous data were analysed by Student's *t* test. Relative risk (RR) was calculated by the method of Woolf.<sup>9</sup> A logistic regression model was used to determine those variables predicting the appearance of erosive and deforming disease.

## RESULTS

Seventy one patients were studied, 44 men and 27 women with a mean age of 47 (SD 12) years. The duration of psoriasis was 18 (SD 10) years, and the duration of arthritis was 12 (SD 8) months at the recruitment period. Psoriasis preceded the onset of arthritis in 53 (75%) of the patients. A positive family history of psoriasis was present in 14 (20%) of these patients.

During the first six months of follow up, five (7%) patients showed isolated distal interphalangeal joint (DIP) disease, 30 (42%) oligoarthritis, 20 (28%) polyarthritis, and 16 (23%) axial disease. None of our patients presented with arthritis

mutilans. At the end of the study, 17 (24%) showed spondylitis, 24 (34%) polyarthritis, 28 (39%) oligoarthritis, and two (3%) developed arthritis mutilans. Thirty four (48%) patients developed DIP joint disease, but they could be assigned to the other articular categories. Thirty nine (55%) had onychopathy.

HLA-B27 was present in 25 of 71 patients (35% *v* 7% in controls, relative risk (RR) 7,  $p < 0.001$ ); 11 of 17 (65%) patients with spondylitis had this allele compared with 10 of 30 (33%) with oligoarthritis and four of 17 (24%) of those having polyarthritis ( $p < 0.05$ ). Thirty nine out of 71 (55%) carried the HLA-Cw\*0602 antigen compared with a normal distribution of this allele of 18% in our control population (RR 5.5,  $p < 0.0001$ ); however, it was equally distributed among the articular categories.

At the end of the study 32 of 71 (45%) patients had developed erosive and deforming arthritis (including two patients with arthritis mutilans). Of these 32 patients, 18 (56%) had a polyarticular onset, two (6%) showed a DIP disease onset, six (19%) had an oligoarticular onset, and six (19%) presented with axial disease as the form of onset ( $p = 0.001$ ). The mean time to detect erosions or narrowing of joint spaces in this series was 20 (SD 4) months.

Table 1 summarises the main characteristics of patients with and without erosive and deforming disease, and table 2 shows the radiological features of patients with erosive and deforming disease.

Among those variables which correlated positively with erosive and deforming disease in a univariate analysis, only a polyarticular onset of disease remained as an independent risk factor predicting erosive and deforming disease over time (OR 37, 95% CI 3.6 to 88,  $p = 0.025$ ).

## DISCUSSION

In the past few years it has been clearly established that PsA is not as benign as it was once thought, and in fact, it can lead

to an important functional limitation as well as to an erosive and deforming arthropathy.<sup>1</sup> In this sense, in a wide cohort of patients with PsA studied by Torre-Alonso *et al*, 57% of patients had erosive arthritis and 19% of them were in American Rheumatology Association classes III-IV of functional impairment.<sup>3</sup> This misconception regarding the benign nature of PsA may be explained in part by the fact that these patients have less pain than patients with rheumatoid arthritis.<sup>1</sup>

With the increasing potential for early intervention, for longer term treatment, and for the use of more aggressive drugs, it would be very useful to be able to predict the course of rheumatic conditions to assess the risk : benefit ratio of treatments and to start treatment as early as possible to modify the prognosis of these diseases.

In rheumatoid arthritis, several factors have been implicated in an unfavourable prognosis, including the presence of rheumatoid factor, the so-called shared epitope of HLA-DR, the early presence of bony erosions, extra-articular features (rheumatoid nodules), or a high number of swollen joints in early phases of the disease.<sup>10</sup> Similar investigations in PsA are sparse; however, the possible indicators of a poor prognosis in PsA include a younger age at onset, extensive skin involvement, polyarticular disease, association with HIV infection, and the presence of certain HLA antigens.<sup>11</sup>

In the present report we undertook a prospective cohort study to establish which variables discriminated those patients destined to develop an aggressive form of PsA. At the end of the study when data were compared between patients with and without erosive and deforming disease, there was no difference in age at onset of disease, extension of skin involvement (it is known that the relationship between psoriasis and PsA in terms of disease activity is poor, as patients may have a severe exacerbation of dermatitis but not of arthritis or vice versa), or HLA distribution. In the third aspect, Gladman and Farewell showed that HLA antigens were predictive of progression in PsA; thus, in their cohort of patients, those who carried the HLA-B27 antigen, particularly in the presence of HLA-DR7, were likely to progress, as were patients who were HLA-B39 positive and those with the HLA-DQw3 antigen.<sup>4</sup> In our series most patients with HLA-B27 did not develop erosive disease, whereas HLA-Cw\*0602 was equally distributed among patients with and without erosive disease. Therefore we cannot make additional considerations on the role of HLA antigens in the worsening of disease over time. On the other hand, many clinicians treating patients with PsA do not have haplotyping techniques available, and this means that HLA determination to assess disease progression in PsA is probably of limited value in clinical practice.

Although more patients with DIP disease had erosive and deforming arthritis in this study, this probably represented a true association with polyarthritis rather than with erosive disease. In a similar manner, the tendency to male predominance in non-erosive disease indicated that men exceeded women in the oligoarticular and axial subgroups (table 1), although we cannot rule out a protective effect of male sex, or, vice versa, a tendency to more aggressive disease among women. In this sense, our own group found that in psoriatic spondylitis women showed more aggressive disease than men.<sup>12</sup>

Gladman *et al* showed that patients who presented with five or more swollen joints in an early phase of disease were at increased risk for progression of joint deformities, as were

those who had been given high doses of drugs.<sup>3</sup> We confirmed that a high level of inflammation represented by a high number of inflamed joints in a phase of disease where erosions and deformities were absent, was the main independent risk factor to detect those patients destined to develop erosive and deforming disease over time. The level of DMARD and corticosteroid use was similar between both groups of patients; however, it is necessary to underline that the pattern of DMARD use in our patients with PsA has changed in the past six to eight years with an increasing use of treatments with mainly methotrexate, cyclosporin A, and sulfasalazine. Thus it is difficult to predict the protective effect of these drugs on the appearance of erosions and deformities during the first 20 months of disease evolution, a time when many of our patients were not taking these drugs.

In summary, a substantial proportion of our patients with PsA developed erosive and deforming arthropathy, confirming that PsA is not as benign as previously thought.<sup>1</sup> In addition, those patients who developed erosive disease were more severely limited in their functional performance than those with non-erosive disease. For this reason, we support the use of treatment with DMARDs as early as possible, particularly in patients with PsA with polyarticular onset.

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