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Jaccoud's arthropathy in systemic lupus erythematosus: clinical, laboratory and ultrasonographic features

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ABSTRACT

Objective. *Jaccoud's arthropathy (JA) is a deforming, non-erosive arthritis, occurring in 2–35% of systemic lupus erythematosus (SLE) patients. We aimed to evaluate JA patients in a wide monocentric SLE cohort in terms of clinical, serological and ultrasonographic features.*

Methods. *Consecutive SLE patients (ACR criteria 1997) were evaluated. The JA index was applied for patients with reducible deformities. Patients with a JA index ≥5 underwent physical examination, blood testing and ultrasound (US) assessment. Detection of anti-citrullinated protein antibodies (ACPA) and rheumatoid factor (RF) was performed. A single rheumatologist performed the US assessment of bilateral wrist and hands.*

Results. *Four hundred and eighty SLE patients were evaluated: 17 (3.5%) showed a JA index ≥5 (M:F 1:16; mean age±SD 50.7±11.1 years; mean disease duration±SD 247.8±116.2 months). Four patients (23.5%) showed ACPA positivity. Fifteen patients (88.2%) showed at least one US abnormality. Bone erosions were found in 10 patients (58.8%). ACPA+ve patients showed erosive damage more frequently in at least one joint compared with ACPA-ve (75% vs. 53.8%, p=0.002).*

Conclusion. *JA should no longer be considered a non-erosive condition since bone damage can occur in more than half of patients. Moreover, the erosive damage seems to be associated with the presence of ACPA.*

Introduction

Musculoskeletal involvement is one of the most frequent manifestation in systemic lupus erythematosus (SLE) patients, occurring in up to 90% of cases and characterised by a wide heterogeneity (1). Jaccoud's arthropathy (JA) is one of the possible phenotypes of SLE joint involvement. This is a deforming but usually considered non-erosive arthritis, described in 2% to 35% of patients (2). The deformities are similar to those identified in rheumatoid arthritis (RA), but are typically reducible (2). The concept of JA non-erosive arthritis has been revised thanks to more sensitive imaging techniques: among these, musculoskeletal ultrasonography (US) is a technique that is able to capture synovitis and bone erosions even in the early disease stages and in asymptomatic patients (3). A growing number of studies have analysed joint US features in SLE patients, identifying the presence of erosions in patients without radiographic damage (3-4).

The identification of specific markers and pathogenic mechanisms for JA is an interesting topic. The prevalence of different autoantibodies has been evaluated, suggesting an association with anti-RNP, anti-SSA and anticardiolipin (aCL) antibodies (5, 6). Moreover, some studies have evaluated the presence of rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA) in JA patients (2).

The aim of the present study was to evaluate the prevalence and the clinical, serological and ultrasonographic features of JA in a wide monocentric cohort of SLE patients.

Patients and methods

Consecutive SLE patients (revised 1997 American College of Rheumatology criteria) were enrolled at the Lupus Clinic of the Sapienza University of Rome ("Sapienza Lupus Cohort") (7). The local ethics committee approved the study and informed consent was signed. JA index was assessed in all SLE patients with reducible joint deformities: patients are classified as affected by JA in the case of the index showing ≥5 points (8).

All the JA patients underwent clinical evaluation including the count of swollen and tender joints and the patient's/physician's global disease assessment [visual analogue scale (VAS; 0–100 mm)]. Disease activity was measured according to the disease activity score in 28 joints (DAS28) (9) and disability by the health assessment questionnaire disability index (HAQ-DI).

We registered data on C-reactive protein (CRP) values (nephelometry, cut-off 0.5 mg/dl) and erythrocyte sedimentation rate (ESR, mm/h). Antinuclear antibodies (ANA) were determined by indirect immunofluorescence on HEp-2 and anti-dsDNA by indirect immuno-

Table I. Demographic and clinical features of SLE patients with and without JA.

	SLE patients with JA (n=17)	SLE patients without JA (n=463)	*p*-value
Demographic features			
Sex (M:F)	1:16	36:444	NS
Mean age ± SD (years)	50.7 ± 11.1	45.2 ± 12.5	NS
Mean disease duration ± SD (months)	247.8 ± 116.2	157.1 ± 106.4	0.001
Mean SLEDAI-2K ± SD value	3.4 ± 3.3	3.6 ± 3.9	NS
Clinical manifestations (n/%)			
Mucocutaneous	15/88.2	288/62.2	0.00003
Musculoskeletal	17/100	277/59.8	<0.000001
Serositis	9/52.9	82/17.7	<0.000001
Renal	9/52.9	128/27.6	0.0005
Haematological	8/47.0	287/61.9	NS
Neuropsychiatric	5/29.4	64/13.8	0.008
Autoantibodies (n/%)			
anti-SSA/Ro	4/23.5	155/33.5	NS
anti-SSB/La	1/5.9	71/15.3	NS
anti-Sm	0/0	67/14.5	0.00003
anti-RNP	2/11.8	79/17.0	NS
anti-CL	6/35.3	166/35.8	NS
anti-β2GPI	4/23.5	78/16.8	NS
LA	6/35.3	105/22.7	NS

Table II. Clinimetric, laboratory and ultrasonographic evaluation of SLE patients with JA (n=17).

Clinimetric assessment	
Tender joints count (mean ± SD)	1.5 ± 2.7
Swollen joints count (mean ± SD)	1.3 ± 2.0
DAS28 (mean ± SD)	3.3 ± 1.1
Low activity (DAS28≤2.6, %)	30.8
Moderate activity (>2.6 DAS28≤5.1, %)	61.4
High activity (DAS28>5.1, %)	0.8
Pain-VAS (mean ± SD)	37.0 ± 20.5
Physician VAS (mean ± SD)	28.8 ± 15.4
HAQ-DI (mean ± SD)	0.74 ± 0.62
HAQ>0.5 (n/%)	10/58.8
Laboratory assessment	
CRP, mg/dl (mean ± SD)	3.2 ± 5.8
Higher values (% pts)	45.4
ESR, mm/h (mean ± SD)	33.2 ± 22.5
Higher values (% pts)	72.7
RF (n/%)	7/41.2
ACPA (n/%)	4/23.5
Low C3 and/or C4 (n/%)	14/82.3
Ultrasonographic assessment	
SE in at least one joint (n. patients/%)	15/88.2
SH in at least one joint (n. patients/%)	13/76.5
PD in at least one joint (n. patients/%)	5/29.4
Total Joint Synovitis score (mean ± SD)	6.1 ± 3.9
Total Tenosynovitis score (mean ± SD)	1.2 ± 0.8
Total erosion score (mean ± SD)	1.3 ± 1.8
Erosions in at least one joint (n. patients/%)	10/58.8%

SE: synovial effusion; SH: synovial hypertrophy; PD: power Doppler.

fluorescence on *Crithidia Luciliae* (Orgentec Diagnostika, Mainz, Germany). Anti-SSA/Ro, anti-SSB/La, anti-Sm and anti-RNP, anti-cardiolipin (CL) and anti-b2GPI antibodies were measured by commercial ELISA kit (Diamedix, Miami, FL, USA); LA was assessed according to the International Society on Thrombosis and Haemostasis guidelines. C3 and C4 concentrations were determined (radial immunodiffusion). RF (nephelometry, cut-off 20 UI/ml) and ACPA (ELISA kit Delta Biological, Italy) were determined in all JA subjects and in an age- and sex-matched SLE control group with other than JA joint involvement. The Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2 K) and Systemic Lupus International Collaborating Clinics Damage Index (SDI) assessed disease activity and chronic damage, respectively (10, 11).

A single rheumatologist, blinded to the clinical and laboratory data, performed the US assessment of bilateral wrists and hands [MyLab70 X-Vision Gold (Esaote, Genova, Italy) machine (multifrequency linear array transducer 6–18 MHz; power Doppler (PD) settings: PD pulse repetition frequency 750 Hz, Doppler frequency 11.1 MHz, gain 50% and low filters] according to the international guidelines (12). Metacarpo-phalangeal (MCP), proximal interphalangeal (PIP) and radio-ulno-carpal joint were examined to identify signs of synovitis [synovial effusion (SE), synovial hypertrophy (SH) and PD signal]. Wrist extensors compartments 1–6 and finger flexors 2–5 in both hands were evaluated. Moreover, the presence of erosions was assessed at MCP and PIP level. All abnormalities were defined according to the ultrasongraphic OMERACT definitions (13). SE, SH and PD were evaluated with a dichotomous score (absence or presence). Then, the US synovitis scores (SE, SH and PD) at, respectively, the joint and the tendon level, were summed in order to obtain the "global score" of the patient.

Statistical evaluation

We used version 13.0 of the SPSS statistical package. Normally distributed variables were summarised using the mean ± SD, and non-normally distributed variables by the median and range. Frequencies were expressed by percentage. Wilcoxon's matched pairs test and paired *t*-test were performed accordingly. Univariate comparisons between nominal variables were calculated using chi-square test or Fisher's exact-test when appropriate. Spearman test was used to assess the correlation. Two-tailed *p*-values were reported, *p*-values <0.05 were considered significant.

Results

Four-hundred and eighty consecutive SLE patients were evaluated. Among

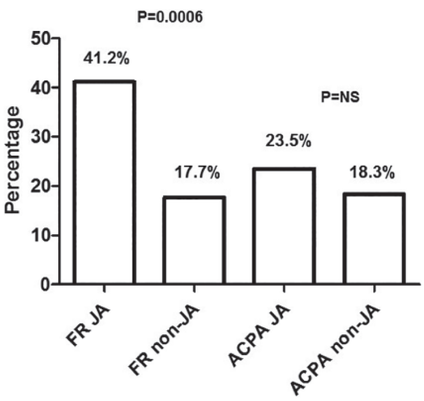

Fig. 1. Frequency of ACPA and RF in SLE patients with and without JA.

these, 17 patients (3.5%) showed a JA index ≥5. Demographic and clinical features of SLE patients with and without JA are summarised in Table I.

Mean disease duration was significantly longer in JA patients compared with SLE patients without JA (247.8±116.2 *vs*. 157.1±106.4, *p*=0.001). The most frequent joint deformity was ulnar drift of MCP joints (15 patients, 88.2%) and followed by Z distortion of thumbs (14 patients, 82.3%).

Table II reports the clinimetric, laboratory and ultrasonographic parameters of JA patients.

At the time of the evaluation JA patients showed a mean ± SD SLEDAI-2K of 3.4±3.3 and a mean ± SD SDI of 2.1±1.5. Bone erosions, found in 58.8% of patients, were most frequently detected at the 1st and 2nd MCP level (17.6% each). The radioulnar carpal joint was the most frequently involved in terms of synovitis at the US evaluation (15 patients, 88.2%). Concerning tendon involvement, the 3rd flexor digitorum tendon was the most frequently affected.

RF and ACPA were evaluated in JA patients and in a subgroup of 62 consecutive age- and sex-matched SLE patients with joint involvement other than JA (M/F 3/59; mean age 46.7±4.8 years; mean disease duration 168.6±99.6 months). RF was significantly more prevalent in JA patients (41.2% *vs*. 17.7%, respectively; *p*=0.0006; Fig. 1). Conversely, no significant difference in ACPA frequency was found between the two groups (23.5% *vs*. 18.3%, *p*=NS; Fig. 1). No differences were found in the titre of RF (JA SLE 24.9±31.7 UI/ml; non-JA SLE 12.2±17.0 UI/ml, *p*=NS) and ACPA (JA SLE 798.2±873.6 UI/ml; non-JA SLE 488.4±639.1 UI/ml, *p*=NS).

Subgrouping JA patients according to ACPA status, ACPA+ve patients showed erosive damage more frequently in at least one joint compared with ACPA-ve (75% *vs*. 53.8%, *p*=0.002). The evaluation of 4 ACPA+ patients allowed the identification of 2 Rhupus subjects.

The US synovitis global score significantly correlated with HAQ (r=0.5; *p*=0.02), patients (r=0.4; *p*=0.04) and physician VAS (r=0.5; *p*=0.02). No other correlations were observed.

Discussion

In agreement with previously published studies, in our large monocentric cohort of SLE patients, we identified a JA prevalence of 3.5% (2). According with the classical definition, JA is a peculiar disease phenotype characterised by reducible deformities and spared by x-ray bone erosions (8). However, we here demonstrate by using US the presence of erosive bone damage in 58.8% of JA patients, frequently localised at first and second MCP. The only previous study providing an US evaluation on JA patients, performed by Gabba *et al*., described bone erosions in a lower percentage of patients: only 1 out of 6 patients (14). This discrepancy could be related to the smaller size of the cohort.

Although JA has been defined as a non-erosive arthropathy, erosions have been demonstrated in some radiological studies. These erosions, well defined and with a sclerotic margin, are usually localised on the heads of the metacarpal or metatarsal joints, resulting in a hook-shaped deformity (2). It is noteworthy that an erosive arthritis was described in SLE patients in a percentage varying from 2 to 47% of patients (3).

Nevertheless, JA is a condition that significantly impairs the quality of life of affected patients. In our cohort, we found an HAQ >0.5 in 58.8% of the cases, highlighting the frequent disability of these patients. Moreover, we found that our JA patients had a longer disease duration and higher prevalence of mucocutaneous, renal and neuropsychiatric manifestations and serositis. Contrary to our results, previous studies have reported a higher frequency of anti-SSA, anti-RNP and aCL in JA patients compared with non-JA SLE patients (5, 6). The relatively small size of the studied cohorts or the ethnic differences could explain such discrepancies. On the other hand, our study suggest that RF and ACPA may play a role in the development of JA. Indeed, RF is more prevalent in JA patients than in a non-JA SLE confirming previous data (2, 15). At the same extent, despite ACPA have a similar prevalence between these two SLE groups, they are significantly associated with US-detected erosive damage in JA.

In conclusion, in the light of our and previous observations, the definition of non-erosive arthritis is no longer appropriate for JA. The relatively high prevalence of RA-specific antibodies suggests possible shared mechanisms between these two pathologic conditions. This observation may change the pathogenic scenario, and consequently the therapeutic targets of JA. Moreover, the presence of patients with JA and erosions without ACPA, suggests that other pathways may concur to the development of bone damage.

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