Ultrasound imaging for the rheumatologist XXIV. Sonographic evaluation of wrist and hand joint and tendon involvement in systemic lupus erythematosus

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ABSTRACT

Systemic lupus erythematosus (SLE) is an autoimmune multisystem disorder characterised by frequent musculoskeletal manifestations. Joint involvement in SLE is usually not erosive or destructive but some patients develop hand erosive arthritis or deforming arthropathy of the hand (respectively "rhupus" hand and Jaccoud arthritis). To date, few studies, evaluated joint and tendon involvement in SLE patients by US. We studied wrist and hand structure, using ultrasound, in 50 patients affected by SLE, detecting inflammatory joint involvement in 80% of them at the wrist and in 50% at the hand. Tenosynovitis was visualised in 14 patients, while structural damage was present in 12% of the SLE group. Those results reinforce the importance of including musculoskeletal ultrasound in the patient assessment, especially in those cases in which physical examination is not conclusive.

Introduction

Systemic lupus erythematosus (SLE) is an autoimmune multisystem disorder characterised by frequent musculoskeletal manifestations. Arthralgia or arthritis which may affect any joint (even if wrist, hand and knee are most commonly involved) are reported in up to 94% of the patients (1). Joint involvement in SLE is usually not erosive or destructive but some patients develop hand erosive arthritis or deforming arthropathy of the hand (respectively "rhupus" hand and Jaccoud arthritis).
It is well known that by musculoskeletal ultrasound (US) it is possible to evaluate articular and periarticular structures in different rheumatic diseases, such as rheumatoid arthritis (RA) (2), spondyloarthritis (3), crystal-related arthritis (4), osteoarthritis (5) or vasculitis (6). The features of sinovium or tendon inflammation and the structural damages of bone are well imaged by US examination as extensively described (7). Furthermore, the use of Doppler techniques, mainly power Doppler (PD), provides detailed information on synovial perfusion thus reflecting the activity of the inflammatory process (8, 9).
To date, few studies, the majority of which enrolling a low number of patients, evaluated joint and tendon involvement in SLE patients by US (10-14). We decided to study wrist and hand structures, using US as the imaging technique, because of the frequency of their involvement in SLE patients (15), and also since previous papers had focused on those anatomic sites (10-12, 14).

Patients and methods

Patients

Fifty patients affected by SLE, diagnosed according to the American College of Rheumatology (ACR) criteria for SLE (16), referred as in- or out-patients to four different Rheumatology Units in Italy (University of Pisa, University of Pavia, Università Politecnica delle Marche and the "Sapienza" University of Rome) were enrolled in the study. The US examinations were performed in all the patients independently of the presence or absence of pain and/or swelling at hands. The study was conducted according to the good clinical practices guidelines and the Declaration of Helsinki principles.
For every patient we recorded the clinical characteristics including disease

duration (expressed in months from the diagnosis), multisystem involvement (renal, cardiovascular, pulmonary, central nervous system and skin involvement) and the presence at the time of the examination or only from the referred history of pain and/or swelling of hand joint and tendon. For the evaluation of disease activity we used the European Consensus Lupus Activity Measurement (ECLAM). Moreover samples were taken from all the patients to test for erythrocyte sedimentation rate (ESR) (normal value <25 mm/h), C-reactive protein (CRP) (normal value <0.5 mg/dl), C3 and C4 levels (normal value >90 mg/dl and >10 mg/dl, respectively), serum creatinine (normal value <0.9 mg/dl), 24/h proteinuria and autoantibody profile (ANA, ENA, dsDNA, rheumatoid factor and anti-CCP antibodies). The most relevant demographic and clinical data are reported in Table I.

Control group

Fifty healthy subjects (HS) sex and age-matched with SLE patients were used as control group. No personal or family history of rheumatic disorders were elicited from any normal subject. Demographic data are reported in Table I.

US assessment

The US examinations were performed, in each Rheumatology Unit, by a rheumatologist experienced in musculoskeletal US (blinded to the diagnosis, clinical and laboratory data), using a Logiq 9 (General Electrics Medical Systems, Milwaukee, WI) with a linear probe operating at 14 MHz. The inter-observer agreement of sonographers in detecting and scoring US features of joint inflammation and bone erosions has been previously calculated and reported in a recent study (17). Good-to-excellent agreement rates were found in the detection and semi-quantitative evaluation of inflammation and bone erosions, and good agreement rates between sonographers were also found in the detection of tenosynovitis.

Using a multiplanar scanning technique according to EULAR guidelines for musculoskeletal US in rheumatology (18), we performed bilateral US examination of radiocarpal (RC) and intercarpal (IC) joint and of extensor ulnaris carpi tendon at the wrist, of the 2nd and 3rd metacarpo-phalangeal (MCP) and proximal interphalangeal (PIP) joint, of flexor tendons of the 2nd and 3rd finger at the hand, of cartilage (over the head of the 2nd metacarpal bone) and of cortical bone involvement (head of the ulna and 2nd metacarpal bone in dorsal, lateral and volar aspects). Hyaline cartilage of the 2nd metacarpal head was examined using a multiplanar scanning technique with the MCP joint in maximal flexion. Particular attention was paid on maintaining the US beam direction perpendicular to the cartilage layer. Joint effusion, synovial hypertrophy, bone erosion and tenosynovitis were diagnosed by US according to the preliminary definitions provided by the Outcome Measures in Rheumatoid Arthritis Clinical Trials (OMERACT) Special Interest Group for Musculoskeletal Ultrasound in Rheumatology (19). A semi-quantitative grading method (0 to 3) for scoring joint effusion, synovial proliferation and intra-articular power Doppler (PD) signal was used (9, 20-23).

Table I. Demographic data of SLE patients and controls.

	SLE patients group (n=50)	Control group (n=50)
F/M	49/1	49/1
Mean age±SD (yrs)	39.6 ± 12.3	41.1 ± 9.1
Mean disease duration±SD (months)	124.8 ± 96.2	–

Table II. US findings in SLE patients and controls.

Finding	SLE Patient group n/50 (%)	Control group n/50 (%)
Wrist joints synovitis	40/50 (80)	2/50 (4)*
radiocarpal	23/50	2*
intercarpal	20/50	0*
Hand joints synovitis	25/50 (50)	3/50 (6)*
metacarpo-phalangeal	21/50	3/50*
proximal interphalangeal	13/50	0/50*
Wrist tenosynovitis extensor ulnaris carpi tenosynovitis	6/50 (12)	0/50**
Hand tenosynovitis	11/50 (22)	2/50 (4)°
flexor tendons of the 2nd finger	11/50	1/50°°
flexor tendons of the 3rd finger	6/50	1/50
Structural damage	6/50 (12)	0#
bone erosion	1/50	0
cartilage defects	6/50	0#

*p<0.0001; **p=0.027; °p=0.014; °°p=0.004; #p=0.027.

Statistical analysis

Contingency table analysis and Fisher's exact test were used to compare qualitative differences between the groups, while the student *t*-test was chosen to compare quantitative parameters in large samples of similar variance. The findings were expressed as mean and standard deviation from the mean. Values of p<0.05 were considered to be statistically significant.

Results

Thirty out of 50 (60%) SLE patients referred a history of arthritis/arthralgia or complained of pain with or without swelling at wrist and/or hand at the examination time. Only 3 patients were positive for rheumatoid factor while anti-CCP antibodies were not detected in any patients. Both ESR and CRP were elevated in 33% of patients while mean values for ESR and CRP were respectively 38.6±28.6 mm/h and 1.47±2.16 mg/dl. A reduction in C3 and/or C4 was present in 25/50 patients while mean values for C3 and C4 were respectively 79.16±15.5 mg/dl and 12.6±8.1 mg/dl. Serum creatinine and proteinuria (>1.0

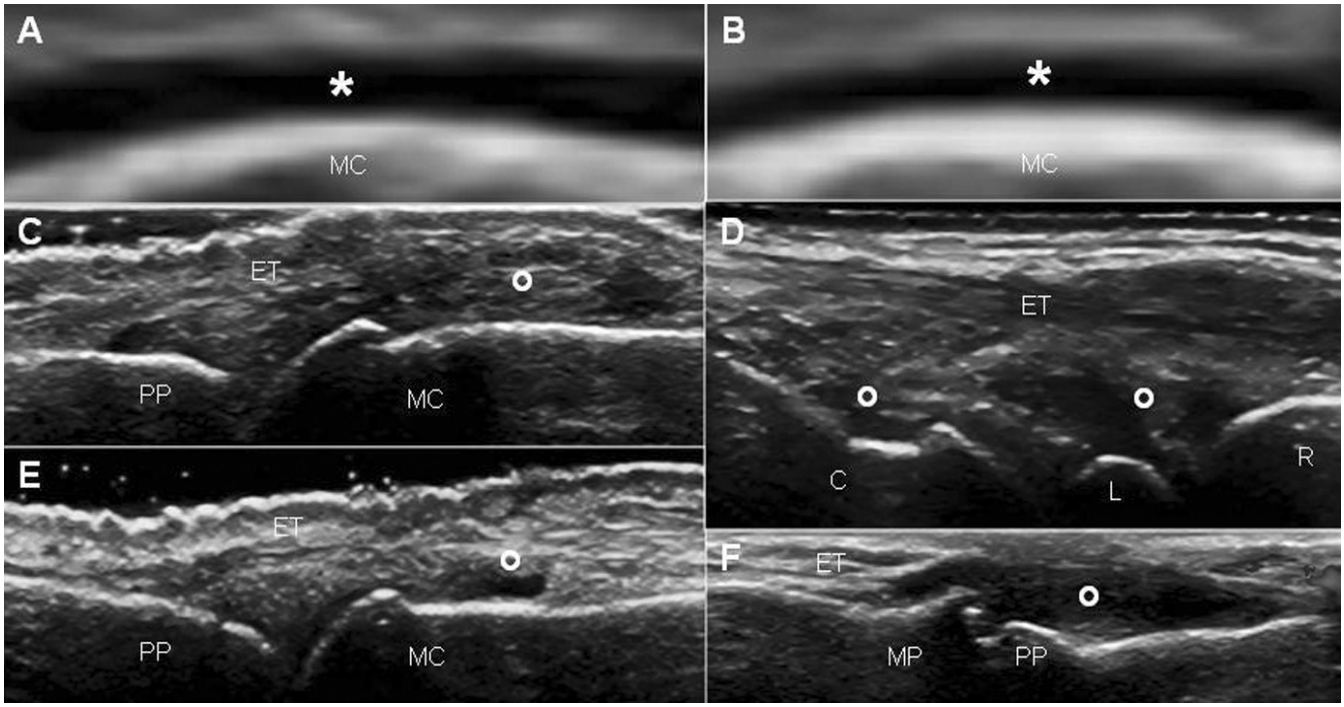

Fig. 1. Systemic lupus erythematosus. Second metacarpophalangeal joint, transverse dorsal scan showing normal aspect (**A**) and thinning (**B**) of the cartilage layer of the 2nd metacarpal head. MC: metacarpal bone; *: cartilage layer. (**C**) and (**E**) dorsal longitudinal scan of the 2nd metacarpophalangeal joint showing a synovitis. MC: metacarpal bone; PP: proximal phalanx; ET: extensor tendon; °: effusion and synovial proliferation. (**D**) dorsal longitudinal scan of the wrist showing radiocarpal and intercarpal joint synovitis. R: radius; L: lunate; C: capitatus; ET: extensor tendon; °: effusion and synovial proliferation. (**F**) dorsal longitudinal scan of the 2nd proximal interphalangeal joint showing a synovitis. PP: proximal phalanx; MP: medium phalanx; ET: extensor tendon; °: effusion and synovial proliferation. Images taken with a Logiq 9 (General Electrics Medical Systems, Milwaukee, WI) using a 14 MHz linear probe.

g/24h) were elevated in 10/50 patients. Pericardial effusion was observed in 13/50 patients, while pleural effusion was detected in 9/50 subjects. Thirty-four out of 50 patients were on therapy with steroids, 9 of them had been treated with high dose pulse 6-methylprednisolone. Various disease modifying anti-rheumatic drugs (DMARDs), as monotherapy or combined therapy were used in the cohort of SLE: 27 patients on hydroxycloroquine, 13 on azatioprine, 11 on mycophenolate mofetil, 6 on cyclosporine, 5 on methotrexate and, finally, 1 on leflunomide and another patient on cyclophosphamide.

US findings related to inflammatory joint involvement were observed in 40 out 50 (80%) patients at the wrist and in 25 out 50 (50%) patients at the hand (synovitis at RC and IC joint in 23 and 20 patients respectively and at MCP and PIP joint in 21 and 13 patients respectively). Tenosynovitis was visualised in 14 (28%) patients, in 3 only at wrist, in 8 at hand and in 3 patients both at wrist and hand. Structural damage was present in 6 (12%) patients who showed thinner cartilage layer and in one of them also bone erosion was visualised. The US findings are reported in Table II.

By US we did not observe any statistically significant correlation between the occurrence of joint or tendon involvement and disease activity parameters levels, systemic involvement or disease duration.

US examination of HS showed slight wrist joint effusion at wrist in 2 subjects while MCP or PIP joint inflammation was found in 6 out of 50 (12%) subjects, 5 of whom without synovial proliferation and 1 with mild synovial proliferation but no PD signal. No tendon involvement was detected. No osteoarthritic changes or structural damages were shown in any controls.

The prevalence of joint effusion, synovial proliferation and tenosynovitis appeared increased (with a statistically significant difference) in SLE patients when compared with the findings in HS.

Discussion

Joint involvement, mostly of wrists and hands, is very frequent in SLE patients with various clinical manifestations ranging from mild arthralgia to the severe non erosive deforming arthritis of Jaccoud's arthropathy or even to the erosive arthritis resembling RA the so-called "Rhupus".

In 2008 we reviewed the available data concerning the application of US to study the articular and periarticular involvement in connective tissue diseases (24) but very few papers on SLE were reported (10, 11). Iagnocco *et al.* (10), in 2004, used US to examine both wrists in a group of 26 unselected SLE patients, demonstrating synovitis in 22/52 radio-ulno-carpal joints, mostly with effusion (13 joints) and/or synovial proliferation (10 joints), while PD signal was present in 5 wrists joints and bone erosions were detected in only one patient (in both wrists). Tenosynovitis was visualised in 15/26 pts (58%) while 27% of the examined wrists shown no alterations. The Authors found that the SLE disease activity index (SLEDAI) score was significantly higher in the group without tendon involvement. The Authors did not observe any correlation

between the presence of joint synovitis and the signs of systemic activity, identified as ESR and C3 levels and SLEDAI score, and suggested that the low articular inflammation found at the wrists does not influence systemic disease activity. Two years later, Wright *et al*. (11), studied a group of 17 SLE patients who showed hand involvement. Joint effusion or synovial proliferation were visualised in 16/17 patients in the wrists and in 12/17 patients at the MCP joints. In this study only the 2nd and 3rd MCP and PIP joints were assessed, detecting bone erosions in 8 subjects. Tendon involvement was also investigated, imaging the 2nd, 3rd and 4th finger flexor and tenosynovitis in 11 patients was showed.

In 2007 a case report by Saketkoo *et al*. (12) was published, on the detection of bone erosion with US in a SLE patient, then revisiting the deformities caused by Jaccoud's arthropathy and stressing the role of US in the better definition of joint involvement in SLE patients.

More recently, Iagnocco *et al*. (13) published the results of a new study on joint involvement in SLE patient demonstrating that knee effusion was present in almost half of the group of 26 unselected SLE patient, with a prevalence not statistically different from that observed in a group of rheumatoid arthritis (RA) patients, while proliferation, erosions and PD signal were more frequent in the RA group.

In the same year, Demirkaya E *et al*. (14) studied 30 juvenile SLE patients (comparing them to HS), and an increased involvement of the knee, ankle, wrist and elbow joint, as well as of flexor and extensor tendons of the hand was shown, with an interesting decreased tendon thicknesses in the third finger of the juvenile SLE patients group. This last finding did not correlate with disease duration or SLEDAI scores but underscored the potentially disabling scenario of tendon pathologies in those patients.

Our results differ both from those reported in Iagnocco (10) and in Wright's study (11), probably because we examined IC joints also (not studied by Iagnocco *et al*) in an unselected group of patients, while Wright *et al*. enrolled a few patients who complained of hand and wrist pain at the examination time. We underline that we observed such a high prevalence of wrist synovitis which is an unexpected result in a population of unselected SLE patients (20/50 patients did not complain of wrist pain). We found wrist tenosynovitis in only 10% of the patients but, also in this case, the different choice of the anatomic structures to examine could explain the difference with respect to Iagnocco's results (10). No erosions of the distal part of the ulna were shown in our work.

When examining the hand, we found joint synovitis in 50% of the patients, which is lower than the one reported by Wright (11), but we have to remember that 40% of our SLE patients had no pain at this anatomic site, then we could hypothesise that subclinical inflammation could be a widespread phenomenon in SLE patients, while a more important disease, which correlates with articular symptoms, is more rare. In fact we noted bone erosions in only one patient [but if we look to the US examination of every joint in the hand, it goes up to 4 patients (8%)]. In any case, the percentage of bone erosion is very low with respect to the 47% of patients reported by Wright *et al*. (11), but similar to the 4% reported by Iagnocco *et al*. (10) (observed while scanning only the wrist). We also evaluated cartilage damage, with 12% of structural changes in our cohort of patients, which we can assume is due to synovitis and not to osteoarthritis because of the kind of US findings (no alteration of the bone-condral profile) and, most of all, because of the mean age of the population studied. In any case, the percentage of structural damage (cartilage damage plus bone erosion) remain lower with respect to the symptomatic SLE patients included in the paper by Wright *et al*. (11).

Finally, while Iagnocco (10) reported tendon involvement in 58% of the patients (at the wrist level) and Wright (11) showed 65% of inflammation (assessing 2nd, 3rd and 4th finger flexor tendons), we found only 22% of patients with tenosynovitis of the hands. Once again the marked difference with respect to Wright's study (11) could be explained not only by the fact that we scanned only the 2nd and 3rd finger and that our SLE patients are unselected and consecutively enrolled in the study, but also that the population included in our study is markedly larger than the one involved in Wright's examination.

We conclude by remarking the fact that, even if more exhaustive studies have to be produced, the findings we noted by wrist and hand US examination in SLE patients, probably reflect the existence of a mild joint (possibly more frequent at the wrists), as well as tendon, inflammation which, most of the time, does not reach such a level of activity which is able to produce structural damage, as hypothesised by Ossandon *et al*. (13).

Finally, the absence of correlation between systemic disease activity parameters and US joint findings, reinforces the importance of a patient assessment that also includes musculoskeletal US, as an imaging technique that allows to better classify SLE patients, especially in those cases in which physical examination is not conclusive.

Link

For further ultrasound images, please go to www.clinexprheumatol.org

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