

Wrist joint involvement in systemic lupus erythematosus. An ultrasonographic study

A. Iagnocco, A. Ossandon, G. Coari, F. Conti, R. Priori, C. Alessandri, G. Valesini

Rheumatology Unit, Department of Applied Clinical and Medical Therapy, University of Rome "La Sapienza", Italy

Annamaria Iagnocco, MD; Alejandra Ossandon, MD; Giulio Coari, MD; Fabrizio Conti, MD; Roberta Priori, MD; Cristiano Alessandri, MD; Guido Valesini, MD, Professor of Rheumatology.

Please address correspondence and reprint requests to: Annamaria Iagnocco, MD, Cattedra Reumatologia, Dipartimento di Clinica e Terapia Medica Applicata, Università di Roma "La Sapienza", V.le del Policlinico 155, Roma 00161, Italy.

E-mail address: annamaria.iagnocco@uniroma1.it

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ABSTRACT

Objective. To define joint alterations in the wrists of patients with systemic lupus erythematosus (SLE) by ultrasonography (US).

Methods. Fifty-two wrists of 26 SLE patients and 30 wrists of 15 healthy controls were evaluated using US by two different experienced operators, blinded to the clinical data. A 14 MHz linear probe was used. Power Doppler (PD) was applied to evaluate the presence of synovial neoangiogenesis as a parameter of active local synovitis. The findings were correlated to the clinical evaluation, serological systemic disease activity parameters (ESR, C3 levels) and the SLE-disease activity score (SLEDAI). Statistical analysis was performed by the EPISTAT program.

Results. Signs of synovitis were found in 22 wrists (42.3%). Synovial proliferation was present in 10 joints (19.2%), PD positivity in 5 (9.6%) and joint effusion in 13 (25%). Erosions were present in both wrists (3.8%) of one patient. Signs of tenosynovitis of one or more tendons were shown in 23 cases (44.2%). Ganglia were found in 2 joints (3.8%). Changes of the median nerve, joint dislocations, tendons' ruptures, cysts and nodules were never detected. In 14 wrists (26.9%) no alterations were found. There was no correlation between sonographic findings and clinical, laboratory and indexes signs of disease activity. In the control group the only alteration found was tenosynovitis in 1 joint ($p < 0.0001$).

Conclusion. US proved to be an useful technique to detect wrist joint alterations in SLE. These findings may help the physician to modulate treatment strategies and to perform a low cost monitoring of joint disease activity.

Introduction

Musculoskeletal symptoms represent the chief complaint in systemic lupus erythematosus (SLE), affecting up to 94% of the patients (1). Manifestations include stiffness and pain, that may be persistent or evanescent and may be accompanied or not by objective clinical signs of inflammation. Recurrent synovitis is described in about 10-30% of patients, with joint deformities

occurring in a minor percentage (Jacoud's arthropathy). Bone erosions are rare (2). Involvement of tendons in different sites are usually described as frequent (3) but, as far as we know, there are no previous studies that have quantified its incidence. Tendons tears and ruptures are associated both to inflammation and to corticosteroid usage (2, 4).

High resolution ultrasonography (US) is a reliable diagnostic technique in the evaluation of musculoskeletal disorders. Due to its high sensitivity in the detection of changes within joint structures, it has recently been widely applied to the study of rheumatic diseases. In particular, the recent advances in ultrasound technology and the development of high resolution transducers have made it possible to obtain accurate sonographic depiction of small joints of the hand and wrist. Moreover, the use of new techniques such as power Doppler (PD) has given higher value to ultrasound in the detection of inflammatory joint changes (5).

The aim of this study was to detect alterations of the wrists in patients with SLE using US and PD. The imaging findings were correlated to clinical, laboratory and disease activity score parameters.

Materials and methods

Twenty-six patients were recruited consecutively from the in- and out-patient population of the "La Sapienza" University Rheumatology Unit, Policlinico Umberto I of Rome, Italy, between March and July 2002. All patients fulfilled the SLE classification revised criteria of the American College of Rheumatology (6). Patients underwent a medical interview which included past and recent medical history, a general physical examination and transcription of serological data. A serum sample was collected from each patient at the time of the visit to determine the erythrocyte sedimentation rate (ESR) and C3 values, which were taken as a measure of serological disease activity. ESR > 15mm/h and C3 < 170 mg/dl were considered as abnormal values. Measures were performed in the same laboratory. Clinical and

serological parameters were collected in a protocol form that included age at diagnosis, ESR and C3 values, number of current painful joints and SLE-disease activity (SLEDAI) scores. Therapy and associated autoimmune diseases present at entry were also recorded. Information was transferred to a computerized database. Both wrists of 15 healthy subjects were evaluated as controls.

The same day the patients and controls underwent an ultrasonographic examination of both wrists. In all subjects sonography was performed separately by two different experienced operators (both rheumatologists), who were blinded to the patient diagnosis and clinical data and repeated each examination twice. After the US examination the two operators compared their findings. In case of discrepancies about the presence/absence of alterations within the single structures studied, they reached a consensus after performing a third examination together. An Agilent-HP Image point Hx machine, with a 14 MHz linear transducer and PD was used. Sonographic examinations were performed in all patients using a multiplanar scan technique around the wrist, according to previous reports (7, 8). We used the following PD settings: PFR 1100 Hz; gain 60-65 dB; low filter. Increased synovial perfusion was defined as a high colour persistence of PD signal in the synovial tissue.

The following structures were studied:

1. radio-ulno-carpal joint, searching for the signs of synovitis and for the

presence of irregularities of the bone profile (erosions, osteophytes, fractures, joint dislocations).

2. tendons (abductor pollicis longus, extensor pollicis brevis, extensor carpi radialis longus, extensor carpi radialis brevis, extensor pollicis longus, extensor digitorum communis, extensor indicis proprius, extensor digiti minimi, extensor carpi ulnaris, flexor carpi radialis, flexor pollicis longus, flexor digitorum superficialis and flexor digitorum profundus), searching for the signs of tenosynovitis and tendons' rupture.
3. Moreover, alterations of other peri-articular soft tissues such as changes in the median nerve (9), nodules, cysts and ganglia were searched for.

Definition sonographic criteria for the different findings are reported in Table I.

Statistical methods

The chi-square and Fisher exact tests were performed to detect qualitative differences. The Student t-test was used to compare quantitative parameters in large samples of similar variance. Values of quantitative variables were expressed as mean \pm standard deviation (SD) of the mean. P values less than 0.05 were considered statistically significant. Statistical analysis was performed by the EPISTAT program.

Intra-observer and inter-observer agreement were calculated using the unweighted Kappa test. The test was applied to evaluate agreement avoiding the random concordance (poor agree-

ment: Kappa < 0.40; moderate agreement: Kappa 0.40 – 0.60; good agreement: Kappa 0.60 – 0.80; excellent agreement: Kappa > 0.80).

Results

The cohort of 26 SLE patients included 23 women (88.5%) and 3 men (11.5%), with a female to male ratio of 8:1. Mean age at entry was 40.3 years (SD \pm 9.6; range 23-64). Mean time from diagnosis was 15.1 (SD \pm 7.1 years; range 1-27). Serological activity parameters showed mean ESR levels 28.9 mm/h (SD \pm 28.3; range 4-101) and mean C3 levels 111 mg/dl (SD \pm 43; range 38-173). The mean number of painful joints was 3.2 (SD \pm 5.4; range 0-21) and the mean SLEDAI score was 2.3 (SD \pm 1; range 0-6). Swollen wrists were never present.

Treatment included, for most of the patients, corticosteroids and/or immunosuppressors such as hydroxychloroquine, cyclosporine, methotrexate and cyclophosphamide. There was no correlation between disease activity, measured by ESR, C3 values and SLEDAI scores at entry, and the type of treatment. Since there was a high variability in the treatment between the patients, we did not evaluate them according to the different therapy.

Controls were matched for age and sex. Regarding the sonographic assessment, intra-observer and inter-observer agreement was from good to excellent (intra-observer Kappa values: 0.82-1.00; inter-observer Kappa values: 0.73-0.89).

Sonographic signs of synovitis of the radio-ulno-carpal joint were found in 22 wrists (42.3%) of 15 patients (57.7%). In particular, synovial proliferation was present in 10 joints (19.2%), PD positivity in 5 (9.9%) and joint effusion in 13 (25%). Erosions of the radio-ulno-carpal joint were present in both wrists (3.8%) of one patient. Signs of tenosynovitis (Fig.1) of one or more tendons were shown in 23 wrists (44.2%) of 15 patients (57.7%). Ganglia were present in 2 joints (3.8%). Changes of the median nerve, joint dislocations, tendons' ruptures, cysts and nodules were never found.

In 14 wrists (26.9%) no alterations were found.

Table I. Definition criteria of sonographic findings.

Erosion	Cortical break or defect with an irregular floor seen in longitudinal and transverse plans
Synovitis	Intra-articular synovial proliferation (presence of hypertrophic synovial tissue), with or without joint effusion (intra-articular anechoic/hypoechoic fluid collection) determining capsular distension, with or without hyperemia (increased local perfusion demonstrated by PD)
Tenosynovitis	Fluid collection around the tendon and within its sheath with sheath's distension, with or without local synovial proliferation, with or without hyperemia (PD)
Median nerve pathology	Cross sectional area > 10 mm ² , Flattening of the median nerve (height < 3 mm), Palmar displacement (< 4 mm) of flexor retinaculum
Ganglia	Anechoic oval, round, or lobulated cystic structures

Table II. Demographic, clinical and laboratory characteristics of patients divided based the “presence/absence” of tenosynovitis.

	Presence of tenosynovitis	Absence of tenosynovitis	p
Sex	12 females; 3 males	11 females, no males	ns
Age (years)	40.6	39.8	ns
Duration of disease (years)	14.3	16.1	ns
ESR (mm/h)	26.3	33.8	ns
C3 (mg/dl)	123.5	101.6	ns
Number of painful joints	2.2	4.3	ns
SLEDAI	1.5	2.7	<0.05

ns = non significant (p>0.05).

Five joints (9.6%) were referred by the patients as painful. Three of them (60%) didn't show any alterations by ultrasound, 2 (40%) presented signs of synovitis (synovial proliferation) and 1 (20%) of tenosynovitis. The difference between the frequency of clinical involvement and presence of pathological ultrasonographic findings was significant (p < 0.001).

Considering the higher percentage of tenosynovitis in relation to other changes, we divided our cohort in two different groups based on the presence or absence of tenosynovitis (Table II). The first group was composed by 12 females and 3 males, mean age 40.6 (SD±10; range 23-64), mean time from diagnosis 14.3 (SD ± 7 years; range 1-23). Mean ESR levels were 26.3 mm/h (SD ± 26.8; range 4-96) and mean C3 levels 123.5 mg/dl (SD ± 47.1; range 38-182). Mean number of painful joints was 2.2 (SD ± 4.2; range 0-16) while mean SLEDAI score was 1.5 (SD ± 1.5; range 0-4).

The group in which no tenosynovitis was revealed was composed by 11 females, mean age 39.8 years (SD ± 8.7; range 23-55), mean duration time from diagnosis 16.1 years (SD±7.9; range 0-27). Mean ESR levels were 33.8 mm/h (SD±30.9; range 5-101) and mean C3 levels 101.6 mg/dl (SD ± 37.3; range 66-159). Mean number of painful joints was 4.3 (SD ± 6.7; range 0-21), while mean SLEDAI score was 2.7 (SD ± 24; range 0-6).

There was no statistical difference between the two groups regarding the mentioned parameters, with the exception of SLEDAI which was higher in the group without tenosynovitis (p < 0.05).

In the control group, the only ultrasonographic alteration found was tenosynovitis in one wrist (p < 0.001).

Discussion

Musculoskeletal complaints are frequent in SLE patients (1). Nevertheless there are no previous studies, other than those published in patients with particular clinical subsets, investigating joint involvement in SLE (10).

We studied the wrists of 26 lupus patients by US. The wrist was chosen among other joints because of its frequent lupus articular involvement (11), while US was selected because of its high sensitivity in detecting soft tissues and bone profile alterations in this joint (12). In comparison to other techniques, US demonstrated more sensitivity than conventional radiography in detecting destructive joint lesions at metacarpophalangeal joints (13) and more sensitivity than MRI in detecting synovitis at finger joints (14). Moreover, PD showed to be reliable in assessing inflammatory activity in rheumatoid arthritis (RA) patients using dynamic MRI as the reference method (15). Other advantages of US include the low cost of the examination, optimal patient compliance, quickness and accuracy in detecting soft tissues and bone surface alterations (16).

Our study highlighted the presence of synovitis in a high number of joints (42.3%), being joint effusion and synovial proliferation the main alterations found. PD was positive in only 9.6% of the joints. This percentage is lower than the value reported in other pathologies such as RA (17). The difference seems higher than what could be expected only on account of the different

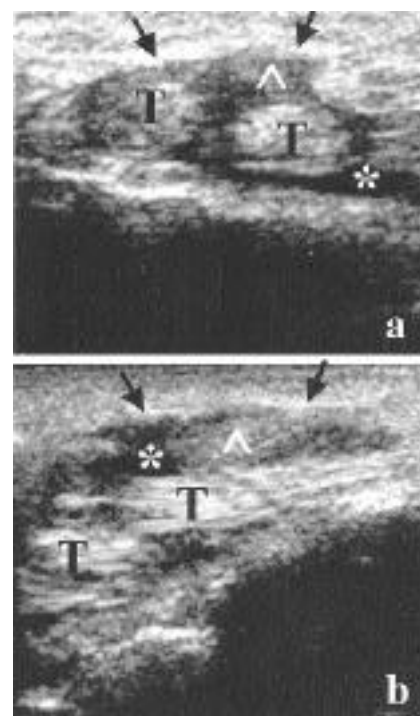


Fig. 1. Tenosynovitis of flexor tendons in the wrist. (a) transverse scan; (b) longitudinal scan. T: flexor digitorum profundus tendons; * : fluid distension of tendon's sheath. ^: peritendinous synovial proliferation. *: peritendinous effusion.

techniques or the different machine settings although further information may be obtained only by studies of comparison between SLE and RA. The fact that there was no correlation between the presence of synovitis and the signs of systemic activity (ESR, C3, SLEDAI) may be related to the evanescence, oligoarticular, migrating and non-erosive/non-deformant characteristics of articular involvement in this disease (18) and suggests that probably low local articular inflammation at this location does not influence systemic disease activity or the involvement of other organs.

The high percentage of tenosynovitis (44.2%) was an unexpected finding. We therefore divided the patients in 2 groups based on the presence or not of this alteration. The only significant difference between the groups was found for SLEDAI, which was higher in patients without tenosynovitis (p< 0.05). This aspect suggests that probably tenosynovitis at the wrist is not able to influence systemic disease activity. Our study confirms the low incidence

of erosions (3.8%) and of other alterations of periarticular soft tissues at this joint site. In particular, we did not find alterations of the median nerve, probably due to the fact that synovitis at the wrist is not as serious as in other pathologies such as RA and, therefore, it is not able to determine a compression of the median nerve in the majority of cases. Tendon lesions were not found probably because spontaneous ruptures or lesions in SLE usually involve other tendons than the ones present at the wrist, such as the Achille's tendon and the patellar tendon. These ruptures are thought to be associated with underlying systemic disease, oral corticosteroid therapy and concurrent strain in weight bearing areas and are a relatively rare occurrence (2, 4).

We demonstrated a high percentage of sonographic pathologic findings (73.1%) compared to the low percentage of articular manifestations (9.6%). This is probably due to the high sensitivity of the technique that is able to show even minimal alterations in asymptomatic joints. The dissociation between clinical and imaging findings has been previously reported (14,19).

In conclusion, as far as we know, this is the first ultrasonographic study on lupus musculoskeletal involvement. We have demonstrated that US is able to detect and locate the site of joint inflammation in the wrists of lupus patients. The pattern of inflammatory involvement evidences a slight prevalence of tenosynovitis over joint synovitis. The fact that at the moment of the sonographic examination the patients did not always refer symptoms in

the studied area, could be due to the migrating, evanescent characteristics of lupus articular involvement. Nevertheless, the detection of such inflammation by US may help the clinician to objectify pain complaints and, if necessary, to modify treatment.

References

- VITALI C, BENCIVELLI W, ISENBERG DA *et al.*: Disease activity in systemic lupus erythematosus: report of the Consensus Study Group of the European Workshop for Rheumatology Research. I. A descriptive analysis of 704 European lupus patients. European Consensus Study Group for Disease Activity in SLE. *Clin Exp Rheumatol* 1992; 10: 527-39.
- WALLACE DJ: The musculoskeletal system. In WALLACE DJ and HAHN BH (Eds.): *Du Bois' Lupus Erythematosus*, Baltimore, Williams & Wilkins, 1997: 635-51.
- EDWORTHY SM: Clinical manifestations of systemic lupus erythematosus. In RUDDY S, HARRIS ED JR and SLEDGE CB (Eds.): *Kelly's Textbook of Rheumatology*, Philadelphia, W.B. Saunders, 2001: 1105-23.
- FURIE RA, CHARTASH EK: Tendon rupture in systemic lupus erythematosus. *Semin Arthritis Rheum* 1988; 18: 127.
- GRASSI W, FILIPPUCCI E: Is the Doppler sonography the new frontier in therapy monitoring? *Clin Exp Rheumatol* 2003; 21: 424-8.
- TAN EM, COHEN AS, FRIES JF *et al.*: The 1982 revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum* 1982; 25: 1271-7.
- BACKHAUS M, BURMESTER GR, GERNER T *et al.*: Guidelines for musculoskeletal ultrasound in rheumatology. *Ann Rheum Dis* 2001; 60: 641-9.
- SARRIA L, CABADA T, COZCOLLUELA R, MARTINEZ-BERGANZA T, GARCIA S: Carpal tunnel syndrome: usefulness of sonography. *Eur Radiol* 2000; 10: 1920-5.
- SWEN WA, JACOBS JW, BUSSEMAKER FE, DE WAARD JW, BILJLSMAJW: Carpal tunnel sonography by the rheumatologist versus nerve conduction study by the neurologist. *J Rheumatol* 2001; 28: 62-9.
- OSTENDORF B, SCHERER A, SPECKER C, MÖDDER FU, SCHNEIDER M: Jaccoud's arthropathy in systemic lupus erythematosus. *Arthritis Rheum* 2003; 48: 157-65.
- LAHITA RG: The clinical presentation of systemic lupus erythematosus. In LAHITA RG (Ed.): *Systemic Lupus Erythematosus*, San Diego, Academic Press, 1999: 325-36.
- LUND PJ, HEIKAL A, MARICIC MJ, KRUPINSKI EA, WILLIAMS CS: Ultrasonographic imaging of the hand and wrist in rheumatoid arthritis. *Skeletal Radiol* 1995; 24: 591-6.
- WAKEFIELD RJ, GIBBON WW, CONAGHAN PG *et al.*: The value of sonography in the detection of bone erosions in patients with rheumatoid arthritis: a comparison with conventional radiography. *Arthritis Rheum* 2000; 43: 2762-70.
- BACKHAUS M, KAMRADT T, SANDROCK D *et al.*: Arthritis of the finger joints: a comprehensive approach comparing conventional radiography, scintigraphy, ultrasound, and contrast-enhanced magnetic resonance imaging. *Arthritis Rheum* 1999; 42: 1232-45.
- SZKUDLAREK M, COURT-PAYEN M, STRANDBERG C, KLARLUND M, KLAUSEN T, OSTERGAARD M: Power doppler ultrasonography for assessment of synovitis in the metacarpophalangeal joints of patients with rheumatoid arthritis: a comparison with dynamic magnetic resonance imaging. *Arthritis Rheum* 2001; 44: 2018-23.
- GRASSI W, FILIPPUCCI E, CAROTTI M, SALAFFI F: Imaging modalities for identifying the origin of regional musculoskeletal pain. *Best Pract Res Clin Rheumatol* 2003; 17: 17-32.
- WEIDEKAMM C, KOLLER M, WEBER M, KAINBERGER F: Diagnostic value of high-resolution B-mode and doppler sonography for imaging of hand and finger joints in rheumatoid arthritis. *Arthritis Rheum* 2003; 48: 325-33.
- DUBOIS EL, TUFFANELLI DL: Clinical manifestations of systemic lupus erythematosus. *JAMA* 1964; 190: 104-11.
- MAILLEFERT JF, DARDEL P, CHERASSE A, MISTRIH R, KRAUSE D, TAVERNIER C: Magnetic resonance imaging in the assessment of synovial inflammation of the hind-foot in patients with rheumatoid arthritis and other polyarthritis. *Eur J Radiol* 2003; 47: 1-5.