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● *Original Contribution*

ULTRASOUND FINDINGS ON HANDS AND WRISTS OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: RELATIONSHIP WITH PHYSICAL EXAMINATION

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Abstract—Diagnosis of synovitis/tenosynovitis by physical examination can be difficult. Ultrasound (US) can be an effective tool for the evaluation of joint involvement in systemic lupus erythematosus (SLE). This study will describe musculoskeletal findings by US in SLE patients and the evaluation of their correlation with physical examination. SLE patients underwent clinical/sonographic evaluation of hand/wrists. In total, 896 joints were evaluated: at least 1 change on physical examination was found in 136 joints and at least 1 US abnormality was found in 65 of 896 joints. Out of the 65 joints with US changes, only 13 had findings on physical examination. Conversely, 111 joints had tenderness on physical examination with no sonographic abnormalities. Tenosynovitis was statistically significant more frequently with joint edema (41%) (*p* = 0.0003). US can detect musculoskeletal changes in only a minority of symptomatic SLE patients. Clinical findings may be related to some reasons that cannot be explained using US. (E-mail: kerolins@yahoo.com.br)   © 2017 World Federation for Ultrasound in Medicine & Biology.

Key Words: Systemic lupus erythematosus, Musculoskeletal ultrasound, Physical examination.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a multi-systemic autoimmune disease whose course is marked by remissions and relapses that may affect various organs simultaneously (Ceccarelli et al. 2015). The musculoskeletal involvement in SLE occurs in 95% of cases and may be a result of the disease itself or its treatment (Lins and Santiago 2015). Regarding the joints, it is difficult to detect synovitis or tenosynovitis on the basis of only physical examination. Hence, some researchers have suggested the inclusion of ultrasound (US) as a tool in articular evaluation in SLE patients (Dale et al. 2014; Zayat et al. 2016).

US is a non-invasive diagnostic procedure, with good accuracy for detecting abnormalities such as synovial effusion, tendon/soft tissue involvement and visualization of cartilage/bone surface (Backhaus et al. 2001; Ball and Bell 2012; Kang et al. 2014) even in the subclinical phase. In some rheumatic diseases, such as rheumatoid arthritis, the use of sonographic imaging for joints is well defined; however, this procedure is not established in SLE yet (Filer et al. 2011; Kane et al. 2004).

The main objective of this study is to describe the US evaluation of joints and soft tissues in a group of SLE patients and correlate them with physical examination.

MATERIALS AND METHODS

This is a cross-sectional study on a group of SLE patients. The study was performed at the Rheumatology Clinic of Escola Bahiana de Medicina e Saúde Pública, Salvador, Brazil. Using the American College of Rheumatology criteria (Hochberg 1997), we diagnosed and enrolled patients with SLE in this study. All patients signed the informed consent, and this study was approved by the Research Ethics Committee of our institution.

The exclusion criteria were (i) patients younger than 18 y of age and those older than 65 y of age (excluding patients in an older age range to avoid those who may have degenerative joint changes) and (ii) those with Jaccoud's arthropathy (excluding patients who might show positive findings even with no evidence of arthritis in the physical examination).

All patients underwent clinical evaluation, including demographic data and disease duration. A physical examination of the hands and wrists was performed by a rheumatologist with 5 y of experience. The rheumatologist used a standard evaluation for rheumatologic disease, according to a previous study by Almoallim et al. (2012), focusing on findings related to arthritis (joint edema and tenderness). In this way, radiocarpal (RC), proximal interphalangeal (PIP) and metacarpophalangeal (MCP) joints from the second to fourth fingers in both hands and wrists were analyzed. These anatomic sites were chosen because they are pathologically more representative sites according to previous studies (Delle Sedie et al. 2009; Yoon et al. 2014).

Physical examination was based on dichotomic evaluation (positive and negative). During the visual inspection of patients' hands and wrists, the rheumatologist observed the presence of edema by increasing the volume and reduction in skin roughness. The PIP joints were palpated with the physician's thumb and index finger positioned to assess the joint studied in the vertical and transversal planes, alternating between these planes. Palpation on MCP joints was also held between the physician's thumb and index finger, but the rheumatologist's hands were in the scissors position (ring and little fingers separated from the middle and index fingers by the patient's fingers). At the RC joints, palpation was performed by placing the thumbs on the dorsal side and index fingers on the ventral part of the examined joint.

Hands and wrists US

The US of all the patients' hands and wrists was performed using the HD11 XE US System (Koninklijke Philips N.V., Eindhoven, The Netherlands) with a 10- to 14-MHz transducer by a radiologist (C.F.L.) specialized in musculoskeletal system (>10 y of experience). In accordance with the guidelines for musculoskeletal US recommended by the European League Against Rheumatism (Backhaus et al. 2001), images were obtained in the transverse and longitudinal planes of RC joint at the dorsal wrist, second to fourth joints of both MCP and PIP joints and flexor tendons of the second to fourth fingers of both hands (Delle Sedie et al. 2009; Yoon et al. 2014).

The presence of synovial hypertrophy, joint effusion, tenosynovitis and bone erosions was evaluated. Synovitis was defined as the presence of non-compressible unusual hypoechoic material in the joint recess (Fig. 1), according to the protocol Outcome Measures in Rheuma-
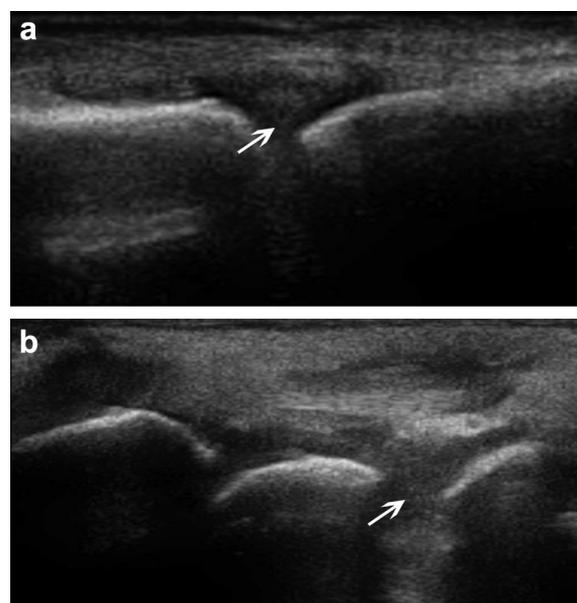

Fig. 1. (a) Ultrasonographic example of mild synovitis in the second metacarpophalangeal joint (*arrow*); (b) ultrasonographic example of radiocarpal moderate synovitis (*arrow*).

tology Clinical Trials (Mukherjee et al. 2016; Wakefield et al. 2005). Bone erosions were defined as defects in the superficial cortical bone that are identified both in the longitudinal and transversal planes. Tenosynovitis was defined as thickened and hypoechoic tendon with or without liquid in its synovial sheath (Fig. 2) (Delle Sedie et al. 2008; Filer et al. 2011).
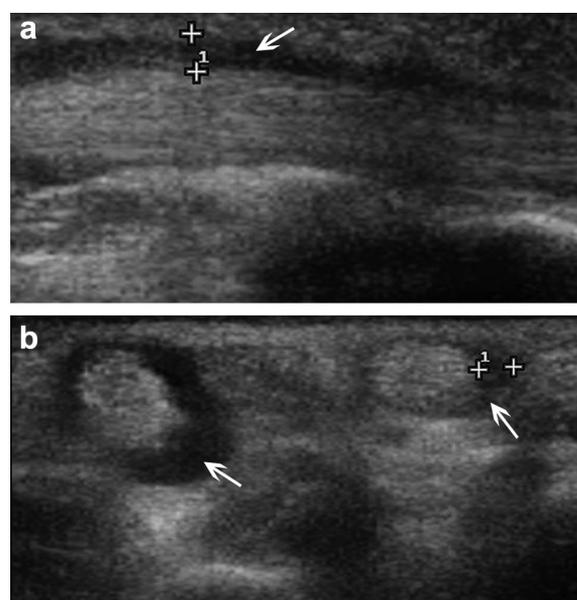

Fig. 2. (a) Ultrasonographic example of tenosynovitis at the third finger's flexor, in the longitudinal plane (*arrow*); (b) ultrasonographic example of tenosynovitis at the second and third fingers' flexors, in the transverse plane (*arrows*).

A semi-quantitative scale from 0 to 3 was used to evaluate synovitis and tenosynovitis in the gray-scale, as previously suggested (Delle Sedie et al. 2008; Filer et al. 2011; Mukherjee et al. 2016).

The degree of synovitis was classified as follows: 0 = no effusion/synovial hypertrophy; 1 = least effusion/synovial hypertrophy, hypoechoic/anechoic line beneath joint capsule; 2 = moderate effusion/synovial hypertrophy, elevation of joint capsule parallel to joint area and 3 = extensive effusion/synovial hypertrophy, bulge extending to at least one bone diaphysis either proximally or distally.

The degree of tenosynovitis was graded on a scale of 0 to 3: Grade 0 = no signs of tenosynovitis (diameter of synovial tendon sheath ≤0.3 mm); grade 1 = mild tenosynovitis (diameter of the synovial tendon sheath ≤2 mm); grade 2 = moderate tenosynovitis (diameter of the synovial tendon sheath ≤4 mm); and grade 3 = severe tenosynovitis (synovial sheath tendon diameter >4 mm).

Statistical analysis

Statistical analysis was performed by using SPSS, version 20 (Chicago, IL, USA). The associations between categorical variables (changes on physical examination vs. US alterations) were analyzed using χ^2 or Fisher's exact test. For all statistical tests, the significant p value was considered as <0.05.

RESULTS

Clinical and US findings

The study included 64 participants, 63 women (98.4%) and 1 man (1.6%). The mean age was 42.9 y (±10.7 y).

In total, 896 joints were evaluated in 64 patients with SLE. At least 1 change on physical examination was found in 136 joints (15.2%). Of these, 124 (13.8%) had joint tenderness and 12 (1.3%) had joint swelling. At least 1 US abnormality was found in 65 of 896 joints of SLE patients (7.2%). In total, we found 25 joints with synovitis (2.8%), 42 with tenosynovitis (4.7%), two with synovitis and tenosynovitis simultaneously (0.2%) and no bone erosion. On physical examination, most changes were observed in PIP joints followed by MCP; while in sonographic study, more changes were identified in the wrist, followed by MCP joints (Table 1).

Synovitis and tenosynovitis were classified as moderate in only 5 joints, from 2 patients. In other joints the sonographic findings were categorized as mild. Isolated synovitis of the wrist was found in 18 cases and in the hand in 7 cases (involving MCP joints). Tenosynovitis occurred only in the flexor tendons.

Table 1. Distribution of analyzed joints and their clinical and sonographic features

Joint	Physical examination		Ultrasonography examination	
	Edema, n (%)	Tenderness, n (%)	Synovitis, n (%)	Tenosynovitis, n (%)
PIP (n = 384)	7 (1.8)	59 (15.4)	0 (0)	17 (4.4)
MCP (n = 384)	3 (0.8)	39 (10.1)	7 (1.8)	15 (3.9)
Wrist (n = 128)	2 (1.6)	26 (20.3)	18 (14.1)	8 (6.2)
Total (n = 896)	12 (1.3)	124 (13.8)	25 (2.8)	42 (4.7)

PIP = proximal interphalangeal; MCP = metacarpophalangeal.

Association between physical examination and US study

Out of the 65 joints with US changes, only 13 had findings on physical examination: 8 with tenosynovitis had edema and/or tenderness, 4 with synovitis had tenderness and 1 had tenosynovitis and synovitis simultaneously with tenderness. On the other hand, 52 joints had US changes (19 with synovitis, 32 with tenosynovitis and 1 with tenosynovitis and synovitis simultaneously) without abnormalities on physical examination. Conversely, 111 joints had tenderness on physical examination with no sonographic abnormalities.

Synovitis occurred in a small percentage of the joints 25/896 (2.8%), it was slightly more prevalent in patients with tenderness (5 of 124; 4.0%) in comparison with asymptomatic individuals (20 of 772; 2.6%), but it was not statistically significant (p = 0.307). Tenosynovitis occurred in 42 of 896 of the examined joints (4.7%), it was more frequent with joint edema (5 of 12; 41%) than without it (37 of 884; 4.2%), and it had statistical significance (p = 0.0003) (Table 2). It should be noted that asymptomatic joints also had anatomic injury on US: 2.5% of synovitis and 4.4% of tenosynovitis.

DISCUSSION

Musculoskeletal involvement is the most common clinical finding seen in SLE patients. In this study, US abnormality was observed even in asymptomatic joints, thus it could characterize them as a subclinical disease. This phenomenon has also been observed in other rheumatic diseases such as RA and Sjogren's syndrome (Naredo et al. 2005; Riente et al. 2008).

As pointed out in a recent systematic review (Lins and Santiago 2015), there are only a few studies that have addressed US findings in joints of patients with SLE. An even smaller number of articles comment on the relationship between physical examination and US evaluation in SLE patients. Gabba et al. (2012) studied both symptomatic and asymptomatic SLE patients and found that asymptomatic patients have mainly tendon

Table 2. Association between US findings and physical examination on analyzed joints

	Physical examination					
	Edema			Tenderness		
	Yes n = 12 (1.3%)	No n = 884 (99.7%)	*p* value	Yes n = 124 (13.8%)	No n = 772 (86.2%)	*p* value
US findings						
Synovitis	-	25 (2.8%)	0.415	5 (4.0%)	20 (2.6%)	0.307*
Tenosynovitis	5 (41%)	37 (4.2%)	0.0003*	8 (6.4%)	34 (4.4%)	0.343

US = ultrasound.
* Fisher's test.

sheet inflammation. Ogura et al. (2017) found a major prevalence of tendon involvement (tendinitis/tenosynovitis) in SLE patients than in individuals with RA. These findings are in accordance with what we found in this study, as some of our patients had US abnormalities with no alteration at physical examination and we detected a higher frequency of tendon involvement than synovitis.

In our study, we did not observe an association between US findings and physical examination, except for the item tenosynovitis compared with joint edema, which had poor association. In contrast, Corzo et al. (2017) found US as a useful imaging technique for predicting and evaluating musculoskeletal outcomes in SLE patients, mainly in patients who are symptomatic. On the other hand, in absolute numbers, we found a higher frequency of US changes in asymptomatic patients, suggesting subclinical disease. Similarly, Dreyer et al. (2015) identified that some asymptomatic patients had US abnormalities, emphasizing the value of US utilization in SLE patients, particularly the asymptomatic ones.

The prevalence of US findings in our study was lower than that observed in other reports. Moreover, some authors believe that US is a more sensitive method than physical examination in the detection of synovitis in SLE patients, as it identifies changes in the absence of clinical manifestations (Dreyer et al. 2015; Gabba et al. 2012; Iagnocco et al. 2004). On the other hand, Mosca et al. (2015) found lower sensitivity and higher specificity of US in relation to physical examination. Thus, not all clinical changes necessarily correspond to anatomic lesion in US (synovitis/tenosynovitis) and US cannot be used as a confirmatory diagnostic method of symptomatology. However, US can provide complementary information to physical examination, which is the reason why some rheumatologists defend the use of this method as part of their clinical consultations (Belloli et al. 2015; Dougados et al. 2010; Vlad et al. 2011).

From our data, we observed that a reasonable number of patients had physical examination changes (joint tenderness) without any US finding, suggesting that clinical findings may be related to other unidentifiable reasons when using US. On the basis of the available information retrieved from the studies by Mosca et al. (2010) and Dreyer et al. (2015), we could deduct that a few of their symptomatic patients had normal US findings. It can be explained by muscle, nerve or other soft tissue injuries not rarely seen in SLE patients. On the other hand, it is also known that arthralgia is not necessarily secondary to inflammation in SLE; other conditions may explain their appearance, such as the presence of neuropathic pain (with central sensitization mechanisms); pain related to depression, fatigue or even overlap with fibromyalgia, which has no relation to disease activity, but may generate an inadequate interpretation of symptomatology (Di Franco et al. 2014; Friend and Bennett 2011; Greco et al. 2003; Woolf 2011).

Our study has some limitations such as the lack of Power Doppler evaluation associated with the B-mode analysis, but a recent systematic review (Zayat et al. 2016) observed that Power Doppler as a marker of disease activity in SLE has unknown significance, because of the lack of standardization of its criteria of evaluation. Also, we did not use a gold standard method as magnetic resonance for comparison (we performed physical examination and US, which are considered more viable methods in the conventional clinical environment), finally we did not assess disease activity (although none of the indices can demonstrate disease activity at joint level). However, our findings allow us to conclude that US can detect musculoskeletal changes in a minority of symptomatic SLE patients and it can rule out inflammation in tendon sheets or synovium in some patients with peripheral articular complaints. Thus, US may complement physical examination. As this was a cross-sectional study, new studies with a prospective design are required to assess the real contribution of US of the joints in the management of SLE patients.

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