Tendinous and Ligamentous Derangements in Systemic Lupus Erythematosus

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ABSTRACT. ***Objective.*** We assessed the prevalence of selected clinical and radiological features of tendinous and ligamentous derangements in a consecutive sample of patients with systemic lupus erythematosus (SLE).

Methods. Consecutive patients with SLE with no comorbidities attending a tertiary care center were prospectively assessed and underwent plain radiographic evaluation of the pelvis. Radiographs were analyzed by 2 blinded observers; radiographic sacroiliitis was graded 0 to IV. To better assess sacroiliac (SI) involvement, a computed tomography (CT) scan of the SI joints was performed in patients with grade III sacroiliitis. Hip joints and pubis were also assessed as described.

Results. Of the 192 included patients, 89% were female, mean age was 36 years, and mean disease duration was 10 years. Inflammatory low back pain was reported by 10% of patients. Sacroiliitis of any grade was observed in 31 patients (16%), and grade III (confirmed on CT scan) sacroiliitis was observed in 6% (95% CI 3% to 9%). Osteitis pubis was diagnosed in 6% (95% CI 3% to 10%) and coxofemoral migration in 8% (95% CI 2% to 9%). Jaccoud's arthropathy was found in 23%. Demographic and clinical variables were not statistically associated with radiographic sacroiliitis.

Conclusion. Sacroiliitis and other tendinous and ligamentous derangements are not uncommon in patients with SLE. Based on these features and on previous reports, the term "SLE-related tendinous and ligamentous derangements" may be used to establish a common framework for further research and reporting. (First Release Sept 1 2008; J Rheumatol 2008;35:2187–91; doi:10.3899/jrheum.080255)

Key Indexing Terms:
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The musculoskeletal system is involved in nearly all patients with systemic lupus erythematosus (SLE), including arthralgias and arthritis as the most frequent manifestations. However, diverse tendon and ligament derangements have been sporadically reported as manifestations of SLE since 1975; these manifestations include tendinous laxity[1-3], spontaneous tendon rupture[4,5], Jaccoud's arthropathy[6,7], atlantoaxial subluxation[1], osteitis pubis[8], and radiographic sacroiliitis[8-22]. Recent studies using powerful imaging techniques such as magnetic resonance imaging (MRI), high-resolution ultrasonography, and power Doppler have demonstrated inflammatory pathology in the tendons of these patients[23-25].

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However, in several cases it was not clear if the tendons or ligamentous derangements were part of the SLE manifestations or comorbid conditions. For instance, radiological sacroiliitis has been described in case reports or case series of highly selected SLE patients[8-22]; some reports selected male SLE patients, some were associated with seronegative spondyloarthritis and others as part of SLE manifestations; there are, however, no studies of the frequency of sacroiliitis in consecutive SLE patients lacking other comorbidities. Sacroiliitis may also be found in infections and noninfectious diseases such as acne conglobata, familial Mediterranean fever, polymyalgia rheumatica, hyperparathyroidism, osteoarthritis, and even in seropositive rheumatoid arthritis[26,27].

The aim of our study was to assess the prevalence of selected clinical and radiological features of tendinous and ligamentous derangement (Jaccoud's arthropathy and radiographic features of sacroiliitis, coxofemoral migration, and osteitis pubis) in otherwise unselected consecutive patients with SLE.

MATERIALS AND METHODS

This study included consecutive patients with a diagnosis of SLE according to the revised (1997) American College of Rheumatology (ACR) criteria for classification of SLE[28]. All patients attended a single tertiary care outpatient rheumatology clinic in Guadalajara, Mexico, during a 3-month period of recruitment. Patients with mixed connective tissue disease, over-

lap syndromes, rhupus, inflammatory bowel disease, psoriasis, or brucellosis or a history of major trauma were excluded. SLE patients who used wheelchairs (for any reason), or who had endstage renal failure or a history of infectious arthritis were also excluded.

Our study was approved by the Ethics Committee of the Hospital de Especialidades, IMSS, and all patients gave consent to participate.

Musculoskeletal assessment. All patients' assessments were performed by the same rheumatologist (GSJ). Demographic data, disease characteristics, comorbid conditions, and clinical characteristics of patients' low back pain history were documented using a structured questionnaire and medical chart review. Examination included axial mobility measurements[29]. Inflammatory back pain was defined as proposed by Calin, *et al*[30], consisting of 5 features: (1) insidious onset, (2) age at onset < 40 years, (3) duration of back pain ≥ 3 months, (4) was associated with morning stiffness, and (5) improved with exercise. Inflammatory back pain was considered to be present if at least 4 of the 5 features were fulfilled[30]. Jaccoud's arthropathy was diagnosed as described[31,32].

Enthesopathy was defined as tenderness when pressure was applied during the examination to the ischial tuberosities, greater trochanters, spinous processes, costochondral and manubriosternal junctions, and the iliac crests or over calcaneal and tibial tubercles[33].

Radiographic assessments. Patients underwent standard pelvis radiography (anterior-posterior view). The first 50 radiographs were mixed with 10 other pelvis radiographs from healthy subjects, and the assessments were performed independently by 2 rheumatologists blinded to patients' clinical data. The interobserver correlation calculated for these radiographs was 0.79. The following radiographs were evaluated simultaneously by these rheumatologists, who were also blinded to the patient's identity and clinical status: pelvic radiographs were specifically assessed for sacroiliitis using a 5-stage system (0 = normal to IV = ankylosis)[34]; osteitis pubis, femoral head shape changes, and migration of femoral head were assessed as described[35]. Computed tomography (CT) scan of the sacroiliac (SI) joints was performed only in patients with grade III findings.

Statistical analysis. Differences between 2 continuous variables were compared using the 2-tailed t-test. Differences between proportions were compared using the chi-squared test and Fisher's exact test. Statistical significance was set at $p \leq 0.05$. Confidence intervals (CI) are reported at 95%.

RESULTS

Two hundred forty-two consecutive eligible patients were seen at the clinic within the 3-month recruitment period. Of these, 50 patients were excluded: 15 due to comorbid conditions (7 undergoing hemodialysis, 4 using wheelchairs due to central nervous system involvement, and 4 with hip replacements due to avascular osseous necrosis); 15 other patients had mixed connective tissue disease, 7 had overlap syndromes, and 3 did not meet SLE criteria after chart review; 10 other SLE patients were further excluded due to poor radiograph quality. The total number of included patients was 192.

Patients' demographic and clinical characteristics are summarized in Table 1. Most patients were young (range 17 to 79 yrs) and female. Disease duration (i.e., time after initial symptoms) ranged from 6 months to 42 years. Fifteen patients (8%) had 4 ACR criteria for SLE, 146 (76%) had between 5 and 8 criteria, and 31 (16%) had 9 or more criteria. SLE involvement of at least one major organ was observed in 123 patients (64%); all patients were taking steroids. Although low back pain was frequently reported by patients, the inflammatory type was reported by 10% (95% CI 4.5% to 16%). Results of the modified Schober test were abnormal (≤ 5 cm) in 56 patients (29%). Enthesopathy or SI pain was detected during the examination in 27% of the patients.

Table 1. Selected demographic, clinical, and radiographic characteristics of 192 patients with SLE.

Variable	Value	95% CI
Age, mean yrs ± SD	36 ± 11.8	34 to 38
Sex, n (%)		
Female	170 (89)	
Male	22 (11)	
Disease duration, mean ± SD	10 ± 8	9 to 11
History of low back pain, n (%)	108 (56)	49 to 63
Inflammatory	11 (10)	4.5 to 16
Mechanical	77 (71)	63 to 80
Undifferentiated	20 (19)	11 to 25
Jaccoud's arthropathy, n (%)	44 (23)	17 to 29
History of peripheral arthritis, n (%)	170 (89)	84 to 93
Modified Schober test, mean cm ± SD	5.8 ± 2.1	—
Modified Schober (≤ 5 cm), n (%)	56 (29)	23 to 36
Enthesopathy, n (%)	52 (27)	21 to 33
Sacroiliac pain at examination, n (%)	48 (25)	19 to 31
Sacroiliitis grade, n (%)		
Normal	161 (84)	79 to 89
I	12 (6)	3 to 10
II	8 (4)	2 to 8
III	11 (6)	3 to 9
IV	0	0
Osteitis pubis, n (%)	12 (6)	3 to 10
Coxofemoral migration, n (%)		
Left side, n = 189*	5 (3)	0.4 to 5
Right side, n = 186*	10 (5)	2 to 9

* Excluded hip replacement/prosthesis.

Patients' radiological findings are summarized in Table 1. SI abnormalities were observed in 31 (16%) patients; 27 of the abnormalities (87%) were bilateral: 11 of grade III, 8 of grade II, and 8 of grade I sacroiliitis. Sacroiliitis (any grade) was observed in 30 of 171 (17.5%) female patients and in one of 21 (5%) male patients. A CT scan of SI joints was performed in the 11 (6%) patients with grade III sacroiliitis; sacroiliitis was confirmed by this technique in all of them (Figure 1, panels A and B).

Five patients had abnormally shaped femoral heads suggesting osteonecrosis; these patients were asymptomatic. However, 15 other cases had femoral head migration; the type of migration was medial in 5, superior in 5, and lateral in 5 cases (Figure 1, panel A). None of the 15 patients showed signs of osteonecrosis. Osteitis pubis was documented in 6 cases (Figure 1, panels C and D).

For statistical purposes, radiographic sacroiliitis was recoded in 3 different forms: as a nominal variable (absent or present), as an ordinal variable (sacroiliitis grade), and as a nominal variable using the criteria that sacroiliitis grade III was marked as "present" and all other forms (including none) were marked as "absent." Age, sex, disease duration,

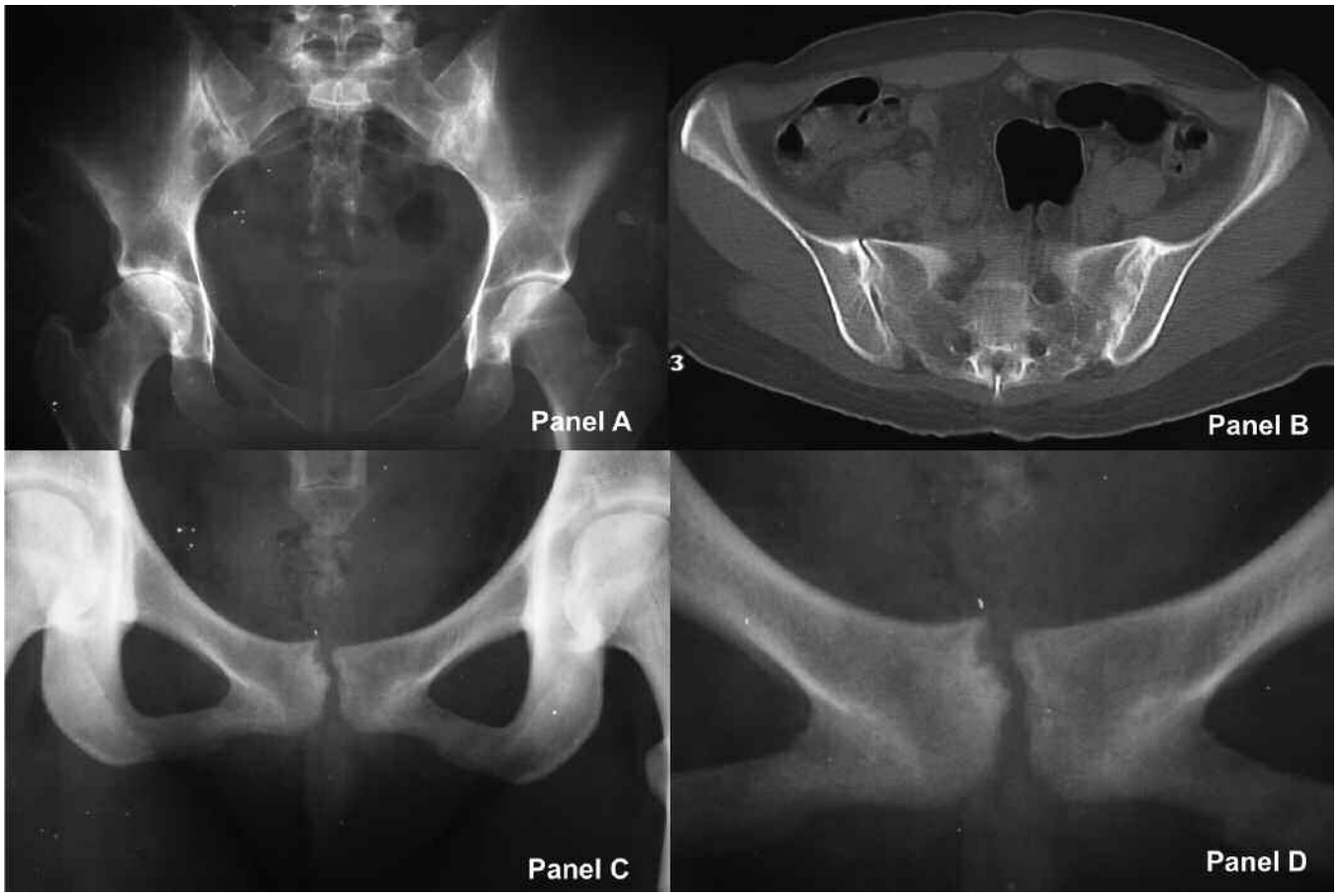

Figure 1. Panels A and B: A 35-year-old female with SLE for 15 years. A simple X-ray shows right coxofemoral migration and sacroiliitis. The CT scan, a transaxial image through the middle portion of the sacroiliac joint, shows articular abnormalities. The abnormalities are more pronounced on the left side, and consist of joint surface irregularity and erosion in both the ilium and the sacrum along with associated new bone formation. Panels C and D: A 23-year-old female with SLE for 7 years with no pregnancies. A simple X-ray shows erosion in the pubis; in a close-up view, erosions on both sides of the pubis are evident.

low back pain, enthesitis, peripheral arthritis, and Jaccoud's arthropathy were not statistically associated with any of the recoded sacroiliitis variables.

DISCUSSION

Our study has 3 main findings. First, ligamentous derangements, in the form of sacroiliitis or osteitis pubis, were documented in at least 6% of the SLE patients. Second, tendinous derangements, expressed either as Jaccoud's arthropathy or femoral head migration, were present in 5% to 23% of our patients. Third, no significant association was found between sacroiliitis and demographic or clinical variables.

Involvement of tendons and ligaments in patients with SLE has been reported, mostly in small series, since 1975. There are around 45 case reports of spontaneous rupture of diverse tendons, including extensor pollicis longus, patellar, and Achilles' tendons[4,5]; there are also reports of patellar tendon elongation and articular hypermobility[1-3]. Recent studies using powerful techniques such as MRI, high resolution ultrasonography, and power Doppler have demonstrated tenosynovitis[23], tendonitis[24], and proliferative tenosynovitis[25]. Jaccoud's arthropathy is considered a form of tendinous derangement in patients with SLE, and the reported frequency in these patients is from 5% to 40%[6,7]; the frequency of it in our study was in the middle range.

Ligamentous weakening and laxity in SLE patients may be manifested as atlantoaxial subluxation[1,7], radiographic sacroiliitis, osteitis pubis, femoral head migration, etc. The literature regarding the association of SLE, ankylosing spondylitis (AS), and noninfectious sacroiliitis falls into 3 categories. The first includes 3 case reports of patients with clear clinical and radiological signs of AS that developed into SLE with major organ involvement[10,15,22]; the authors of these reports considered their patients to have the 2 diseases. The report of Alekberova, *et al*[14] may also be included in this group: this study reported that 4 of 5 cases of SLE with aortal valvular disease also had bilateral sacroiliitis, but all were HLA-B27-negative. The second category of publications includes reports of the development of an autoimmune phenomenon that seems to be SLE in patients with AS

using anti-tumor necrosis factor drugs[22]; most of the authors of these studies considered the autoimmune phenomenon to be an unexpected side effect of the drugs. The third category includes reports of SI joint involvement in patients with otherwise typical SLE. Thirteen case reports or case series and 2 cross-sectional studies fall into this category. One example is the report by Nassonova, *et al*[21], who studied 43 male patients with SLE. About half these patients showed radiological signs of SI abnormalities and 7 had different degrees of iliosacral ankylosis as well; the rationale to select only male patients for this study was not provided [21]. Vivas, *et al*[8] also restricted their study to male patients, and found that 8 of 16 showed radiological evidence of sacroiliitis; they also found osteitis in 3 patients.

It has been reported that elevated quantitative radionuclide SI joint uptake may occur in some patients with active SLE[9,11,13]. However, in the only study of consecutive SLE patients, Leone, *et al*[20] found sacroiliitis in 6 of 41 patients (15%); 2 had grade III sacroiliitis. The authors found no significant associations between clinical symptoms or laboratory findings and sacroiliitis. This is in agreement with our study, where we found radiographic sacroiliitis was not associated with any clinical characteristics, including sex, low back pain, peripheral arthritis, SLE disease duration, etc. Radiographic sacroiliitis was also present in our female patients; thus the evidence from the studies of Nassonova, *et al*[21] and Vivas, *et al*[8] that sacroiliitis was more prevalent in male patients with SLE is not supported by the report from Leone, *et al*[20] and our current study.

Aside from the patients with osteonecrosis, we documented femoral head migration in some of our patients with SLE; this feature may also be explained by ligamentous laxity. These patients did not have radiographic osteoporosis of the femoral head, a crescent sign, or articular collapse; the absence of these signs and the presence of joint space narrowing suggested that osteonecrosis was unlikely. Ligamentous derangements may also be expressed as osteitis pubis; it was diagnosed in 6% of our patients, and in 17% in the report from Vivas, *et al*[8].

Our study has some limitations. First, the pain associated with enthesopathy may be confused with tender points in fibromyalgia[36]. Fibromyalgia is frequently present in patients with SLE and may exacerbate musculoskeletal complaints and hinder the clinical assessment of features such as low back pain or enthesopathy, making it difficult to determine statistical associations between clinical manifestations and radiographic sacroiliitis. Unfortunately, we did not foresee fibromyalgia as a confounder at the time of the patients' assessments. Second, there are new criteria for inflammatory back pain that may perform better than those we used in this study[37]. Third, participating patients were attending a tertiary care, high-referral center and were studied using a cross-sectional design precluding generalization of the reported frequencies of our main features.

Several questions remain concerning the relation of tendinous and ligamentous derangement in SLE, such as the clinical influence, pathogenesis, enthesis involvement, and treatment; these issues warrant further investigation. We propose that the term "SLE-related tendinous and ligamentous derangements" be used to establish a common framework for further research and reporting.

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