Ultrasound imaging for the rheumatologist
XXIII. Sonographic evaluation of hand joint involvement in primary Sjögren’s syndrome

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ABSTRACT

Objective. To study the frequency and features of joint and tendon involvement in the hand of patients with primary Sjögren’s syndrome (pSS) by musculoskeletal ultrasound (US) examination.

Methods. Forty-eight patients with pSS diagnosed according to the preliminary classification criteria proposed by the American-European Classification Criteria Group were enrolled in the study. Bilateral US examination of the 1st – 5th metacarpophalangeal (MCP), 2nd – 5th proximal interphalangeal (PIP) joints and of flexor tendons were performed. A semi-quantitative grading method (0 to 3) for scoring joint effusion, synovial proliferation and intra-articular power Doppler (PD) signal was used.

Results. We observed clear evidence of inflammatory arthritis in 9 (18.7%) patients. Bone erosions at MCP and/or PIP joint were visualized in 6 out of 48 (12.5%) patients. In 10 (20.8%) patients we imaged flexor tenosynovitis which appeared more frequent than in healthy subjects even if no statistically significant difference was detected.

Conclusion. US examination appears to be a useful imaging technique to study joint and soft tissue involvement in connective tissue diseases. The presence of bone erosions in pSS patients is unexpected. Future studies will hopefully concentrate more on defining the erosive capability of connective tissue disorders together with inflammatory involvement of tendons.

Patients and methods

We performed a multicentre study in 4 different Rheumatology Units in Italy: University of Pisa, University of Pavia, Università Politecnica delle Marche and the Sapienza University of Rome. In each unit, US examinations were performed by a rheumatologist experienced in musculoskeletal US 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 semiquantitative

Competing interests: none declared.
assessment of US signs of both joint inflammation and bone erosions, and good agreement rates between sonographers were also found in the detection of tenosynovitis.

Patients
Forty-eight patients (3 males and 45 females, mean age: 57 years, ranging from 81 to 24 years; mean disease duration: 4.7 years, ranging from 1 to 31 years) with pSS were enrolled in the study. The diagnosis of pSS was established according to the preliminary classification criteria proposed by the American-European Classification Criteria (AECC) Group (18). At the time of the US examination, 31 out of 48 (64.5%) patients complained of pain in the hands and 12 out of 48 (25%) also showed swelling of metacarpophalangeal (MCP) or proximal interphalangeal (PIP) joints. However, a history of painful hands was mentioned by 47 out of 48 patients.

After informed consent was obtained, serum samples were taken from the patients and immediately stored at -20°C until tested for IgG antibodies to viral citrullinated peptides (VCP) (19), rheumatoid factor (RF), antinuclear antibodies and antibodies to Ro(SSA) and La(SSB) antigens. Only patients negative for anti VCP antibodies were eligible for the study. Moreover, all the patients were submitted to minor salivary gland biopsy. Focus score ≥1 was detected in 40 patients (grade 3 and 4 according to the Chisholm and Mason scoring) (20). Patients with a focus score <1 were positive for antibodies to Ro(SSA) and La(SSB) antigens and fulfilled the AECC criteria. The clinical characteristics of the patients are summarized in Table I.

Control group
As controls we enrolled 40 healthy volunteers (3 males and 37 females) with mean age 52 years, max. 75 and min. 28 years.

US assessment
Bilateral US examination of the 1st – 5th MCP, 2nd – 5th PIP joints and of flexor tendons were performed using a multiplanner scanning technique. 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 (21). A semi-quantitative grading method (0 to 3) for scoring joint effusion, synovial proliferation and intra-articular power Doppler (PD) signal was used (17, 22-24).

Statistical analysis
Qualitative variables were compared using contingency table analysis and Fisher’s exact test. P-values <0.05 were considered statistically significant.

Results
pSS patients
In 20 out of 48 (41.6%) patients US examination disclosed joint effusion with or without synovial proliferation. More precisely, we observed synovial proliferation (grade 2) with joint effusion in at least one MCP or PIP joint in 4 out of 48 (8.3%) patients and in 3 of them also a positive PD signal. Osteophytes were not imaged in any of the 4 patients, but in 1 of them bone erosions (at the 2nd and 5th metacarpal heads) were visualized. Only one of the 4 patients was positive for RF; both autoantibodies to Ro(SSA) and La(SSB) were present in another patient, while only anti Ro(SSA) antibodies were detected in the last two subjects. In 5 other patients, synovial proliferation (grade 1) with joint effusion, but no PD signal, was visualized at MCP and PIP joints with no evidence of osteoarthritic change.

In the remaining patients we imaged only mild effusion without signs of synovial hypertrophy in 11 out of 20. Bony irregularities due to osteoarthritis were present in 2 subjects within this last group.

In 10 out of 48 (20.8%) patients we observed flexor tendon effusion with synovial hypertrophy but no PD signal. Bone erosions at MCP and/or PIP were visualized in 6 out of 48 (12.5%) patients and in 5 of them features of inflammatory arthritis were not detected by US. In addition, there was no US evidence of osteoarthritis change in any of these 6 individuals who had hand pain or gave a history. Laboratory tests revealed positivity for RF in 5 of the 6 subjects, both antibodies to Ro(SSA) and La(SSB) in 1 out of 6 and only antibodies to Ro(SSA) in 4 patients.

Pathological findings detected by US examination of hand in pSS patients are reported in Table II.

Healthy control group
In the group of healthy controls minimal effusion without synovial proliferation at MCP or PIP was discovered in 12 out of 40 (30%) subjects. There was no significant difference in the frequency of effusion without synovial proliferation in pSS and the control group (p=0.27). In 2 other individuals, who also showed osteoarthritic change, mild effusion at MCP or PIP was associated to slight synovial proliferation but no PD signal. No bone erosions were detected in any controls.

Flexor tenosynovitis was visualized in 2 out of 40 (5%) normal subjects. The frequency of tenosynovitis in pSS patients is higher than in healthy controls (20.8% vs. 5%, p=0.057) with a statistically significant trend.

Table I. Main characteristics of patients with pSS.

<table>
<thead>
<tr>
<th>Patient number</th>
<th>M/F</th>
<th>Mean age (years)</th>
<th>Autoantibodies (prevalence %)</th>
<th>Positive lip biopsy</th>
<th>Antibodies to Ro(SSA)</th>
<th>Antibodies to La(SSB)</th>
</tr>
</thead>
<tbody>
<tr>
<td>48</td>
<td>3/45</td>
<td>57 (81-24)</td>
<td>28/48 (58%)</td>
<td>0/48 (0%)</td>
<td>40/48 (83%)</td>
<td>29/48 (60%)</td>
</tr>
</tbody>
</table>

M/F: male/female ratio; VCP: viral citrullinated peptides.
**Discussion**

Articular signs and symptoms are frequent in pSS. The true prevalence of joint and tendon involvement in this connective tissue disorder remain unclear. In 1993, Pease et al. reviewed the clinical course of 48 pSS patients and reported that the incidence of arthritis and/or arthralgia was 54% and in a third of these patients it was the presenting feature prior to the sicca syndrome (25). A study in elderly patients revealed that articular involvement was present in 29% of the subjects (26). Furthermore, arthritis was reported in 12.5% and 9.8% of patients with early and late onset pSS respectively (27).

Kruize et al. failed to observe arthritis (4) in a small number of subjects followed longitudinally (1, 5). Important advances have been made in the field of musculoskeletal US confirming its eminent position in the detailed depiction of the anatomical changes in joints and tendons in rheumatic disorders. The study by Iagnocco et al. remains the pivotal study using US to investigate focal joint involvement in pSS describing the presence of synovial thickening and slight synovitis within the knee (16). Our study showed a high proportion of patients with pSS reporting hand pain. Subsequent US examination showed clear evidence of inflammatory arthritis in 9 (18.7%) patients. This is consistent with most of the smaller studies performed to date (1, 5). Interestingly, 6 patients had MCP and PIP erosions, detected in 5 out of these 6 patients in the absence of cardinal signs suggestive of active inflammatory disease. The origin of these findings is unclear but may represent hallmark features of previous inflammatory activity within these particular joints.

The study by Wright et al. reported erosive changes within the MCP joints of patients with systemic lupus erythematosus (SLE) (8 out of 17) (28). Some lupus patients may develop arthritis with erosive features (the “rhupus” hand) but usually radiographs of hands in these patients do not reveal erosive changes and the disorder is widely viewed as being non-erosive. The presence of bone erosions in both pSS and SLE patients is unexpected. US is able to visualize even minimal interruptions of the bony cortex so the US technique is now recognized as an imaging modality with higher sensitivity than x-ray in the detection of small erosions.

### Table II. Pathological findings detected by US examination of hand in pSS patients.

<table>
<thead>
<tr>
<th>Pathological finding</th>
<th>no. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Joint effusion with synovial proliferation in at least one MCP or PIP joint (grade 2)</td>
<td>4/48</td>
</tr>
<tr>
<td>Joint effusion with synovial proliferation in at least one MCP or PIP joint (grade 1)</td>
<td>5/48</td>
</tr>
<tr>
<td>Joint effusion without synovial proliferation</td>
<td>11/48</td>
</tr>
<tr>
<td>Flexor tenosynovitis</td>
<td>10/48</td>
</tr>
<tr>
<td>Bone erosions at MCP and/or PIP joints</td>
<td>6/48</td>
</tr>
</tbody>
</table>

![Fig. 1. A. Dorsal longitudinal scan of the 3rd metacarpo-phalangeal joint. Power Doppler technique showing the presence of signal in the fat pad. pp: proximal phalanx; m: metacarpal head; et: extensor tendon; *: fat pad. B. Dorsal longitudinal scan of the 1st metacarpo-phalangeal joint. Gray scale US. pp: proximal phalanx; m: metacarpal head; the arrow indicates an erosion. C. Dorsal longitudinal scan of the 2nd interphalangeal joint. Gray scale US. pp: proximal phalanx; mp: middle phalanx; °: shows the effusion in the capsula. D. Volar longitudinal scan of the 2nd interphalangeal joint. Gray scale US. pp: proximal phalanx; mp: middle phalanx; ft: flexor tendons; °: shows the effusion in the capsula.](image-url)
which evade traditional radiography (7, 8, 29). Our 6 patients with bone erosion on US examination had had regular clinical follow up at our Rheumatology Units and the typical manifestations of pSS, according to the preliminary classification criteria proposed by the American-European Classification Criteria, had been observed. None of the 6 patients described symmetrical arthritides or had rheumatoid nodules. The sonographic demonstration of bone erosion might however suggest the possibility of co-existing rheumatoid arthritis or suggest the presence of a subset of pSS patients with aggressive arthritides. We think that a strict US follow up should be performed in pSS patients, particularly when positive for RF, to establish the more correct diagnosis and effective therapy in order to avoid structural damage.

A minimal effusion at MCP or PIP, without synovial proliferation, was visualized in 11 out of 48 pSS patients and also in 12 out of 40 healthy subjects with no statistically significant difference (30).

Flexor tenosynovitis in pSS patients appeared more frequent than in healthy subjects but no statistically significant difference was detected. Further studies on larger populations may help to clarify the prevalence further. US examination appears to be a useful imaging technique to study joint and soft tissue involvement in connective tissue diseases. Future studies will hopefully concentrate more on defining the erosive capability of these disorders together with inflammatory involvement of tendons. Future comparisons between US and MRI could be very interesting in the follow-up of pSS patients and could help further our understanding of this disease.

**Link**

For ultrasound images, go to: www.clinexpneumato.org/ultrasound

**References**


**Hand ultrasound in primary Sjögren’s syndrome**