Differentiation between early rheumatoid and early psoriatic arthritis by the ultrasonographic study of the synovio-entheseal complex of the small joints of the hands

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Abstract

Objective

To determine whether ultrasonographic findings of the synovio-entheseal complex of the hand small joints could be used to differentiate between early rheumatoid and early psoriatic arthritis.

Methods

Thirty-four early rheumatoid and 26 early psoriatic arthritis patients with a prevalent involvement of the hands were examined with ultrasound (US). All exams were performed at the first visit by evaluating synovitis, peritendon extensor digitorum tendon oedema, enthesitis of the central slip of extensor tendon, flexor tenosynovitis and soft tissue oedema. In the same patient, the two most clinically involved joints, if possible of the same digit, were evaluated.

Results

Sixty-eight clinically involved joints were evaluated in 34 early rheumatoid arthritis patients and 52 joints in 26 early psoriatic arthritis patients.Synovitis was significantly more frequently detected in early rheumatoid arthritis compared to early psoriatic arthritis patients (p=0.0001), in 91.1% joints of the former and in 59.6% joints of the latter.
At metacarpohalangeal joint, the presence of peritendon extensor digitorum tendon inflammation was observed in 2.5% of the joints in the early rheumatoid arthritis group and in 54.1% of the joints in the early psoriatic arthritis group (p=0.0001). At PIP joints, central slip enthesitis was exclusively observed in EPsA (p=0.0045).
When considering the most clinically involved finger per patient, soft tissue oedema was detected almost exclusively in psoriatic arthritis (p=0.0002).

Conclusion

The US involvement of synovio-entheseal complex and US extrasynovial features may be helpful in the differential diagnosis between early rheumatoid and early psoriatic arthritis.

Key words

early rheumatoid arthritis, early psoriatic arthritis, enthesitis, ultrasound

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Introduction

Drug-free remission, or drug remission, is the new aim for the treatment of chronic arthritis and the "window of opportunity" is the time to act to turn the tide of the disease.

For this purpose, the early diagnosis is essential for the early treatment of the patient, and ultrasound (US) is useful to improve the diagnostic process and to predict progression from undifferentiated to differentiated arthritis (1, 2).

Rheumatoid arthritis (RA) and Psoriatic Arthritis (PsA) are the two types of chronic inflammatory arthritis most frequently found in clinical practice and they share similar progressive damage and irreversible joint function. However, chronic arthritis in its early stages may have a lower clinical and immunologic expression and the differential diagnosis may be rather complicated, in particular in seronegative patients: thus, the diagnostic process in the early phase of the disease needs additional tools.

To date, the evidence of the role of US and Magnetic Resonance Imaging (MRI) in the differential diagnosis between early RA (ERA) and early PsA (EPsA) is still limited, although US and MRI seem to demonstrate a greater extra-synovial involvement in PsA if compared to RA (3, 4, 5).

These imaging findings support the concept of the involvement of the synovio-entheseal complex (SEC) and of enthesitis related inflammation as an early event in PsA and in spondyloarthritis (SpA) (6, 7).

The aim of this study was to highlight the US findings (*e.g.* peritendon inflammation of the extensor digitorum tendon) of the hand small joints in patients with ERA and EPsA.

Material and methods

Patients

Patients, attending the outpatient Early Arthritis Clinic at the Rheumatology Clinic of Udine University Hospital (Italy) with articular symptoms lasting for less than 12 months, were evaluated from June 2013 to December 2014.

Among them, consecutive patients with a prevalent involvement of the hands were selected.

An ultrasonography study was performed in 34 patients with a diagnosis of ERA and in 26 patients with a diagnosis of EPsA; all the included patients satisfied either the 2010 ACR/EULAR criteria for RA or the CASPAR criteria for PsA (8, 9).

All the patients underwent both clinical evaluation and ultrasonography analyses at the time of their first access to the Early Arthritis Clinic and they were taken no treatment at all (including NSAIDs or steroids).

Within one month from baseline visit, all patients were examined with traditional hands and feet x-ray.

Clinical assessment was carried out by an expert rheumatologist (SS), who recorded tenderness and swelling of the joints and the presence of dactylitis and then chose the two more involved joints of the hands and the most involved finger for the ultrasound assessment.

Distal interphalangeal joints were clinically evaluated but not selected for ultrasound examination.

No patient with a known or suspected concomitant diagnosis of osteoarthritis or crystal arthritis was included and these diagnoses were ruled out with clinical examination and x ray of hands and feet.

The study was conducted according to a protocol for the characterisation of early arthritis approved by the local Ethical Committee, in conformity with the Declaration of Helsinki and with the guidelines for good clinical practice. A written informed consent was obtained from all participants.

Ultrasound protocol

Sonographic evaluations were performed by the same rheumatologist (AZ), expert in US, blinded to the clinical and laboratory data.

Two joints of the hand per patient were scanned, *i.e.* the most clinically involved joints, if possible of the same digit; the ones with clinical dactylitis were excluded from sonographic evaluation.

All joints were scanned dorsal and volar adopting the indications provided by the EULAR guidelines for musculoskeletal ultrasound in rheumatology (10) and each feature was evaluated in two perpendicular scans.

All ultrasound scans were performed using a MyLabClassC (Esaote, Genova, Italy) equipped with a 6-18 MHz linear transducer and it was paid specific attention not to apply transducer pressure on the anatomical structures under examination.

Both longitudinal and transverse scans were performed by slightly moving the probe from radial to ulnar and from proximal to distal areas on dorsal and volar view to overall assess the anatomical surface. US examination took about 5 minutes for each patient, including documentation.

US grey-scale (GS) imaging parameters were optimised for maximal image resolution and power Doppler (PD) settings were standardised at the following values: 750 Hz for pulse repetition frequency, 3 for wall filter, 4 for persistence and colour gain between 50-55%.

The pathological US findings were graded in GS and PD with 0 when absent and 1 if present.

Synovitis at metacarpophalangeal (MCP) and proximal-interphalangeal (PIP) joints was defined according to the OMERACT definition (11) as an abnormal hypoechoic intra-articular tissue that is non-displaceable and poorly compressible (Syn) and that may exhibit PD signal (PD-Syn).

Furthermore, at MCP joints articular synovitis was analysed semiquantitavely in GS (0 = absence, 1 = mild, 2 = moderate, and 3 = severe) and in PD (0 = no intra-articular colour signal, 1 = mild, single vessel signal, grade 2 = moderate, greater than grade 1 to <50% of the intra-articular area filled with colour signals and grade 3 = ≥50% of the intra-articular area filled with colour signals) (12).

Erosion was defined as a discontinuity of the bone surface that was visible in two perpendicular planes (11) and was only evaluated in a binary method (presence/absence).

Peritendon inflammation of the extensor digitorum tendon was investigated by dorsal scan of the MCP joints and defined as present in GS (PTI), with or without peri-tendinous PD signal (PD-PTI), if it was present a hypoechoic swelling of the soft tissue surrounding the extensor tendon (5) (Fig. 1).

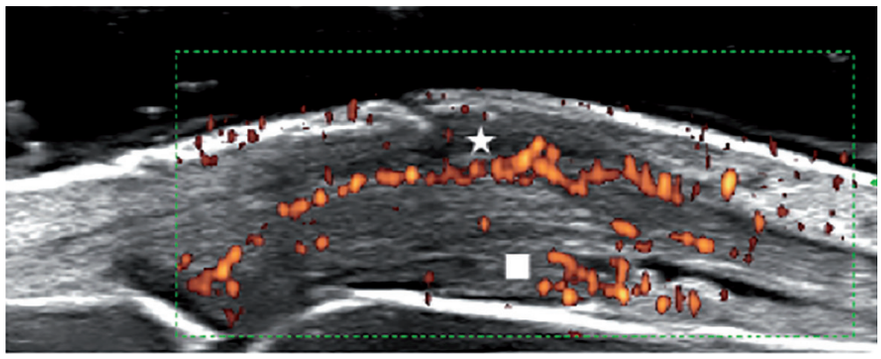

Fig. 1. Dorsal longitudinal scan on MCP joint. Peritendon inflammation of the extensor digitorum tendon with PD signal (white star) and articular synovitis with PD signal (white square).

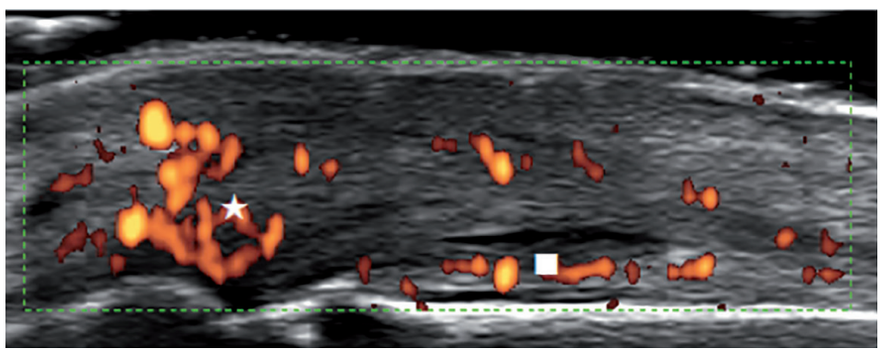

Fig. 2. Dorsal longitudinal scan on PIP joint. Central slip enthesitis with PD signal (white star) and articular synovitis with PD signal and a small effusion (white square).

At PIP joints central slip enthesitis (CSE) was graded as present in grey scale when it was found hypoechoic and increased thickness in the insertion of the central slip of extensor tendon on PIP joint. The thickness of the extensor tendon at the level of insertion was assessed as thickened by comparing it to the proximal part of the tendon and to the controlateral joint. Particular attention was given in the evaluation of PD (PD-CSE) in the insertion site (13-14), (Fig. 2).

Tenosynovitis was defined in grey-scale (Teno) as abnormal anechoic and/or hypoechoic tendon sheath widening which could be related to both the presence of tenosynovial abnormal fluid and/or hypertrophy. The presence of PD (PD-Teno) was characterised by the presence of peritendinous doppler signal within the synovial sheath (15).

Soft tissue oedema was defined as a diffuse enlargement of soft tissue around the flexor tendon, with an increased power doppler signal, from finger pad to MCP joint and it was evaluated by volar scan (16-17).

On the contrary, localised soft tissue oedema (*e.g.* around the extensor digitorum tendon in PTI pattern, extracapsular soft tissue inflammation in PIP joint) was not included in the previous definition.

Tenosynovitis and soft tissue oedema were evaluated only in the most clinically involved finger joints.

Statistical analysis

• *Sample size*

Based on the findings from Gutierrez *et al.* (5), where the difference in the prevalence of peritendon inflammation of the extensor digitorum tendon in RA and PsA was about 55% when considering the number of joints, and the prevalence of peritendon inflammation of the extensor digitorum tendon in patients with disease duration <18 months was 70%, a sample size of 52 joints for each group was calculated in order to observe a difference of at least 30% of articular joints with peritendon inflammation of the extensor digitorum tendon between ERA and EPsA, with an estimated power of 90% and an alpha error of 5%.

• *Statistics*

Descriptive statistics, reported as mean ± standard deviation, were used to summarise data and comparison between the US features was performed using Chi-square test. A p-value <0.05 was considered as significant. Furthermore, for each of the US features, sensitivity, specificity, predictive positive value (PPV), negative predictive value (NPV), were calculated by considering in turn ERA or EPsA patients as control group.

Results

Sixty-eight clinically involved joints (39 MCP and 29 PIP) were evaluated by US in 34 ERA patients and fifty-two joints (24 MCP, 28 PIP) in 26 EPsA patients. Two joints of the same digit were studied in 17/34 (50%) patients with ERA and in 17/26 (65.3%) with EPsA.

The clinical characteristics of the patients are reported in Table I.

Table II shows the US findings in patients with ERA and EPsA, while Table III and IV show the sensitivity, specificity, PPV, and NPV, for each feature in ERA and EPsA, respectively.

Extrasynovial involvement

At MCP joint, only 1/39 (2.5%) joint of ERA patients showed the presence of PTI, while this feature was present in 13/24 (54.1%) of EPsA patients (p=0.0001) and the same data was found with PDUS examination (PD-PTI) (p=0.0001).

Evaluating only the joints with PTI in EPsA patients, it was found that there was a concomitant presence of Syn in 6/13 (46.2%) joints while in 7/13 (53.8.%) PTI was the only pathological feature.

Concerning PIP joints, CSE was exclusively observed in EPsA, in 7/28 (25%) joints (7/28 *vs*. 0/29, p=0.0045). The presence of PD in the insertion of extensor tendon was found only in psoriatic joints with pathological changes in GS; in particular, it was found in 6/28 (21.4%) (6/28 *vs*. 0/29 p=0.01). CSE associated with Syn was found in 5/7 (71.4%) joints.

The identification of PTI or CSE resulted the US findings with the highest specificity and the highest PPV for EPsA if compared with ERA (Table IV).

Table I. Clinical findings at baseline of patients with ERA and EPsA.

	ERA (n=34)	EPsA (n=26)
Age in years (mean ± sd)	49.2 ± 12.7	52.0 ± 12.1
Women/men	27/7	15/11
Duration of symptoms, months (mean ± sd)	6.4 ± 3.8	7.0 ± 3.5
DAS28 (mean ± sd)	4.4 ± 0.9	3.6 ± 0.7
CRP mg/dl (median, range)	1.42 (0.06-5.01)	0.4 (0.05-5.17)
Total tender joints (68) (mean ± sd)	10.4 ± 5.6	7.0 ± 3.2
Total swollen joints (66) (mean ± sd)	6.3 ± 4.4	3.6 ± 2.1
Rheumatoid factor +	16/34	0/26
ACPA +	18/34	0/26
Current Psoriasis	0/34	22/26

ERA: early rheumatoid arthritis; EPsA: early psoriatic arthritis; DAS28: Disease Activity Score 28; CRP: C-reactive protein; ACPA: anti-cytrullinated peptide antibodies; sd: standard deviation.

Table II. Frequency of US findings at MCP and PIP joints in ERA and EPsA patients.

US-feature	ERA	EPsA	p-value
Syn (total)	62/68 (91.1%)	31/52 (59.6%)	**0.0001**
PD-Syn (total)	59/62 (95.1%)	25/31 (80.6%)	0.055
Syn (MCP joints)	38/39 (97.4%)	15/24 (62.5%)	**0.0004**
PD-Syn (MCP joints)	36/38 (94.7%)	13/15 (86.6%)	0.56
PTI	1/39 (2.5%)	13/24 (54.1%)	**0.0001**
PD-PTI	1/39 (2.5%)	13/24 (54.1%)	**0.0001**
Syn (PIP joints)	24/29 (82.7%)	16/28 (57.1%)	**0.045**
PD-Syn (PIP joints)	21/24 (87.5%)	12/16 (75%)	0.40
CSE	0/29 (0%)	7/28 (25%)	**0.0045**
PD-CSE	0/29 (0%)	6/28 (21.4%)	**0.01**
Erosions (total)	9/68 (13.8%)	2/52 (3.8%)	0.11
Teno (most clinically involved finger)	22/34 (64.7%)	14/26 (53.8%)	0.43
PD-Teno (most clinically involved finger)	10/34 (29.4%)	7/26 (26.9%)	1.00
Soft tissue oedema (most clinically involved finger)	1/34 (2.9%)	11/26 (42.3%)	**0.000**2

Syn: grey-scale synovitis; PTI: peri-extensor digitorum tendon inflammation at MCP joint; CSE: central slip of extensor tendon enthesitis at PIP joint; Teno: flexor tenosynovitis.

Soft tissue oedema was detected in 1/34 (2.9%) in ERA group and in 11/26 (42.3%) in EPsA group (p=0.0002). The eleven cases with soft tissue oedema could be divided into two groups: in 4/11 (36.4%) there was soft tissue oedema associated with flexor tenosynovitis and in 7/11 (63.4%) there was soft tissue oedema without flexor tenosynovitis. Considering only the most clinically involved finger per patient, soft tissue oedema showed a high specificity for EPsA (specificity 97.1%, PPV 91.7%).

Considering the most clinically involved finger joint, Teno and PD-Teno did not differ between ERA patients (Teno: 22/34, 64.7%; PD-Teno: 10/34, 29.4%) and EPsA patients (Teno: 14/26, 53.8%; PD-Teno: 7/26, 26.9%) (Table II).

Synovial involvement

In the EPsA group, 17/26 (65.4%) patients showed symmetric hand polyarthritis similar to RA, while 9/26 (34.6%) showed asymmetric oligoarthritis, predominantly involving the hand joints.

Regarding all joints evaluated, Syn was significantly more detected in ERA patients compared to EPsA patients (p=0.0001). It was observed respectively in 62/68 (91.1%) of the former and in 31/52 (59.6%) of the latter; the presence of PD in Syn positive cases, found in 59/62 (95.1%) in ERA patients and in 25/31 (80.6%) in EPsA patients, was not significantly different.

In detail, at the MCP joints, Syn was statistically more frequent in ERA patients resulting in 38/39 (97.4%) joints compared to 15/24 (62.5%) in EPsA (p=0.0004), while no statistically significant difference was found for the presence of PD-Syn, grade of Syn and the grade of PD-Syn.

Table III. Sensitivity, specificity, PPV, NPV of the different US features for ERA.

ERA	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Syn (total)	91.2% (81.8-96.7)	40.4% (27.0-54.9)	66.7% (56.1-76.1)	77.8% (57.7-91.4)
PD-Syn (total)	95.2% (86.5-98.9)	19.3% (7.4-37.4)	70.2% (59.3-79.8)	66.7 (29.9-92.6)
Syn (MCP)	97.4% (86.5-99.9)	37.5% (18.8-59.4)	71.7% (57.6-83.2)	90.0% (55.5-99.7)
PD-Syn (MCP)	94.7% (82.2-99.3)	13.3% (1.6-40.4)	73.4% (58.9-85.0)	50.0% (6.7-93.2)
PTI	2.6% (0.1-13.4)	45.8% (25.5-67.1)	7.1% (0.2-33.8)	22.4% (11.7-36.6)
PD-PTI	2.6% (0.1-13.4)	45.8% (25.5-67.1)	7.1% (0.2-33.8)	22.4% (11.7-36.6)
Syn (PIP)	82.8% (64.2-94.2)	42.9% (24.5-62.8)	60.0% (43.3-75.1)	70.6% (44.0-89.7)
PD-Syn (PIP)	87.5% (67.6-97.3)	25.0% (7.2-52.3)	63.6% (45.1-79.6)	57.1% (18.4-90.1)
CSE	0.0% (0-11.9)	75.0% (55.1-89.3)	0.0% (0.0-40.9)	42.0% (28.1-56.8)
PD-CSE	0.0% (0-11.9)	78.5% (59.0-91.7)	0.0% (0.0-45.9)	43.1% (29.3-57.8)
Erosions (total)	13.2% (6.2-23.6)	96.1% (86.8-99.5)	81.8% (48.2-97.7)	45.9% (36.3-55.7)
Teno	67.4% (46.4-80.2)	46.1% (26.5-66.7)	61.1% (43.4-76.9)	50.0% (29.1-70.9)
PD-Teno	29.4% (15.1-47.5)	75.0% (55.1-89.3)	58.8% (32.9-81.6)	46.7% (31.7-62.1)
Soft tissue oedema	2.9% (0.1-15.3)	57.7% (37.0-76.7)	8.3% (0.2-38.5)	31.2% (18.7-46.2)

Table IV. Sensitivity, specificity, PPV, NPV of the different US features for EPsA.

EPsA	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Syn (total)	59.6% (45.1-73.0)	8.8% (3.3-18.2)	33.3% (23.9-43.9)	22.2% (8.6-42.2)
PD-Syn (total)	80.7% (62.5-92.5)	4.9% (1.0-13.5)	29.8% (20.2-40.7)	33.3% (7.5-70.7)
Syn (MCP)	62.5% (40.6-81.2)	2.6% (0.1-13-5)	28.3% (16.8-42.3)	10.0% (0.5-44.5)
PD-Syn (MCP)	86.7% (59.5-98.3)	5.2% (0.6-17.8)	26.5% (14.9-41.0)	50.0% (6.8-93.2)
PTI	54.1% (32.8-74.4)	97.4% (86.5-99.9)	92.9% (66.1-99.8)	77.5% (63.4-88.2)
PD-PTI	54.1% (32.8-74.4)	97.4% (86.5-99.9)	92.9% (66.1-99.8)	77.5% (63.4-88.2)
Syn (PIP)	57.1% (37.1-75.6)	17.2% (5.9-35.8)	40.0% (24.9-56.7)	29.4% (10.3-56.0)
PD-Syn (PIP)	75.0% (47.6-92.7)	12.5% (2.7-32.3)	36.3% (20.4-54.9)	42.9% (9.9-81.6)
CSE	25.0% (10.7-44.9)	100% (88.0-100)	100% (59.0-100)	58% (43.2-71.8)
PD-CSE	21.4% (8.3-40.9)	100% (88.0-100)	100% (54.0-100)	56.8% (42.2-70.6)
Erosions (total)	3.8% (0.5-13.2)	86.7% (76.3-93.7)	18.2% (2.2-51.8)	54.1% (44.3-63.7)
Teno	53.8% (33.3-73.4)	35.3% (19.8-53.1)	38.9% (23.1-56.5)	50.0% (29.1-70.9)
PD-Teno	26.9% (11.6-47.8)	70.6% (52.5-84.9)	41.2% (18.4-67.0)	55.8% (39.9-70.9)
Soft tissue oedema	42.3% (23.3-63.0)	97.1% (84.7-99.9)	91.7% (61.5-99.8)	68.8% (53.8-81.3)

Regarding the PIP joints, Syn was statistically more frequent in ERA patients resulting in 24/29 (82.7%) joints compared to 16/28 (57.1%) in EPsA (p=0.045), while no statistically significant difference was found for the presence of PD-Syn.

Overall erosions were observed in 9/68 (13.8%) joints of 8/34 (23.5%) ERA patients and in 2/52 (3.8%) joints of 1/26 (3.8%) EPsA patient but these features, although more frequent in ERA group, did not reach a statistical significance (p=0.11 for the erosions, p=0.06 for the patients with erosions). At traditional x-ray, 2/9 (22.2%) erosions were recorded in the ERA group while none were observed in the EPsA group.

Synovitis at the MCP joint was the US finding with the highest sensitivity and NPV, while erosions were the US finding showing the highest specifivity and PPV for ERA if compared to EPsA (Table III).

Comparisons between seronegative patients

Interestingly, while no differences were observed in US findings between seronegative and seropositive ERA patients (data not shown), frequencies of PTI and synovitis were still significantly different between seronegative ERA and EPsA (seronegative ERA vs EPsA: 1/13 vs 13/24, p=0.01 for PTI, 20/22 *vs*. 31/52 for synovitis, p=0.01).

Discussion

This study provides novel evidence for the usefulness of US in the early diagnosis of EPsA *versus* ERA, detecting significantly extra-synovial findings in the former. In fact, PTI, CSE and soft tissue oedema showed the highest specificity for EPsA in comparison with ERA. This observation supports the accepted hypothesis that enthesitis and the involvement of the synovio-entheseal complex may be a very early event in PsA (18, 19).

Enthesitis and the involvement of the SEC represent the earliest lesion in the SpA-like animal model (19, 20). In a mouse model of chronic deregulated TNF production (TNF$^{\Delta ARE}$mouse), which develops arthritis and Crohn's like ileitis, enthesitisis an early disease event and the collateral ligaments of PIP, the SEC of Achilles tendon and greater trochanter of the hip are the first sites of inflammation (19). Subsequently, the extension of the inflammation leads to an involvement of the synovium, finally evolving into synovitis (19, 20). In human beings the same data have not been demonstrated conclusively and additional investigation by imaging (US and MRI) could then be useful to support the experimental data.

Our data point to the role of US as a useful tool in the differential diagnosis in early chronic arthritis. We found the US findings of peritendinitis, enthesitis and soft tissue oedema in joints of the hands as possible hallmarks of EPsA and these results supported the involvement of SEC and extrasynovial structures as a key element for the differential diagnosis between EPsA and ERA.

Conversely, articular synovitis, both at MCP and PIP joints, and erosions were more frequently observed in ERA patients, consistent with the definition of synovitis for ERA and enthesosynovitis for EPsA.

At the MCP joints, the SEC consists in a functional enthesis (21) formed by extensor digitorum tendon, sesamoid fibrocartilage in tendon as it crosses the MCP joints, superficial and deep peritendinous tissues and joint synovia (22). The US evidence of PTI in MCP joints then reflected the inflammation of a functional enthesis, and in this study it was significantly associated with EPsA, extending to early PsA the observation by Gutierrez *et al*. (5) on established PsA.

A second significant hallmark of EPsA was detected in the PIP joints, with the enthesitis of the central slip of extensor

digitorum tendon on the base of middle phalanx. At the PIP joints CSE resulted significantly associated with EPsA. This ultrasonographic feature was previously described in one case of PsA (14).

According to SEC theory, Syn was in combination with PTI in about 50% of MCP joints and with CSE in about 70% of PIP joints.

This association between enthesitis and articular synovitis supports the hypothesis that SEC involvement could be an earlier pathologic event (18, 19) and advises to deeply study this combination in very early psoriatic arthritis in order to establish the first pathological feature.

In our study, another extrasynovial feature was the soft tissue oedema, which was more frequently associated with psoriatic arthritis and it was associated with flexor tenosynovitis in about 40% of psoriatic finger joints.

Dactylitis is not usually clinically detected in early phases of spondyloarthritis, indeed it was found after 5-6 years since first symptom noted (23) and, in US and MRI studies, soft tissue oedema and flexor tenosynovitis are the two most important findings described in works evaluating clinical psoriatic dactylitis (24).

In view of the above, the concomitant presence of soft tissue oedema and flexor tenosynovitis could be evaluated as a preclinical dactylitis and then could be considered as a US marker of EPsA but this hypothesis will be evaluated in larger perspective series.

Overall, oedema of the soft tissue could be defined as an inflammation of the "fibrous skeleton" (16) of the digit, confirming once more the role of the extrasynovial structures and digital enthesitis in the development of psoriatic arthritis.

Finally, histological analyses of synovial biopsies suggest that the psoriatic synovial membrane differs from RA for an increased vascularity and for a lower lining layer thickness (25). However, despite these histological differences, in this study, and according to the MRI data of the hand and wrist (26, 27), the grade of PD activity at MCP joints did not differ significantly between EPsA and ERA. Overall, the evaluation of joint vascularity by US appears at the moment useless for the differential diagnosis. Contrast-enhanced ultrasound might improve the approach to this issue (28).

The limits of this study include, first, the sample size which was not powered to detect significant differences in extrasynovial features other than peritendon inflammation of the extensor digitorum tendon, and synovial features, and, secondly, the a priori choice of the two more clinically involved joints for US investigation. The current results should be then considered as preliminary, and they need replication.

However, this study confirms the importance of US in clinical practice and the role of US in improving the performance of the diagnostic process by increasing the specificity of the diagnosis of early chronic arthritis (29, 30, 31), even in seronegative patients.

In clinical practice, focusing on a small number of active joints (*e.g.* about 5 minutes for the two most clinically involved joints) could easily help the clinician during the diagnostic process of early chronic arthritis.

In conclusion, the US involvement of SEC and US extrasynovial features may be helpful in the differentiation between ERA and EPsA with prevalent involvement of the hand joints. If confirmed, these results may lead to major advances in the management of early chronic arthritis, in particular in the setting of undifferentiated and/or seronegative arthritis.

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