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Original article

Ultrasound study of entheses in psoriasis patients with or without musculoskeletal symptoms: A prospective study

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ABSTRACT

Objective: To estimate the prevalence of ultrasonographic enthesitis in psoriasis patients with or without musculoskeletal symptoms and to investigate their evolution under systemic treatments given for the cutaneous symptoms.
Patients and methods: Prospective bi-centre (rheumatology and dermatology) study over 6 months, including psoriasis pts requiring systemic treatment, with or without musculoskeletal symptoms and/or psoriatic arthritis (PsA). Clinical assessment (M0 and M6) included: BASDAI, HAQ, SPARCC, PASI and nail disease. US assessment (M0 and M6) with Grey Scale and PD of 10 entheses was performed by one trained rheumatologist blinded to clinical and biological data, scoring morphological, structural lesions and PD signal.
Results: Complete data were obtained on 340 entheses in 34 patients. Twenty-two were asymptomatic (PsO) and 12 symptomatic (PsA). They received conventional treatment and/or biologics.
At baseline: US abnormalities were found in 97.1% total population and in 86.4% PsO patients. 95/340 enthesitis were observed, 57/220 in PsO vs 38/120 in PsA ($P = 0.258$). Neither group had PD signal. Presence of 24/90 enthesitis in patients with nail disease vs 33/130 without ($P = 0.831$).
At M6: Twenty-three patients were assessed. US morphological (thickness and hypoechogenicity) abnormalities were improved in PsO ($n = 13$) ($P = 0.021$) and PsA patients ($n = 10$) ($P = 0.164$) with a significant decrease of BASDAI, HAQ, SPARCC.
Conclusion: We observed a high frequency of US enthesitis in psoriasis patients, with or without musculoskeletal symptoms, requiring systemic treatment. At 6 months, US morphological abnormalities were likely to improve. Further studies would be interesting to validate our data and to assess their potential impact on PsA development.

1. Introduction

Enthesitis is a distinctive feature in the pathogenesis of spondyloarthritis (SA), group of diseases, including psoriatic arthritis (PsA) [1,2]. PsA occurs in a variable percentage of psoriasis patients that ranges from 10 to 30% depending on the studied population [3]. Despite their clinical importance, entheseal abnormalities in patients with SA are under-diagnosed and subclinical enthesitis using ultrasonography (US) have been found mainly in lower limbs of patients, including PsA patients. It has been demonstrated that subclinical enthesitis is present in psoriasis patients without musculoskeletal involvement (PsO) compared with healthy controls [4–8]. US is a sensitive technique and appears as a valid and reliable tool for enthesitis evaluation [9–11]. In 2005, consensus definitions of US elementary lesion, including enthesopathy, were published by the OMERACT group [12,13]. Several studies have highlighted the value of US in assessing inflammation and the follow-up of enthesis in SA [14–20]. In fact, few longitudinal US studies have

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evaluated the response to therapy of entheseal abnormalities in SA but none in PsA [14,15]. Some US scoring systems were used both for diagnostic and for assessing changes under treatment [16–18,21], nevertheless their performances varied according to the purpose.

Our study aimed to investigate the prevalence of enthesitis with Power Doppler Ultrasonography (PDUS) in psoriasis patients without articular symptoms (PsO) and in patients with PsA, and to assess their evolution under systemic treatment. In addition, as clinical and imaging observations suggest that there may be a link between systemic enthesopathy and psoriatic nail disease, we planned to investigate if nail disease in psoriasis is linked to a greater degree of enthesitis compared with psoriasis patients without nail disease.

2. Methods

2.1. Patients groups and clinical assessment

PsO patients requiring systemic treatment, and PsA were prospectively recruited in 2 French departments of Rheumatology and Dermatology (University hospital of Nice, France) from January 2011 to June 2012. Inclusion criteria were age over 18 years and a diagnosis of psoriasis without or with articular symptoms (PsA patients being defined by the CASPAR criteria) requiring systemic treatment. The patients were included before the introduction of the first systemic treatment (i.e. methotrexate, cyclosporine and acitretin) or biologic therapies (infliximab, adalimumab, etanercept and ustekinumab). Exclusion criteria were a history of inflammatory musculoskeletal disease except PsA, a chronic infectious disease or a cancer. Informed consent was obtained from all patients before study enrolment.

Patients underwent a clinical and laboratory evaluation at baseline, and after 3 and 6 months of treatment. PDUS evaluation was performed at baseline and after 6 months. Clinical and laboratory assessment were realized by a trained rheumatologist and dermatologist blinded to ultrasound data. The following data were recorded for each patient at the first visit: age, sex, osteoarticular and dermatological symptom duration, psoriatic nail involvement, disease modifying anti rheumatic drugs (DMARD), biologic therapy received for PsA or psoriasis; C-reactive protein (CRP) level (normal 0–5 mg/L), erythrocyte sedimentation rate (ESR) level (normal 5–15 mm/h), HLA B27 status and CCP antibodies. Therapeutic decision was taken independently of the PDUS findings by the dermatologist or the rheumatologist of the patient in real life conditions.

At each visit, psoriasis severity was scored using the psoriasis area and severity index (PASI) and the body surface area (BSA) measurement. The impact of the disease on quality of life was assessed by the Dermatology Life Quality Index (DLQI). Rheumatologic evaluation included: tender and swollen joint count, tenderness of 16 entheses (Spondyloarthritis Research Consortium of Canada, SPARCC), the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and the Functional Index (HAQ = Health Assessment Questionnaire). Data on serum markers of inflammation C-reactive protein (CRP) and ESR were recorded at each clinical visit.

2.2. Ultrasonography

US examinations were performed at the Rheumatology department of the University Hospital (Nice, France) by one rheumatologist experienced in this technique, using a MyLab 70 XVG Esaote (Saint-Germain-en-Laye, France) equipped with multifrequency linear array transducers (6 to 18 MHz).

The rheumatologist performing the US examination was unaware of the clinical and laboratory findings, and was not involved in the treatment decisions. US examination was performed in a darkened room. The patients were asked not to discuss their clinical symptoms to avoid the possibility of bias. In each patient, 5 entheses were scanned bilaterally with a systematic longitudinal and transverse PDUS examination: Achilles tendon, plantar fascia insertion, quadriceps insertion, patellar proximal and brachial triceps tendon insertion. Entheses with previous surgical procedures were not evaluated. Power Doppler (PD) assessment was performed at the bony margins and entheseal site with a Doppler frequency of 8.3 MHz. Pulse repetition frequency of 500 Hz was adjusted to the lowest permissible value to maximize sensitivity. A low-wall filter was used. Flow was additionally demonstrated in 2 planes and confirmed by pulse wave Doppler spectrum to exclude artefacts.

Patients were placed in a supine decubitus position to assess entheses of knee (quadriceps tendon insertion and patella ligament origin) flexed at 45° for gray scale (GS) and power doppler (PD); to assess the entheses of feet (Achilles tendon and plantar aponeurosis): prone decubitus with the feet hanging outside the examination table in slight at 90° dorsal of flexion for GS and in neutral position for PD; to assess brachial triceps enthese: sitting facing the examiner with armed flexed at 90° and palmar surfaces on a table. US enthesitis were identified according to the outcome measures in rheumatoid arthritis clinical trials (OMERACT) definition: abnormally hypoechogenicity (loss of normal fibrillar architecture) and/or thickened tendon or ligament at its bone attachment (may occasionally contain hyperechogenicity foci consistent with calcification), seen in two perpendicular planes, which may exhibit Doppler signal and/or bony changes, including enthesophytes, erosions or irregularity [12]. The following elementary lesions were assessed for each enthesis with a binary score (presence/absence): morphological (i.e. hypoechogenecity and/or thickening at the body of the tendon) and structural abnormalities (entheseal calcific deposits, bone erosion and/or enthesophytes) in GS and intra-enthesis PD signals at the cortical bone insertion. We took as reference value the tendinous thicknesses used in the MASEI score [22].

2.3. Statistical analysis

Categorical data are expressed as frequencies, and continuous variables are given as means (SD). The Wilcoxon signed-rank test was used to compare changes in clinical and functional scores, from baseline to the end of the study (M6). The rates of overall and individual lesions by ultrasound in PsO and PsA patients and in subgroups with or without nail disease were compared by using a χ^2 test. Changes in US morphological abnormalities between baseline and M6 were studied using the Mc Nemar's test for paired binary data. All tests were two sided and the significance level was set to 5%. We used SPSS software, version 11.0 (Chicago, IL, USA) for the statistical analyses.

3. Results

3.1. Patient's characteristics

PDUS were performed on 34 patients (Table 1) who were starting a first systemic therapy with methotrexate (MTX) ($n = 23$, 67.6%) or biologic therapy ($n = 11$, 32.4%), (etanercept, infliximab, ustekinumab, and adalimumab).

We included:

- 22 PsO patients: 19 starting conventional systemic treatment (MTX) and 5 biologics (infliximab $n = 1$, adalimumab $n = 1$, ustekinumab $n = 3$);