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Original Article

Prevalence and risk factors of subclinical enthesitis and synovitis in patients with psoriasis

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Abstract: This study is to investigate the prevalence of subclinical enthesitis and synovitis with PDUS in patients with psoriasis, and identify the risk factors. There were 30 patients with plaque psoriasis and 20 age-matched controls with other skin disease in this study. All patients without arthritis underwent dermatological assessment and PDUS examination. The frequency of US synovitis was higher in psoriasis compared to control (5/30 vs 0/20, P=0.149). But US enthesitis was not found in two groups. Among demographic and clinical data, predictors for US synovitis included first-degree family history of psoriasis [odds ratio (OR) 17.250; 95% CI 1.730, 172.015; P=0.015] and nail involvement (OR21; 95% CI 1.834, 240.508; P=0.014). The prevalence of subclinical synovitis and enthesitis in Chinese patients with psoriasis was low. First-degree family history of psoriasis, nail involvement may be the risk factors for subclinical synovitis and enthesitis.

Keywords: Psoriatic arthritis (PsA), rheumatoid factor (RF), power doppler (PD), ultrasonography (US), enthesitis, synovitis

Introduction

Psoriatic arthritis (PsA) is a chronic inflammatory arthritis associated with psoriasis, usually seronegative for rheumatoid factor (RF). PsA is characterized by intermittent flares and remissions. 70% of patients have progressive joint damage, therefore early diagnosis and management of patients with PsA may prevent joint deformity and associated morbidity [1].

The classification standard of CASPAR (classification criteria for Psoriatic Arthritis) has been commonly used for identifying PsA, but the prerequisite of CASPAR criteria is inflammatory arthritis [2]. So, early recognition of the joint inflammation becomes the key to early diagnosis PsA.

In recent years, magnetic resonance imaging (MRI) and ultrasound (US) have demonstrated to be more sensitive than clinical assessment in detecting early joint inflammation [3]. Furthermore, US is reproducible, rapid and inexpensive. It should be considered as the first choice for screening early PsA among psoriasis patients.

This study was to investigate the prevalence of subclinical enthesitis and synovitis by Power Doppler (PD) ultrasonography (US) in Chinese patients with psoriasis, and to identify the risk factors for subclinical enthesitis and synovitis.

Materials and methods

Patients

A total of 30 patients with psoriasis and 20 age-matched controls were recruited in the study from October 2015 to July 2009. Psoriatic patients and control were assessed by an experienced dermatologist. Inclusion criteria were as follows: age >18 years; vulgaris psoriasis (duration >1 year); other skin diseases without musculoskeletal disorders; no clinical symptoms and signs of joint involvement or enthesitis. Exclusion criteria was as follows: history of gout or arthritis, history of peripheral neuropathy of the lower limbs or trauma; any systemic

Table 1. Clinical and laboratory findings of psoriatic and control patients

	Psoriasis group (n=30)	Control group (n=20)	*P*-value
Age, mean (S.D.), yrs	36.7 (8.1)	36.2 (8.8)	0.826
Sex, n (%)			
Men	22 (73.3)	14 (70.0)	
Women	8 (26.7)	6 (30.0)	0.797
BMI, mean (S.D.)	23.7 (2.2)	23.7 (2.6)	0.952
Glucose, mean (S.D.), mmol/L	4.7 (0.4)	4.8 (0.5)	0.287
Cholesterol, mean (S.D.), mmol/L	4.5 (0.7)	4.0 (0.6)	0.012
Triglycerides, mean (S.D.), mmol/L	1.2 (1.0)	1.0 (0.3)	0.339
Uric acid, mean (S.D.), μmol/L	343.0 (79.4)	231.0 (50.8)	<0.0001
ESR, median (Interquartile range), mm/h	5.5 (2.0, 10.0)	5.0 (3.0, 12.0)	0.486
CRP, median (Interquartile range), mg/L	6.2 (3.6, 13.8)	3.8 (2.5, 4.5)	0.002
Positive RF, n (%)	2 (6.7)	0 (0)	0.510
Positive CCP, n (%)	0 (0)	0 (0)	NA
Positive HLA-B27, n (%)	0 (0)	0 (0)	NA

therapy (i.e. NSAIDs, corticosteroids, immunosuppressants, retinoids or biological agents) in 3 months; pregnant or breast-feeding.

The study was in accordance with the Declaration of Helsinki and was approved by the ethics committee of PLA 306 hospital. Written informed consent was obtained from all patients before study enrolment.

Dermatological assessment

The data were recorded for each psoriatic patients and control: age, sex, Body Mass Index (BMI). In psoriatic patients, age at psoriasis onset, duration, psoriasis area and severity index (PASI) and nail involvement were documented. For each patient, RF (normal 0-30 IU/ml), CCP antibodies (normal 0-20 U), HLA-B27 antigen, CRP (normal 0-6 mg/L) and ESR (normal: male 0-15 mm/h, female 0-20 mm/h), uric acid (150-440 μmol/L), cholesterol (2.8-5.17 mmol/L), triglycerides (0.56-1.7 mmol/L) and glucose (3.9-6.4 mmol/L) were obtained from laboratory tests at study entry.

PDUS assessment

A systematic longitudinal and transverse multidimensional US examination was performed by an experienced ultrasonographer. The ultrasonographer was blind for the clinical data and used a Sequoia512 (Siemens, Germany) machine and a multi-frequency linear transducer (5-15 MHz). Following bilateral joints were investigated for US synovitis: elbow and wrist joints, metacarpophalangeal (MCP) joints, proximal (PIP) and distal (DIP) interphalangeal joints, knee and ankle joins. Following bilateral enthesis were assessed for the presence of US enthesitis: quadriceps enthesis, proximal patellar tendon, distal patellar tendon, Achilles tendon, plantar fascia. Blood flow was examined by PD with a pulse repetition frequency of 750 Hz and a color-mode frequency 7.0 MHz. US synovitis and enthesitis were identified according to the Outcome Measures in Rheumatology Clinical Trials (OMERACT) pathology definitions and Glasgow Ultrasound Enthesitis Scoring System (GUESS) [4, 5].

Statistical analysis

Statistical analysis was performed using IBM SPSS version 20.0. Comparisons between numerical variables were analyzed using t-test or Kruskal-Wallis test. Categorical variables were evaluated by chi-squared test or Fisher's exact test. Logistic regression model was used to identify independent associations between different variables and PDUS abnormalities. Statistical significance was defined as $P<0.05$.

Results

The levels of cholesterol, uric acid, and CRP in the psoriasis group were significantly higher than that in the control. There were no significant differences between psoriatic and control patients in age, sex, mean BMI, glucose, triglycerides, and ESR, positive RF, CCP and HLA-B27 (**Table 1**).

Among 30 psoriatic patients, synovial thickening and abnormal PD signal were found in ankles of three patients (**Figure 1**) and elbows of two patients (**Figure 2**). None of 20 control patients showed PDUS abnormalities.

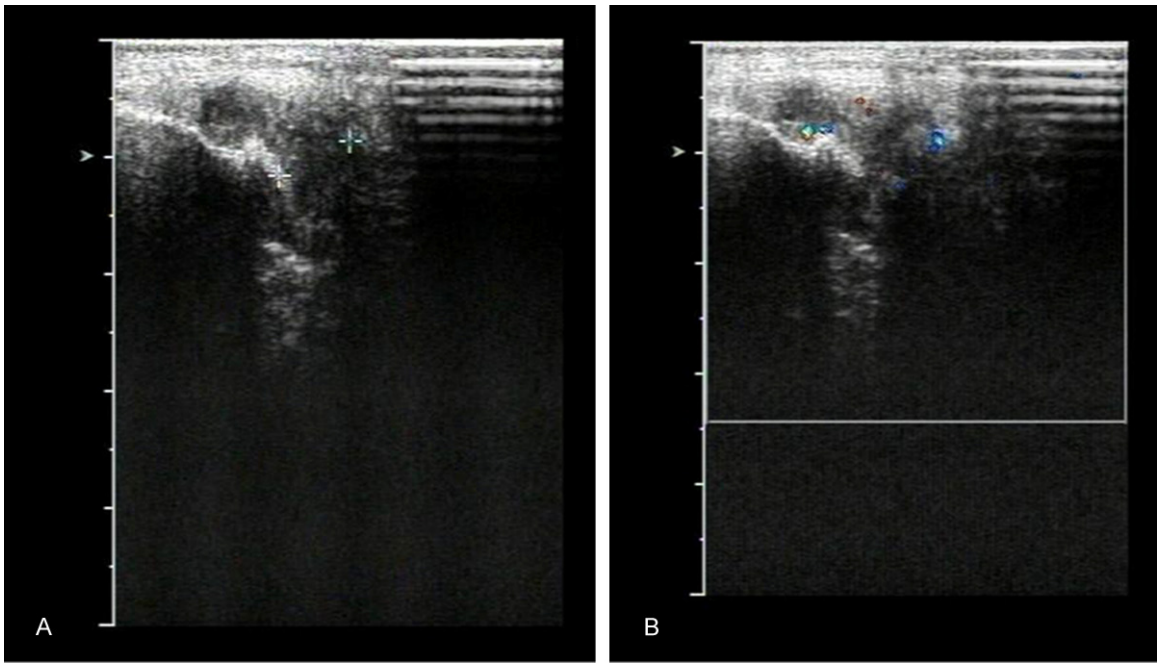

Figure 1. A: Synovial thickening in the ankle; B: Abnormal PD signal in the ankle.

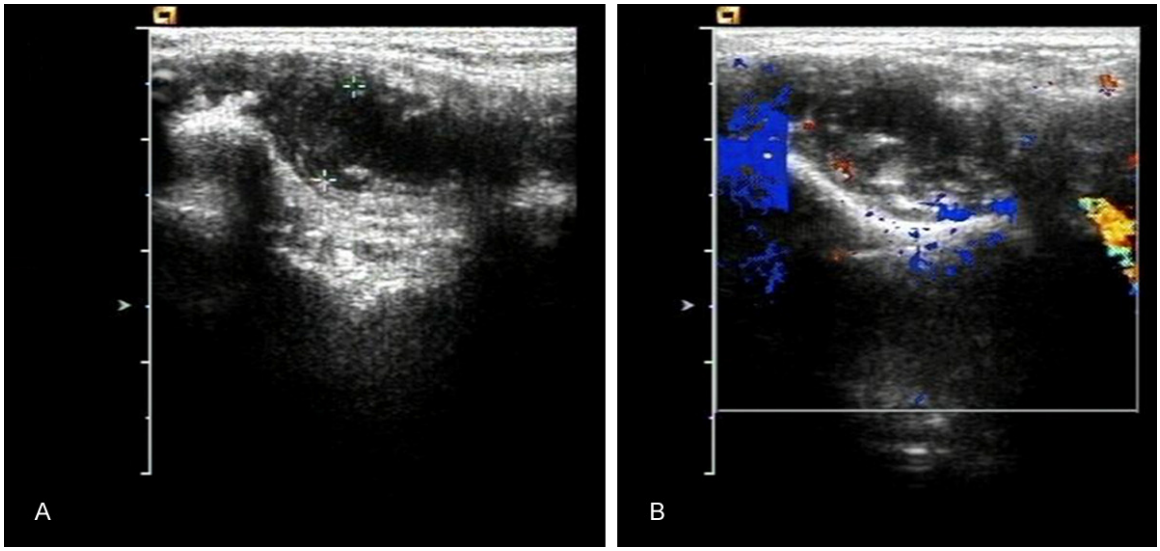

Figure 2. A: Synovial thickening in the elbow; B: Abnormal PD signal in the elbow.

We analyzed psoriatic patients with and without US synovitis (**Table 2**). There were significant differences in first-degree family history of psoriasis, PASI score, nail involvement ($P<0.05$).

To further identify the risk factors of US synovitis in patients with psoriasis, univariate analysis of logistic regression model was performed (**Table 3**). The predictors for US synovitis included first-degree family history of psoriasis (OR 17.250; 95% CI 1.730, 172.015; P=0.015), and nail involvement (OR 21; 95% CI 1.834, 240.508; P=0.014).

Discussion

Enthesitis and/or synovitis are considered as the major features of PsA. Conventional radiography can hardly recognize soft tissues, especially in the early PsA, whilst US has been shown

Table 2. Clinical and laboratory findings of psoriatic patients with and without US synovitis

	Psoriasis patients without US synovitis (n=25)	Psoriasis patients with US synovitis (n=5)	*P*-value
Age, mean (SD), yrs	36.9 (8.7)	35.8 (4.1)	0.783
Sex, n (%)			
Men	19 (76.0)	3 (60.0)	
Women	6 (24.0)	2 (40.0)	0.589
BMI, mean (SD)	23.8 (2.2)	23.6 (2.5)	0.856
Psoriasis duration, mean (SD), months	132.0 (98.5)	159.4 (92.4)	0.571
Age at psoriasis onset, mean (SD), yrs	25.8 (11.0)	22.4 (4.9)	0.508
Family history of psoriasis			
First-degree			
Yes	2 (8.0)	3 (60.0)	
No	23 (92.0)	2 (40.0)	0.022
Second-degree			
Yes	4 (16.0)	1 (20.0)	
No	21 (84.0)	4 (80.0)	1.000
PASI score median, (Interquartile range)	4.2 (2.8, 9.4)	10.4 (7.7, 36.8)	0.021
Nail involvement, n (%)	4 (16.0)	4 (80.0)	0.011
Glucose, mean (SD.), mmol/L	4.7 (0.4)	4.6 (0.4)	0.388
Cholesterol, mean (SD.), mmol/L	4.6 (0.7)	4.2 (0.7)	0.230
Triglycerides, mean (S.D.), mmol/L	1.2 (1.1)	1.2 (0.7)	0.957
Uric acid, mean (S.D.), μmol/L	338.8 (66.0)	364.4 (137.4)	0.702
ESR, median (Interquartile range), mm/h	5.0 (1.0, 9.0)	9.0 (6.0, 14.0)	0.197
CRP, median (Interquartile range), mg/L	5.7 (3.9, 14.6)	7.3 (2.7, 8.2)	0.420
Positive RF, n (%)	1 (4.0)	1 (20.0)	0.310
Positive CCP, n (%)	0 (0)	0 (0)	NA
Positive HLA-B27, n (%)	0 (0)	0 (0)	NA

Table 3. Logistic regression analyses comparing psoriatic patients with and without US synovitis

Covariates	OR (95% CI)	*P*-value
Age, yrs	0.982 (0.869, 1.110)	0.774
Male	0.474 (0.063, 3.538)	0.466
BMI	0.959 (0.621, 1.482)	0.850
Psoriasis duration, months	1.003 (0.993, 1.013)	0.559
Age at psoriasis onset, yrs	0.965 (0.870, 1.070)	0.494
Family history of psoriasis		
First-degree	17.250 (1.730, 172.015)	0.015
Second-degree	1.313 (0.115, 15.033)	0.827
PASI score	1.183 (0.983, 1.423)	0.075
Nail involvement	21.000 (1.834, 240.508)	0.014
Glucose, mmol/L	0.263 (0.013, 5.119)	0.378
Cholesterol, mmol/L	0.365 (0.070, 1.912)	0.233
Triglycerides, mmol/L	0.971 (0.358, 2.637)	0.955
Uric acid, μmol/L	1.004 (0.992, 1.017)	0.506
ESR, mm/h	1.073 (0.937, 1.229)	0.308
CRP, mg/L	0.934 (0.794, 1.099)	0.409
Positive RF	6.001 (0.309, 116.618)	0.237

to be of value in revealing enthesitis and synovitis. PD strongly improves US accuracy in the assessment of enthesitis and synovitis [6]. In the last few years, some studies have reported subclinical enthesitis and synovitis in US in patients with psoriasis.

Gutierrez examined the lower limb entheses of 45 psoriatic patients and 45 healthy controls by US [7]. Grayscale US and PD findings were more frequent in patients with psoriasis than in healthy controls. Moreover, the average GUESS score of patients with psoriasis was significantly higher (P<0.0001).

Naredo reported 162 patients with plaque psoriasis without musculoskeletal disease, and found that patients with psoriasis had a significant prevalence of US synovitis (50.7%) and en-

thesopathy (62.5%). And psoriasis was the only significant predictive factor of US synovitis (OR 2.1; P=0.007) and enthesopathy (OR 2.6; P=0.027) [8].

Tinazzi et al performed a longitudinal study in order to investigate the correlation between US enthesitis and PsA. After follow up of 3.5 years, 7 of 30 patients (23%) fulfilled the CASPAR criteria for the diagnosis of PsA [9]. This study indicated that US enthesitis may be used for identifying psoriatic patients at high risk of developing PsA.

Few studies about the prevalence of PsA in Chinese patients with psoriasis were reported. Yang investigated the prevalence and clinical features of PsA with CASPAR criteria among 1928 outpatients with psoriasis. There were 112 PsA patients (5.8%), 92% of which was newly diagnosed. Enthesitis patients accounted for 26.8%. The most common enthesitis was in the knees (46.67%) [10].

Our study showed that the prevalence of subclinical enthesitis and synovitis in patients with psoriasis was lower than in previous studies. This was probably due to racial/ethnic disparities. Several studies identified potential risk factors for PsA among patients with psoriasis, such as psoriasis severity, psoriasis involving the scalp and intergluteal and/or perianal region, earlier age at onset of psoriasis, psoriatic nail disease [11-13]. Opposite to previous studies, we found first-degree family history was a risk factor of subclinical synovitis. This may be helpful in selecting psoriatic patients at greater risk of subclinical synovitis and enthesitis.

The major limitations of our study were small sample size, multivariate logistic regression model without analyzing the risk factors. So, future large-scale longitudinal studies are needed to value these risk factors in the development of enthesitis and synovitis.

In conclusion, subclinical enthesitis and synovitis was not common in this study. First-degree family history and psoriatic nail involvement were suggested as the risk factors for subclinical synovitis. Careful screening and regular follow-up patients with these risk factors may facilitate early diagnosis of PsA.

Disclosure of conflict of interest

None.

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