Preliminary Evidence That Subclinical Enthesopathy May Predict Psoriatic Arthritis in Patients with Psoriasis

To the Editor:

The importance of enthesitis as the key pathological lesion underpinning the pathogenesis of psoriatic arthritis (PsA) has been increasingly recognized[1]. Studies for more than 3 decades have shown a high frequency of osseous and entheseal abnormalities in patients with psoriasis without clinical signs of arthritis[2,3]. From a clinical viewpoint, about 10% of patients with psoriasis develop PsA over a decade, so there is a need to better define predictive factors for the identification of future PsA in patients with psoriasis[4]. The ability to accurately predict development of PsA in subjects with psoriasis could have implications for prevention of the morbidity associated with PsA and also for studies aimed at elucidation of the early phases of disease.

We previously used ultrasound (US) to show a high frequency of subclinical entheseal involvement in patients presenting with psoriasis but without clinically evident arthritis[5]. We investigated whether subclinical enthesopathy in patients with psoriasis predicted the future development of PsA.

A longitudinal evaluation was performed in a cohort of 30 cases of psoriasis with a mean duration of 3.5 years using clinical and repeat ultrasound assessment of lower-limb tendons, using the Glasgow Ultrasound Enthesitis Scoring System (GUESS)[6]. Of the 30 patients originally evaluated[5], 28 returned for a re-evaluation. No patient received systemic treatment with a disease-modifying antirheumatic drug. The criteria of the ClASsification of Psoriatic ARthritis (CASPAR) study group were used to define the presence or absence of PsA[7]. Evidence for osteoarthritis (OA) was also sought, as this can affect the same joints involved in PsA, including distal interphalangeal (DIP) joints and spine. All patients had evaluation for Psoriasis Area and Severity Index (PASI) score and nail disease status according to standard procedures[8]. Patients had a repeat ultrasound scan using the Glasgow Ultrasound Enthesitis Scoring System (GUESS) score, by the same sonographer that carried out the original study. Once again the sonographer was blinded to the patient's clinical status or joint symptoms and was unaware of the original US scan findings. On followup imaging, ultrasonography was performed using a LOGIQ 5 instrument (GE Healthcare) with a 10–15 MHz probe, whereas an ALT HDI3000 machine with a 10–15 MHz linear probe was used in the baseline assessment[5]. On followup imaging, the power-Doppler settings were standardized, with a pulse repetition frequency of 750 Hz, a color-mode frequency of 9.1 MHz, and low-wall filters. The color gain was increased to the maximum level not generating power-Doppler signals under the bony cortex. All US assessments were performed using a multiplanar scanning technique. US assessment of structure, thickness, bony erosions, and bursitis of quadriceps, patella, and Achilles tendons, and plantar aponeurosis was scored using the GUESS as described[5,6]. US examination was performed in a darkened air-conditioned room. Unfortunately, we have not calculated the coefficients of variation for measurements using the 2 machines at the same timepoint because of the unavailability of the previous machine.

At clinical followup, 7 of 28 patients (23%) fulfilled the CASPAR criteria for the diagnosis of PsA, 5 having active disease at the time of assessment (Table 1). These patients (5 men, 2 women) had a median age of 54 years (range 51–60) and there was a median period of 13 months (range 3–24) between baseline GUESS evaluation and development of PsA. The pattern of joint involvement was polyarticular in 2 patients and oligoarticular in 5, with 3 cases reporting plantar fasciitis and 2 Achilles tendonitis. Skin psoriasis was present in all these patients at baseline (mean PASI 5.5) and in 6 patients it was still present after 3.5 years (mean PASI 2.6); nail disease was present in 4 patients (57%) both at baseline and after 3.5 years, in patients developing PsA. Four patients were also diagnosed as having hand OA based on the development of Heberden's and Bouchard's nodes, with 2 of these being asymptomatic at the time of evaluation. At baseline these patients did not complain of hand joint symptoms or DIP swelling.

The GUESS scores remained remarkably stable over the followup period, with persistent thickening of insertions being noted: the difference of baseline GUESS variance (4.9) and third-year GUESS (2.66) were +2.23 (r = 0.937; p = 0.918). Baseline GUESS scores of patients with psoriasis who developed PsA or OA were significantly higher compared to those who remained asymptomatic after followup of 3.5 years (mean 9.54 ± 2.02 vs 6.61 ± 3.60, respectively; p = 0.0127), whereas after the same followup period, GUESS scores of patients with psoriasis who developed PsA compared to those who did not develop PsA did not reach statistical significance (mean 9.14 ± 2.03 vs 7.72 ± 3.94; p = 0.4115).

Table 1. Characteristics of the study populations.

Characteristic	Psoriasis	Psoriasis and PsA
No. cases	21	7
Male:female	12:9	5:2
Age, mean (SD), yrs	55.7 ± 13.5	54.7 ± 3.6
Body mass index, mean (SD)	28.5 ± 4.2	29.8 ± 3.2
PASI, mean (SD)	8.3 ± 7.7	5.5 ± 6.2
Nail disease, n (%)	11 (52.4)	4 (57.1)
Years from onset of psoriasis, mean (SD)	16 ± 12.5	11.1 ± 8.2
Baseline GUESS, mean (SD)	8 ± 3.8	9.2 ± 2
GUESS at 3rd year followup, mean (SD)	8.6 ± 2.8	9.7 ± 1.6

PsA: psoriatic arthritis; PASI: Psoriasis Area and Severity Index; GUESS: Glasgow Ultrasound Enthesitis Scoring System.

In the logistic regression analysis, baseline thickness of the quadriceps tendon was found to be an independent predictor of the development of PsA (p = 0.029; Table 2). In contrast, baseline thickness of Achilles and patellar tendon was not significantly associated with the development of PsA (there was a trend toward significance). At clinical followup, 2 patients presented a positive power-Doppler US signal at their Achilles tendon insertions, which were also painful.

These preliminary findings in a small group of patients with psoriasis indicate that tendon thicknesses and entheseal abnormalities may be useful in identifying patients with psoriasis who are more likely to develop PsA. It must be noted that the rate of progression of clinical disease in our cohort appeared to be much greater than that evident from epidemiological studies[4]. However, when the frequency of PsA is investigated more deeply, with sophisticated techniques, it is as high as 40%[9]. Although 7 out of 30 patients with psoriasis developed frank PsA, the total GUESS score remained remarkably stable over a 3-year period, which may indicate stable thickening of insertions rather than a continuous active inflammatory reaction. Whether this represents subclinical inflammation or "noninflammatory" thickening of insertions awaits further study, but it is likely to be of importance for detecting the early phases of PsA. In this and in our previous study we decided to use the GUESS score because it is a validated method to assess entheses[5]. Among the lower-limb tendons analyzed by US we found that baseline thickness of the quadriceps appeared to be the

Table 2. Independent predictors of the development of PsA in the study population (n = 28).

Development of PsA, Independent Variables	Standardized ß Coefficient	p
Age, years	–0.001	0.97
Male vs female	–0.04	0.96
Body mass index	0.2	0.12
Psoriasis Area and Severity Index	0.09	0.2
Thickness of quadriceps tendon	1.4	0.02

PsA: psoriatic arthritis.

best predictor of the development of PsA. An important expansion of this study will be identification of a cutoff value of the GUESS and a power-Doppler GUESS in a larger cohort of psoriasis and PsA patients. We will attempt to replicate these findings and to ascertain whether the inclusion of power-Doppler is diagnostically useful to detect active PsA in contrast to patients with OA and psoriasis. The group of patients who developed hand OA also had a higher GUESS score. This is noteworthy because degenerative arthritis of the DIP joint and spine as determined by magnetic resonance imaging (MRI) is associated with entheseal abnormalities[10,11]; indeed there is good evidence that OA of small joints of the hand has a ligament-related microanatomical basis similar to entheseal PsA[12]. Moreover, it may be difficult to distinguish between OA and PsA, as both may affect the DIP joint and the axial skeleton and may show similar entheseal changes on MRI[10]. We therefore combined the PsA and OA groups and examined a link to GUESS scores. The association between baseline GUESS score and development of combined OA and PsA was stronger. The role of psoriasis as a modifier in the expression of hand OA warrants further evaluation in larger studies.

Our study has several strengths, including the complete characteristic of the dataset, the ability to adjust for multiple confounders, and the prospective observation of the patients with psoriasis, which had not to our knowledge been done previously. However, the study has the limitation that the limited number of patients could have attenuated the power of the association between enthesopathy and development of PsA.

We suggest that subclinical enthesopathy deserves further investigation as a predictor for the development of PsA in patients with chronic plaque psoriasis.

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