Nail Psoriasis in Individuals With Psoriasis Vulgaris: A Study of 661 Patients

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Abstract

Background and objectives: The nails are affected in a substantial number of patients with psoriasis. Nevertheless, few epidemiological studies have reported the characteristics of patients with nail psoriasis. Here we describe the epidemiology of nail psoriasis and the main characteristics of affected patients.

Patients and methods: We undertook a prospective case-control study at Hospital Universitario Marqués de Valdecilla and Hospital Universitario Central de Asturias in Spain between January 2007 and December 2009.

Results: Of a total of 661 patients included, 47.4% were diagnosed with nail psoriasis, which was 13.5% more prevalent in men. The group of patients with nail disease had more severe psoriasis (12.82 vs 8.22 points on the psoriasis area and severity index) and a longer disease duration (20.30 vs 13.94 years), and included a larger percentage of patients with psoriatic arthritis (29.7% vs 11.5%), a positive family history of the disease (53.7% vs 42.8%), and a body mass index greater than 30 (31.6% vs 23.9%). A larger percentage of the patients with nail disease had early-onset psoriasis (74.1% vs 65.5%) and fewer were carriers of the human lymphocyte antigen Cw*0602 allele (33% vs 50.3%).

Conclusions: Nail disease is frequent in psoriasis and is associated with greater severity of psoriasis and a larger number of comorbidities.

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Psoriasis ungueal: estudio en 661 pacientes con psoriasis vulgar

Resumen

Introducción y objetivos: La psoriasis ungueal afecta a un número importante de pacientes con psoriasis. No obstante, son raros los estudios epidemiológicos que recojan las características de estos individuos. Describimos la epidemiología y principales características de los pacientes con psoriasis ungueal.

Material y método: Se trata de un estudio prospectivo de casos y controles realizado en el Hospital Universitario Marqués de Valdecilla y Hospital Universitario Central de Asturias entre enero de 2007 y diciembre de 2009.

Resultados: De un total de 661 pacientes la psoriasis ungueal fue diagnosticada en el 47,4% de los pacientes. La prevalencia fue 13,5 puntos mayor en hombres que en mujeres. Los pacientes con afectación ungueal presentan mayor severidad de la enfermedad (PASI 12,82 vs 8,22), mayor duración de la misma (20,30 vs 13,94 años), incidencia superior de artritis psoriásica (29,7% vs 11,5%), mayor frecuencia de antecedentes familiares positivos (53,7% vs 42,8%) y mayor proporción de obesidad IMC > 30 (31,6% vs 23,9%). La psoriasis en el grupo con afectación ungueal se inicia de forma precoz (74,1% vs 65,5%) y se asocia con menor frecuencia a HLA*0602 (33% vs 50,3%).

Conclusiones: La afectación ungueal es una manifestación frecuente en los pacientes con psoriasis y se asocia a mayor gravedad de la enfermedad y mayor número de comorbilidades.

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Introduction

The umbrella term psoriasis embraces several clinical forms that differ according to lesion site, clinical features (size, thickness, shape, erythema, scaling), association or otherwise with psoriatic arthritis, presence or absence of nail disease, time since onset, family history (and the genetic factors implicated), and disease course in relation to these characteristics.

Nail psoriasis, which can present alone or as part of more extensive psoriasis, is a very important disease but one that is often overlooked. First, patients with disease of the nails and periungual tissue, often with painful consequences, have difficulty performing fine manual tasks; 58.9% of patients, for example, are restricted in simple everyday activities such as dressing and 49% experience reduced professional capacity. Second, given the highly visual nature of the disease, 90% of affected individuals have a distorted perception of their physical appearance that considerably impairs their quality of life. Moreover, nail psoriasis is a chronic disease that is refractory to conventional treatment, explaining why its importance tends to be overlooked in medical settings. Another important point is its high incidence. Nail involvement in the course of psoriasis is very common, with a prevalence of between 15% and 53% depending on the series, and even higher figures have been reported for hospitalized patients (78%) and for lifetime prevalence (90%). Only 1% to 5% of patients have exclusive nail disease.

The aim of this study was to determine the prevalence of nail disease in patients with psoriasis in our setting and to explore the corresponding clinical implications.

Patients and Methods

Recruitment and Clinical Evaluation of Patients and Controls

We performed a cross-sectional hospital-based study in which we compared 661 patients with psoriasis divided into 2 groups according to whether or not they had nail disease. All of the patients were evaluated consecutively at the outpatient clinics of Hospital Universitario Central de Asturias and Hospital Universitario Marqués de Valdecilla, both in the north of Spain, between January 2007 and December 2009. The inclusion criteria were an age of over 18 years and a clinical diagnosis of chronic plaque psoriasis. The diagnosis was confirmed in all cases by at least 2 dermatologists based on established clinical criteria. Special attention was paid to the recording of data such as the date of onset of psoriasis and a family history of psoriasis, defined by the presence of this disease in at least 1 first-degree relative. We also recorded patients’ age and sex and whether or not they had nail or joint disease. All patients with joint symptoms were examined and diagnosed by a rheumatologist. Patients receiving systemic therapy at the time of inclusion or who had received systemic medications in the month leading up to this time were excluded. The study was approved by the Institutional Review Board of Hospital Universitario Central de Asturias and performed in accordance with the principles established in the Declaration of Helsinki.

Anthropometric Assessments

All of the patients underwent physical examination, which included weight and height measurements. Height
was expressed as centimeters and weight as kilograms, with rounding off to the nearest 0.1 kg. Body mass index (BMI) was calculated as weight in kilograms divided by the square of the height in meters. Patients were then classified into 3 groups (normal weight [BMI, <25 kg/m²], overweight [BMI, 25-29.9 kg/m²], and obese [BMI, ≥30 kg/m²]) according to the cutoffs determined by the World Health Organization.¹⁰ Waist circumference was measured in centimeters.

Skin Evaluation

Psoriasis severity was evaluated using the Psoriasis Area and Severity Index (PASI) according to the method originally described by Fredriksson and Pettersson.¹¹ Inter-rater agreement, which was analyzed by comparing the scores given by different dermatologists at the time of the first visit, was acceptable. Patients were divided into 2 groups according to whether they had a PASI score of over 10 (moderate to severe psoriasis) or of 10 or less (mild psoriasis).

Nail Examination

The presence of nail disease was evaluated on the finger nails only using the method described by Mallbris et al.,⁹ with evaluation of nail pitting, onycholysis, subungual hyperkeratosis, and dystrophy. Toe nails were not evaluated.¹² Samples were not systematically taken for potassium hydroxide staining, direct visualization, or fungal culture.

Laboratory Tests

Blood samples were routinely drawn after 12 hours’ fasting and analyzed by the biochemistry departments of the participating hospitals for serum levels of aspartate aminotransferase, alanine aminotransferase, γ-glutamyl transpeptidase, total cholesterol and triglycerides, and low-density lipoprotein (LDL) cholesterol and high-density lipoprotein (HDL) cholesterol. Testing for the Cw*0602 allele of the human lymphocyte antigen (HLA)-C locus was performed by the immunology department at Hospital Universitario Central de Asturias.

Definition of Metabolic Syndrome

Patients were considered to have metabolic syndrome (according to the Adult Treatment Panel III criteria) if they had 3 or more of the following risk factors:

1. A waist circumference of >102 cm for men and >88 cm for women
2. A serum triglyceride level of ≥150 mg/dL (≥1.7 mmol/L)
3. Blood pressure of ≥130/85 mm Hg
4. A HDL-cholesterol level of <40 mg/dL (<1.0 mmol/L) for men and <50 mg/dL (<1.3 mmol/L) for women.
5. A fasting glucose level of 110 to 126 mg/dL (6.1-7.0 mmol/L)

<table>
<thead>
<tr>
<th>Table 1 Characteristics of Patients With Psoriasis (n=661)*</th>
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<tbody>
<tr>
<td><strong>Psoriasis (n=661)</strong></td>
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<tr>
<td><strong>Men</strong></td>
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<tr>
<td>Mean (SD) age (range), y</td>
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<tr>
<td>Early-onset psoriasis</td>
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<tr>
<td>Severe psoriasis (PASI &gt;10)</td>
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<tr>
<td>Family history</td>
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<tr>
<td>Nail disease</td>
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<tr>
<td>Psoriatic arthritis</td>
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<tr>
<td>HLA-Cw*0602 positivity</td>
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<tr>
<td>BMI &gt;30</td>
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<tr>
<td>High blood pressure</td>
</tr>
<tr>
<td>Elevated triglycerides</td>
</tr>
<tr>
<td>Type 2 diabetes mellitus</td>
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<tr>
<td>Waist circumference</td>
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<tr>
<td>Metabolic syndrome (ATP III)</td>
</tr>
<tr>
<td>HDL cholesterol</td>
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</tbody>
</table>

Abbreviations: ATP III, Adult Treatment Panel III guidelines; BMI, body mass index (kg/m²); HDL, high-density lipoprotein; LDL, low-density lipoprotein; PASI, psoriasis area and severity index.

*Data shown as number (%) of patients unless otherwise indicated.

Logically, factors 2 to 5 were considered to be risk factors in patients who had normal values but who were receiving treatment for the corresponding conditions.

Statistical Analysis

Statistical analysis was performed using R 2.10 software (www.r-project.org). Comparisons between patients and controls were performed using the t test, the Pearson χ² test, and analysis of odds ratios. The Fischer exact test was used to compare dichotomous variables between groups and the t test was used to compare continuous variables. All the tests were 2-tailed. The cutoff for statistical significance was set at P = 0.05.

Results

In total, 661 patients with plaque psoriasis were included in the study. Their characteristics are summarized in Table 1.

Nail involvement was diagnosed in 313 (47.4%) of these patients. The corresponding 95% confidence interval (CI) was 43.47% to 51.23% indicating that the true prevalence would be within this range. On comparing sexes, it was seen that 188 men (53.7%) and 125 women (40.2%) had nail psoriasis. The proportion of men with and without nail involvement was 60.1% (n=188) and 46.6% (n=160), respectively (OR, 1.73; 95% CI, 1.27-2.35; P=0.001). The mean (SD) age of patients with nail disease was 47.47 (15.71) to 51.23 years, indicating that the true prevalence was 27.03 (16.23) years compared to 33.31 (19.06) years in patients without nail disease (47.39 (16.99) years; range, 18-90 years). The Mann-Whitney U test was used to compare continuous variables between groups and the t test was used to compare continuous variables. All the tests were 2-tailed. The cutoff for statistical significance was set at P=.05.
Factors Associated With Nail Disease

Patients with nail disease had a significantly higher mean PASI score than those without (12.82 [12.86] vs 8.22 [8.23], \( P < .001 \)). On analyzing PASI scores by sex, both men and women in the nail-disease group had significantly higher PASI scores than their counterparts in the control group (12.71 [14.14] vs 8.15 [8.58] for men and 12.89 [11.97] vs 8.30 [7.85] for women; \( P < .001 \) in both cases). Figure 1 shows these results, alongside results for a similar series of German patients. In our series, the proportion of patients with severe psoriasis (PASI >10) was over 20% higher in the nail-disease group than in the control group.

Table 2 shows the different study parameters analyzed in both groups.

Of the 313 patients with nail psoriasis, 93 (29.7%) had associated psoriatic arthritis; this was over twice the proportion of patients with this condition in the control group (11.5% [40 of 348 patients], OR, 3.25; 95% CI, 2.16-4.90; \( P < .001 \)).

The proportion of patients with a family history of psoriasis was 10.9 percentage points higher in the nail group than in the control group (Figure 2); the proportions were also higher for early onset of psoriasis (almost 9% higher) and a BMI of over 30 (almost 8% higher); there was also a difference for the proportions of patients carrying the HLA-DRw0602 allele (almost 20% lower in the nail-disease group). The results for elevated triglyceride levels, type 2 diabetes mellitus, and HDL-cholesterol were similar for both groups. While no statistically significant differences were found between the 2 groups for waist circumference according to the ATP III criteria (\( P = .054 \)), a significant difference was detected on comparing waist circumference measurements (Table 3).

Table 3 shows the mean values for biochemistry profile, waist circumference, and time since onset of psoriasis; no statistically significant differences were detected between

Discussion

Few studies of the epidemiology, clinical features, and probable systemic repercussions of nail psoriasis have been published to date. The aim of the present study was to determine the prevalence of nail disease in a group of patients with psoriasis referred to 2 dermatology departments in the north of Spain and to characterize the differences in disease patterns between patients with and without nail involvement. To strengthen the validity of the study, all the data related to nail involvement were collected by at least 2 trained dermatologists in each case.

Our findings show that 47.7% of patients with psoriasis had nail involvement. This proportion is somewhat higher than that reported by Augustin et al\textsuperscript{14} in Germany (40.9%), lower than that reported by Taieb et al\textsuperscript{15} in France (61%),\textsuperscript{15} and almost identical to that reported by Baran\textsuperscript{16} (50%). Of the patients in the nail-psoriasis group in our study, 53.7% were men and 40.2% were women. This difference in prevalence between men and women (over 10%) has also been reported by Reich\textsuperscript{2} and Augustin et al\textsuperscript{14}. Reich, in addition, found a correlation between greater body weight and a higher prevalence of nail psoriasis in men. The percentage of patients with psoriasis treated in primary care in Spain once diagnosed varies greatly, although it can probably be assumed that most cases are treated by dermatology specialists. As has been reported previously,\textsuperscript{14} we cannot rule out the possibility that nail psoriasis might
It is known that nail psoriasis has a genetic component, which has been linked on occasions to HLA-B27, HLA-Aw19, and HLA-Bw3 and even to polymorphisms in the coding regions for the interleukin (IL) 23 and IL-12 receptor; nail psoriasis has also been shown not to be associated with HLA-Cw*0602. Our study confirms this lack of association, as this allele was only found in 33% of patients with nail psoriasis compared to 50.3% of those without this condition (OR, 2.05; 95% CI, 1.36-3.09). Nonetheless, we did find a relatively weak association between psoriasis and HLA-Cw*0602 in our patients, supporting previous findings by our group. Patients with this genetic component would develop autoinflammatory disorders involving innate immunity and probably linked to mechanical stress at the enthesis (microtrauma).

The pathogenic mechanism described in the above paragraph highlights the importance of identifying nail involvement in patients with psoriasis as it might be a marker.
of psoriatic arthritis.\textsuperscript{21} Indeed, extensive involvement might be associated not only with more severe forms of psoriasis and longer disease duration,\textsuperscript{4} but also with enthesis, polyarticular involvement, and progressive arthritis.\textsuperscript{22} Indeed, histology studies, high-resolution ultrasound, and nuclear magnetic resonance have all shown that the nail is part of the musculoskeletal system, and is connected, both anatomically and functionally, to the distal interphalangeal joint.\textsuperscript{23-25} Furthermore, several authors consider the enthesis to be the centerpoint of the inflammatory process, which leads to effects in cartilage and bone as well as in the nail matrix and the nail bed (via extensor tendon fibers attached to the matrix and lateral ligaments that connect the tendon, the nail bed, and the periosteum).\textsuperscript{17,25} This subclinical enthesis would also explain why patients with psoriasis but not psoriatic arthritis develop nail pain, and it might also explain why nail involvement is associated with a greater risk of psoriatic arthritis, as has been suggested by previous studies.\textsuperscript{26-28} Nevertheless, not all authors have found a correlation between the presence of nail psoriasis and the severity of psoriatic arthritis.\textsuperscript{29-31} Others, such as Williamson et al\textsuperscript{32} have identified a link between the severity of nail dystrophy and that of joint disease. It has indeed been postulated that nail involvement in psoriasis could serve as a marker for increased immunoreactivity, which would lead to onset of psoriatic arthritis in certain patients.

In a recent study, Scarpa et al\textsuperscript{33} suggested that almost all patients with psoriatic arthritis have nail involvement, even though it is not always clinically evident. The results of that study again suggested that nail involvement might be a marker of disease in the distal interphalangeal joint.

In our group of patients, psoriatic arthritis was present in 29.7% of patients with nail disease and 11.5% of those without. Also, of the patients with psoriatic arthritis (133), 69.9% had nail disease. Augustin et al\textsuperscript{14} reported similar results (26% and 12% for those with and without nail involvement, respectively). Nonetheless, the percentage

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Biochemical Profile, Waist Circumference, and Time Since Onset of Psoriasis in Patients With and Without Nail Psoriasis</th>
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</thead>
<tbody>
<tr>
<td>No Nail Psoriasis (348 Patients)</td>
<td>Nail Psoriasis (313 Patients)</td>
</tr>
<tr>
<td>Total AST</td>
<td>24.28 (12.82)</td>
</tr>
<tr>
<td>Men</td>
<td>22.03 (12.46)</td>
</tr>
<tr>
<td>Women</td>
<td>26.94 (12.75)</td>
</tr>
<tr>
<td>ALT</td>
<td>27.17 (15.82)</td>
</tr>
<tr>
<td>Men</td>
<td>22.71 (13.38)</td>
</tr>
<tr>
<td>Women</td>
<td>32.42 (16.88)</td>
</tr>
<tr>
<td>GGT</td>
<td>32.32 (47.48)</td>
</tr>
<tr>
<td>Men</td>
<td>26.11 (43.61)</td>
</tr>
<tr>
<td>Women</td>
<td>39.62 (50.83)</td>
</tr>
<tr>
<td>LDH</td>
<td>291.51 (92.78)</td>
</tr>
<tr>
<td>Men</td>
<td>294.90 (91.42)</td>
</tr>
<tr>
<td>Women</td>
<td>287.51 (94.48)</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>203.44 (42.74)</td>
</tr>
<tr>
<td>Men</td>
<td>198.40 (41.16)</td>
</tr>
<tr>
<td>Women</td>
<td>209.38 (43.93)</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>55.23 (15.66)</td>
</tr>
<tr>
<td>Men</td>
<td>58.23 (14.52)</td>
</tr>
<tr>
<td>Women</td>
<td>51.71 (16.26)</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>126.58 (33.85)</td>
</tr>
<tr>
<td>Men</td>
<td>122.41 (32.78)</td>
</tr>
<tr>
<td>Women</td>
<td>121.48 (34.54)</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>120.73 (87.42)</td>
</tr>
<tr>
<td>Men</td>
<td>108.50 (80.81)</td>
</tr>
<tr>
<td>Women</td>
<td>143.12 (85.75)</td>
</tr>
<tr>
<td>Waist circumference, cm</td>
<td>93.97 (13.12)</td>
</tr>
<tr>
<td>Men</td>
<td>90.88 (14.49)</td>
</tr>
<tr>
<td>Women</td>
<td>97.52 (10.31)</td>
</tr>
<tr>
<td>Time since onset, y</td>
<td>13.94 (14.90)</td>
</tr>
<tr>
<td>Men</td>
<td>12.83 (14.31)</td>
</tr>
<tr>
<td>Women</td>
<td>14.91 (15.36)</td>
</tr>
</tbody>
</table>

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; CI, confidence interval; GGT, γ-glutamyl transferase; HDL, high-density lipoprotein; LDH, lactate dehydrogenase; LDL, low-density lipoprotein.

\textsuperscript{a}Values expressed as mean (SD).
of nail dystrophy in patients with psoriatic arthritis in our
group was slightly lower than that reported elsewhere. Of
Contrasting with most reports in the literature, we
found a high percentage of family history of psoriasis in our
patients (53.7% and 42.8% in those with and without nail
involvement, respectively). Our data, thus, are similar to
those reported by Augustin et al14 (Figure 2).

Furthermore, 231 (74%) of the patients with nail
involvement in our study had early-onset psoriasis
(<40 years), compared to 227 (65.4%) of those without nail
involvement (OR, 1.51; 95% CI, 1.08-2.11; P=0.018). These
data are also similar to those reported by Augustin et al,14
indicating a longer duration of disease in patients with nail
psoriasis.

The presence of nail disease in our patients was
associated with more severe clinical manifestations, with
161 patients in the nail-psoriasis group (51.4%) scoring over
10 on the PASI compared to just 107 patients (30.7%) in
the control group (OR, 2.39; 95% CI, 1.74-3.28; P<0.001). According
to our data, thus, nail psoriasis appears to be a
risk factor for the development of more severe forms of
psoriasis (Figure 1). This observation, however, is not
supported by findings of a study of Chinese patients.18

We also found a link between nail psoriasis and body
weight. Specifically, 31.6% of patients with nail involvement
and just 23.9% of those without had a BMI of over 30 (OR,
1.47; 95% CI, 1.05-2.08). In our review of the literature,
we found just 1 study that has analyzed the relationship
between BMI and nail psoriasis.35 The study, performed in
Han Chinese patients, did not find a statistically significant
association between the 2 variables. Nonetheless, the
findings of that study and ours are probably not comparable
as the prevalence of nail involvement in Asian patients
with psoriasis is surprisingly low (<2%).36 It is also of note
that waist circumference was larger in patients with nail
psoriasis than in those without. This was the case when
the groups were compared according to the ATP III component
measure for diagnosing metabolic syndrome and according
to mean circumference measurements. On comparing mean
waist circumference by sex, we saw that the differences
were due to the subgroup of women.

Finally, although 25.2% of patients with nail psoriasis
and 22.4% of those without had metabolic syndrome, the
difference was not significant.

We found no differences between patients with and
without nail psoriasis for hypertension, type 2 diabetes
mellitus, cardiovascular events, dyslipidemia, smoking, or
alcohol consumption (data not shown).

The main limitation of our study is that we did not
collect data to distinguish between nail matrix and nail bed
involvement in patients with nail disease. Love et al36 found
that of all the clinical forms of nail psoriasis they analyzed,
only onycholysis was associated with joint involvement;
the main limitation of that study, however, was the small
sample size. Gudjonsson et al,1 in contrast, found that all
4 parameters analyzed (onycholysis, nail pitting, subungual
hyperkeratosis, and nail dystrophy) were associated with
psoriatic arthritis. Another limitation is the fact that we
conducted a prevalence study. Accordingly, the association
detected between nail psoriasis and other parameters
might be due to an increased incidence of nail disease or
indeed to the fact that this disease had been present for
longer (chronic nail psoriasis), either because of the natural
history of the disease or because the patients had received
no treatment or had received less efficient treatment. Our
results are also limited by the fact that we did not analyze
toe-nail involvement. Similarly to other studies,1 we chose
to analyze toe nails due to the high prevalence of
onychomycosis in patients with nail psoriasis37 as the
clinical features of both conditions are similar.

Based on the data from the present study, a typical
patient with nail psoriasis would be a man (60.1%), have
an age of onset of psoriasis of before 40 years (74%), as well
as a history of psoriasis among first-degree relatives (54%),
psoriatic arthritis (29.7%), moderate to severe disease
(51.4%), and a BMI of over 30 (31.6%).

Until further studies are conducted on the value of
nail psoriasis as a marker of the severity of skin disease,
probable clinical and subclinical enthesitis, and possible
cardiovascular risk (BMI >30), the importance of this
clinical form of psoriasis, which has been mentioned as
the most common comorbidity in psoriasis,38 should not be
underestimated.

Conflict of Interest

The authors declare that they have no conflict of interest.

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