Distal extremity swelling with pitting edema in psoriatic arthritis: A case-control study

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Abstract

Objective
To evaluate the frequency and the clinical characteristics of distal extremity swelling with pitting edema in patients with psoriatic arthritis (PsA).

Methods
This was a case-control study of consecutive outpatients with PsA (old and new diagnosis) observed over a 3-month period in three secondary referral centers in Italy. As controls we used the two consecutive rheumatic outpatients, excluding those with spondylarthropathies, observed after a PsA patient. The demographic and clinical features were assessed by clinical examination and review of the medical records.

Results
A total of 183 patients with PsA and 366 controls were evaluated. Distal extremity swelling with pitting edema was recorded in 39/183 (21%) PsA patients and in 18/366 (4.9%) controls (p < 0.0001). In 8/39 (20%) patients this feature presented as a first, isolated manifestation of PsA, and in 8 others it was associated with other features of PsA at diagnosis. The upper and lower extremities were affected, predominantly asymmetrically, in 40% and 60% of the cases respectively. In patients with pitting edema compared to those without this feature, the frequency of Achilles enthesitis and plantar fasciitis, calculated together, was higher (p < 0.05) and the duration of arthritis was significantly lower (p = 0.02). In 7 patients the clinical evidence of a predominant involvement of tenosynovial structures was confirmed by MRI.

Conclusion
Upper or lower distal extremity swelling with pitting edema due to tenosynovitis, usually unilateral, is a common feature in PsA patients and may represent the first, isolated manifestation of the disease.

Key words
Psoriatic arthritis, distal swelling with pitting edema, tenosynovitis.
Distal pitting edema in PsA / F. Cantini et al.

Introduction

Remitting distal extremities swelling with pitting edema is a clinical manifestation that has been described in different rheumatic conditions such as remitting seronegative symmetrical synovitis with pitting edema (RS3PE syndrome) (1), polymyalgia rheumatica (2, 3), late onset undifferentiated spondyloarthropathies (4), ankylosing spondylitis (5), rheumatoid arthritis (6) and acute sarcoidosis (7). Furthermore, clinical findings of distal swelling with pitting edema may represent in some cases a para-neoplastic condition (8-11). The edema is characterised by an acute onset and by a rapid response with complete remission after short-term, low dose corticosteroid therapy. MRI studies have confirmed the marked tenosynovitis of the extensor and flexor tendons, associated with less marked joint synovitis, seen on clinical examination in these patients (12).

A clinical picture of distal extremity swelling with pitting edema can also be observed in psoriatic arthritis (PsA) and may be due to two different pathological processes. In some PsA patients the edema may be attributed to an altered lymphatic drainage (13-16). This type of edema is usually not responsive to therapy. Moreover, we have described patients with PsA with distal swelling and pitting edema showing a predominant involvement of the tenosynovial structures and a rapid response to corticosteroid therapy (17). In order to evaluate the frequency and clinical characteristics of this type of distal extremity swelling with pitting edema in patients with PsA we carried out this a case-control study. Magnetic resonance imaging (MRI) was used to investigate the anatomical structures involved in patients presenting this feature.

Patients and methods

A review of the clinical charts and physical findings for all the consecutive outpatients with PsA (old and new diagnosis) observed over a 3-month period in 3 Italian hospitals (Reggio Emilia, Prato, Bologna) was performed. Our clinics are secondary referral centers and over the considered period we observed a total of 2,580 outpatients.

The clinical evaluation was made by 4 rheumatologists (FC, CS, IO, LM) with an interest in PsA, and the diagnosis of psoriasis was made by a dermatologist in all cases. The diagnosis of PsA was considered in patients who were seronegative for rheumatoid factors (Rose-Waaler titer ≤ 1:40 or nephelometric determination ≤ 20 Iu/ml on 2 or more occasions) and who presented psoriasis and arthritis affecting the axial and/or peripheral joints. All past clinical manifestations were assessed by the review of the medical records and carefully registered in the patients’ charts.

For each patient the following clinical characteristics were examined: sex, age, type of PsA (axial, peripheral, both), duration of PsA, extremities involved by pitting edema (upper, lower, both), type of involvement (symmetric, asymmetric), distribution of pitting edema, relapse/recurrence of pitting edema, the presence of dactylitis, tendonitis or peripheral enthesitis (Achilles tendinitis and plantar fasciitis) and the duration of follow up (months). Peripheral arthritis was defined by the history or by the presence of one or more swollen and tender joints for at least 3 months. Axial involvement was assessed by the presence of inflammatory spinal pain as defined by Calin’s criteria (18), alternating buttock pain, physical examination (spinal mobility and chest expansion were evaluated) and radiographs of the pelvis and spine.

The diagnosis of distal swelling with pitting edema was accepted if a diffuse unilateral or bilateral swelling of the upper or lower extremities or both, usually distributed along a well defined tenosynovial structure, associated with pitting, was present at the time of the visit or recorded in the patients’ charts.

As we have a special interest in this clinical feature, in order to avoid a possible bias related to overestimation, the presence of past episodes of distal swelling with pitting edema was accepted if registered in the medical records and confirmed by the patient.
who was shown a picture illustrating this feature at the time of the visit. Dactylitis was defined by the history (the patient learned to recognise this manifestation by looking at a photograph showing finger or toe dactylitis) or evidence of a sausage-shaped digit with pain.

Tenosynovitis was considered present in a patient showing pain and swelling over a well-defined tenosynovial structure (hand flexor and extensor tendons, peroneal, tibialis or extensor tendons of the foot).

Achilles enthesitis was defined by the presence of a history of severe pain (difficulty walking) and swelling over the site of the calcaneal insertion of the Achilles tendon of at least one month’s duration or evidence at examination of tenderness at a calcaneal insertion. Plantar fasciitis was considered in the presence of a history of severe pain (difficulty walking) at the calcaneal insertion of the plantar fascia of at least one month’s duration or evidence at examination of tenderness at the calcaneal insertion.

As controls we used the two successive outpatients, with any rheumatic disorder, consecutively observed after a patient with PsA over the same 3-month period, excluding those meeting the ESSG classification criteria for the spondylarthropathies (19). The presence of distal swelling with pitting edema was assessed by the same method used for PSA patients.

In 7 PsA patients presenting distal extremity swelling with pitting edema on examination, a hand and/or foot MRI was performed. This MRI was performed using two 0.5 T superconductive magnet systems (MR Max Plus, GE Medical Systems, Milwaukee, WI; Philips Gyroscan T5 II, Eindhoven, The Netherlands). Patients were placed in a prone position with their arms extended above the head. Both hands, joined in the “prayer position” with a foam pad between them and immobilized with tape, were positioned in the center of a 17-cm bore transmit-receive extremity coil. To study the proximal and intermediate parts of the feet, each foot was placed, in a neutral position with the knee extended, in the center of the same 17-cm bore transmit-receive coil that was used for hand MRI. To avoid alterations due to overturn, the forefoot was covered in aluminium foil.

Pulse sequences included sagittal T1-weighted (460/20/4-repetition time msec/echo time msec/excitations), axial proton-density (2000/25/2) and T2-weighted (2000/90/2 or 4000/120/8) and STIR (1400/25/2; IT 110) scans. Sagittal and axial section thicknesses were 3 mm and 7 mm, respectively, with an intersection gap of 1 mm. The field of view was 20 cm, and the matrix size was 160 x 224 or 128 x 192.

Scan images were examined by three radiologists (AB, LB and PP) who had no knowledge of the results of the physical examination. The joint space and synovial sheaths of the hand and/or foot tendons were evaluated for fluid collection.

Statistical analysis was done using the SPSS statistical package (SPSS Inc., Chicago, Illinois). Chi-square and T-tests for independent values were used.

### Results

183 patients with PsA, 103 men (56%) and 80 women (44%) with a mean age at the visit of 49.8 ± 12.2 years (range: 25 to 80 years), and 366 controls (167 men and 199 women; mean age 54 ± 8.3 years; range: 20 to 76 years) were studied. Table I shows the demographic and clinical features of the 183 patients with PsA. None of the patients had associated conditions, such as congestive heart failure, marked obesity, venous insufficiency, hypertension or renal failure, that could cause distal edema.

The control group consisted of 132 patients with osteoarthritis, 84 with rheumatoid arthritis, 66 with polymyalgia rheumatica/giant cell arteritis, 41 with fibromyalgia, 22 with connective tissue diseases, 5 with acute sarcoidosis, 7 with chondrocalcinosis, 3 with RS3PE syndrome, 4 with vasculitis, 1 patient with reflex sympathetic dystrophy and 1 patient with infectious arthritis.

Distal extremity swelling with pitting edema was recorded in 39/183 (21%) PsA patients and 18/366 (4.9%) controls (P < 0.0001). 7/39 (18%) episodes of distal pitting edema were observed at the time of the visit, while the remaining 32 resulted from the medical records and the patient’s confirmation. Distal edema was diagnosed at the time of the visit in 6 controls. The lower limbs were affected in 8/18 (44%) control patients.

The following rheumatic disorders were associated with distal extremity swelling with pitting edema in the controls: polymyalgia rheumatica in 8 cases, rheumatoid arthritis in 2, acute sarcoidosis in 2, RS3PE in 3, and infectious arthritis, reflex sympathetic dystrophy and chondrocalcinosis in 1.

### Table I. Demographic and clinical features of the 183 patients with PsA.

<table>
<thead>
<tr>
<th>Females/males (%)</th>
<th>44/56</th>
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<tbody>
<tr>
<td>Age at visit (ys)</td>
<td>49.8 ± 12.2</td>
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<tr>
<td>Age at onset of psoriasis (ys)</td>
<td>34 ± 11.6</td>
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<tr>
<td>Age at onset of PsA (ys)</td>
<td>43.4 ± 10.1</td>
</tr>
<tr>
<td>Duration of psoriasis (months)</td>
<td>188.1 ± 144.4</td>
</tr>
<tr>
<td>Duration of arthritis (months)</td>
<td>77.3 ± 70.5</td>
</tr>
<tr>
<td>Type of PsA: axial/peripheral/both (%)</td>
<td>9/64/27</td>
</tr>
<tr>
<td>Patients presenting distal extremity swelling with pitting edema (%)</td>
<td>21</td>
</tr>
<tr>
<td>Dactylitis (%)</td>
<td>34</td>
</tr>
<tr>
<td>Enthesitis (%)</td>
<td>40</td>
</tr>
<tr>
<td>Achilles enthesitis (%)</td>
<td>13</td>
</tr>
<tr>
<td>Plantar fasciitis (%)</td>
<td>16</td>
</tr>
<tr>
<td>Both achilles enthesitis and plantar fasciitis (%)</td>
<td>11</td>
</tr>
<tr>
<td>Duration of follow-up (months)</td>
<td>46.7 ± 27.3</td>
</tr>
</tbody>
</table>

Data are expressed as percentage or mean ± SD
The frequency of distal swelling with pitting edema was also significantly higher in PsA patients with respect to that observed in patients with rheumatoid arthritis and polymyalgia rheumatica calculated together (39/183 vs 10/150; P=0.002). Distal extremity swelling with pitting edema was observed in 2/84 (2.3%) patients with rheumatoid arthritis and in 8/66 (12%) patients with polymyalgia rheumatica. Most of the 39 patients with PsA had only 1 episode of distal swelling with pitting edema, while 4 patients (10%) had 2 episodes, for a total of 43 episodes. In these 4 patients the second episode occurred 16, 54, 72 and 84 months after the first episode. The analysis of the ten-year age groups distribution of the episodes showed the highest frequency, corrected for multiple comparisons, in the age group 40-49 years (49%, p = 0.0006). Eight patients (4 men and 4 women) had distal swelling with pitting edema as a first, isolated manifestation of PsA. They were treated with low-dose corticosteroids (CS) for 1 to 2 months (range: 1-6) after the suspension of CS, when they developed peripheral arthritis.

In 8 other patients distal swelling with pitting edema was associated with other features of PsA at diagnosis. In the remaining 23 (59%) distal edema complicated the course of the disease with a mean interval from the diagnosis of 46.7 ± 42.6 months. The upper extremities were affected in 5/17 (29%) episodes and hand extensor tenosynovitis in 17/17 (100%) episodes. In the 26 episodes affecting the lower limbs, peroneal tenosynovitis was evidenced in 22 (85%), tibialis tenosynovitis in 20 (80%) and foot extensor tenosynovitis in 22 (85%). Joint synovitis of the hands and feet was more difficult to detect at the clinical examination due to the marked swelling and edema of the hands and feet. However, wrist synovitis was present in 10/17 episodes of pitting edema involving the upper extremities and ankles synovitis was clinically detectable in 12/26 episodes affecting the lower extremities. All episodes of distal swelling with pitting edema promptly remitted after a short period (1-2 months) of 12.5 mg/day/os prednisone therapy.

Table II shows the comparisons between patients with and without pitting edema. Taken together, Achilles enthesitis and plantar fasciitis were significantly higher (p < 0.05) and the duration of arthritis was significantly lower (p = 0.02) in the patients with distal pitting edema.

Among the 7 patients who underwent hand or foot MRI, all showed impressive soft tissue edema and marked tenosynovitis. These findings were associated with fluid collection within the joint spaces (Figures 1A, 1B, 1C).

### Discussion

Few patients with PsA and distal extremity swelling with pitting edema due to lymphedema have been reported (13-16). The edema involved the upper limbs in all cases, more often asymmetrically, and in the majority of the patients was unresponsive to therapy. However, we observed some patients with PsA who presented distal swelling and edema characterized by a predominant involvement of the tenosynovial structures with a rapid response to CS (17).

Therefore, we decided to carry out a case-control study in order to evaluate the frequency and clinical characteristics of this finding in patients with PsA. The presence of past episodes of distal extremity swelling with pitting edema was assessed by a review of the medical records and by showing the patients a picture illustrating this clinical feature and asking them to recall any such episodes. Although not perfect, our methodological approach was the most reliable way to retrospectively identify patients with distal swelling and pitting edema.

Since the aim of the study was to assess the frequency of distal swelling with pitting edema in PsA patients we used as controls the two successive outpatients with any rheumatic disorder observed after a patient with PsA, over the same period. Moreover, considering that arthritis may precede the onset of psoriasis even by several years, we decided to exclude patients who met the ESSG classification criteria for the spondylarthropathies (19).

| Data are expressed as percentage or mean ± SD. |  |
|---|---|---|
| Pts with PsA with distal pitting edema (n=39) | Pts with PsA without distal pitting edema (n=144) | P value |
| Female/male (%) | 38/62 | 55/45 | NS |
| Age at onset of arthritis (years) | 45 ± 11 | 43 ± 9 | NS |
| Age at onset of psoriasis (years) | 33 ± 11 | 34 ± 11 | NS |
| Duration of psoriasis (months) | 201 ± 133 | 185 ± 148 | NS |
| Duration of arthritis (months) | 55 ± 45 | 83 ± 75 | 0.02 |
| Duration of follow-up (months) | 48 ± 36 | 46 ± 25 | NS |
| Type of PsA: axial/peripheral/both (%) | 13/69/18 | 8/63/29 | NS |
| Dactylitis (%) | 44 | 31 | NS |
| Both Achilles tendinitis and plantar fasciitis (%) | 54 | 37 | 0.05 |
These criteria encompass patients with undifferentiated spondyloarthropathy, who may potentially develop psoriasis in the future. Therefore, the inclusion of these patients in the control group could create some confusion in the evaluation of the real frequency of distal swelling with pitting edema in PsA patients. Distal extremity swelling with pitting edema was recorded in 39/183 (21%) PsA patients and in only 18/366 (5%) controls with a highly significant statistical difference (p < 0.0001). Furthermore, in 20% of the patients this feature represented the first manifestation of PsA. The edema was more often unilateral and the lower extremities were more frequently affected. Patients with distal edema also more frequently had plantar fasciitis or Achilles tendinitis.

The high frequency of distal swelling with pitting edema due to tenosynovitis found in the present series may be explained by the well-known frequent involvement of tenosynovial structures in PsA (20-21). In our study, the inflammatory involvement of the tenosynovial sheaths was confirmed in the...
cannot be ruled out, the predominant pathogenic mechanism seems to be a strenuous tenosynovitis rapidly responding to CS. Awareness of this clinical sign could help facilitate a proper diagnosis.

References