LETTERS

Remitting distal lower extremity swelling with pitting oedema in acute sarcoidosis

Remitting distal extremity swelling with pitting oedema is a clinical manifestation that may be observed in different rheumatic conditions such as RS3PE syndrome, polymyalgia rheumatica, late onset undifferentiated spondyloarthritis, ankylosing spondylitis, psoriatic arthritis, and more rarely in other rheumatic diseases. In RS3PE the swelling with pitting oedema predominantly involves the upper extremities symmetrically. This clinical finding may occur unilaterally in polymyalgia rheumatica and upper and lower limbs may be equally affected, whereas in seronegative spondyloarthropathies it has been described more frequently in lower extremities with asymmetric involvement.

The oedema is characterised by a rapid response to small doses of corticosteroids. The pathogenesis of swelling with pitting oedema has not been completely defined, but the distribution along the tenosynovial membranes suggests that it probably results from tenosynovitis.

Sarcoidosis is a systemic granulomatous disease that is associated with rheumatic manifestations in 6% to 39% of patients. The most common form of arthritis occurs acutely, involves preferentially the ankles, and it is often the initial feature of sarcoidosis. Frequently, erythema nodosum and bilateral hilar adenopathy are associated with arthritis (Lofgren’s syndrome). Erythema nodosum may also be absent.

Peripheral oedema and tenosynovitis accompanying arthritis have been emphasised in some reports. However, remitting distal lower extremity swelling with pitting oedema of the dorsa of the feet in patients with acute sarcoidosis has not been mentioned in previous reports.

We describe five patients with acute sarcoidosis who presented as first manifestation of the disease an impressive distal lower extremity swelling with pitting oedema of the dorsum of both feet.

We made a retrospective review of all patients with acute sarcoidosis seen in two Italian Divisions of Internal Medicine (Prato and Reggio Emilia Hospitals) over a two year period. The diagnosis and presenting clinical features were assessed by clinical examination and review of the patient’s chart.

Remitting distal extremity swelling with pitting oedema was the presenting manifestation in five (29%) of 17 consecutive patients with acute sarcoidosis seen between January 1995 and December 1996.

Table 1 summarises the demographic and clinical characteristics of the five patients. All patients presented with pain and swelling of both ankles and feet.

The swelling and pitting oedema were most prominent over the dorsum of both feet and ankles, malleolar and perimalleolar areas were also involved (fig 1). In perimalleolar areas the oedema followed the distribution of tendons and peroneal tendons. It is possible that pitting oedema in our series may have been present in some other cases, but less pronounced and not considered by the examiner.

Swelling and oedema completely resolved after a few days of corticosteroid treatment.

To investigate the structures responsible for the swelling and oedema we examined three patients by magnetic resonance imaging.

Table 1 Demographic, clinical, and magnetic resonance imaging features of the five patients with acute sarcoidosis

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex/age at disease onset (y)</th>
<th>Pitting oedema of the dorsum of the feet</th>
<th>Systemic symptoms</th>
<th>Erythema nodosum</th>
<th>ESR/CRP*</th>
<th>SACE concentration†</th>
<th>Bilateral hilar adenopathy (x rays)</th>
<th>Gallium scan</th>
<th>Bronchovascular uptake</th>
<th>Transbronchial biopsy</th>
<th>Foot and ankle MRI findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M/32</td>
<td>present</td>
<td>low grade fever</td>
<td>absent</td>
<td>42/35</td>
<td>58</td>
<td>present</td>
<td>increased</td>
<td>not performed</td>
<td>not performed</td>
<td>not performed</td>
</tr>
<tr>
<td>2</td>
<td>F/48</td>
<td>present</td>
<td>low grade fever</td>
<td>present</td>
<td>65/52</td>
<td>65</td>
<td>present</td>
<td>not performed</td>
<td>not performed</td>
<td>CD4+ lymphocytic alveolitis</td>
<td>mild joint synovitis, severe tenosynovitis of all extensor tendons</td>
</tr>
<tr>
<td>3</td>
<td>F/34</td>
<td>present</td>
<td>low grade fever, fatigue</td>
<td>present</td>
<td>70/56</td>
<td>70</td>
<td>not performed</td>
<td>mild joint synovitis</td>
<td>mild joint synovitis, severe tenosynovitis of all extensor tendons</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>M/31</td>
<td>present</td>
<td>low grade fever</td>
<td>absent</td>
<td>61/45</td>
<td>57</td>
<td>not performed</td>
<td>mild joint synovitis</td>
<td>non-caseating granulomas</td>
<td>mild joint synovitis, severe tenosynovitis of all extensor tendons</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>F/28</td>
<td>present</td>
<td>low grade fever</td>
<td>absent</td>
<td>71/48</td>
<td>62</td>
<td>present</td>
<td>mild joint synovitis</td>
<td>non-caseating granulomas</td>
<td>non-caseating granulomas</td>
<td></td>
</tr>
</tbody>
</table>

* ESR= erythrocyte sedimentation rate (mm 1st hour), CRP= C reactive protein (normal value: < 5 mg/l); † SACE= serum angiotensin converting enzyme (normal value: 18–55 U/l).

Figure 1  Patient 2. Soft tissue swelling of malleolar and perimalleolar areas with pitting oedema of the dorsum of the right foot. The distribution of the oedema follows the course of peroneal, tibialis, and extensor tendons of the foot.

Figure 2  Patient 4. Right ankle axial magnetic resonance imaging (SE T2weighted): pronounced tenosynovitis of posterior tibial tendon (arrow). Subcutaneous oedema and mild joint synovitis with scanty intrarticular fluid may be observed.
Further evidence that low androgen values are a cause of rheumatoid arthritis: the response of rheumatoid arthritis to seriously stressful life events

It is well established that androgen concentrations are low in patients with rheumatoid arthritis (RA).

(1) Low androgen values are a consequence of RA. The association of low androgen values with RA, in turn, is associated with the presence of nodule-like lesions in RA patients.

(2) Acute and chronic administration of exogenous glucocorticosteroids can lower testosterone and DHA-S. (See Masi et al. for reference.) Therefore, low androgen concentrations are a cause of RA in patients who survive RA.

(3) However, there are very substantial grounds for suspecting that low androgen concentrations are a cause of RA too: (a) RA is more common in women than in men. (b) RA is associated with low androgen values in men. Hence the suggestion that low testosterone is a genetically determined precursor, rather than a consequence of RA or its treatment.

A similar argument may be deployed in regard to RA DR 4 in women. (c) RA abates in about 75% of cases during pregnancy. (See Masi et al. for reference.) Some weeks to months after delivery, the disease flares in more than 90% of RA patients. During pregnancy, increasing quantities of androgens are produced by the corpus luteum, placenta, and fetal Leydig cells in the male fetal reproductive tract.

According to this hypothesis, amelioration during pregnancy is caused by these hormones, and the subsequent relapse is caused by their withdrawal. (d) Controls have shown that higher testosterone concentrations in patients in case-control studies: these data are consistent with any of the three propositions above. But the point has been established in a longitudinal study too: women who live near the equator and RA had significantly lower DHA-S values than controls who did not develop the disease. Such a finding, if it were confirmed would not be adequately explained by propositions 1 or 2. (c) Direct administration of testosterone to male androgen-deficient and postmenopausal female patients has resulted in improvement. It would be interesting to see the effect of such treatment for premenopausal women.

In the attempt to further incite low testosterone values in the aetiology of RA, I wish to draw attention to further confirmatory evidence in the shape of two dramatic cases reported in the behavioural literature.

The first is that of an elderly female RA patient who survived a lightning strike during a thunderstorm. Her walking stick was allegedly charred and her symptoms almost totally abated, though they subsequently returned before her death. I can vouch for the authenticity of this story: the lady was my aunt and she certainly suffered a shock (though not necessarily in the electrical one). She regarded her experience as the occasion of a miracle.

The second case was that of a 53 year old female RA patient who suffered the unexpected deaths of her sister and husband. Her disease went into temporary remission within a week of the deaths.

Stress in both sexes leads to increased pituitary secretion of adrenocorticotropic hormone. In men this causes a rise in gonadal steroid production. In women, adrenocorticotropic hormone activation of the adrenal cortex is suspected of leading to increased androgens.

I suggest that these two cases illustrate the beneficial effects of androgens on RA. There are two ways in which these findings can be tested: (1) If I am right, such seriously stressful life events would have an exacerbating effect on male patients. (2) If I am right, the beneficial effects of pregnancy should be more evident in women carrying male fetuses (because male fetuses secrete more androgens than female fetuses).

WILLIAM H JAMES
The Galton Laboratory, University College London, Wilshon House, 4 Stephenson Way London NW1 2HE

Rемitting distal lower extremity swelling with pitting oedema in acute sarcoidosis

FABRIZIO CANTINI, LAURA NICCOLI, IGNAZIO OLIVIERI, LIBERO BAROZZI, PIETRO PAVLICA, ALESSANDRO BOZZA, PIER LUIGI MACCHIONI, ANGELA PADULA and CARLO SALVARANI

Ann Rheum Dis 1997 56: 565-566
doi: 10.1136/ard.56.9.565

Updated information and services can be found at:
http://ard.bmj.com/content/56/9/565

These include:

References
This article cites 10 articles, 0 of which you can access for free at:
http://ard.bmj.com/content/56/9/565#BIBL

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/