BONE AND JOINT LESIONS ASSOCIATED
WITH PUSTULOSIS PALMARIS ET PLANTARIS

A CLINICAL AND HISTOLOGICAL STUDY

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We have reviewed 41 patients with pustulotic arthro-osteopathy (PAO), all having both the typical skin rash of pustulosis palmaris et plantaris and bone lesions. The most common bones affected were the clavicle, sternum and ribs. Changes in the clavicle started, not as an enthesopathy, but with periosteal bone formation, indicative of a bone marrow disorder. About 30% of the patients also had lesions in the spine, sacroiliac region or the peripheral joints. Bone and joint lesions followed a variable and intermittent clinical course over a long period of time. Biopsies in eight cases showed similar inflammatory changes in skin, bone and synovium, with infiltration of lymphocytes and polymorphonuclear leucocytes. This suggests that there is a common pathogenesis in the three tissues.

Pustulosis palmaris et plantaris (PPP) is a skin disease in which a number of septic vesicles develop, mainly on palmar and plantar surfaces (Fig. 1). The skin rash runs a recurrent course of deterioration and improvement, and an association with bone lesions has been reported (Sonozaki et al. 1974, 1979; Köhler et al. 1975; Probst, Björksten and Gustavson 1978). Bone lesions are found in about 10% of all Japanese patients with PPP and has also been reported in rare cases in Europe and America (Resnick, Vint and Poteshman 1981; Goossens, Vanderstraeten and Claessens 1985; Jurik, Graudal and de Carvalho 1985).

The major symptoms are painful swellings in the anterior chest region, involving clavicle, sternum or rib, which show characteristic hypertrophy and sclerotic changes on radiography. Sonozaki et al. (1974) emphasised that these lesions differed from those of infection and in 1979 they reported this disease as “intersterno-costo-clavicular ossification”. In Europe and America, three similar cases were reported by Köhler et al. (1975) as “sterno-kosto-klavikutäre Hyperostose” and by Probst et al. (1978) as “chronic recurrent multi-focal osteomyelitis”. It has now become apparent that these bony changes may develop not only in the anterior chest region, but also in the spine or the sacroiliac joint. Sonozaki et al. (1981), reporting more cases, proposed the name pustulotic arthro-osteopathy (PAO) as a new rheumatic disease related to seronegative spondylo-arthritis.

All the conditions named in the paragraph above can now be recognised as due to the same disease. The cause of PAO is unknown, and the diagnostic criteria, clinical features and management have not yet been established (Chigira et al. 1986). We have studied 41
patients with PAO with reference to clinical features, radiography, serum biochemistry and histopathology. We present our views on the pathogenesis and clinical features together with a review of the literature.

PATIENTS

We have seen 41 patients with PAO within the past 10 years. Patients without the typical skin rash, even if they had anterior chest symptoms, were excluded. There were 11 males and 30 females, with an age range at onset from 12 to 77 years (mean 46.8 years). In many cases, the skin rash and bone lesions developed almost simultaneously, and in 85% of the patients both types of lesion were seen within one year.

### Table 1. Clinical and radiographic findings in 41 patients with pustulotic arthro-ostitis

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Per cent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristic rash</td>
<td>100</td>
</tr>
<tr>
<td>Anterior chest pain</td>
<td>93</td>
</tr>
<tr>
<td>Anterior chest swelling</td>
<td>93</td>
</tr>
<tr>
<td>Peripheral joint swelling</td>
<td>33</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Radiographic abnormalities</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior chest region</td>
<td>38</td>
</tr>
<tr>
<td>Clavicle + sternum + rib</td>
<td>10</td>
</tr>
<tr>
<td>Clavicle + sternum</td>
<td>15</td>
</tr>
<tr>
<td>Clavicle</td>
<td>3</td>
</tr>
<tr>
<td>Sternum + rib</td>
<td>2</td>
</tr>
<tr>
<td>Sternum</td>
<td>6</td>
</tr>
<tr>
<td>Rib</td>
<td>2</td>
</tr>
<tr>
<td>Spine</td>
<td>15</td>
</tr>
<tr>
<td>Sacroiliac joint</td>
<td>9</td>
</tr>
</tbody>
</table>

Advanced bone lesions in both clavicles and both first ribs with severe osseous hypertrophy and sclerotic change. The technetium scan also shows increased uptake in the second ribs and the sternum.

### RESULTS

**Clinical and radiographic findings** (Table 1)

*Anterior chest area.* Of the 41 patients, 38 (93%) had slight to severe pain in the anterior chest region, with repeated relief and deterioration during its course. The skin rash tended to become worse with the aggravation of the bone lesions. Most patients were treated with indomethacin, which was effective against pain. Radiographs showed that 28 patients (the largest group) had lesions of the clavicles, 15 with bilateral involvement (Table 1; Fig. 2a). Ten of the 28 patients had widespread lesions in the clavicles, sternum and ribs (Fig. 2b). Of the rib lesions, nearly all were of the first rib.

Affected clavicles showed sclerotic hypertrophy associated with some osteolytic changes (Fig. 3). The

![Fig. 3a](image1)

![Fig. 3b](image2)

![Fig. 3c](image3)

Radiographs of a 24-year-old woman. Figure 3a – Six months after the onset of anterior chest pain, the film shows periosteal bone formation (large arrows) and a cystic lesion (small arrow) in the clavicle. Figure 3b – Two and a half years later, hypertrophy is seen, though the original contour of the clavicle is still visible (small arrows). Figure 3c – Six years later more cystic lesions are seen. Anterior chest pain had recurred and settled many times.
osteolytic changes first appeared at the medial end of the clavicle with simultaneous periosteal reaction. This periosteal reaction advanced laterally, and finally osseous hypertrophy involved the medial two-thirds of the clavicle. Most sternal lesions were in the manubriosternal joint, where an osteophyte similar to a spinal syndesmophyte was formed and eventually resulted in a bony bridge (Fig. 4). In the ribs there was sclerotic hypertrophy of the costal cartilage, with some periosteal new bone formation at the anterior end of the bone (Fig. 5).

Bone scintigraphy was useful to identify early lesions, before radiological abnormalities had appeared. Relatively chronic lesions continued to accumulate radioactive isotope (see Fig. 2b).

Spine and sacroiliac joint. Of the 41 patients, spinal hyperostosis was found in 15 (37%) and sclerotic changes in the sacroiliac joint in nine (22%), but at these sites symptoms, if any, were slight. The earliest spinal lesion of hyperostosis was an asymmetrical anterolateral syndesmophyte with an irregular vertebral margin, termed spondylodiscitis (Fig. 6a). The lesion finally

---.d--
[64x530]---.d--
[100x530]
[0x0]---.d--
[156x530]---.d--
[63x518]clavicle
[102x518]with
[128x518]simultaneous
[190x518]periosteal
[238x518]reaction.
[283x518]This
[63x506]periosteal
[110x506]reaction
[149x506]advanced
[195x506]laterally,
[238x506]and
[259x506]finally
[290x506]os-
[63x494]seous
[89x494]hypertrophy
[144x494]involved
[183x494]the
[199x494]medial
[231x494]two-thirds
[277x494]of
[288x494]the
[63x482]clavicle.
[102x482]Most
[126x482]sternal
[158x482]lesions
[190x482]were
[213x482]in
[225x482]the
[242x482]manubrioster-
[64x471]nal
[82x471]joint,
[112x471]where
[144x471]an
[161x471]osteophyte
[214x471]similar
to
[250x471]a
[265x471]spinal
[64x459]syndesmophyte
[132x459]was
[151x459]formed
[184x459]and
[203x459]eventually
[250x459]resulted
in
[286x459]a
[64x447]bony
[90x447]bridge
(Fig.
[146x447]4).
In
[177x447]the
[196x447]ribs
[218x447]there
[245x447]was
[267x447]sclerotic
[64x435]hypertrophy
[118x435]of
[129x435]the
[145x435]costal
[172x435]cartilage,
[215x435]with
[236x435]some
[261x423]periosteal
[63x423]new
[86x423]bone
formation
[111x423]at
[159x423]the
[172x423]anterior
[190x423]end
[229x423]of
[249x423]the
[263x423]bone
(Fig.
[87x411]5).

Spinal radiographs. Figure 6a – A 53-year-old man four years after the onset of anterior chest pain shows osteophyte formation with irregular bony margins (arrow). Figure 6b – Advanced lesions of the lumbar spine, with massive new bone formation and ankylosis similar to that seen in Reiter’s disease and psoriatic arthritis. There is some disc space narrowing in both cases.

Massive ossification of the first costal cartilage with periosteal hypertrophy of the end of the first rib and bony ankylosis of the sternocostal joint. The clavicle is normal in this case.

Changes in the pelvis of a 52-year-old woman. Figure 7a – Bilateral sacroiliac sclerosis. Figure 7b – Twelve years later, there are osteolytic changes on the right and sclerosis of the whole of the left ilium.
became a thick bony bridge between two vertebrae (Fig. 6b) in association with slight narrowing of the disc space. Patients with advanced spinal lesions often showed symmetrical sclerosis on the iliac side of the sacroiliac joint (Fig. 7a), and rarely did this sclerosis spread to the entire ilium (Fig. 7b).

Peripheral joints. Nine of 27 patients (33%) had obvious peripheral arthritis: this was mono-articular in five (knee 3, hip 1, ankle 1) with effusion and slight pain. In four of these, intermittent swelling persisted for more than one year. Four patients with polyarthritis had transient pain in knee, wrist and shoulder. Radiographs were normal but bone scintigraphy was positive.

Serum biochemistry and histopathology
Laboratory findings suggested inflammation with an increased erythrocyte sedimentation rate in 73%, a positive carbohydrate reactive protein test in 62%, and leucocytosis in 46% (Table II). However, during the course of the disease these sometimes became normal, tending to vary with the severity of the disease. RA factor was positive in only 13% and HLA-B27 was absent in all of 14 cases examined.

Histology of the skin rash showed multiple spongiotic vesicles with surface hyperkeratosis (Fig. 8). Many polymorphonuclear leucocytes (PMNs) were seen in the vesicles, and there was an infiltration of mononuclear cells (MNs) between the epidermis and dermis. Bone lesions of clavicle and rib were biopsied in four patients as were arthritic peripheral joints in four others. In the clavicle severe marrow fibrosis was seen (Fig. 9a), but the areas of active infiltration showed many MNs and PMNs (Fig. 9b). The synovium from knee and ankle joints showed infiltration of MNs with slight hypertrophy of the lining layer (Fig. 10a), and in two patients there was some infiltration of PMNs in the sublining layer (Fig. 10b). Tissue culture of all eight biopsy specimens was negative for bacteria and for tuberculosis.

DISCUSSION
It is now recognised that various bone and joint lesions may develop as complications of PPP (Enfors and Molin 1971; Sonozaki et al. 1974; Köhler et al. 1975; Ishibashi et al. 1977; Probst et al. 1978). The incidence of bone and joint lesions in Japanese patients is about 10% with around twice as many female as male cases (Sonozaki et al. 1981; Kojima 1982). The major site is the anterior chest region, but lesions are also found in the spine and the sacroiliac joint in 10% to 40% of cases (Miyagawa et al. 1981; Sonozaki et al. 1981). We found a similar incidence, and also found peripheral arthritis in 33% of patients. A higher incidence may be found during continued observation because the lesions do not necessarily appear simultaneously.

The aetiology and characteristic features of PAO and its relation to PPP have not yet been clarified. In our study the onset of skin and bone lesions was frequently coincidental, and the worsening of bone symptoms was

Table II. Laboratory findings in 41 patients with pustulotic arthro-ostitis

<table>
<thead>
<tr>
<th>Finding</th>
<th>Per cent</th>
</tr>
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<tbody>
<tr>
<td>Positive RA factor</td>
<td>13</td>
</tr>
<tr>
<td>Elevated ESR</td>
<td>73</td>
</tr>
<tr>
<td>Positive CRP</td>
<td>62</td>
</tr>
<tr>
<td>Leucocytosis</td>
<td>46</td>
</tr>
<tr>
<td>Elevated ALP</td>
<td>40</td>
</tr>
<tr>
<td>Liver dysfunction</td>
<td>8</td>
</tr>
<tr>
<td>Renal failure</td>
<td>0</td>
</tr>
<tr>
<td>Positive Wasserman</td>
<td>0</td>
</tr>
<tr>
<td>HLA-B27</td>
<td>0 (14 cases)</td>
</tr>
</tbody>
</table>

CRP, carbohydrate reactive protein
ALP, alkaline phosphatase

Skin lesions. Figure 8a – Low-power photomicrograph of a biopsy specimen from a skin lesion. There is a spongy vesicle in the epidermis (× 30). Figure 8b – Higher magnification shows a large number of polymorphonuclear leucocytes in the vesicle, with mononuclear cell infiltration in the transitional zone between epidermis and dermis (× 140).
Bone lesions. Figure 9a - A low-power photomicrograph of the clavicular lesion from a 27-year-old woman shows bone marrow fibrosis and new bone formation (×30). Figure 9b - Higher magnification of a different area shows inflammatory cells, mainly polymorphonuclear leucocytes and lymphocytes (×70).

Bone lesions. Figure 9a - A low-power photomicrograph of the clavicular lesion from a 27-year-old woman shows bone marrow fibrosis and new bone formation (×30). Figure 9b - Higher magnification of a different area shows inflammatory cells, mainly polymorphonuclear leucocytes and lymphocytes (×70).

usually associated with aggravation of the skin rash. Histology showed similar inflammatory cell infiltration in the lesions of the skin, the bone and the synovium (Figs 8, 9 and 10). This similarity has not been previously described, and suggests a common aetiology for the lesions at all three sites. The aetiology of the skin rash has been studied from an immunological approach (Husby, Rajka and Larsen 1973; Yamanaka, Sambe and Kataura 1982) and the similarity of the histology suggests that the bone and joint lesions may be triggered by a similar mechanism to that of the skin rash. However, the immunological study of the bone and joint lesions has not yet been reported.

The painful swellings in the anterior chest area have been considered to be an enthesopathy, beginning with ossification in the costoclavicular ligament (Sonozaki et al. 1979). We would emphasise, however, that osseous hypertrophy caused by periosteal bone formation occurs in the entire circumference of the clavicle before ossification takes place in the costoclavicular ligament (Fig. 3). This periosteal reaction suggests some type of bone marrow disorder rather than an enthesopathy, but radiographs of the sternum and spine show abnormalities similar to both enthesopathy and hyperostosis.

The spinal changes resemble those of psoriatic arthropathy and Reiter's disease. The vertical osteophytes seen in PAO appear to be different from those of spondylitis deformans in which the osteophytes grow more horizontally and rarely result in a bony bridge. However, in PAO some disc narrowing was frequently seen, unlike cases of enthesopathy but more like those of spondylitis deformans. In advanced sacroiliac involvement, sclerosis was observed in the entire ilium (Fig 7b), again suggesting, as in the clavicle, a lesion of

Synovial lesions. Biopsy specimens from an ankle show collections of mononuclear cells (×70) and polymorphonuclear leucocytes (×140).

Fig. 10a

Fig. 10b
the bone marrow. Previous reports on peripheral arthritis in PAO have stated that transient rheumatoid-like polyarthritis occurs (Enfors and Molin 1971) and heals in one to two months (Sonozaki et al. 1981). In our series also, peripheral arthritis was mild and radiographs showed no obvious abnormality over several years, but variable symptoms continued over many years.

Pustulotic arthro-osteitis has clinical features of spondylitis, sacroiliitis and peripheral arthritis, and changes in serology which are similar to those of seronegative spondylo-arthritis (SNSA). But when PAO is compared with SNSA (Wright and Moll 1976), some differences can be found: there is no familial tendency and no specific HLA antigen (Ishii et al. 1982). Moreover, the main manifestations of PAO involve the anterior chest area and, especially in the clavicle, the lesion seems to develop by periosteal bone formation. These latter features indicate that PAO may not belong in the SNSA group of diseases.

REFERENCES


