SAPHO Syndrome[1]

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Palmoplantar pustulosis and severe acne are sometimes associated with peculiar aseptic skeletal conditions, but such skeletal lesions can be found without skin lesions. The term *SAPHO syndrome* has been coined for this cluster of manifestations. (The acronym SAPHO refers to synovitis, acne, palmoplantar pustulosis, hyperostosis, and osteitis.) The most common site of the disease is the upper anterior chest wall, characterized by predominantly osteosclerotic lesions, hyperostosis, and arthritis of the adjacent joints. Osteosclerosis of the vertebral bodies, hyperostosis, and erosions of the vertebral plates can be encountered. Unilateral sacroiliitis is frequently observed. Long bone involvement consists of osteosclerosis or osteolysis with periosteal new bone formation. Peripheral arthritis can be present but is rarely associated with joint destruction. The pathogenesis of this syndrome remains unknown, but a link with seronegative spondyloarthropathies is probable. Radiologists should be aware of this unusual syndrome to avoid misdiagnosis (eg, tumor, infection), unnecessary surgery, and antibiotic therapy.

■ INTRODUCTION

The osteoarticular manifestations of psoriasis are well known. Recently, attention has been drawn to a variety of bone and joint lesions associated with other skin diseases, especially palmoplantar pustulosis (1-3), acne (4,5), and hidradenitis suppurativa (4). To stress the association between these rheumatologic and cutaneous features, the term *SAPHO syndrome* was coined in 1987 (6). (The acronym SAPHO refers to synovitis, acne, palmoplantar pustulosis, hyperostosis, and osteitis.) However, not all the syndrome components need to be present for a diagnosis of SAPHO syndrome, especially the dermatologic components, as osteoarticular involvement can manifest alone without known skin lesions. The aseptic skeletal inflammatory process is the common denominator of these manifestations. Synonymous conditions have been discussed under a variety of names, including "pustulotic arthroosteitis" (1,2,7) and "sternocostoclavicular hyperostosis" (3). SAPHO syndrome is probably rare, but its frequency remains

Abbreviation: SAPHO = synovitis, acne, palmoplantar pustulosis, hyperostosis, and osteitis

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unknown. In 1987, a French national retrospective study (6) found 85 cases of SAPHO syndrome, including 13 cases of severe acne, 44 cases of palmoplantar pustulosis, and 28 cases of hyperostosis without dermatitis.

The radiologic appearance of the skeletal lesions may be helpful in diagnosis, particularly when the sternocostoclavicular joint is involved, but can lead to misdiagnosis in cases in which the sites are atypical or the patient does not have skin lesions. In this article, we describe the SAPHO syndrome and emphasize the sites and radiologic features of the skeletal lesions. The following topics are discussed: (*a*) the pathogenesis of the syndrome, including the relationship with psoriasis; (*b*) pathologic features; (*c*) clinical findings; (*d*) radiologic findings in the sternocostoclavicular region and axial and appendicular skeleton; (*e*) diagnosis; and (*f*) treatment and prognosis.

■ PATHOGENESIS

The pathogenesis of this syndrome remains unknown. Bacterial (*Propionibacterium acnes*) or viral infection and autoimmune disease have been suggested as possible causes (3). However, in most cases, neither an infectious agent nor an immune complex or autoantibodies have been isolated. No known link exists between acne and psoriasis; however, the proportion of patients with palmoplantar pustulosis who also have psoriasis is much higher than in the normal population and varies between 8% (6) and 30% (8). Some investigators suggest that palmoplantar pustulosis is only a variant of psoriasis (7), which would explain the similarity of the skeletal lesions. Other authors state that palmoplantar pustulosis is distinct from psoriasis on account of the differences in the histologic features of the skin lesions and in the distribution of HLA antigens, the less severe destruction of peripheral joints in palmoplantar pustulosis, the rare involvement of distal interphalangeal joints, and the presence of multifocal aseptic osteomyelitis (9). However, a relationship between SAPHO syndrome and seronegative spondyloarthropathies is probable (1,3,4).

■ PATHOLOGIC FEATURES

Pathologic examination of biopsy specimens from the bone lesions shows nonspecific inflammatory changes indistinguishable from those of conventional bacterial osteomyelitis, but abscess formation is rare. In the acute stage, active resorption of bone and invasion by polymorphonuclear leukocytes are often noted. Occasionally, Paget disease–like features are seen. Long-standing lesions show a predominance of lymphocytes, with the occasional presence of plasma cells, histiocytes, and polymorphonuclear leukocytes. Still later, lesions show fibrosis and an increased occurrence of osteoblasts with new bone formation (9).

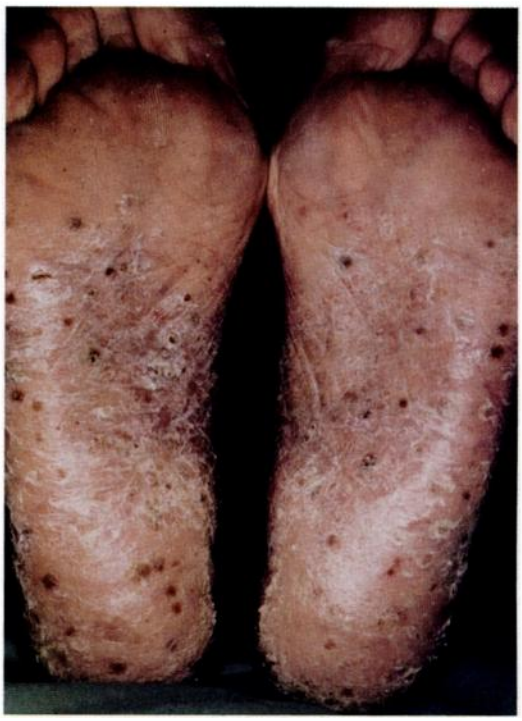
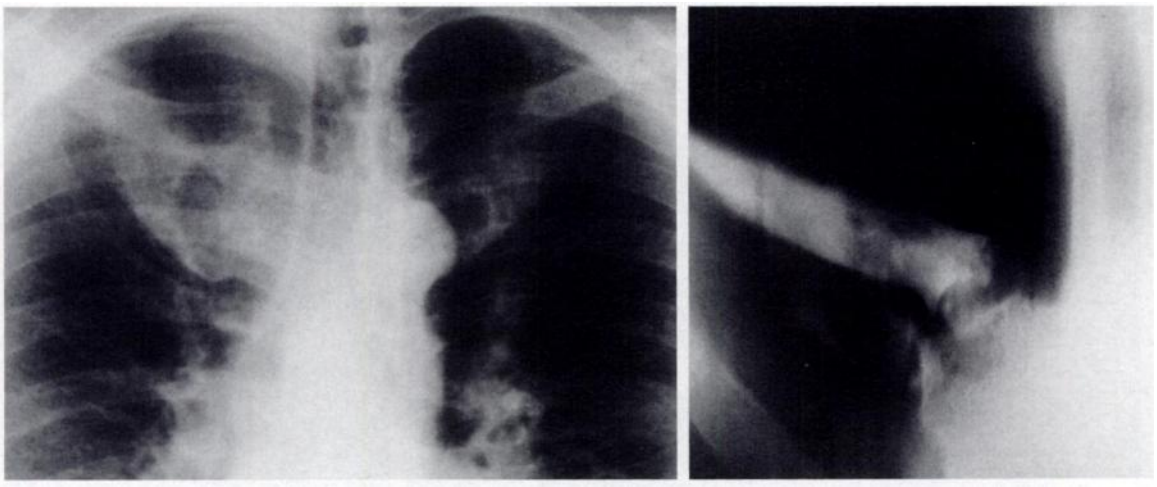


Figure 1. Photograph of the feet of a patient with SAPHO syndrome shows the characteristic skin lesions on the plantar surface of each foot.

■ CLINICAL FINDINGS

This rare condition is observed mainly in young or middle-aged adults, but children can also be affected. The sex ratio is nearly 1:1, but there is a male predominance in cases of acne and a female predominance in cases of palmoplantar pustulosis. Palmoplantar pustulosis and acne have been reported in 51.7% and 15.3% of patients with SAPHO syndrome, respectively (6). Palmoplantar pustulosis is a chronic eruption of yellowish, intradermal, sterile pustules on the palms and soles (Fig 1). The prevalence of bone lesions in patients with palmoplantar pustulosis varies from 1% to 22%. When present, acne is usually severe (acne fulminans, acne conglobata). However, osteoarticular abnormalities can occur without associated skin disease, as the latter may be episodic and precede or follow bone lesions (1). A 20-year interval between the skin lesions and bone involvement



3. 4.

Figures 3, 4. (3) Anteroposterior chest radiograph shows osteosclerosis and hypertrophy of both first ribs. (Reprinted, with permission, from reference 10.) (4) Frontal tomogram demonstrates osteosclerosis and osteolytic changes in the medial end of the clavicle with erosions at the sternoclavicular joint. (Reprinted, with permission, from reference 10.)

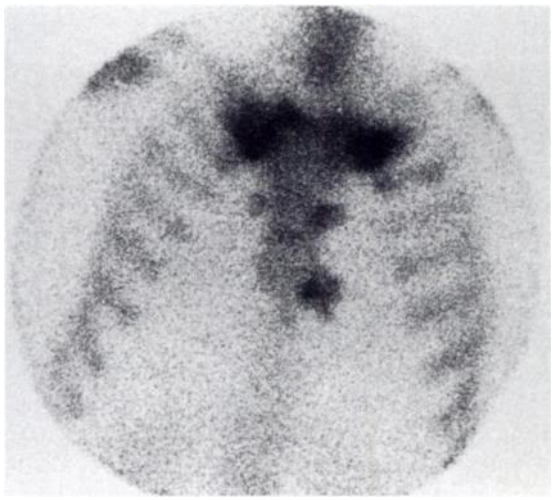


Figure 2. Technetium-99m methylene diphosphonate bone scan shows increased uptake in the sternocostoclavicular regions. Also note increased uptake of the radioisotope in several other sternocostal joints.

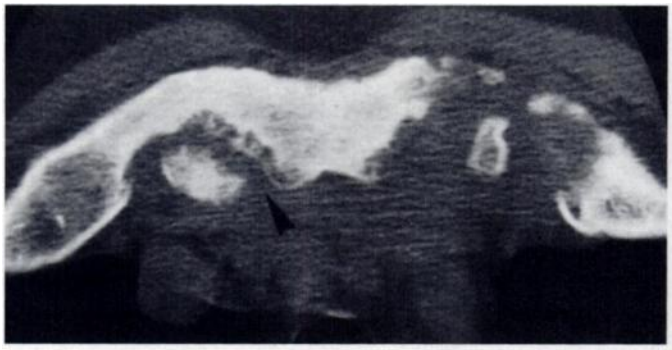
has been reported in one case (9). Most patients experience pain, soft-tissue swelling, and limitation of motion referable to the involved skeletal sites. Systemic manifestations are unusual, but fever is sometimes encountered. The erythrocyte sedimentation rate is frequently elevated, but all other laboratory values are usually within normal limits (2,5).

■ RADIOLOGIC FINDINGS

One or more skeletal sites can be involved. When multiple, lesions can occur either simultaneously or successively. In view of the possible fluctuation of the clinical symptoms, a technetium bone scan that shows increased uptake in asymptomatic regions is helpful. The sternocostoclavicular region is the most frequent site of the disease, but other sites in the axial and appendicular skeleton may be involved. There is usually a combination of osteoproliferative and osteodestructive changes in the involved bone. Accompanying synovitis may manifest as joint space narrowing, juxta-articular osteoporosis, and even osseous erosions.

• Sternocostoclavicular Region

The sternocostoclavicular region is the most frequent site of the disease, being affected in 70%–90% of patients (1,3,6) (Fig 2). The most frequently involved area is the region of the costoclavicular ligament, with abnormal ossifications and erosions seen in this area, but all the components of the anterior chest wall can be involved, particularly the clavicles and manubrium sterni (Figs 3–7). Hyperostosis is highly characteristic of SAPHO syndrome and is usually associated with osteosclerosis. Osteolysis is sometimes observed, especially at the be-



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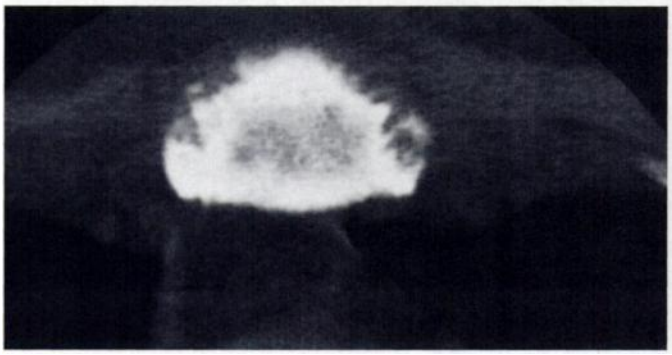

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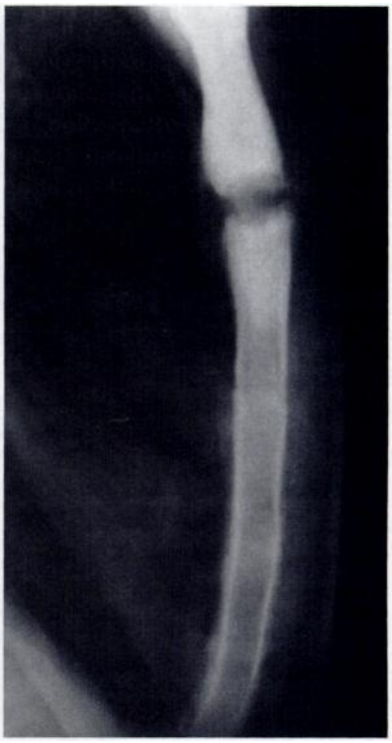

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Figures 5–7. **(5)** Computed tomographic (CT) scan shows sternoclavicular erosions (arrowhead) and bony ankylosis between the sternum and the right first rib. Retrosternal fat infiltration is also seen. **(6)** CT scan demonstrates hyperostosis and osteosclerosis of the sternum. **(7)** Multidirectional plain tomogram in the lateral projection shows osteosclerosis and periostitis of the sternum with erosions at the manubriosternal joint.

ginning of the disease. More often, there is an association of both features. Soft-tissue involvement around hyperostotic bones can be found and is sometimes responsible for venous thrombosis (11). Associated arthritis and ankylosis of the adjacent articulations are frequently seen.

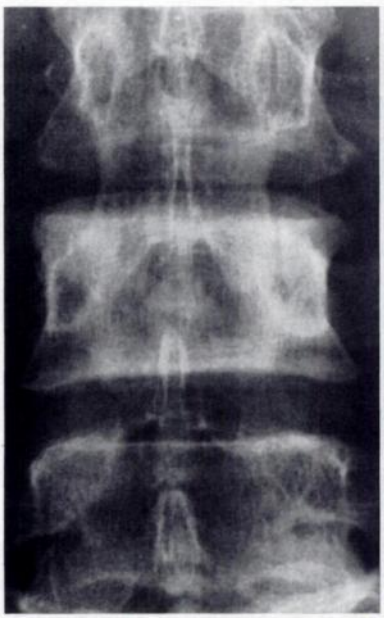
• Axial Skeleton

The spine is the second most common site of the disease, being involved in about one-third of patients. Three radiographic manifestations are seen, often in combination: osteosclerosis of one or more vertebral bodies (Figs 8, 9) (1,9), paravertebral ossifications mimicking marginal syndesmophytes but most frequently nonmarginal syndesmophytes or massive bridging (5,9,11), and lesions of the diskovertebral junction whose appearance can be similar to that of infectious spondylitis (1,7). Magnetic resonance (MR) images demonstrating a normal appearance of the disks can be helpful (Fig 10).

Sacroiliitis can occur. Unilateral involvement is frequent and is characteristically associated with extensive osteosclerosis of the adjacent iliac bone (Fig 11) (5,9).

• Appendicular Skeleton

Involvement of the long bones occurs in approximately 30% of patients. The disease predominantly affects the metaphyseal regions of the distal femur and proximal tibia, but the fibula, humerus, radius, and ulna can also be involved (2,7,9). At radiography, the lesions often appear aggressive, consisting of osteosclerosis or osteolysis and periosteal new bone forma-



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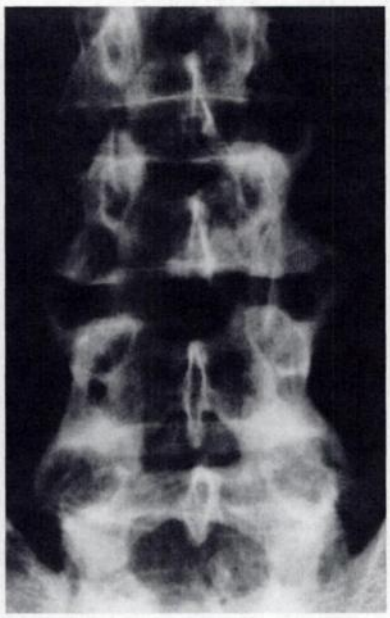

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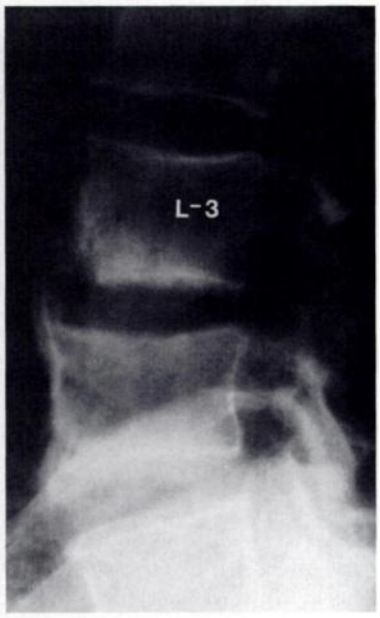

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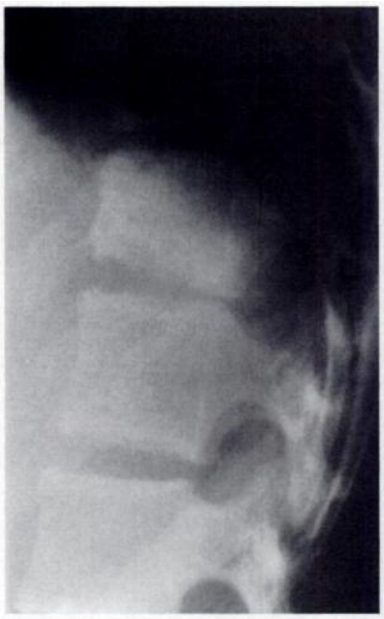

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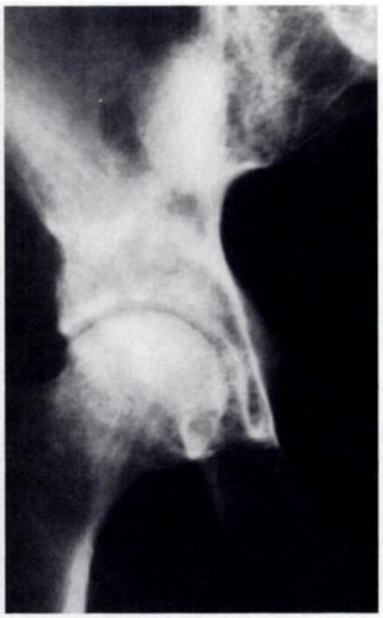


11.

Figures 8–11. **(8)** Anteroposterior radiograph of the lumbar spine shows diffuse homogeneous osteosclerosis of L-4. (Reprinted, with permission, from reference 10.) **(9a)** Anteroposterior radiograph of the lumbar spine shows prominent syndesmophytes. (Reprinted, with permission, from reference 10.) **(9b)** On a lateral radiograph, end-plate erosions and osteosclerosis are seen at L-3 to L-4 and L-4 to L-5 together with anterior syndesmophytes. An erosion along the anterior aspect of the L-3 vertebral body, L3-4 disk space narrowing, and loss of definition of the adjacent vertebral end plates are also present. **(10a)** Lateral radiograph of the thoracic-lumbar region shows disk space narrowing at T12-L1 with inferior end-plate erosions at the T-12 vertebral body. **(10b)** On a sagittal spin-echo T2-weighted MR image, the deformed T-12 vertebral body has high signal intensity, consistent with osteitis. **(11)** Anteroposterior radiograph of the right hip reveals erosions and fusion of the right sacroiliac joint with osteosclerosis of the adjacent iliac bone. Osteosclerosis about the hip and loss of the right hip joint space are also seen.

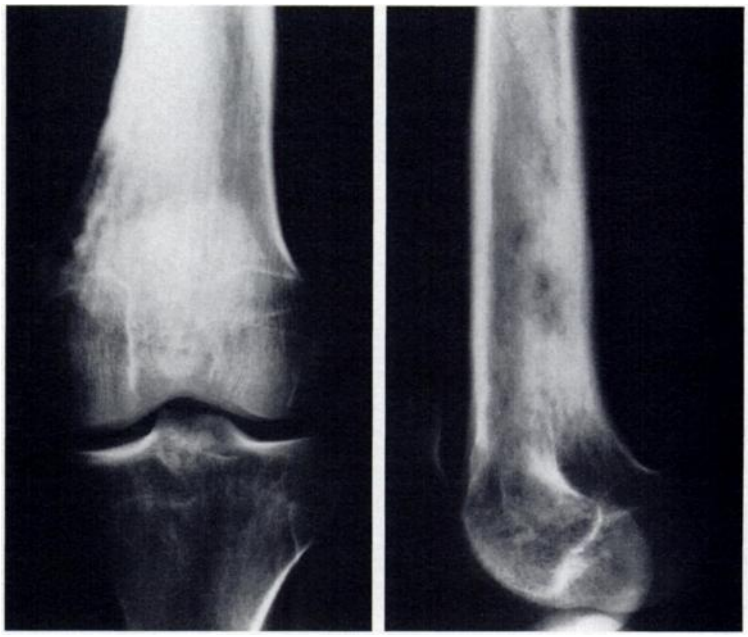


Figure 12. Anteroposterior **(a)** and lateral **(b)** radiographs of the femur show osteosclerotic and osteolytic lesions in the distal shaft. (Reprinted, with permission, from reference 10.)

a. b.

tion, usually with enlargement of the bone (Figs 12, 13). Radiologic findings may suggest infectious or tumorous conditions.

Synovitis and arthritis are usually associated with more characteristic bone involvement but can also be found in isolation. The knees, hips, and ankles are the most frequently affected joints, but small joints of the hands and feet, especially distal interphalangeal joints of the hands, can also be involved (1–3). Radiographic features of the acute phase of the disease include synovial inflammation with juxta-articular osteoporosis; in more advanced cases, the involved joint may show joint narrowing, marginal erosions, hyperostosis, and enthesopathy (Fig 14).

■ DIAGNOSIS

A skeletal lesion, especially at the sternocostoclavicular site, associated with palmoplantar pustulosis or acne is highly characteristic but not pathognomonic of SAPHO syndrome. Diagnosis is much more difficult if the sites of involvement or radiographic findings are atypical or if the patient is free of skin disease. However, the questioning of the patient has to be detailed, as a delay of several years can separate cutaneous and skeletal lesions (9). In such cases, biopsy of the bone lesions and follow-up—in some cases, over several years—may allow confirmation of the diagnosis of SAPHO syndrome. The main differential diagnoses are infectious osteomyelitis or spondylitis, osteo-

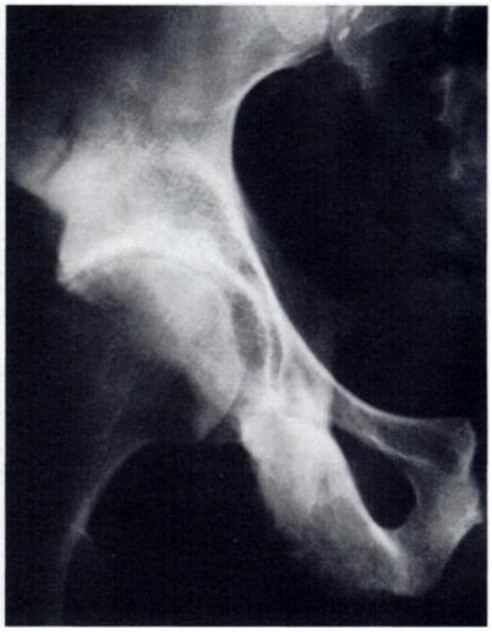
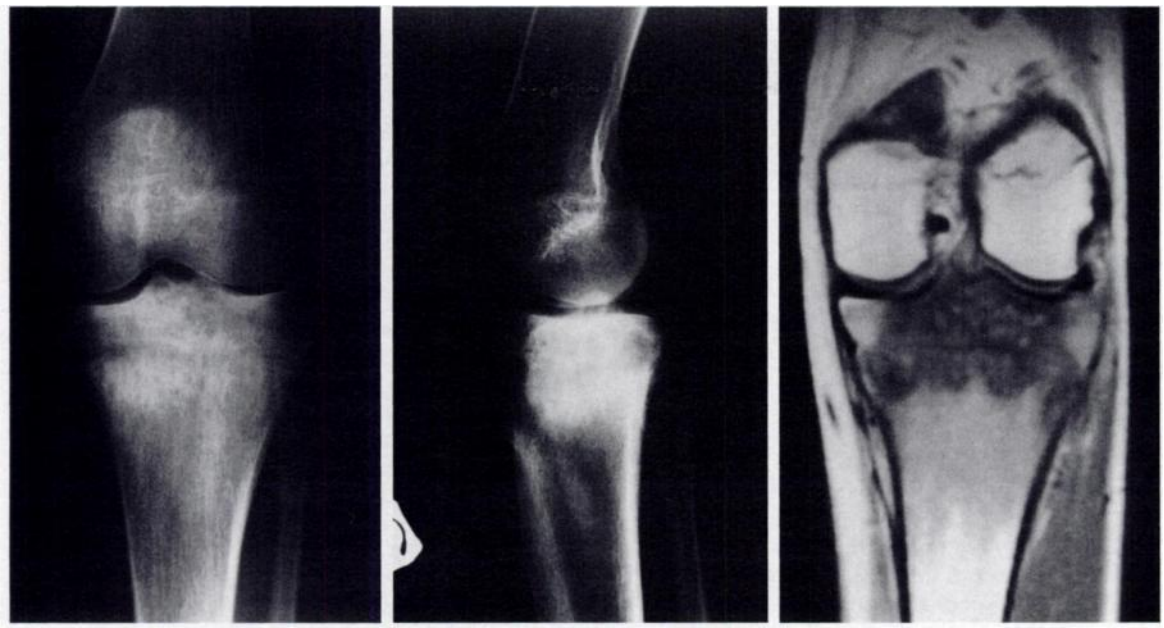
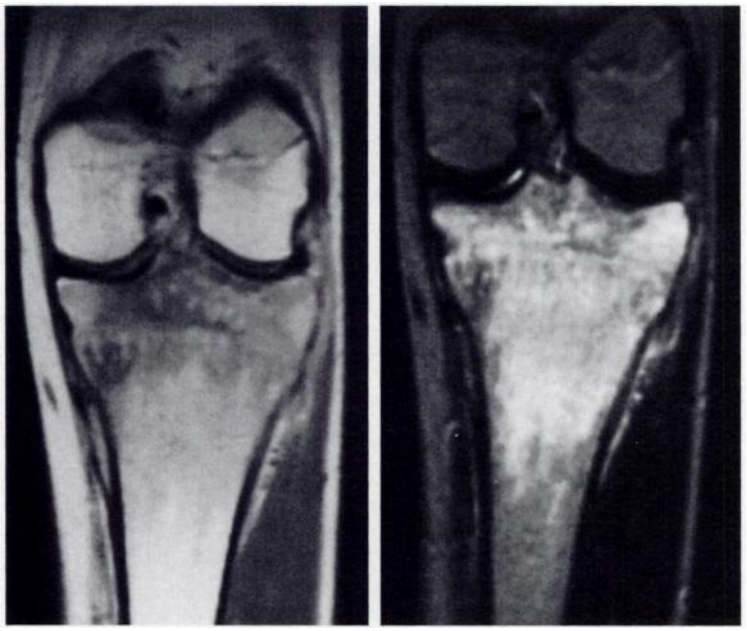


Figure 14. Anteroposterior radiograph of the right hip shows osteosclerosis of the right ischial bone with enthesopathy along the inferior border of the ischial tuberosity. Note the loss of the superior joint space in the right hip.



a. b. c.



d. e.

Figure 13. Anteroposterior **(a)** and lateral **(b)** radiographs of the knee demonstrate diffuse osteosclerosis of the proximal tibia with periostitis. **(c)** Coronal spin-echo T1-weighted MR image shows low signal intensity in the proximal tibia. **(d)** Gadolinium-enhanced coronal spin-echo T1-weighted MR image shows increased signal intensity in this region. **(e)** Coronal spin-echo T2-weighted MR image shows diffuse enhancement in the proximal tibia, representing osteitis.

sarcoma, Ewing sarcoma, metastasis, Paget disease, and aseptic necrosis of the clavicle.

■ TREATMENT AND PROGNOSIS

Nonsteroidal anti-inflammatory drugs are usually effective for the relief of pain (1,4). In cases of severe pain, a low dose of corticosteroids, analgesics such as codeine, or cyclosporine can be prescribed (7). The disease usually has a chronic course with unpredictable exacerbations and remissions of skeletal or skin lesions for many years. However, it is important for patients to know that the course of the disease is benign and that the long-term functional prognosis is good.

■ CONCLUSIONS

The common denominator of SAPHO syndrome is the peculiar aseptic skeletal involvement, which represents a link between the different manifestations. Awareness of the SAPHO syndrome should facilitate proper diagnosis and treatment.

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