

# An Infrequent Presentation of SAPHO Syndrome

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We describe a case of SAPHO (synovitis, acne, pustulosis, hyperostosis, and osteitis) with an unusual presentation in a 14 year-old girl with low grade fever which lasts 8 months, left low back pain and elevated erythrocyte sedimentation rates and protein C-reactive with chronic anaemia. A radiography of the lower limbs showed a lytic image with osteitis and hyperostose in the right fibula, as a casual finding. This information, in addition to the acne, pustulosis, sternoclavicular arthritis, and the studies got from the magnetic resonance image (MR) of spine, pointed out the diagnosis of SAPHO.

**Key words:** SAPHO syndrome. Spondyloarthropathy. Chronic recurrent multifocal osteomyelitis (CRMO).

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### Síndrome SAPHO de presentación infrecuente

Describimos un caso de síndrome SAPHO (sinovitis, acné, pustulosis, hiperostosis y osteítis) con una forma de presentación poco habitual, en una niña de 14 años de edad con febrícula de 8 meses de duración, dolor lumbar izquierdo y reactantes de fase aguda elevados con anemia normocítica y normocromica. En una radiografía de miembros inferiores se evidenció una imagen lítica con osteítis e hiperostosis en peroné derecho, como hallazgo casual tras una caída accidental. Estos datos, además del acné, la pustulosis, la artritis esternoclavicular y los estudios obtenidos por resonancia magnética (RM) de columna y gammagrafía ósea, orientaron el diagnóstico de SAPHO.

**Palabras clave:** Síndrome SAPHO. Espondiloartropatía. Osteomielitis multifocal recurrente crónica (OMRC).

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### Introduction

SAPHO syndrome<sup>1</sup> (synovitis, acne, pustulosis, hyperostosis, and osteitis) includes a variety of rheumatic alterations associated to skin lesions.<sup>2</sup> It generally presents during infancy and adolescence, mainly in females patients.

The distribution of the illness depends on the age of presentation. In adolescents and during middle adulthood, it mainly is localized to the sternoclavicular region, followed by the lumbar spine, the pelvis, and long bones. During infancy it affects long bones (tibia, femur, and ulna), the clavicle and the lumbar spine. The diagnosis of SAPHO syndrome is not difficult when the osteoarticular lesions are localized in the characteristic target areas. The gammagraphic bone scan image simulating a "cow horn" of the sternoclavicular joint is very specific to this syndrome.<sup>3</sup>

We present the case of an adolescent diagnosed with SAPHO syndrome, whose study was motivated by a low-grade fever and an elevation of the acute phase reactants.

### Clinical Case

A 14 year-old girl, followed at our hospital due to mid-afternoon low grade fever of 37.6°C during 8 months and normocytic, normochromic anemia with an elevation of the acute phase reactants, was seen for a 10 day episode of continuous pain in the left lumbar spine without urinary symptoms.

Among the relevant history of the patient we found an episode of hemolytic-uremic syndrome at age 4, an appendectomy (catarrhal appendicitis) at 12 years of age and was currently being followed for recurrent abdominal pain (with normal gastrointestinal transit studies, abdominal echography, and abdominal computerized tomography), and extrinsic asthma. Her mother had Sjögren's syndrome without treatment. There was no history of spondyloarthropathy or inflammatory intestinal disease.

On physical exploration we found obesity, pustulosis on the pubis and the internal part of the thighs (Figure 1), and palmoplantar keratoderma; she had noticeable selective pain upon palpation at the sternoclavicular joint and in the left lumbar spine area, without any signs of



**Figure 1.** Pustulosis of the internal part of the thighs.

nerve root compression. She also presented pain on the left Achilleal entheses. She did not have pain on the fibromyalgia trigger points and had no ulcers on the vulvae.

#### Complementary testing

Hemogram: hemoglobin, 11.7 g/dL; hematocrite, 33.9%; MCV, 81 fl; normal leucocytes; CRP, 20 mg/L; ESR, 42 mm/1st h.

Blood chemistry: uric acid, 6.5 mg/dL; ferritin, 65 ng/mL; immunoglobulin, C3, C4, and TSH, normal; rheumatoid factor, ANA, HLA-B27, urine culture, and a pharyngeal exudate were all negative; serology for mononucleosis and yersinia were negative; Schirmer's test, saliva secretion, and pathergy testing were negative.

The following imaging techniques were carried out: peroneal x-ray, showing a lytic image with osteitis, and hyperostosis in the right peroneal bone (Figure 2); normal chest x-ray; lumbar MRI showing a protrusion of L5-S1, with a diminished signal and a nodular lesion <1 cm, isointense on T1 and hyperintense on T2, adjacent to the right vertebral margin of D8, non-specific, and a thoracic bone scan that presented an increased uptake of the sternoclavicular joint that simulated a "cows horn" as well as an increased uptake in the right sternoclavicular joint (Figure 3).

SAPHO syndrome was diagnosed and treatment was initiated with naproxen and cloxacillin, showing a discreet improvement, after which the use of disease modifying anti-rheumatic drugs (DMARD) was proposed to the family (methotrexate and sulfasalazine) and pamidronate, which they rejected. The patient is currently receiving no treatment and symptoms, pain and elevated acute phase reactants persist.

**Figure 2.** Peroneal x-ray: lytic image with osteitis and hyperostosis in the right peroneal.

**Figure 3.** Thoracic bone scan: increased uptake of the sternoclavicular joint.

## Discussion

SAPHO syndrome is a controversial entity.<sup>3-6</sup> It was described by Kahn et al<sup>7</sup> to group a series of conditions with common findings, such as bone affection with aseptic osteitis that affects determined zones and the skin lesions in the form of palmar and plantar pustulosis as well as acne conglobata. In many of these cases, sacroileitis is found additionally, evolving as a spondyloarthropathy. On the other hand, chronic, recurrent, multifocal osteomyelitis (CRMO)<sup>8</sup> is a chronic, aseptic, non suppurative bone inflammation that affects multiple localizations, generally long bones and the clavicle, and less frequently the spine and pelvis, frequently affecting children and adolescents. It is also frequently associated with palmar and plantar pustulosis and has a favorable evolution.<sup>9</sup> This similarity between entities makes it impossible to reach a consensus on whether they are separate diseases or a spectrum of the same disease,<sup>10</sup> though it seems that SAPHO syndrome carries a worse prognosis in the long term.

The fundamental component of SAPHO is an inflammatory osteitis that can or cannot be associated to skin lesions, presenting negative bacterial cultures. These skin lesions typically are palmar and plantar pustulosis and acne (55.7 and 19.3%, respectively). They can either precede, occur simultaneously or after the start of the skin lesions. The osteoarticular lesions include synovitis, hyperostosis, and osteitis. The distribution depends on the age of presentation, predominantly on the sternoclavicular region during adolescence, while during infancy it affects long bones (tibia, femur, and ulna), the clavicle and lumbar spine. Systemic manifestations are rare, but fever can sometimes be present.<sup>3</sup>

In the SAPHO syndrome with skin lesions, a high percentage of cases have detectable *Propionibacterium acnes* in the synovial fluid, but its role in the pathogenesis of the disease is not clear.<sup>9</sup> Imaging in this patient helped us orient the diagnosis, in spite of a negative joint fluid culture.

Conventional treatment<sup>11</sup> of the SAPHO syndrome (with non steroidal antiinflammatories, steroids and methotrexate) have not proven effective. There are currently several studies that support the superiority of pamidronate<sup>12-15</sup> for pain reduction and an improvement in functionality with few adverse events. This is a second-generation bisphosphonate that suppresses bone resorption and has anti-inflammatory properties. We think that knowledge on this syndrome is important because its diagnosis is unique and requires a high index of suspicion. We hope to stimulate pediatric rheumatologists to the careful inspection of the skin and the anterior thorax that, in our opinion, are key points in elucidating this condition.

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