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The challenging diagnosis of synovitis–acne–pustulosis–hyperostosis–osteitis (SAPHO) syndrome: A rare case report

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Abstract

Considered rare, the synovitis–acne–pustulosis–hyperostosis–osteitis (SAPHO) syndrome is a distinct clinical entity, associating skin manifestations and osteoarticular symptoms. Anterior chest wall pain centered at sternoclavicular and sternocostal joints is an important and characteristic clinical finding that can lead to its diagnosis. Radiologists and clinicians must be aware of synovitis–acne–pustulosis–hyperostosis–osteitis syndrome as it can mimic some of the more common disease entities such as Paget's disease. We report the case of a 63-year-old male patient, with no significant medical history, who presented to the dermatology department, with severe palmar and plantar pustulosis associated with polyarthralgia. Computerized tomography scan showed sternoclavicular hyperostosis, in favor of SAPHO syndrome, with regression of clinical symptoms after non-steroidal anti-inflammatory drug treatment.

Keywords

Hyperostosis, pustulosis, synovitis–acne–pustulosis–hyperostosis–osteitis, CT scan

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Introduction

SAPHO syndrome is an acronym referring to an uncommon form of spondyloarthropathy that is manifested by a combined occurrence of synovitis (S), acne (A), pustulosis (P), hyperostosis (H), osteitis (O). It was first described by Chamot et al.[1] in 1987 as a unifying theory to explain the association between cutaneous symptoms and osteoarticular diseases. This syndrome was known by more than 50 names, such as sternoclavicular hyperostosis, pustulotic arthro-osteitis, acne-associated arthropathy, and chronic recurrent multifocal osteomyelitis, which reflect the confusing claims made in the medical literature.[2,3] Therefore, this descriptive term encompasses the range of radiological and clinical presentations. The hallmark of the syndrome is anterior chest wall osteitis while extrathoracic sites of synovitis may also be seen, especially sacroiliac joint involvement in a bilateral or unilateral pattern. Skin abnormalities associated with the SAPHO syndrome are palmoplantar pustulosis (PPP) and acne. The value of laboratory analyses is limited, with only 13–30% of SAPHO patients being reported as having a positive human leukocyte antigen (HLA) B27 antigen. Thus, the radiologist plays a valuable role due to the characteristic osteoarticular manifestations which can help in determining the diagnosis. We report the case of a 63-year-old male patient, who presented to the dermatology department with severe palmar and plantar pustulosis associated with polyarthralgia. Computerized tomography (CT) scan showed typical sternoclavicular hyperostosis, which led to the diagnosis of SAPHO syndrome.

Case report

A 63-year-old male patient with no significant medical history, presented to the dermatology department with bilateral pustules on his feet for 1 year without any clear predisposing

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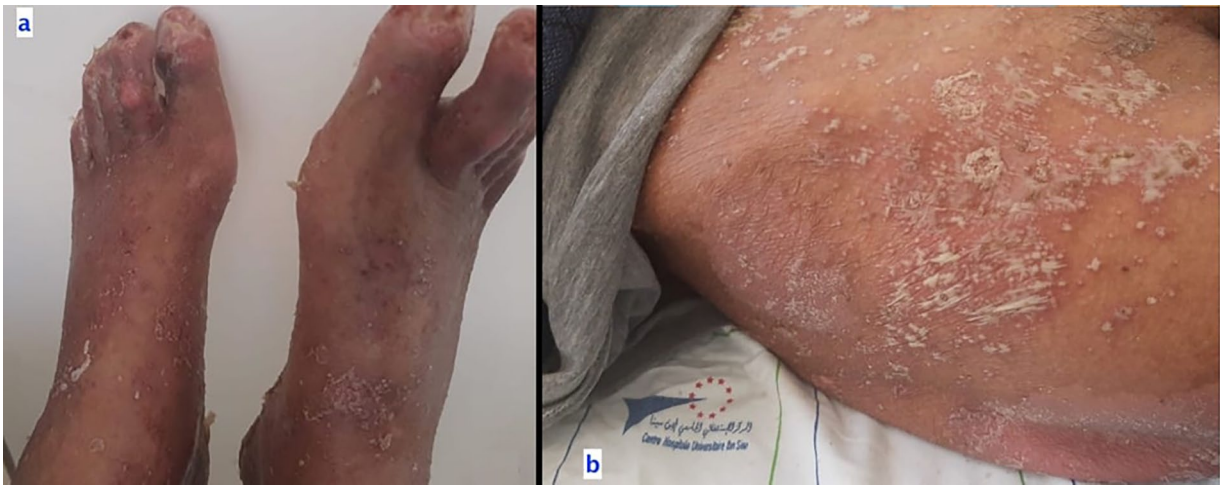

Figure 1. Bilateral pustules on the feet and interdigital surfaces associated with onychosis and anonychia (a), associated with confluent pustules on the groin and the hip giving the appearance of bubbles (b).

cause. He later developed confluent pustules on the groin and interdigital surfaces of the feet. Clinical examination on admission revealed nodulocystic acne involving the patient's face and back. Bilateral pustules on the soles and interdigital surfaces of the feet were found associated with onychosis and anonychia (Figure 1(a)). There were also pustules on the groin, some of which were confluent giving the appearance of bubbles (Figure 1(b)). No fever was noted and the patient's vitals were normal. Blood tests revealed an elevated erythrocyte sedimentation rate and C-reactive protein (60 mm/h and 101 mg/l respectively). Routine blood analysis showed slight increases in leukocytes (11×109/l). The HLA-B27 test was negative, and the rheumatoid factor was below 20 UI/ml (also negative).

A pelvis CT scan was realized revealing hyperostosis and sclerosis on the right side of the symphysis pubis, evoking Paget disease (Figure 2). The patient then reported polyarthralgia, chest pain, and swelling in the left sternoclavicular joint area. A thorax and abdomen CT scan was then realized, revealing hyperostosis of the manubrium with irregularities and sclerosis on the edges of the manubrio-sternal, the first sternocostal joints bilaterally, and the left sternoclavicular joint (Figure 3). After consulting the rheumatology and internal medicine teams, the dermatologists evoked three main diagnoses: osseous tuberculosis, SAPHO syndrome, and osteomyelitis. A QuantiFERON-TB Gold test was realized which was negative, and according to the clinical manifestations (skin lesions and osteoarticular involvement) and CT results, the diagnosis of SAPHO syndrome was made. The patient was then started on non-steroidal anti-inflammatory drugs (NSAIDs) by a multidisciplinary team formed of dermatologists and rheumatologists. On his 2-week follow-up consultation, we noted a significant regression of clinical symptoms.

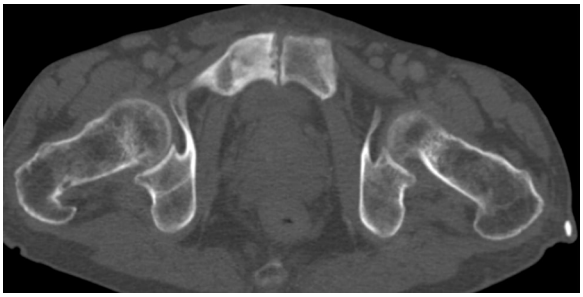

Figure 2. Axial computerized tomography scan of the pelvis showing sclerosis and irregular edges on the right side of the symphysis pubis.

Discussion

When the term "SAPHO" was first proposed, it described a group of diseases with similar osteoarticular involvement (mainly anterior chest wall osteitis), that were usually associated with various forms of dermatological symptoms. Its etiopathogenetic mechanism remains unclear, although several hypotheses have been reported involving bacteriologic, immunologic, and genetic factors. According to Hayem, SAPHO syndrome is a type of "reactive osteitis," a pathogenic sequence in which Propionibacterium acnes, an opportunistic organism, exploits genetically established weaknesses in antibacterial defense mechanisms, subsequently inducing auto-amplification of the inflammatory response, possibly with an autoimmune component.[4]

Diagnosing SAPHO syndrome is based on characteristic skin manifestations, and radiological results, with no history of other inflammatory arthropathy or primary cancer.[5] It is usually seen in young or middle-aged patients (30–50 years

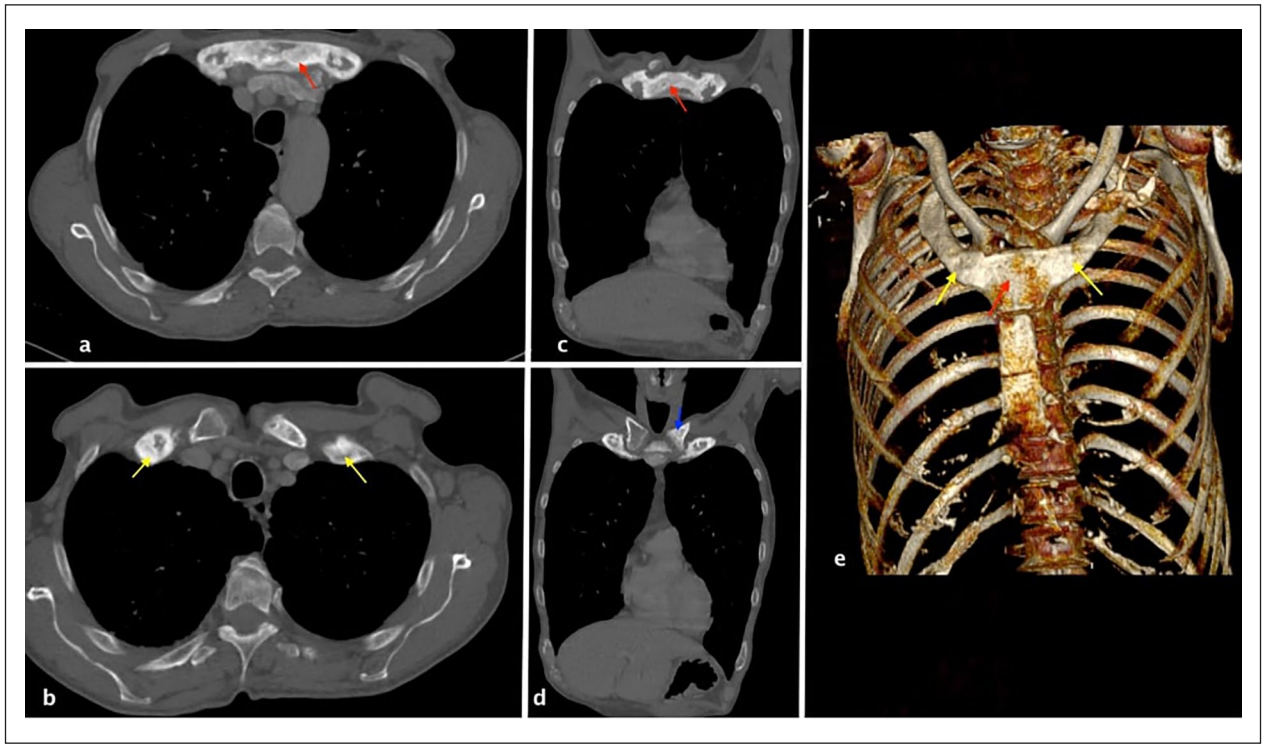

Figure 3. Axial thorax computerized tomography scan (a) and (b), coronal reformatted images (c) and (d), and three-dimensional volume rendering (e) showing hyperostosis of the manubrium (red arrow), with irregularities and sclerosis on the edges of manubriosternal, and the first sternocostal joints (yellow arrow) bilaterally and the left sternoclavicular joint (blue arrow).

as an age average).[6] Nevertheless, it has also been reported in children, and at present it can be seen at any age.[7] In general, males and females are almost equally affected, with a possible gender predilection regarding some skin symptoms such as PPP being more common in females and acne being more common in males.[8] Dermatological and skeletal diseases don't usually occur parallelly, and they may be separated by several years. Thus, it makes the final diagnosis of SAPHO syndrome difficult in some cases, especially when skin manifestations are absent.[9] Palmoplantar pustulosis and acne have been reported in 51.7% and 15.3% of patients with SAPHO syndrome, respectively.[8] Most patients report soft-tissue edema, discomfort, and mobility restriction related to the affected skeletal locations. Although systemic symptoms are uncommon, a low-grade fever might occasionally occur.[10] Laboratory findings include often an increased erythrocyte sedimentation rate with sometimes an increase in C-reactive protein.[6] The majority of other laboratory values fall within acceptable bounds. Early studies have suggested that the frequency of HLA-B27 increases in patients with SAPHO syndrome compared to the general population.[3] However, possession of this antigen was nowhere near as frequent as seen in ankylosing spondylitis (where 85% are positive).[9] Radiology plays an important role in diagnosing SAPHO syndrome since anterior chest wall osteitis is the hallmark of the SAPHO syndrome.[2] If clinical signs and symptoms are not very obvious, characteristic radiological findings can help prompt the diagnosis. Polyostotic involvement is usually seen with the sternoclavicular junction being the most common site of involvement in adults, followed by the spine and sacroiliac joints.

On X-rays and CT scans, there can be diffuse thickening of the periosteum, cortex, and endosteum associated with osteolysis and osteosclerosis. An ossified costoclavicular ligament and hyperostosis at the sternal end of the first ribs are important early findings.[11] Sacroiliitis can be seen in up to 50% of the cases with erosions and sclerosis along the iliac side of the joint usually occurring unilaterally.[9] These abnormalities can be seen on plain radiographs; CT remains the modality of choice to determine the extent of the lesions. Spine involvement is the second most common site, with the thoracic spine most commonly affected.[12] The lesions may start at the vertebral body or end plates, and nonspecific spondylitis and diskitis are the most common imaging findings.[11]

Magnetic resonance imaging (MRI) can help in revealing subclinical foci thus identifying active lesions which are shown by bone marrow edema on water-sensitive sequences such as T2 weighted and STIR (short tau inversion recovery).[12] The bony changes may sometimes extend to adjacent soft tissues on MRI. In the spine, high T2 signal in the disc, vertebral sclerosis, hyperostosis, and paravertebral ossification can be seen. In addition, a lack of abscess formation, sequestra, or paravertebral soft tissue involvement can differentiate SAPHO syndrome from pyogenic spondylodiskitis.[11]

Table 1. Comparison between the diagnostic criteria of SAPHO syndrome and the elements of our case report.

SAPHO syndrome	Our case
Diagnostic criteria by Benhamou et al.: At least one of the following four conditions[1]: 1. Osteoarticular manifestations of acne conglobate, acne fulminans, or hidradenitis suppurativa; 2. Osteoarticular manifestation of PPP; 3. Hyperostosis (of the ACW, limbs or spine) with or without dermatosis; 4. CRMO involving the axial or peripheral skeleton with or without dermatosis	Hyperostosis with dermatosis
Diagnostic criteria by Kahn and Khan: At least one of the following three conditions[3]: 1. Chronic recurrent multifocal sterile and axial osteomyelitis, with or without dermatosis 2. Acute, subacute, or chronic arthritis associated with PPP, pustular psoriasis, or SA 3. Any sterile osteitis associated with PPP, pustular psoriasis, or SA	Sterile osteitis associated with palmoplantar pustulosis

ACW: anterior chest wall; CRMO: chronic recurrent multifocal osteomyelitis; PPP: palmoplantar pustulosis; SA: severe acne.

Whole-body bone scintigraphy with technetium-99m methylene diphosphonate (Tc-99m MDP) is also another modality to help diagnose this syndrome, particularly for detecting multiple and early bone involvement. It has been used to differentiate between active and inactive lesions and distinguish SAPHO lesions from bony metastases.[13] Symmetric high radionuclide uptake in the sterno-costoclavicular joints can be seen and is termed a "bull's head sign."[11]

Differential diagnosis can include other diseases such as osteomyelitis, Paget's disease, osteitis condensans of the clavicle, POEMS (polyneuropathy, endocrinopathy, monoclonal gammopathy, and skin changes), osteosarcoma, Ewing Sarcoma, and metastases, since having similar imaging findings.[11] Nevertheless, some features can raise suspicion thus helping in reaching a proper diagnosis. SAPHO should be strongly suspected in patients with multiple bony abnormalities involvement including joints, axial and appendicular skeleton associated with anterior chest wall pain, unremarkable lab tests, and no history of inflammatory arthropathy or primary cancer. A biopsy can be needed to exclude other diagnoses, in cases where clinical and radiological features are ambiguous.[10]

To sum up, Benhamou and colleagues[1] proposed diagnostic criteria in 1988 for SAPHO syndrome based on clinical manifestations and radiological examinations, including bone, articular, or skin manifestations. Kahn and Kahn[3] proposed another commonly used diagnostic criterion mainly based on clinical symptoms. These criteria are summarized in Table 1 along with a comparison to our case report.

No specific guidelines regarding the treatment of SAPHO are proposed, and it remains mainly symptomatic. NSAIDs are usually the mainstay of treatment. Others such as corticosteroids, bisphosphonates antirheumatic drugs, can be used as second-line agents.[14] Antibiotics are used in cases where a biopsy culture is positive for *Propionibacterium acnes*, while in other cases, antibiotics have no effect.[10] Some open-label studies and case reports suggested anti-TNF-alpha agents, which have usually led to sustained improvement of osteoarticular involvement.[15,16] However, skin manifestations may follow a less predictable course and relapses of PPP have been observed.[16]

Conclusion

As its acronym says, SAPHO syndrome is *a distinct clinical entity representing the involvement of the musculoskeletal and dermatologic systems*. Typically, it is a chronic condition that progresses slowly over many years and is characterized by recurrent episodes of remission and recurrence. Radiologists should be aware of its manifestations since their role is crucial in diagnosing it and differentiating it from other diseases. Treatment outcomes are frequently poor, particularly when it comes to skin involvement. However, because there is frequently an eventual spontaneous remission, the long-term prognosis is favorable.

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Author contributions

Y.E.H. was responsible for manuscript concept, design as well as editing and literature search. K.I. helped in manuscript editing, literature search, and manuscript review. S.E.S. contributed to the conception and design. N.M.B. contributed to acquisition, analysis, and interpretation. I.N. critically revised the manuscript and gave final approval.

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Ethics approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed consent

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