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Constitutional Syndrome: First Case Reported as a Debut of Synovitis, Acne, Pustulosis, Hyperostosis and Osteitis Syndrome

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Abstract

SAPHO syndrome (Synovitis, Acne, Pustulosis, Hyperostosis and Osteitis) is a rare, heterogeneous, chronic autoinflammatory disease characterized by dermatological and osteoarticular clinical manifestations affecting multiple regions. Systemic manifestations are rare. We present the case of a middle-aged man with polyarthralgia and constitutional syndrome under study. He underwent diagnostic imaging tests that helped establish the differential diagnosis as SAPHO syndrome without skin involvement. To our knowledge, this is the first reported case of SAPHO syndrome that debuted as a constitutional condition, and this syndrome should be considered in the diagnostic spectrum.

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Introduction

SAPHO syndrome (Synovitis, Acne, Pustulosis, Hyperostosis and Osteitis) is an autoimmune-autoinflammatory disorder. It is linked to genetic determinants associated with Human Leukocyte Antigens (especially HLA-A26, HLA-B27, HLA-B39, HLA-B61), infections (e.g., *Propionibacterium acnes*, *Staphylococcus aureus*, *Haemophilus parainfluenzae*, *Actinomyces*), and immunological factors (e.g., increased Th17 cells in the peripheral blood, undetectable plasma IL-10 levels) [1].

Epidemiologically, the annual prevalence of SAPHO syndrome ranges from 0.00144 per 100,000 people (in Japan) to nearly 10 in 100,000 (in people of European descent) [2]. It generally affects people in middle age and is more frequent in women. Despite its low prevalence, the syndrome can be masked by other diseases, such as invasive neoplasms, so it is important to be familiar with it and know which diagnostic tests are the most appropriate to identify it. Among the available tests, we focus on PET-CT due to its usefulness in supporting and establishing the differential diagnosis (ruling out seronegative spondyloarthropathies, psoriatic arthritis, anterior chest wall syndrome, and neoplasms), since SAPHO syndrome can be considered a diagnosis of exclusion [3-10].

Case Presentation

We present the case of a 51-year-old man with an unremarkable pathological history who presented with a constitutional syndrome, following three weeks of joint pain and bouts of fever of up to 39ºC. Physical examination revealed pain at the level of the bilateral sternoclavicular junction and in both tibiotalar joints, as well as weakness in the shoulder and pelvic girdle. The patient had no skin changes or other accompanying symptoms.

Blood tests showed leukocytosis (14,700 cells/μL), neutrophilia (76% neutrophils), C-reactive protein of 14.63 mg/dL, and an erythrocyte sedimentation rate of 65 mm in the first hour. Muscle enzymes (CPK, LDH, aldolase, GOT, GPT) and tumor markers were normal. ANA (<1/80), ASMA (<1/80), and anti-LKM (<1/80) titers were negative, as was anti-citrullinated peptide antibody (<1

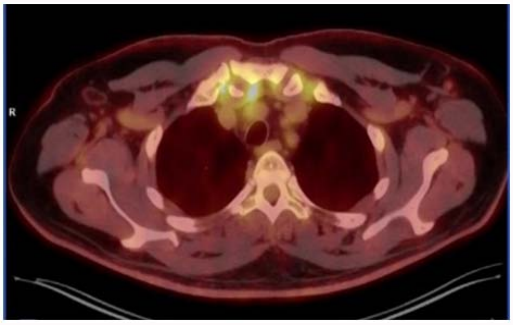


Figure 1: Thickening of both sternoclavicular joints on the CT. On performing a right shoulder arthrocentesis, a fluid with inflammatory characteristics was obtained, with 30,000 leukocytes (84% neutrophils), glucose of 89 mg/dL, and negative culture.

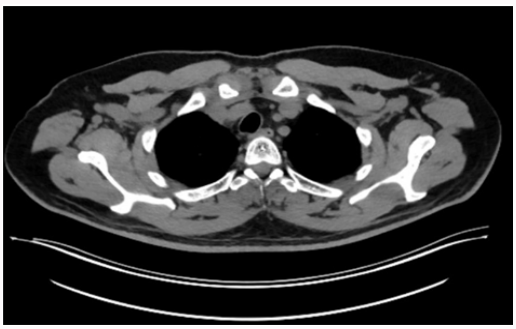


Figure 2: With increased uptake of the radiotracer at that level in the PET study. On performing a right shoulder arthrocentesis, a fluid with inflammatory characteristics was obtained, with 30,000 leukocytes (84% neutrophils), glucose of 89 mg/dL, and negative culture.

IU/mL).

The ultrasound showed increased space in the right subacromiodeltoid bursa and at the level of the tibiotalar joint, an increase in the bilateral Doppler flow and diffuse thickening of both Achilles tendons. There was a dramatic increase in the Doppler flow in both metacarpophalangeal joints and an increase in the adjacent soft tissues. The cervical-thoracic-abdominal CT showed bilateral thickening of the sternoclavicular joints (Figure 1), with increased uptake in the PET images (Figure 2) along with signs of arthropathy in the dorsal column and two instances of spinous apophysitis.

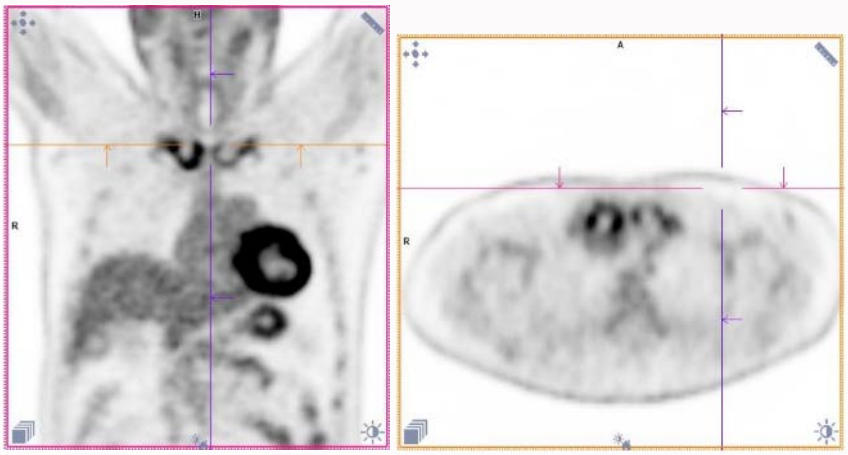
On suspicion of SAPHO syndrome, a bone scintigraphy was requested, confirming increased uptake in the sternoclavicular joints, predominantly the right one (Figure 3A and 3B).

Discussion

We present a clinical case of an adult male with polyarthralgia and constitutional symptoms, fever, increased acute phase reactants, and imaging tests that helped guide the clinical judgment and establish the differential diagnosis. SAPHO syndrome is an entity that affects middle-aged adults and presents as frequent osteoarticular pain. In most cases, there is true axial and peripheral arthritis (which most frequently affects the sternoclavicular joints), sternoclavicular and spinal hyperostosis, and recurrent foci of osteitis [3,4,7,8]. The syndrome may be accompanied by skin lesions such as acne, palmoplantar pustulosis, and hidradenitis suppurativa. In fact, skin involvement usually precedes the onset of joint symptoms, although it can occur at any time during the disease. The epidemiology of this entity is difficult to define given its low prevalence (approximately 1/10,000 people, with a certain predominance of middle-aged women), and it frequently goes undetected or has a delayed diagnosis [1,10].

Diagnostic imaging techniques help to establish a differential diagnosis. CT can show the presence of hyperostosis, bone hyperplasia at the insertion points of the costoclavicular ligament, foci of osteitis, and other chest wall abnormalities at an early stage of the disease [11-14]. Whole-body bone scintigraphy can show the classic "bull's head sign" in approximately a third of patients (reflecting the elevated uptake at the level of the sternal angle and sternoclavicular joint), which helps to confirm the suspected diagnosis of SAPHO syndrome [11,15,16]. Bone scintigraphy is especially important for diagnosing atypical or incomplete forms of SAPHO syndrome (for example, in the absence or atypical presentation of skin lesions) [9,17]. In early stages of the disease, 85% to 95% of cases will present hyper-uptake of the tracer in the anterior part of the thoracic cavity and the characteristic inflammatory involvement of the sternoclavicular and costosternal joints, with true arthritis in 90% of cases [2,8-14]. The chest X-ray was normal in our patient, as is typical in the initial stages of the disease [15].

In recent years, the use of PET-CT for the differential diagnosis of SAPHO has increased notably. These scans can reveal multiple skeletal lesions in the anterior or spinal chest wall, low-moderate FDG uptake,



Figures 3: A and B) Bone scintigraphy with increased uptake of the radiotracer in both sternoclavicular joints, predominantly in the right one.

and the coexistence of osteolysis and osteosclerosis. The convergence of the functional information on 18FDG uptake demonstrates the presence of anatomically located active inflammatory lesions. Diagnostic PET-CT is also useful to determine the stage of SAPHO syndrome. Early-stage disease is characterized by osteolytic bone destruction with increased FDG uptake, whereas the bone lesions are inactive in the late stage, resulting in normal FDG uptake. 18FDG-PET/CT also allows us to differentiate benign lesions from metastatic bone lesions [18-20]. In our case, the FDG uptake shown in the PET-CT was low/moderate, which allows the differential diagnosis with other diseases.

In our case, no skin lesions were observed. The appearance of these lesions is not essential for reaching the diagnosis, as they can appear after arthritis in 30% to 60% of cases, especially if the patient does not start and maintain adequate treatment. Typical skin involvement includes palmoplantar pustulosis, persistent conglobata acne, and hidradenitis suppurativa [2,3].

Following the initiation of treatment with a descending regimen of prednisone 30 mg and follow-up in outpatient clinics, the patient reported adequate pain control and presented synchronous resolution of polyarthralgia and constitutional symptoms. Acute phase reactants showed normalization on successive visits, with no appearance of skin lesions to date. The course of the disease is usually chronic and eventually resolves spontaneously.

In patients who present constitutional syndrome associated with polyarthritis, especially with joint involvement in the anterior part of the thorax, and elevated acute phase reactants, SAPHO syndrome must be included in the differential diagnosis, even without skin alterations. Bone scintigraphy, CT, and PET/CT will help establish the definitive clinical judgment. To the best of our knowledge, this is the first case of SAPHO syndrome presenting as a constitutional syndrome.

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