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Case Report

Clinical manifestation and diagnostic challenges of SAPHO Syndrome: a case report

Thami Ellen Busanello Spanevello [1,*], Lucas Teodoro Rodrigues [1], Márcia Regina Rosa Scalcon [2]

[1] Hospital Universitário de Santa Maria, Federal University of Santa Maria, Rio Grande do Sul, RS, Brazil.
[2] Departamento de Clínica Médica, Federal University of Santa Maria, Rio Grande do Sul, RS, Brazil.

* Correspondence: thamiellen@hotmail.com.

Abstract: The SAPHO syndrome, characterized by synovitis, acne, pustulosis, hyperostosis, and osteitis, is a rare disease of unknown prevalence and probably underdiagnosed. Its diagnosis can be confirmed by correlating the clinical symptoms with the radiological findings. However, it is challenging to do so since the clinical manifestations of this disease are diverse, with no confirmatory serological marker, and the radiological alterations can be nonspecific. This study is aimed to report the case of a patient with SAPHO syndrome, with an unusual clinical presentation, and the challenges faced to establish the diagnosis.

Keywords: Synovitis; Acne; Pustulosis; Hyperostosis; Osteitis.

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1. Introduction

SAPHO syndrome is a rare condition characterized by synovitis, acne, pustulosis, hyperostosis, and osteitis [1]. It is probably underdiagnosed and has an estimated prevalence of less than 1/10,000, with the most reported cases being from eastern and northern Europe and Japan [2-4]. It mainly affects young and middle-aged adults, predominantly in the average age of 30 and 50, and is more common in women [5,6]. The pathogenesis remains uncertain and includes a multifactorial condition that associates genetic susceptibility, autoimmunity, and infectious components [5,7]. Clinical and imaging findings guide the diagnosis, and with no specific serological marker, pose a challenge in clinical practice [1].

Here, we describe a case of unusual presentation of SAPHO syndrome, highlighting clinical and radiological aspects of the disease and drawing attention to diagnostic challenges. Thus, it aims to warn about the importance of considering SAPHO syndrome as a differential diagnosis of osteoarticular and skin conditions.

2. Case Report

A 64-year-old female patient, with chronic low back pain for more than ten years, had been under investigation for osteoblastic lesions in the lumbar and thoracic spine for four years. She underwent tests to investigate solid neoplasia and multiple myeloma, all of which were negative. Bone scintigraphy showed increased radioisotope uptake in different locations, such as the dorsal, lumbar, and sacral spine, costovertebral joint of the first left rib, joint of the first metacarpal of the left hand, and minor trochanter of the right femur. She underwent a vertebral bone biopsy, wherein the anatomopathological examination showed bone tissue with a predominance of plasmocytes, however, with negative immunohistochemistry for neoplasia. The patient even underwent empiric radiotherapy,

slightly improving the lesions radiologically. Despite this, the pain persisted, requiring treatment with analgesics, anti-inflammatories, and dual-action antidepressants. During follow-up, the patient developed pustular lesions on the palms of the hands and in the frontal region of the hair implantation.

A dermatologist ruled out pustular and palmoplantar psoriasis. A new computed tomography scan of the lumbar spine showed, among other findings, sclerosis and hypertrophy of the spinous processes of the lumbar vertebrae (Figure 1). Additionally, she had persistently high erythrocyte sedimentation rate and C-reactive protein level; human leukocyte antigen B27 was negative. Following the diagnostic hypothesis of SAPHO syndrome, treatment with methotrexate was initially instituted, with the need for a subsequent switch to immunobiological therapy (etanercept), progressing with appropriate symptomatic relief.

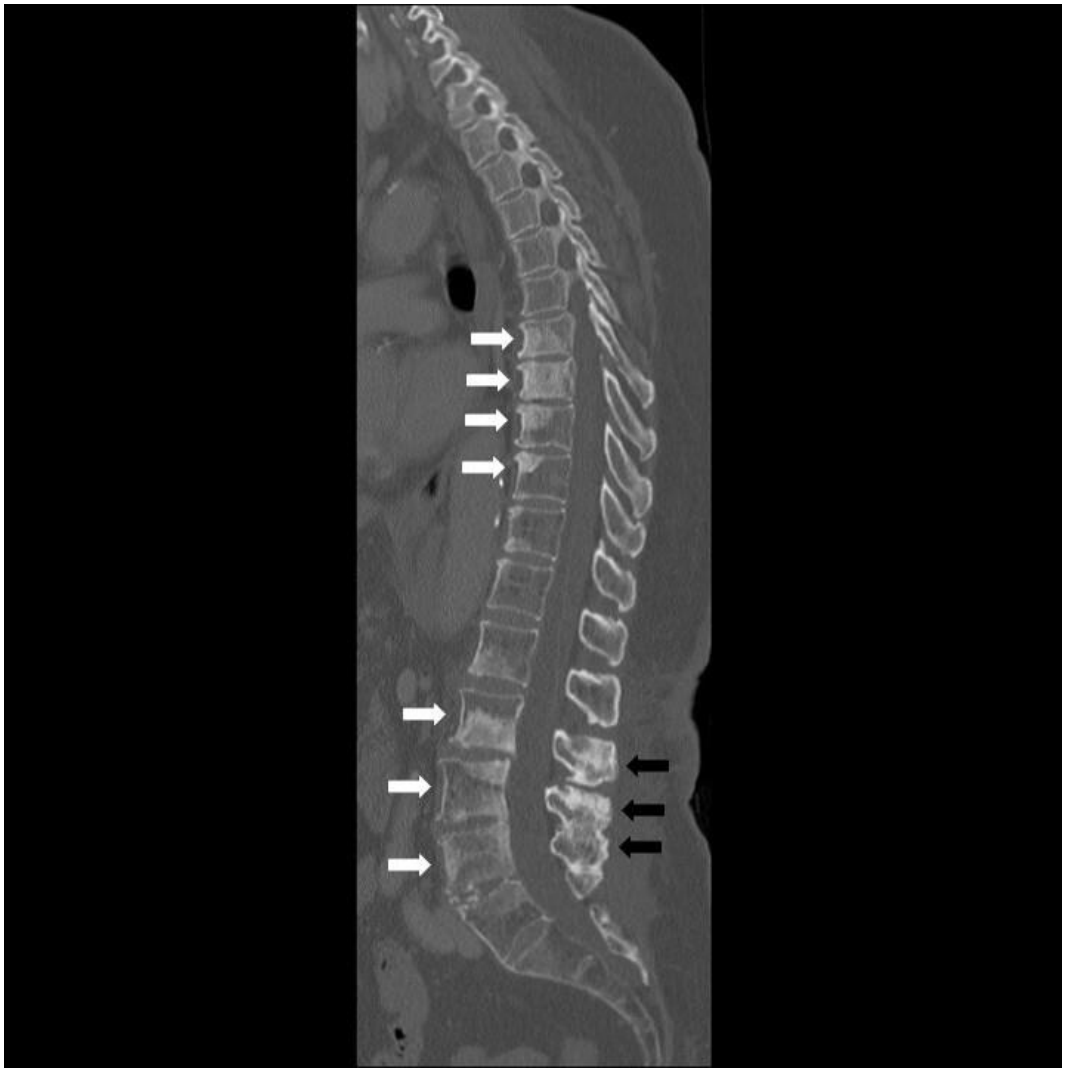

Figure 1: Computed tomography shows sclerosis in vertebral bodies, mainly T8 to T11 and L3 to L5 (white arrows), and sclerosis and hypertrophy of spinous processes of lower lumbar bodies (black arrows).

3. Discussion

Considering the clinical manifestations of SAPHO syndrome, arthritis is the most prevalent, observed in up to 92.5% of cases. Involvement is primarily of the axial skeleton (mainly anterior chest wall, followed by spinal and sacroiliac joints), but peripheral joints

may also be affected [5,6]. Cutaneous manifestations are varied (typically palmoplantar pustulosis and severe acne) and may appear before, concomitantly, or after the onset of joint lesions. Some patients, however, may not have skin lesions [1, 5, 6]. Nonspecific systemic signs, such as increased inflammation markers and fever, are uncommon [1]. Imaging exams, such as computed tomography, magnetic resonance imaging, and bone scintigraphy, play vital roles. The clinical findings comprise arthritis, synovitis, and chronic bone inflammation, with a predominance of osteitis and hyperostosis [8].

There is circumstantial evidence about the genetic influence on the pathogenesis, as there are reports of familial cases, including between twins. A study has attempted to associate genes *PSTPIP2*, *LPIN2*, and *NOD2* with the development of the SAPHO syndrome. However, this association was not significant. In this context, there are even more questions than answers [9,10]. Therefore, the study´s patient did not undergo genetic testing because there was no access to a laboratory or financial conditions.

Some authors propose different diagnostic criteria for SAPHO syndrome (Table 1), with those from 2003 being considered more accurate [1,5]. Diagnosis can be challenging when there are atypical osteoarticular lesions in non-characteristic sites, particularly with no associated skin lesion [7]. Due to its complexity and varied clinical presentation, differential diagnoses may involve several inflammatory, neoplastic, and infectious diseases, like rheumatoid or psoriatic arthritis, Behçet's disease, chronic bacterial osteomyelitis, osteosarcoma, and metastatic tumors [1].

Figure 1: Proposed diagnostic criteria for SAPHO syndrome based on Rukavina [5] and Liu [1].

Benhamous and colleagues, 1988	**Kahn and Kahn, 1994**	**Kahn modified, 2003**
At least 1 of the 4:	**At least 1 of the 3**:	**At least 1 of the 5**:
1) Osteoarticular manifestation and severe acne (fulminans, conglobata, hidradenitis suppurativa).	1) Axial and sterile recurrent multifocal chronic osteomyelitis, with or without dermatosis.	1) Osteoarticular involvement associated with vulgar psoriasis and palmoplantar pustulosis.
2) Osteoarticular manifestation and palmoplantar pustulosis.	2) Acute, subacute or chronic arthritis associated with palmoplantar pustulosis, severe acne, or pustular psoriasis.	2) Osteoarticular impairment associated with severe acne.
3) Hyperostosis with or without dermatosis.	3) Any sterile osteitis associated with palmoplantar pustulosis, severe acne, or pustular psoriasis.	3) Isolated sterile hyperostosis/osteitis (exception: Propionibacterium acnes growth).
4) Recurrent multifocal chronic osteomyelitis in the peripheral or axial skeleton, with or without dermatoses.		4) Recurrent chronic multifocal osteomyelitis (children).
		5) Osteoarticular involvement associated with inflammatory bowel disease.
		- Exclusion criteria: bone tumors, infectious osteitis, non-inflammatory bone lesions.

4. Conclusion

This case report shows how variable the presentation of the SAPHO syndrome can be and the challenges associated with establishing the diagnosis. Despite proposed diagnostic criteria and the aid of imaging tests, SAPHO syndrome does not have a specific serological marker, which requires thorough knowledge about the disease and high clinical suspicion for the hypothesis to be confirmed, representing, in most cases, a clinical challenge.

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Conflicts of Interest: None.

Supplementary Materials: None.

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