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Case Report

SAPHO Syndrome Mimicking Metastatic Breast Cancer: A Challenging Presentation

Maria Alejandra Jaimes-Reyes[1], Kia Persaud[2], James Jelinek[3], Florina Constantinescu[2]

Abstract

Synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome is a rare inflammatory disease characterized by typical skin lesions and aseptic osteoarticular involvement. Difficulties arise in diagnosing SAPHO syndrome due to its heterogeneous clinical presentation. A challenging case is presented involving a patient with chest pain and multiple bone lesions initially suspicious for metastatic breast cancer, in which the magnetic resonance imaging findings of bone marrow edema and osteitis were crucial to differentiate SAPHO from metastatic disease. The importance of a rigorous evaluation, advanced imaging, and a multidisciplinary approach to diagnosing SAPHO syndrome is emphasized.

Keywords: Case reports, hidradenitis suppurativa, osteitis, SAPHO syndrome

Introduction

Synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome is a rare disease in the autoinflammatory spectrum first described in 1987 by Chamot et al[1] based on 85 cases characterized by these clinical and radiological findings. Since the 1960s, up to 50 different terminologies were used for the conditions that involved concomitant skin and bone lesions until 1994, when Khan et al[4] proposed the diagnostic criteria.[2] Its pathogenesis is thought to be multifactorial, involving a combination of genetic, infectious, and immunological processes.[3] The incidence of SAPHO is unknown, likely due to misdiagnosis, misclassification of the disease, and lack of observational studies to estimate its frequency. Most of the initial cases were reported in Japan and northern Europe with few cases in the United States and the United Kingdom. Diagnosing SAPHO syndrome is challenging due to its clinical heterogeneity. Herein, a challenging case of SAPHO is presented that required multiple imaging modalities and multidisciplinary collaboration for diagnosis.

Case Presentation

A 43-year-old female with hidradenitis suppurativa (HS) previously treated with Adalimumab presented with a 1-year history of progressive back and chest pain associated with poor appetite, weight loss, and night sweats. On examination, active subcutaneous nodules with sinus tract formation located in the bilateral axillae consistent with active HS were noted (Figure 1). In addition, a tender and swollen bony prominence was noted over the upper sternum, along with tenderness to palpation of the thoracic spine. No other abnormalities including synovitis were noted. Initial basic metabolic panel and complete blood count were remarkable for mild anemia with a hemoglobin of 10.3 g/dL (reference range 11.1-15.9 g/dL), and inflammatory markers were elevated with a C-reactive protein of 59 mg/L (0-10 mg/L) and ESR of >130 mm/hr (0-20 mm/hr). Informed consent was obtained from the patient for publication purposes.

An initial computed tomography (CT) scan of the chest incidentally revealed extensive bilateral axillary lymphadenopathy, a necrotic right breast mass, and sclerotic bone metastases in the sternum and multiple thoracic vertebral bodies (Figure 2); these findings initially raised concern for metastatic breast cancer. As part of her diagnostic evaluation, a whole-body bone scan demonstrated abnormally increased activity in the proximal third of the sternal body, the costovertebral junction within the thoracic spine, and the bilateral acromioclavicular joints (Figure 3). The findings within the sternum and thoracic bodies were interpreted as metastatic disease, and the other findings were consistent with arthritis or degenerative changes (Figure 4A).

A multidisciplinary discussion was held between Dermatology, Musculoskeletal Radiology, Rheumatology, and Oncology, and the decision was to proceed with biopsies. A CT-guided biopsy of the sternal lesion

ORCID iDs of the authors:
M.A.J-R. 0000-0002-1186-4010;
K.P. 0009-0000-9894-4875:
J.J. 0000-0003-1367-3776:
F.C. 0000-0003-3978-6226.

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[1] Department of Internal Medicine, MedStar Washington Hospital Center, Washington D.C, USA
[2] Department of Rheumatology, MedStar Washington Hospital Center, Washington D.C, USA
[3] Department of Radiology, MedStar Washington Hospital Center, Washington D.C., USA

Corresponding author:
Maria Alejandra Jaimes-Reyes
E-mail: maria.a.jaimesreyes@medstar.net

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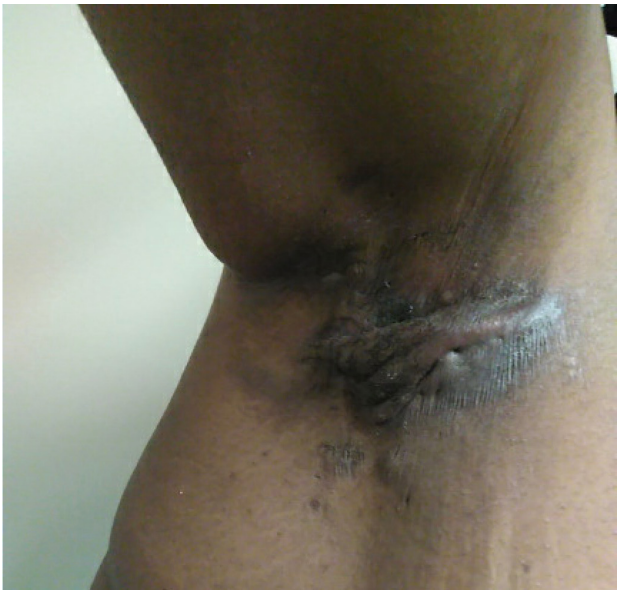

Figure 1. Photo of the right axilla showing hidradenitis suppurativa with nodules.

showed reactive changes but was negative for osteomyelitis or malignancy. A core biopsy of the left axillary lymph node showed no evidence of carcinoma or lymphoma (Figure 4B). Subsequent mammography revealed bilateral necrotic axillary masses corresponding to extensive sebaceous cysts/hidradenitis but no mass or malignant lesion.

Due to the absence of malignancy on histopathologic examination, further imaging was performed; an magnetic resonance imaging (MRI) of the thoracic spine showed diffuse patchy marrow changes suggestive of edema. Reactive inflammatory/degenerative changes were observed along the anterior discs at the T3-T4 and T4-T5 segments; osteitis with patchy sclerosis was present at the endplates and left paraspinal tissues of T8-T9 and T9-T10 (Figure 5A and B). After this work-up, the consensus among the multidisciplinary team was that the MRI findings were characteristic of SAPHO syndrome. She was discharged with a plan to start treatment with an anti-IL12/23 monoclonal antibody (Ustekinumab) and Rifampin and Clindamycin for her skin lesions. Bone-related symptoms initially improved with treatment. However, after 3 doses of Ustekinumab, skin manifestations worsened, and a repeat MRI of the spine showed the persistence of edema in the upper and mid-thoracic spine. These findings prompted modification to IL-17 blockade (Secukinumab). Informed consent was obtained from the patient for publication purposes.

Main Points

- Synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome is a benign autoinflammatory disease that can be mimicked by bone metastases.
- The evidence of bone marrow edema and osteitis on magnetic resonance imaging is characteristic of SAPHO syndrome and a key finding to differentiate this entity from metastatic disease.
- A multidisciplinary approach in patients with SAPHO syndrome might reduce the time from diagnosis to treatment and avoid unnecessary diagnostic and/or therapeutic interventions.

Discussion

Bone involvement is highly characteristic of SAPHO syndrome. It can present as osteitis, hyperostosis, or synovitis;[1] the former is characterized by tenderness or swelling involving the anterior chest wall in 65%-90% of patients.[5] Typically affected areas include the sternocostal, sternoclavicular joints, and the costoclavicular ligament; the soft tissue surrounding these areas may develop erythema and swelling that presents with pain and tenderness, as seen in the patient.[6] Axial involvement has also been reported. In a retrospective case series, 63% of patients had abnormalities in the spine with corner lesions noted in MRI, and approximately 20% had endplate lesions.[7] In this case, MRI identified osteitis with sclerosis at the endplates of the thoracic spine.

Skin involvement can be seen in 60%-90% of SAPHO cases. However, the correlation of these different skin conditions with SAPHO is challenging, given that lesions can appear before, simultaneously, or after the osteoarticular findings.[8] The most common dermatological findings associated with SAPHO are psoriasis, acne, and palmoplantar pustulosis, and less frequently, an association with HS has been reported.[9,10] A prospective study from France described spondylarthritis as the most

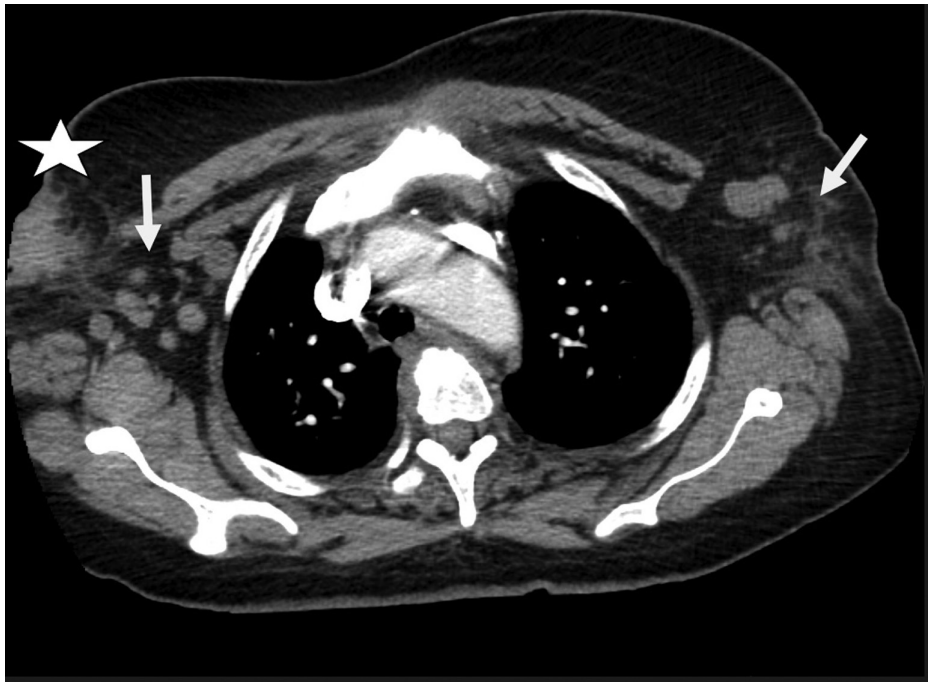

Figure 2. Axial CT scan of the chest showing bilateral axillary adenopathy (arrows) and breast lesion (star).

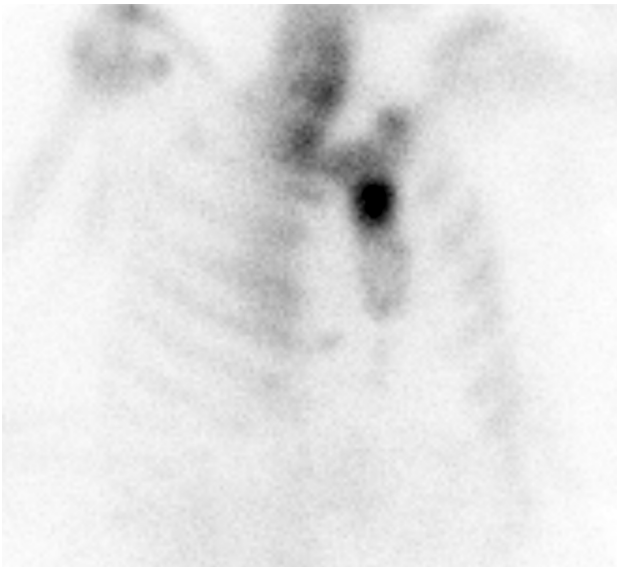

Figure 3. Whole body CT scan showing markedly increased activity of the sternum and milder patchy uptake of the thoracic spine.

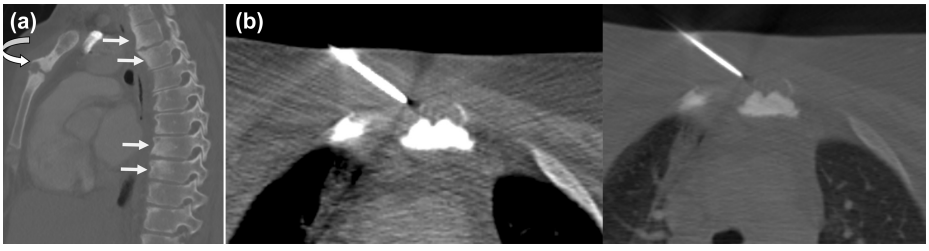

Figure 4. (A) Sagittal CT of the chest shows the diffuse sclerotic changes of the sternum (arrow) and patchy sclerosis of the thoracic spine (arrowheads) mimicking osteoblastic breast metastases. Note the sclerotic changes predominantly involve the anterior aspect of the thoracic spine and multiple contiguous levels. (B) Axial CT of the sternum at the time of the biopsy.

frequent osteoarticular manifestation among 640 patients with HS. In this study, 81% of patients had axial involvement, and 4 patients met SAPHO syndrome criteria.[11]

Malignancy is a key differential diagnosis for SAPHO syndrome. Primary bone malignancies (e.g., osteosarcoma, Ewing's sarcoma) can be questioned when there is localized bone pain, swelling, and tenderness in a single bone segment. Bone metastases should also be considered when there are symptoms and radiographic changes in multiple locations, especially in the vertebra, as SAPHO and metastatic lesions are multifocal.[5] In this case, initial radiographic findings were highly concerning for malignancy given the multifocal bone involvement along the extensive HS lesions that mimicked necrotic breast masses. Other alternative diagnoses include osteomyelitis, rheumatoid arthritis, and costochondritis.[5] In this case, biopsy was notable for reactive changes and negative for infectious or malignant processes which is consistent with prior reports that evidenced nonspecific inflammatory changes in SAPHO cases.[12] Furthermore, rheumatoid factor/anti-cyclic citrullinated peptide antibodies were negative.

The radiographic findings depend on the stage of the disease. Hyperostosis and osteitis are chronic inflammatory reactions that are characterized by increased sclerosis of the bone. The MRI has certain advantages in evaluating the early stages and activity of SAPHO syndrome. Bone marrow edema (BME) shown on MRI can differentiate active from inactive lesions and might detect the involvement of the adjacent joints of the anterior chest wall.[13] The MRI of the thoracic spine was crucial in differentiating SAPHO from bone metastases. Lytic bone metastases are usually sharply defined hypointense lesions on T1 and relatively well-defined on fat-saturated T2 and STIR sequences. In contrast, the BME suggestive of SAPHO syndrome has a patchier appearance on fat-saturated T2 and STIR, and minimal changes on T1, as seen in this case.[14]

There are no randomized clinical trials to guide treatment in patients with SAPHO. First-line medications include antibiotics, non-steroidal anti-inflammatory drugs, and steroids. Bisphosphonates and disease-modifying antirheumatic agents (e.g., methotrexate) have been used as second-line treatments with varying outcomes.[5] Those with refractory symptoms are empirically treated with biological therapy, including TNFα blockers, interleukin-1 (IL-1) inhibitors, and most recently, IL-17/IL-23 inhibitors like Ustekinumab. Daoussis et al[15] reported 5 cases of patients treated with Ustekinumab with approximately 50% efficacy in skin lesions and 60% efficacy in bone/joint manifestations. In the patient, Ustekinumab provided initial improvement of symptoms; however, due to persistent skin manifestations and follow-up MRI findings, treatment was modified to Secukinumab (IL-17 blockade).

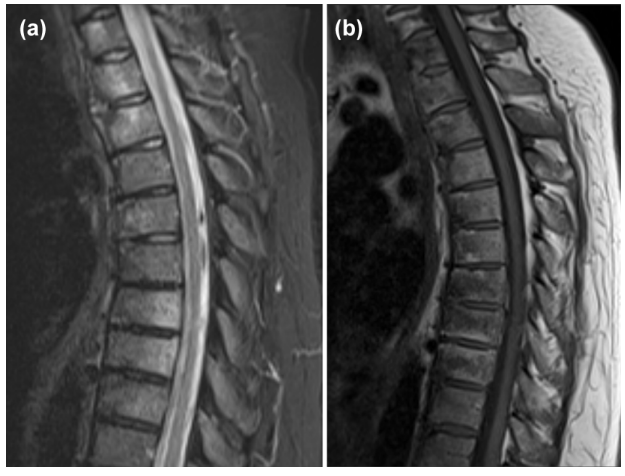

Figure 5. A) Sagittal STIR imaging of the spine shows patchy hyperintense lesions of the spine. B) Sagittal T1-weighted image shows marrow changes but without well-defined margins as typically seen with metastatic disease.

Further studies assessing the effectiveness of these agents are needed to guide the therapy of SAPHO syndrome, as the current evidence is insufficient to make clinical recommendations.

Conclusions

Awareness and early recognition of SAPHO syndrome might prevent individuals from unnecessary diagnostic or therapeutic interventions. The characteristic BME seen in MRI might aid in an early diagnosis. Due to its complexity, a multidisciplinary approach is essential in the diagnosis and prompt treatment of this condition. Larger studies are needed to evaluate the efficacy and safety of the therapeutic options for this disease.

Data Availability Statement: The data that support the findings of this study are available on request from the corresponding author.

Ethics Committee Approval: This case report did not require approval from an ethics committee as it describes a single patient encounter and does not constitute research according to MedStar Health Research Institute guidelines

Informed Consent: Written informed consent was obtained from the patient who agreed to take part in the study.

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