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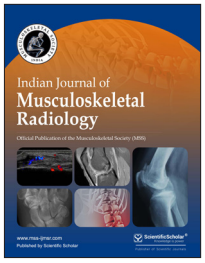

Pictorial Review

Synovitis, Acne, Pustulosis, Hyperostosis, and Osteitis Syndrome – A Pictorial Review

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ABSTRACT

Synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) is an acronym which encompasses SAPHO. SAPHO is a distinct clinical syndrome which involves the musculoskeletal and dermatological systems. The clinical presentation can be variable, and therefore, patients may present to non-specialists who are not familiar with the disease. It is, therefore, important for the radiologist to be aware of the imaging manifestations of SAPHO; as often, it is them who are the first to propose the diagnosis. Imaging allows differentiation of SAPHO from other disease processes such as inflammatory arthropathy, infection, and malignancy which can share similar features and also to demonstrate potentially subclinical areas of disease involvement. Treatment is empirical and aimed at symptom control and modifying the inflammatory process. Nonsteroidal anti-inflammatory drugs are the first-line agents. The disease has a good long-term prognosis, despite the challenges in diagnosis and treatment.

Keywords: Synovitis, Acne, Pustulosis, Hyperostosis, Osteitis, Seronegative, Infection, Joint disease, Spondyloarthropathy

INTRODUCTION

The acronym synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome was coined in 1987[1] in an attempt to form a unifying diagnosis for a rare group of chronic relapsing, inflammatory osteoarticular disorders with dermatological manifestations. Many different names such as sternocostoclavicular hyperostosis and acne-associated spondyloarthropathy have been used to describe this syndrome. SAPHO can be considered to be on the spectrum of seronegative spondyloarthropathy but with defined cutaneous manifestations, which can show periods of exacerbation and remission, the latter of which may contribute to a delay in the diagnosis.

In children, the disease most commonly presents as a chronic recurrent multifocal osteomyelitis, favoring the long bone metaphysis.[2] However, in adults, the anterior chest wall joints, such as the sternoclavicular and manubriosternal, are most commonly affected [Figures 1 and 2].

The pathogenesis of SAPHO remains obscure but is likely multifactorial likely due to a combination of immunological, infectious, and genetic factors.

In this article, we present multiple cases of SAPHO covering all the modalities of imaging.

CLINICAL FEATURES

SAPHO is a rare disease, with limited data available regarding its prevalence;[3] it is estimated to be 1 in 10,000 in Caucasians.[4,5] There are limited reports of SAPHO syndrome involving other ethnic backgrounds such as in African Americans, Chinese, and Japanese suggestive of a worldwide distribution.[4,5]

Osteoarticular manifestations of SAPHO syndrome are characteristic of the disorder and can occur with or without active dermatologic findings. However, more than 60% of patients diagnosed with SAPHO develop an associated cutaneous manifestation.[6]

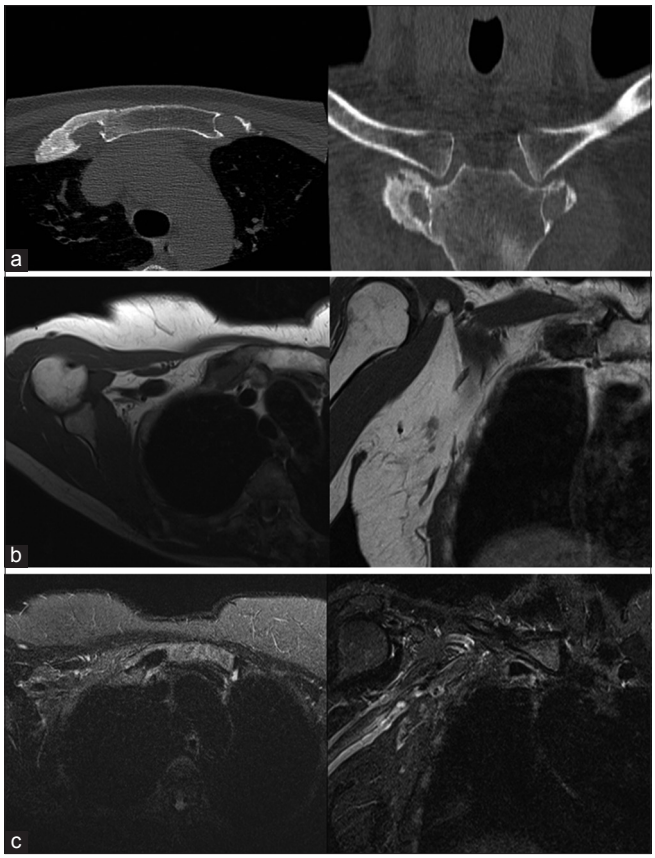

Figure 1: A 52-year-old female presented with anterior chest pain. (a) Selected computed tomography (CT) bony reformats of the upper thorax in the axial and coronal planes demonstrates sclerosis and hyperostosis of the right first sternocostal joint. The sternoclavicular joints are normal. (b) Axial and coronal T1-weighted imaging through the sternum demonstrates low T1 signal centered on the right sternocostal joint, corresponding to the sclerosis and hyperostosis seen on the preceding CT [Figure 1a]. (c) Axial and coronal short-tau inversion recovery weighted magnetic resonance imaging through the sternum demonstrates low-grade bone marrow edematous change related to the right sternocostal joint. Imaging confirmed the final diagnosis of isolated sternocostal hyperostosis/synovitis, acne, pustulosis, hyperostosis, and osteitis.

SAPHO syndrome can affect patients of any age though the average age onset is between 30 and 50 years old. There is a known female predominance, particularly in patients aged <30 years of age.[6]

Palmoplantar pustulosis is the most common cutaneous manifestation,[7,8] followed by acne involving the chest, back, and face. The time interval between the onset of cutaneous and osteoarticular manifestations is <2 years in approximately 70% of patients.[9] Exacerbations of cutaneous and osteoarticular manifestations are often unrelated.[10]

The affected individual typically presents with osteoarticular complaints. This includes pain, swelling, and restricted movement in the affected joints. Patients may present with single or multiple sites of joint involvement. If there is involvement of the axial skeleton, there may be radicular pain. Vertebral destruction is seen in a minority of severe cases. Fever and fatigue may also be present.

There is no pathognomonic biochemical test for SAPHO. In the assessment of SAPHO, it is important to order a full blood count, liver and renal function tests, inflammatory markers (C-reactive protein/CRP and erythrocyte sedimentation rate/ESR), rheumatoid factor, and HLA-B27 to assess for other disease processes. It is important to note that SAPHO can cause raised inflammatory markers and can co-exist in patients who have rheumatoid or more commonly seronegative spondyloarthropathy. Recent small-scale studies have shown raised complement levels (C3 and C4) and immunoglobulin A levels in some patients with SAPHO syndrome, but these remain casual associations.[11,12]

IMAGING FEATURES

Imaging plays a key part in determining the diagnosis of SAPHO syndrome. The anterior chest wall followed by the spine and sacroiliac joints is the most common sites of involvement in adults.

Conventional radiographs

Radiographs can remain normal in early disease, but with disease progression, 80% of patients develop radiographic evidence of osteoarticular involvement.[13] Radiographic findings are of hyperostosis, osteolysis, or osteosclerosis.[6,14] In the bone, osteitis generally precedes sclerotic lesions.[14] Joint involvement is often depicted by joint space narrowing, cortical erosions, and periarticular osteopenia. Ankylosis can be present. Established sacroiliitis can be seen and is most commonly unilateral with erosions on the iliac side of the joint;[14] this is in contrast to the bilateral sacroiliac joint involvement seen in typical spondyloarthritis.

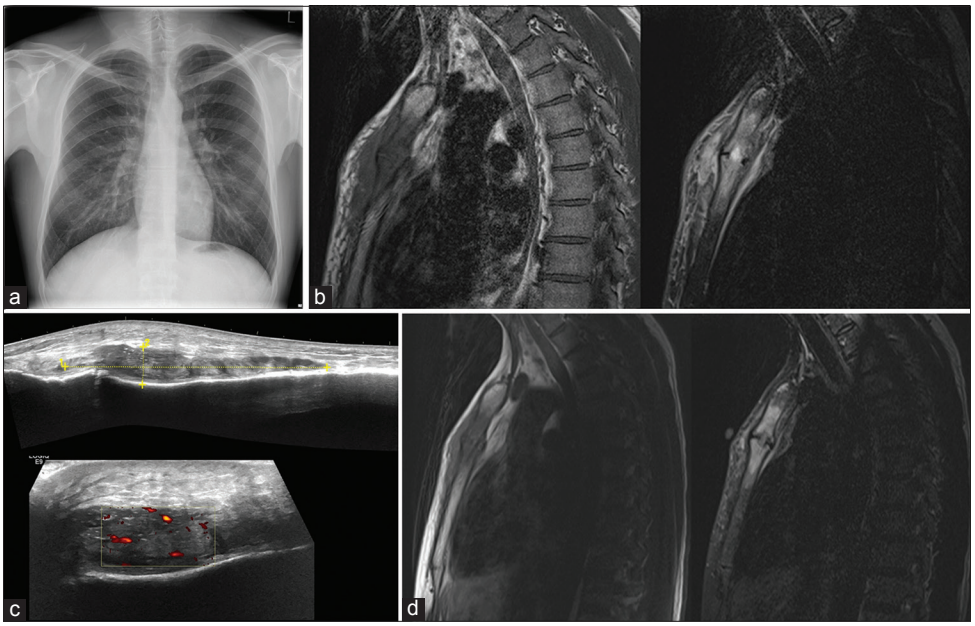

Figure 2: A 30-year-old male presented with a 4-week history of chest discomfort and pain. Blood tests including white cell count and inflammatory markers were normal and the patient suffered from no systemic symptoms. (a) Posteroanterior chest radiograph did not show any abnormality. The patient proceeded to magnetic resonance imaging for further evaluation. (b) Selected sagittal T1-weighted (left) and short-tau inversion recovery (STIR) (right) magnetic resonance imaging (MRI) through the manubriosternal joint. T1-weighted imaging demonstrates hypointense signal within both the manubrium and proximal sternal body with corresponding high signal on STIR imaging consistent with bone marrow edema. In addition, there is a low T1 weighted and intermediate to high STIR signal subcutaneous soft tissue changes seen at and anterior to the manubriosternal joint. (c) Ultrasound images at the level of the manubriosternal joint show a mixed echogenicity subcutaneous abnormality with increased Doppler flow corresponding to the MR findings. (d) Septic arthritis and SAPHO syndrome were raised as possible differentials. The case was discussed at a multidisciplinary meeting and decided a trial treatment with nonsteroidal anti-inflammatory drugs and follow-up imaging in 1 month. No antibiotics were used in patient management. Follow-up sagittal T1-weighted (left) and STIR (right) MRI show improved appearances and the diagnosis of synovitis, acne, pustulosis, hyperostosis, and osteitis was confirmed at this point.

Radiographs can underestimate the disease process and so a combination of magnetic resonance imaging (MRI) and computed tomography (CT) is, therefore, utilized for better evaluation.

Magnetic resonance imaging

MRI can detect osteitis (bone marrow edema) not seen on conventional radiographs and also identify subclinical foci of active lesions. The thoracic spine is the most commonly affected site in the axial skeleton [Figures 3].[15,16] Lesions may start at the enthesis and cause osteolysis, synovitis, and eventually ankylosis.[13] There may also be soft tissue involvement adjacent to the bone lesions. Non-specific spondylitis and discitis are also commonly encountered. Lack of abscess formation, sequestra, or paravertebral soft tissue involvement helps differentiate SAPHO from pyogenic spondylodiscitis.[17]

Bone scintigraphy

Radionuclide whole-body planar imaging may show focal or multiple sites of tracer uptake which can then be used as an adjunct to perform target radiographs or CT.

The "bulls head sign" corresponds to increased tracer uptake at both sternocostoclavicular junctions. The manubrium sterni is meant to represent the upper skull of the bull, while the inflamed sternoclavicular junctions with the adjacent clavicles form the horns. In a single-center retrospective study over 16 years, the bulls head sign was observed in only 23% of patients who had SAPHO [Figure 4]. The study concluded that though the bull-head sign is characteristic for SAPHO it is not entirely sensitive.[8]

Positron emission tomography

Fluorodeoxyglucose positron emission tomography CT can differentiate active from inactive lesions in SAPHO syndrome as well as metastatic disease.[18-20]

KEY POINTS

SAPHO syndrome should be considered in adult patients with osteoarticular anterior chest wall or axial skeleton involvement with cutaneous manifestations.

Cutaneous and osteoarticular manifestations do not always coincide; therefore, a thorough history must be sought to assess for cutaneous involvement.

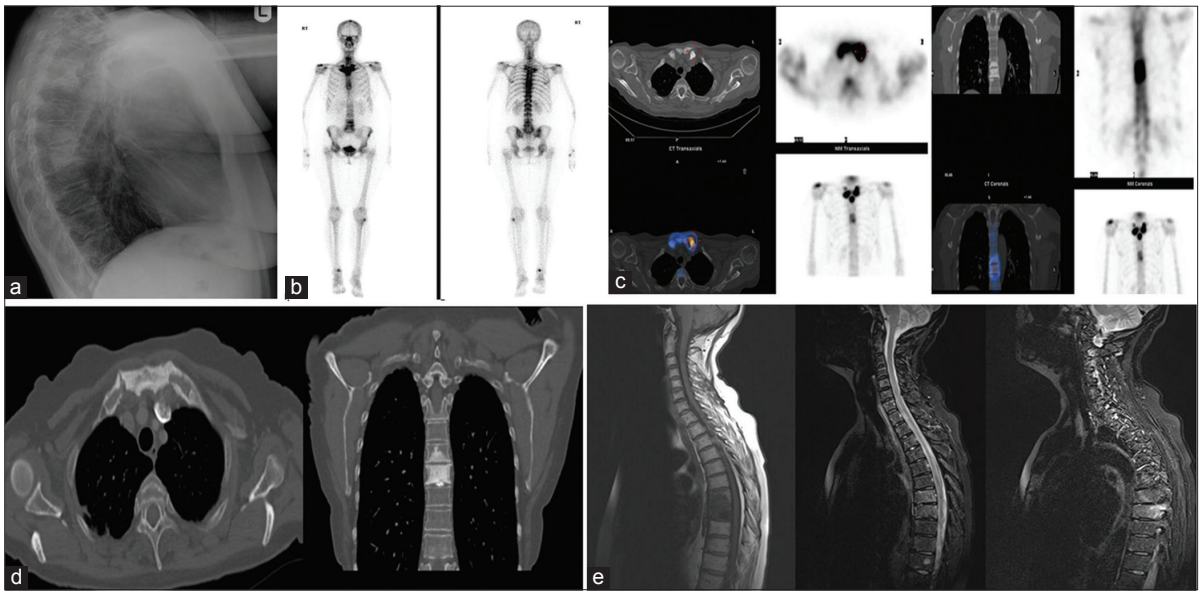

Figure 3: A 53-year-old female who was a known smoker presented with non-specific chest and thoracic back pain. (a) Sclerotic foci were seen on the lateral chest radiograph which raised the concern for potential metastatic disease. (b) Abnormal tracer uptake was noted around both sternoclavicular and sternocostal joints (bull's head sign) and in the thoracic spine. (c) Additional single-photon emission computed tomography (CT)-CT images were acquired of the same patient which demonstrated areas of hyperostosis. The reporting radiologist felt unable to exclude osseous metastatic disease. (d) Selected axial and coronal bony reformats from the whole body CT demonstrates focal areas of sclerosis and hyperostosis centered on the sternocostal joints and the mid-thoracic vertebrae. No primary malignancy or evidence of disseminated metastatic disease. A musculoskeletal radiologists opinion was sought who recommended a magnetic resonance imaging (MRI) for further evaluation with high suspicion of synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) as the diagnosis. (e) Selected sagittal T1-weighted (left) and short-tau inversion recovery (STIR) (middle and right) MRI of the cervicothoracic spine shows T1 hypointense signal in the T7 and T8 vertebral bodies with corresponding high STIR signal here and in the costotransverse junction in keeping with edematous change (osteitis). No further abnormality demonstrated. The patient was referred to rheumatology who confirmed the diagnosis of SAPHO syndrome.

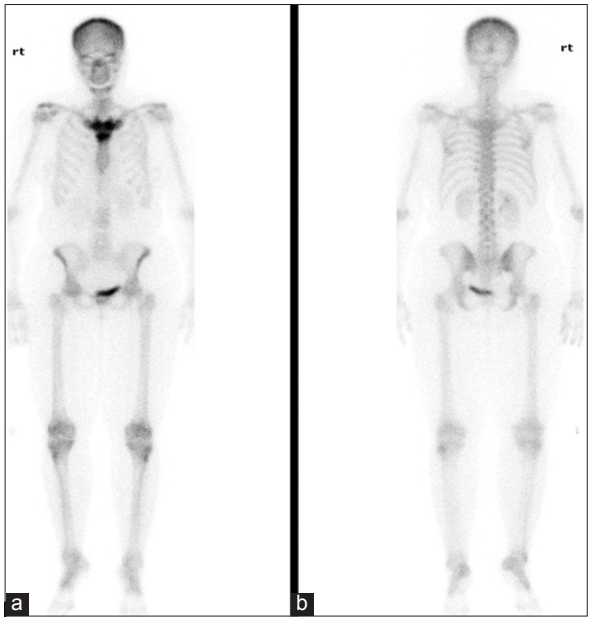

Figure 4: A 52-year-old female with anterior chest pain and prior history of treated breast cancer. (a) A bone scintigram was performed which demonstrated focally increased tracer uptake centered around the proximal sternum and its clavicular and costal articulations bilaterally. "Bulls head" sign.

Another diagnosis should be excluded before diagnosing SAPHO. These other diagnoses include infection, inflammatory arthropathy, and malignancy.

TREATMENT

Treatment is empirical and aimed at symptom control and modifying the inflammatory process.[21] Nonsteroidal anti-inflammatory drugs (NSAIDs) are the first-line agents [Figure 3]. Antibiotics, corticosteroids, disease-modifying antirheumatic drugs, as well as bisphosphonates and biologics have also been used with variable success. Physiotherapy can also be used as an additional treatment. Surgery is reserved for those whose condition has failed to respond to the aforementioned interventions and in those who a complication has developed (vertebral collapse and deformity and temporomandibular joint ankylosis).

CONCLUSION

Imaging plays an important role in the diagnosis of SAPHO syndrome; it is important for the reporting radiologist to recognize the common and typical patterns of osteoarticular involvement to be able to suggest the diagnosis in the correct

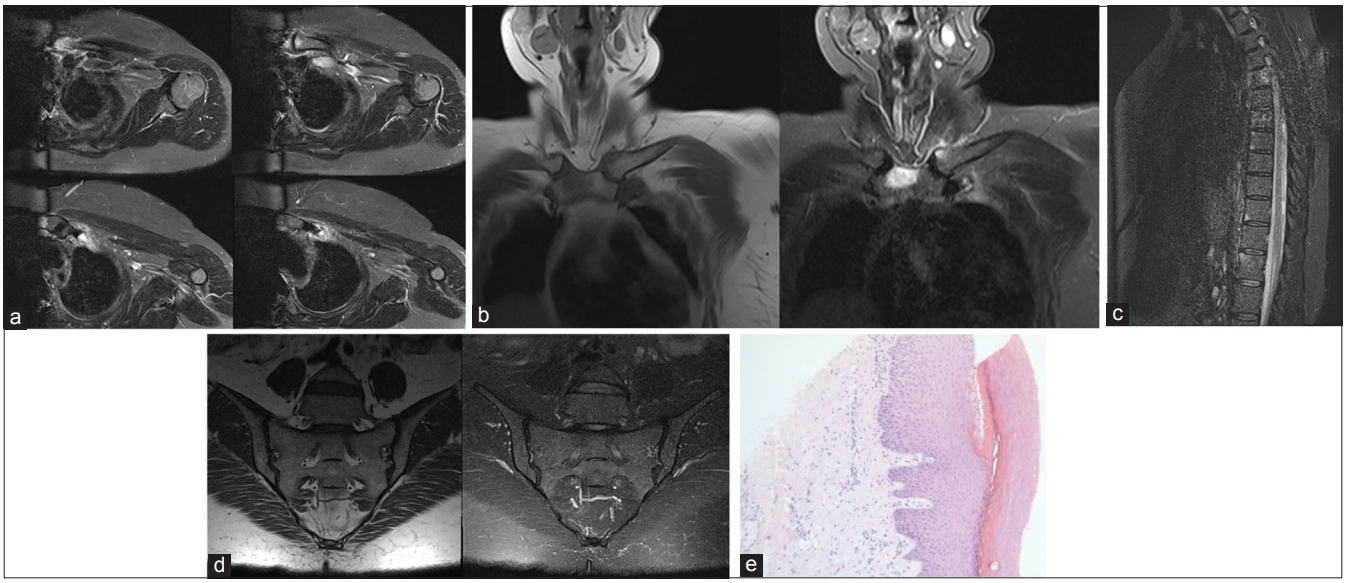

Figure 5: A 52-year-old female presented with non-specific neck and interscapular pain and was referred for a cervical spine magnetic resonance imaging for possible nerve root irritation. (a) No significant central or neural foraminal narrowing within the cervical spine. No abnormality seen relating to scapula on dedicated imaging. Axial short-tau inversion recovery (STIR) imaging demonstrated unexpected findings of edema adjoining the left sternoclavicular joint and also the left first and second costal cartilages. These unexpected findings led to patient recall for dedicated imaging of the anterior chest and SIJ protocol imaging. (b) Coronal T1-weighted (left) and STIR (right) magnetic resonance imaging (MRI) through the sternum demonstrated a couple of foci of low T1 and high STIR signal intensity within the right aspect of the manubrium and left medial clavicle which raised the suspicion for synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome. (c) Sagittal STIR MRI of the lower cervical and upper thoracic spine showed focal areas of bone marrow edema at the anterior aspects of a few vertebral bodies and at the costotransverse junction. This raised the concern for seronegative arthropathy such as ankylosing spondylitis. (d) Normal appearances of the sacroiliac joints. By this time, the patient had given history of palmar rash on direct questioning. The diagnosis of SAPHO syndrome was made. (e) Punch biopsy skin lesion showing a subcorneal pustule. The epidermis and dermis are otherwise within normal limits. *Image courtesy of Dr. Sara Edward, Consultant in Soft tissue and Dermatopathology. Leeds Teaching Hospital Trust.

setting [Figure 5]. It is also important to remember that though SAPHO is a distinct clinical syndrome which involves the musculoskeletal and dermatological systems, cutaneous manifestations may not coincide with osteoarticular manifestations. If there is any uncertainty with regard to the diagnosis, a multidisciplinary team approach/discussion should be employed to ensure best patient management.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent. In the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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