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CASE REPORT

Kimihiko Takeuchi · Masatoshi Matsusita
Kenji Takagishi

A case of SAPHO (synovitis-acne-pustulosis-hyperostosis-osteomyelitis) syndrome in which [^{18}F]fluorodeoxyglucose positron emission tomography was useful for differentiating from multiple metastatic bone tumors

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Abstract We report the case of a 50-year-old Japanese woman with SAPHO (synovitis-acne-pustulosis-hyperostosis-osteomyelitis) syndrome. Radiographs showed osteosclerosis of the cervical and lumbar vertebrae, as well as osteosclerosis and osteolysis of the right femoral neck, resembling multiple metastatic bony lesions. Arriving at a diagnosis required hematological and imaging tests. Whole-body bone scintigraphy identified diffuse uptake from the lower cervical vertebrae to the lumbar vertebrae and marked uptake in the right femoral neck. However, with [^{18}F]fluorodeoxyglucose positron emission tomography ([^{18}F]FDG-PET) scanning, abnormal [^{18}F]FDG uptake was not detected in cervical and lumbar spine, or in the femoral neck. Bone biopsy showed signs of chronic nonspecific inflammation, rather than tumor or infection. Based on these findings, the patient was diagnosed with SAPHO syndrome unaccompanied by skin lesions, and administration of non-steroidal anti-inflammatory drugs provided pain relief.

Key words [^{18}F]fluorodeoxyglucose positron emission tomography · Metastatic bone tumor · Pulmoplantar pustulosis · Synovitis-acne-pustulosis-hyperostosis-osteomyelitis syndrome (SAPHO) · Seronegative spondyloarthritis

Introduction

SAPHO (synovitis-acne-pustulosis-hyperostosis-osteomyelitis) syndrome is a type of multiple-organ inflammation producing joint and skin lesions, which was first described by Chamot et al. in 1987.[1] Spinal lesions are present in about 30% of cases. Radiological spinal lesions demonstrated a combination of vertebral osteosclerosis, spondylitis with or without discitis, and syndesmophytes. We here report a patient with SAPHO syndrome with radiological features resembling multiple metastatic bony lesions, and report on the literature regarding SAPHO syndrome to date.

K. Takeuchi (✉) · M. Matsusita
Maebashi Red Cross Hospital, 3-21-36 Asahi-machi, Maebashi 371-0014, Japan
Tel. +81-27-224-4585; Fax +81-27-243-3380
e-mail: k-takeuchi@maebashi.jrc.or.jp

K. Takagishi
Department of Orthopedic Surgery, Graduate School of Medicine, Gunma University, Maebashi, Japan

Case report

We report on a 50-year-old woman who experienced occasional lumbar and back pain from 1988. A herniated lumbar disk was diagnosed based on the results of magnetic resonance imaging (MRI) ordered by another physician. The patient again experienced lumbar back pain in August 2002, and her symptoms improved after the same physician administered an epidural block. In September 2002, she developed pain in the back of her neck without any clear cause, and radiography revealed an abnormal lesion of her cervical spine. She was subsequently referred to our department for further testing.

The patient reported dull pain from the back of her neck to the left scapula, and extension of her cervical spine exacerbated the pain. There was no swelling or redness in this region and range of motion in the cervical spine was maintained. The pain did not spread to involve her upper arms, and while she did not experience numbness, an osseous bulge was apparent at the sternoclavicular joint. The lumbar spine was stiff, and flexion of the lumbar spine was difficult. She had no complaints about peripheral joints, and extra-articular findings such as skin, nail, or eye involvement were absent.

Systemic inflammation was confirmed. Her erythrocyte sedimentation rate (ESR) was 87 mm/h and C-reactive protein (CRP) 2.5 mg/dl. Her total white cell count and differential were normal. While total protein was high at 9.0 g/dl, γ-globulin fraction was not elevated. Liver and renal function were normal. Bence–Jones proteinuria was not detected. Immunological testing did not reveal autoantibodies,

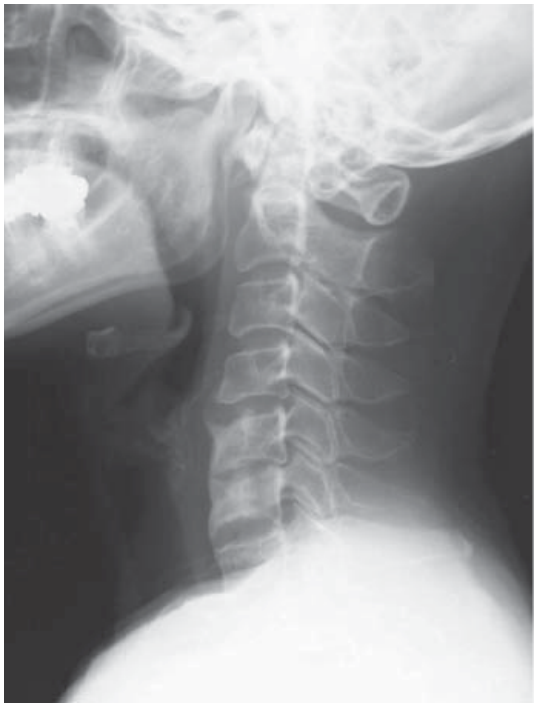

Fig. 1. Lateral view of the cervical spine showing osteosclerosis of the fifth and sixth cervical vertebral body endplates and reduced disk height between these vertebrae

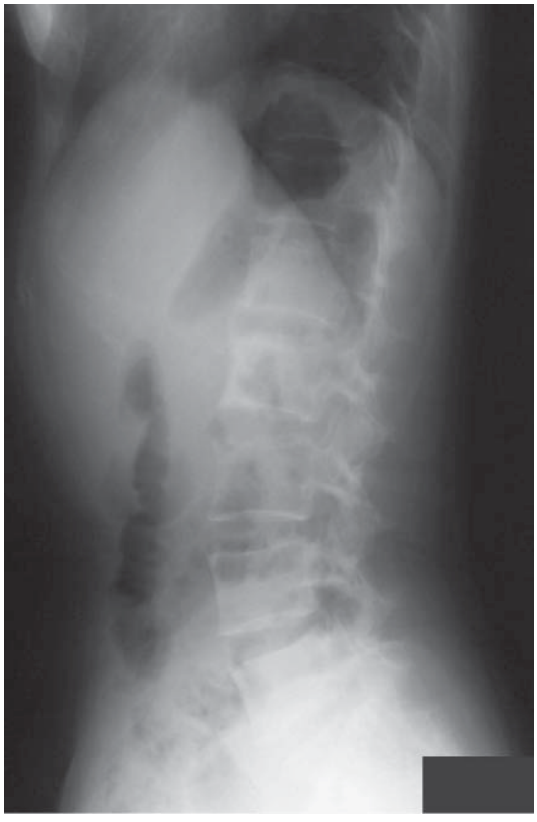

Fig. 2. Lateral view of the lumbar spine showing osteosclerosis, accompanied by syndesmophyte formation, involving the second and fourth lumbar vertebrae

including rheumatoid factor. Various tumor markers were also negative.

Osteosclerosis of the fifth and sixth cervical vertebral body endplates and decreased disk height between these vertebrae were seen (Fig. 1). Osteosclerosis accompanied by syndesmophyte formation was noted in the second and fourth lumbar vertebrae (Fig. 2). Osteosclerosis of bilateral sacroiliac joints and the pubic symphysis as well as osteosclerosis and osteolysis of the right femoral neck were also confirmed (Fig. 3).

Magnetic resonance imaging showed diffuse hypointense signal lesions at the fifth and sixth cervical vertebrae on T1-weighted imaging, and pale hyperintense lesions involving the same vertebrae on T2-weighted imaging. These lesions displayed gadolinium enhancement, suggesting spondylitis or a spinal body tumor (Fig. 4).

Whole-body bone scintigraphy using technetium identified diffuse uptake from the lower cervical vertebrae to the lumbar vertebrae, with marked uptake in the sternocostoclavicular joint, sacroiliac joint and right femoral neck (Fig. 5). Based on her physical status, as well as the hematological and imaging results, inflammatory disease or metastatic lesions of the spine were suspected.

Using [^{18}F]FDG-PET ([^{18}F]fluorodeoxyglucose positron emission tomography) scanning, abnormal uptake was not detected in the cervical and lumbar spine, nor in the sternoclavicular or sacroiliac joints. Abnormal uptake within thoracoabdominal organs was not observed. Mild uptake was observed in the left wrist joint. The standard uptake value (SUV) of this joint was 1.6 (Fig. 6). The possibility of metastatic spinal body tumor was thus low, and while inflammatory disease mainly involving the spine was suspected, biopsy of the femoral neck where uptake was observed on bone scintigraphy was performed on October 23, 2002.

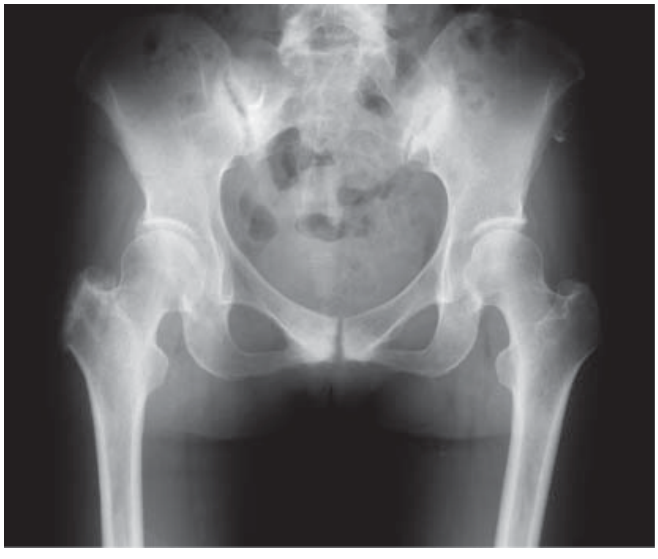

Fig. 3. Anteroposterior view of the pelvis showing bilateral osteosclerosis of the sacroiliac joints, as well as the pubic symphysis. Osteosclerosis and osteolysis of the right femoral neck are also demonstrated

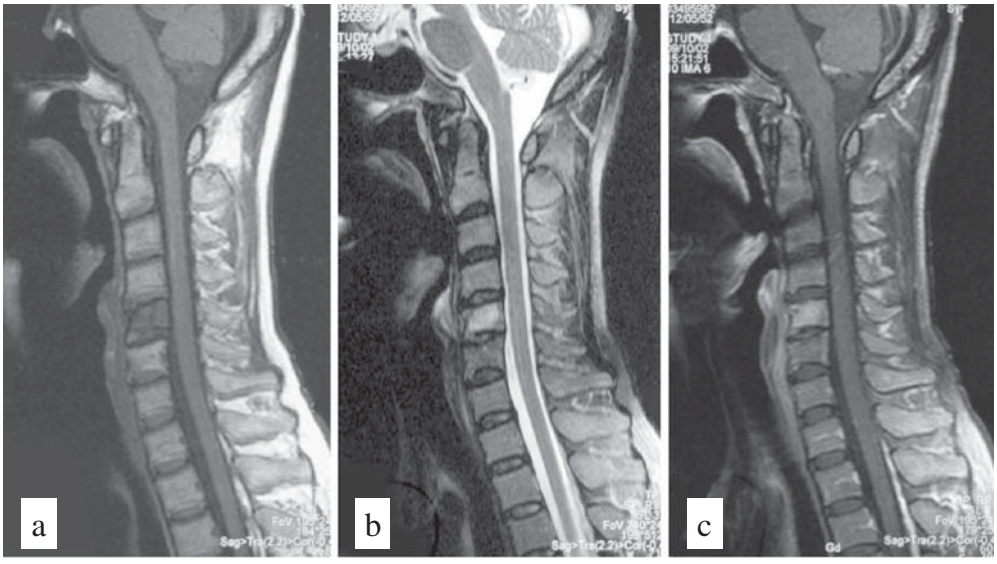

Fig. 4a–c. Sagittal magnetic resonance imaging (MRI) scans of the cervical spine. **a** T1-weighted image showing diffuse low signal intensity at the fifth and sixth cervical vertebrae. **b** T2-weighed image showing high signal intensity lesions involving the same vertebrae. **c** T1-weighed gadolinium-enhanced MRI scans at the same cervical level showing increased gadolinium uptake

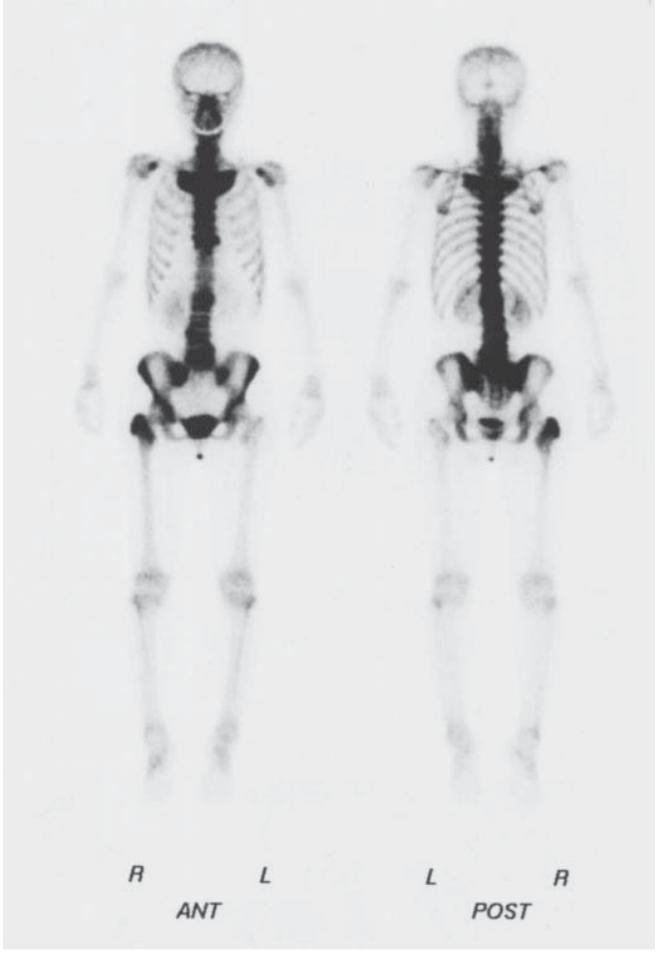

Fig. 5. Technetium scintigrams of whole body demonstrated diffuse uptake from the lower cervical vertebrae to the lumbar vertebrae, and marked uptake in the sternocostoclavicular joint, as well as the sacroiliac joints and right femoral neck

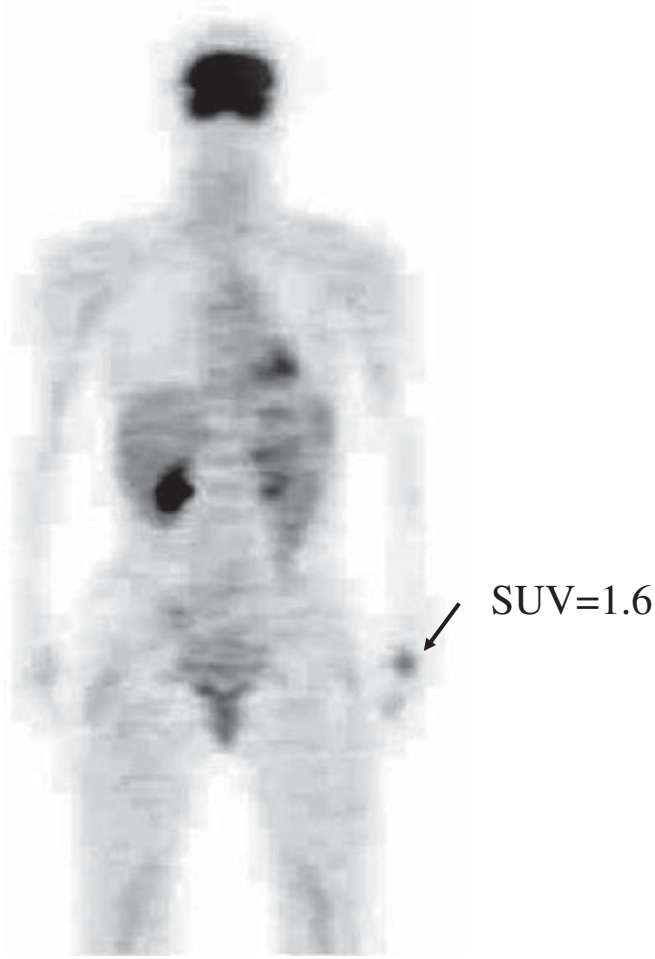

Fig. 6. [^{18}F]Fluorodeoxyglucose positron emission tomography scans show a lack of uptake in the cervical and lumbar spine, as well as the sternoclavicular and sacroiliac joints. The standard uptake value (SUV) of the left wrist joint was 1.6

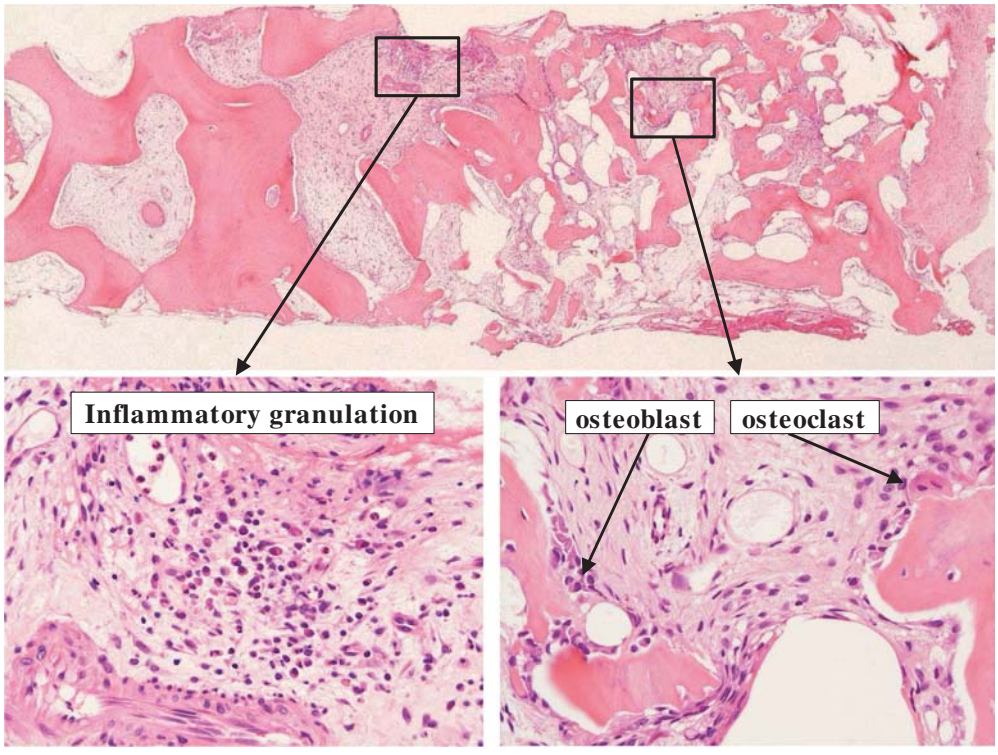

Fig. 7. Microscopy after staining with hematoxylin–eosin indicates chronic inflammation in the femoral bone, involving a combination of bony absorption and new bone formation

Biopsy findings included thickening and sclerosis of bony trabeculae containing osteoblasts and osteoclasts in some areas. Active new bone formation was suspected in these regions. In other areas, relatively immature bony trabeculae were observed, and the bone marrow was fibrotic, and infiltrated by inflammatory cells (Fig. 7). These findings thus suggest chronic nonspecific inflammation, rather than a tumor. The results of bacteriological tests were also negative.

Based on these findings, the patient was diagnosed with SAPHO syndrome unaccompanied by skin lesions, and administration of a nonsteroidal anti-inflammatory drug (Etodolac) was initiated for pain management. Three years after administration of Etodolac, her neck and lumbar pain on movement had diminished and her joint pain had not spread. Inflammatory reactions were kept at bay, and the patient had regained her normal activities of daily living.

Discussion

In 1987, Chamot et al. reported on SAPHO syndrome, describing osteosclerotic lesions of the sternocostoclavicular and sacroiliac joints, as well as the spine, accompanied by skin lesions, such as palmoplantar pustulosis or acne.[1] According to the diagnostic criteria outlined by Benhamou et al.,[2] at least one of the following four criteria must be met: (1) joint lesions accompanying severe acne; (2) joint lesions accompanying palmoplantar pustulosis; (3) osteohypertrophy of the extremities, spine, or sternocostoclavicular joints; or (4) chronic recurrent multiple osteomyelitis. The latter two criteria may be present in the absence of skin lesions.

Hayem et al. followed 120 patients with SAPHO syndrome over an extended period of time, and reported that 84% of patients exhibited skin lesions (palmoplantar pustulosis, 32%; acne, 18%; psoriasis vulgaris, 10%), while 16% did not.[3] According to the above-mentioned diagnostic criteria, the patient described in this report has type 3 SAPHO syndrome.

Type 4 SAPHO syndrome (chronic recurrent multiple osteomyelitis) was first reported by Giedion et al. as "subacute and chronic symmetrical osteomyelitis,"[4] after which Björksten and Boquist proposed the term "chronic recurrent multifocal ostitis" (CRMO).[5] With regard to the clinical symptoms experienced, extremity and precordial swelling and pain are common, and mild systemic symptoms often occur in girls. The illness frequently affects the metaphyses of the long bones of the legs, as well as the spine and pelvis. According to Job-Deslundre et al.,[6] femoral and tibial bones account for more than half (55%) of affected bones, followed by the pelvis (26%) and spine (8%). Plain radiography shows multiple areas of osteolysis or sclerosis or a mixture of the two, resulting in the findings commonly associated with osteomyelitis. Bone scintigraphy and MRI also show findings consistent with osteomyelitis.[7,8]

Pathological findings include bone marrow fibrosis, increased osteogenesis, and chronic inflammation, including inflammatory cell infiltration of predominantly lymphocytes and trabecular thickening.[9] These findings are similar to the clinical, radiological, and pathological findings commonly associated with sternocostoclavicular hyperostosis or palmoplantar pustulosis-related arthritis.[10] We thus believe that these diseases belong to the same disease category as CRMO. The present patient demonstrated a single chronic inflammatory lesion in the marrow of her right femoral

neck, and the site is being carefully monitored for recurrence.

Continuous administration of a nonsteroidal anti-inflammatory drug (NSAID) is the preferred treatment for SAPHO and CRMO. The symptoms of SAPHO syndrome tend to recur after periods of remission, but in general there is little progressive dysfunction of the spine and peripheral joints. Treatment with adrenocorticosteroids, salazosulfapyridine, or bisphosphonates is reportedly effective in some cases who NSAIDs have failed.[6,9,11] Because the spinal lesions in SAPHO syndrome are often multiple and severely destructive,[12,13] differentiation of these lesions from metastatic spinal lesions is important.

As far as diagnosis is concerned, disagreement between the results of bone scintigraphy and [^{18}F]FDG-PET imaging is observed. [^{18}F]FDG-PET detects increased sugar metabolism of tumor cells to ascertain the location of a primary lesion and the presence of metastatic lesions,[14] and has been used in recent years to assess synovitis in inflammatory diseases such as rheumatoid arthritis[15,16] and Takayasu disease.[17] Although metastatic bone tumors cannot be completely excluded by bone scintigraphy alone, [^{18}F]FDG-PET can definitively rule out bone metastases, greatly contributing to the diagnosis of SAPHO syndrome. [^{18}F]FDG-PET is thus expected to play an important role in differentiating spinal inflammatory disease, such as SAPHO syndrome, from metastatic bone tumors.

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