# SAPHO syndrome without dermatologic manifestations: multifocal uptake mismatch on $^{99m}$Tc-MDP and $^{18}$F-FDG-PET/CT imaging

**To the Editor:** We read in HJNM a SAPHO syndrome case presented by Spyridonides et al. (2007) [1]. Our case differs from the above mainly as to demonstrate lytic lesions that show hyper metabolic activity on fluorine-18-fluorodesoxyglucose positron emission tomography/computed tomography ($^{18}$F-FDG-PET/CT). Also the biochemistry tests and magnetic resonance imaging (MRI) findings differ at some point. In contast to the above case, our patient does not have an elevated serum alkaline phosphatase value and the spine imaging using MRI depicted contrast enhancement lesions which was highly suspicious for malignancy.

The acronym SAPHO was introduced in 1987 to describe a syndrome characterized by synovitis, acne, pustulosis, hyperostosis, and osteitis [2]. These disorders were subsequently considered a spectrum of conditions that share clinical, radiographic, and pathologic characteristics [3]. Any one of the following criteria is regarded as sufficient to diagnose SAPHO: (1) joint lesions with severe acne; (2) joint lesions with 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 [4].

An 18 years old female with diffuse osseous pain, most prominent in her back, for nine months was referred to our nuclear medicine department for further evaluation. An elevated erythrocyte sedimentation rate (74 mm/h; normal value: 0-20mmHg/h) was the only remarkable blood test finding. She had no significant medical history. Spinal magnetic resonance imaging demonstrated a mixed pattern of low and high-signal intensity in multiple vertebral bodies on T1- and T2-weighted images with increased contrast enhancement, suspecting malignancy, infection or other inflammatory conditions (Fig. 1 A, B and C). Bone scintigraphy using technetium-99m methylene diphosphonate ($^{99m}$Tc-MDP) revealed increased multifocal tracer activity, evident in the axial skeleton (Fig. 2). Increased uptake also in the manubrium and bilateral sternoclavicular joints previously defined as bull's horn/head appearance [5, 1] were present. The nuclear medicine physician suspected the "SAPHO" syndrome during a multidisciplinary council. To assess the possibility of metastatic vertebral tumors and to find a possible primary malignant neoplasm, $^{18}$F-FDG-PET/CT was performed. The $^{18}$F-FDG PET revealed multi-focal $^{18}$F-FDG activity on lytic lesions in fused-CT, mismatching most of $^{99m}$Tc-MDP uptake sites in spine and pelvic bones (Fig. 3 A, B, C and D). Although the $^{18}$F-FDG-PET/CT images could be suspicious for metastases, no primary malignant neoplasm could be found. The $^{18}$F-FDG negative, $^{99m}$Tc-MDP positive mismatch activity could be partially explained by the inactivity of inflammatory or old bone lesions. As reported previously, the histopathologic findings of SAPHO syndrome was nonspecific osteomyelitis at various stages ranging from acute inflammation to chronic inflammation, and a healing process with osteosclerosis and bone marrow fibrosis [6, 7]. Recently, several case reports have demonstrated the

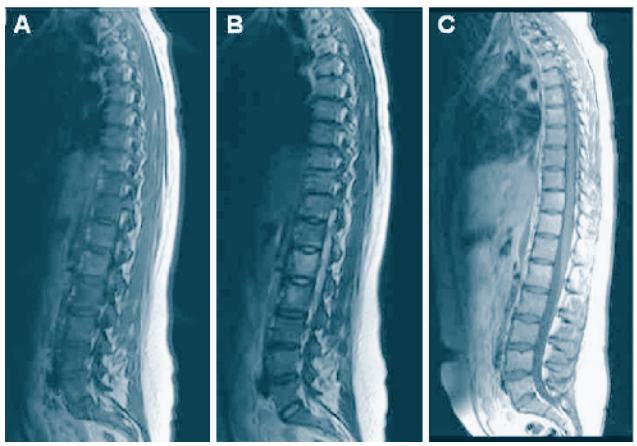



**Figure 1.** Spinal magnetic resonance imaging demonstrated hypo-intensity on T1-weighted images (A) and hyper intensity on T2-weighted images (B) with increased contrast enhancement after gadolinium injection (C) in several vertebral bodies, suspecting malignancy, infection or other inflammatory conditions.

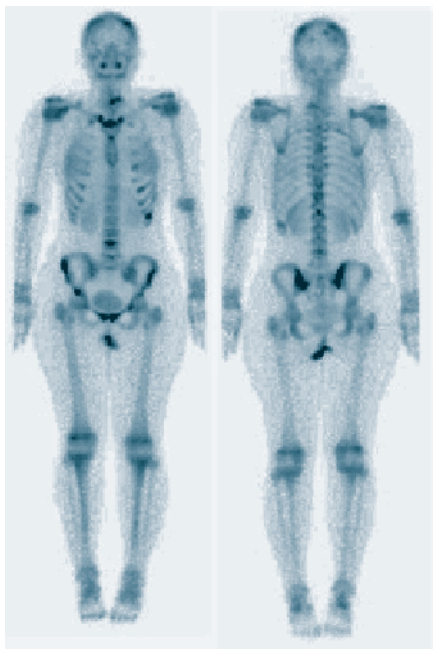


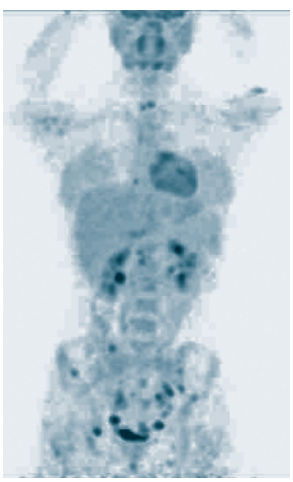
**Figure 2.** Whole body bone scan revealed multifocal increased tracer activity evident in calvarium, manubrium sterni and bilateral sternoclavicular joints (bull's horn sign), anterior ribs prominent in costachondral junctions, bilateral proximal humerus with right dominance, spine and pelvis (bilateral sacroiliac joints, right superior acetabular region, symphysis pubis).

utility of $^{18}$F-FDG-PET in differentiating active inflammatory lesions from chronic sclerotic lesions in the SAPHO syndrome. Although both lesions show increased accumulation in static bone scan, $^{18}$F-FDG-PET reveals augmented uptake exclusively in lesions with active inflammation [8, 9]. There are only a few case reports which demonstrated that $^{18}$F-FDG-PET was effective in distinguishing active inflammatory lesions in SAPHO syndrome, from metastatic bone lesions and healed chronic inflammatory lesions [10].

In SAPHO syndrome lytic lesions have been rarely reported [11]. Interestingly, $^{18}$F-FDG positive lytic lesions were highly noticeable in our case. Bone scan and $^{18}$F-FDG-PET/CT seem complementary in depicting the extent of the disease. Regarding the clinical and imaging findings, malignancy, infection and other inflammatory conditions constituted the differential diagnosis. Because of the multiple bone lesions with blastic and lytic components, to rull out metastatic lesion and for diagnostic purposes, the bone biopsy (Fig. 4) was performed. The specimen was obtained from the 12$^{th}$ vertebral body. This vertebra, highly suspicious for malignancy according to imaging findings, showed contrast enhancement on MRI and increased tracer activity on bone scan. Also transverse process and corpus of the vertebra included lytic lesion exhibiting increased glucometabolic activity on PET/CT (Fig. 5) imaging. The bone biopsy obtained from 12$^{th}$ vertebral body depicted normal marrow with unremarkable cancelous vertebral bone showing minimal sclerosis at some trabeculae with no evidence of malignancy. The specimen acquired from the lytic portion of transverse process was non diagnostic. Also, no microorganism was isolated from biopsy specimens. The final decision of the multidisciplinary council considering all clinical and diagnostic facts was in favour of SAPHO syndrome.

In the absence of dermatologic manifestations, as in this particular case, SAPHO syndrome may be under diagnosed or misdiagnosed as metastatic disease. In the light of the literature and of the presented case, our impression is, that the case of a young adult, mainly female, complaining of osseous pain with elevated sedimentation rate, multiple tracer activity on bone scan prominent on anterior thorax with the characteristic sign bull's horn/head appearance, multifocal $^{18}$F-FDG activity with lytic, sclerotic, or hyperostotic bone lesions but without any extra skeletal abnormality indicating a primary malignancy, should alert the physician to consider the diagnosis of SAPHO syndrome.

*In conclusion*, although optimal treatment for SAPHO syndrome remains unclear, it is crucial to make this diagnosis, to avoid unnecessary investigations and treatment.



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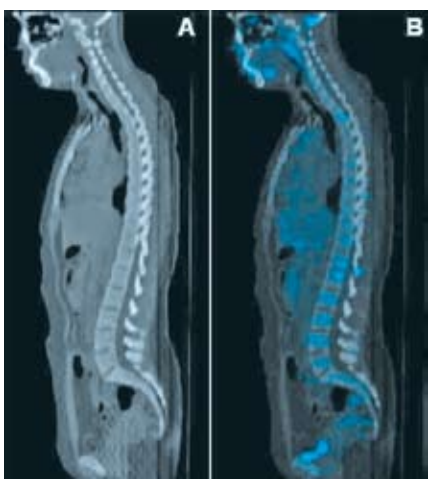
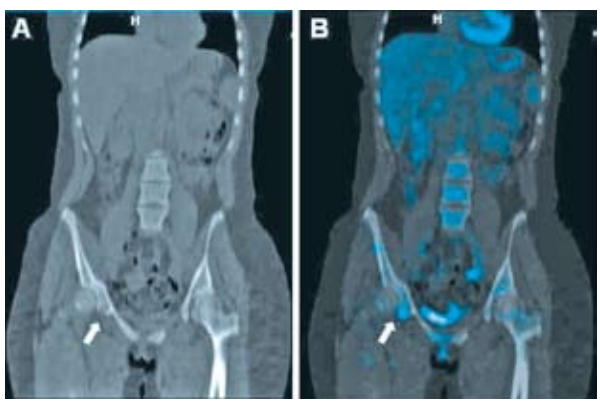



B

**Figure 3.** A $^{18}$F-FDG-PET/CT scan, A: Anterior projection of maximum intensity projection (MIP) image shows multi-focal $^{18}$F-FDG activity mismatching almost all MDP uptake sites in spine and mostly in pelvic bones. B: Sagital projection of low dose CT (A), fused PET/CT (B) showing increased $^{18}$F-FDG activity in the spine prominent in the 1$^{th}$ lumbal and 12$^{th}$ thoracic vertebrae in this slice. Note that the activity abnormality in the $^{18}$F-FDG-PET image is not so marked compared to bone scan in the spine. C: Coronal projection, low dose CT (A), fused PET/CT (B) demonstrates increased focal $^{18}$F-FDG activity (arrow on B) on the lytic lesion (arrow on A) located in the right inferior acetabular region. D: Axial projection of pelvis, low dose CT (A), fused PET/CT (B) shows increased focal $^{18}$F-FDG activity (arrow on B) on the lytic lesion (arrow on A) located in the right posterior iliac bone.

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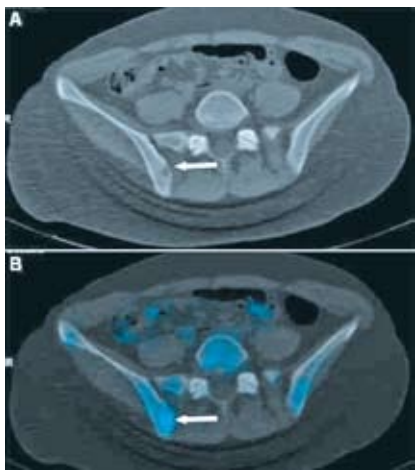


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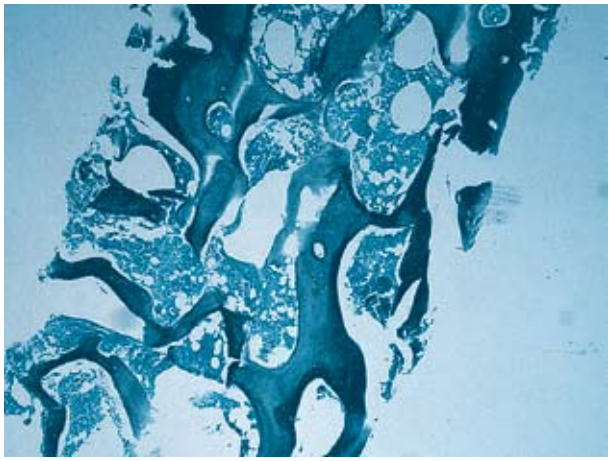

**Figure 4.** Histopathologicaly, normal marrow with unremarkable cancelous vertebral bone showing minimal sclerosis at some trabeculae (hematoxylin-eosin ×25).

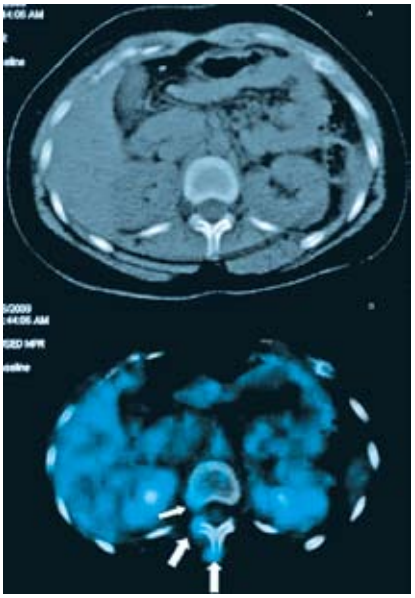

**Figure 5.** Axial projection of 12th vertebra, low dose CT (A), fused PET/CT (B) shows increased focal $^{18}$F-FDG activity on the lytic lesions located in the right posterolateral corpus (thin arrow), transverse and spinous processes (thick arrows).

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*Hell J Nucl Med 2010; 13(1): 73-75*
*Published on line: 10 April 2010*