A case of non-malignant multifocal lesions on the methyl diphosphonate technetium-99m bone scan with enteropathy. SAPHO syndrome

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Abstract

This is a case of a 24-year-old man with non-malignant multifocal bone lesions on the methyl diphosphonate technetium-99m bone scan, that may represent a variant of synovitis, acne, pustulosis, hyperostosis, osteitis (SAPHO) syndrome. The patient complained for diffuse osseous pain, focused mainly in the hip joints. X-rays of the hips were normal but X-rays of the shoulders showed hyperostosis of the right clavicle with no erosions. SAPHO is a rare syndrome of unknown aetiology with no more than a hundred cases reported during the last 10 years. Its typical form consists of characteristic painful osteoarticular manifestations and dermatological findings. In a variant of this syndrome, such as in our case, dermatological manifestations may be absent, but hyperostosis with osseous hypertrophy and enteropathy are present. No other malignant or benign disease was diagnosed. All routine laboratory tests for an inflammatory rheumatoid disease were negative. Treatment with non steroid anti-inflammatory agents was successful and after six months, there were no clinical symptoms and lesions on the bone scan faded. Four years later the patient remained free from symptoms. We discuss the scintigraphic, radiological laboratory clinical findings, the therapeutic criterion and the exclusion of any malignant or other benign bone disease that suggest the diagnosis of SAPHO syndrome. *In conclusion,* although we were unable to perform a bone biopsy, we suggest that no other diagnosis but an enteropathic variant of SAPHO syndrome may better describe the above clinical and laboratory findings. Bone scan findings have a principal diagnostic role in SAPHO syndrome.

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Case presentation

A 24-year-old man was referred to the Nuclear Medicine Department of Evangelismos Hospital for a bone scan. The patient had diffuse osseous pain, focused mainly on the hip joints, without weakness, fever or skin lesions. The patient had a history of ulcerative colitis for the last three years. At physical examination there was nothing remarkable. Erythrocyte sedimentation rate and serum C-reactive protein were within normal range. Blood cell counts and other laboratory tests (Widal test, Wright test, antinuclear antibodies, C3, C4 and RF) were also normal.

Technetium-99m methyl diphosphonate (^{99m}Tc-MDP) was injected intravenously in a dose of 925 MBq. Bone scan showed increased tracer uptake in the right clavicle, in both major trochanters, in the styloid process of the left radius, the medial condyle of left tibia and the right medial malleolus (Fig.1). X-rays of the hips were normal but X-rays of the shoulders showed hyperostosis of the right clavicle with no erosions (Fig. 2). The patient was submitted to treatment with non-steroid anti- inflammatory drugs (NSAID) and sulfasalazine.

The pain subsided within several weeks and six months later the patient had complete clinical remission. A follow–up bone scan at that time, showed incomplete scintigraphic remission (Fig. 3). The above findings could be a typical enteropathic variant of SAPHO syndrome, based on hyperostosis and hypertrophy of the right clavicle, the coexistence of ulcerative colitis, the exclusion of all other possible diseases that could have the same scintigraphic findings (fractures, metastatic bone disease, multifocal osteomyelitis) and response to symptomatic treatment with NSAID and sulfasalazine (Fig. 1).

Discussion

SAPHO syndrome is characterized by osteoarticular and dermatological symptoms that were described by French rheumatologists after a national survey carried out in 1987 [1].

Table 1. *Clinical variants of SAPHO syndrome*

Chronic recurrent multifocal osteomyelitis (CRMO)
Inflammatory anterior thoracic wall syndrome
Acne-CRMO
Triad: CRMO+ Crohn disease+ palmo-plantar pustulosis
Recurrent multifocal periostitis
Pustulo-psoriatic hyperostotic spondylarthritis
Sterno-costo-clavicular hyperostosis
Acne-spondylarthritis

Since then, no more than a hundred cases of SAPHO syndrome have been described [2]. The acronym "SAPHO" stands for [3]: a) Synovitis: inflammation of the joints, b) Acne: (acne conglobata or fulminans) that occurs most commonly on the face and upper back c) Pustulosis on the skin (purulent blisters), often psoriatic, mainly on the palms and on the soles (palmo-plantar pustulosis) d) Hyperostosis: increase in bone substance and e) Osteitis: inflammation of the bones. Typical SAPHO syndrome is consisted of inflammatory, pseudoinfectious, sterile osteitis, with areas of osteosclerosis, hyperostosis and periosteal reaction, associated with arthritis of the adjacent joint [1,3]. The most frequently involved site is the anterior chest wall (65%-90%) with characteristic clavicle osteomyelitis [4, 5]. The vertebral spine or the long bones are also affected in about 30% of the cases, whereas mandible and iliac bones are affected in about 10% [4, 5]. The main clinical features of SAPHO are shown in Table 1.

As described by Kahn et al. in 1994, three diagnostic criteria principally characterize SAPHO syndrome: a) Multifocal osteitis with/without skin lesions, b) Sterile acute or chronic joint inflammation associated with skin lesions and c) Sterile osteitis with skin lesions [6]. Any one of these criteria is sufficient for the diagnosis of SAPHO syndrome. Skin lesions associated with these criteria are of the pustular type of either psoriasis (pustular psoriasis, palmo-plantar pustulosis), or acne (acne conglobata, acne fulminans or follicular occlusion triad) [6].

The enteropathic variant of SAPHO syndrome is associated with chronic inflammatory disease of the intestine (Crohn's disease or ulcerative colitis) and has the clinical picture of chronic recurrent multifocal osteomyelitis (CRMO). Skin lesions are absent in 30% of the cases [4, 7].

The aetiology of SAPHO syndrome is unknown. An interesting hypothesis has been suggested that propionibacterium acnes act as a potential antigenic trigger, causing bone marrow inflammation with lympo-plasmacellular infiltrates, resulting in sclerosing and hyperostosing reactions [8, 9].

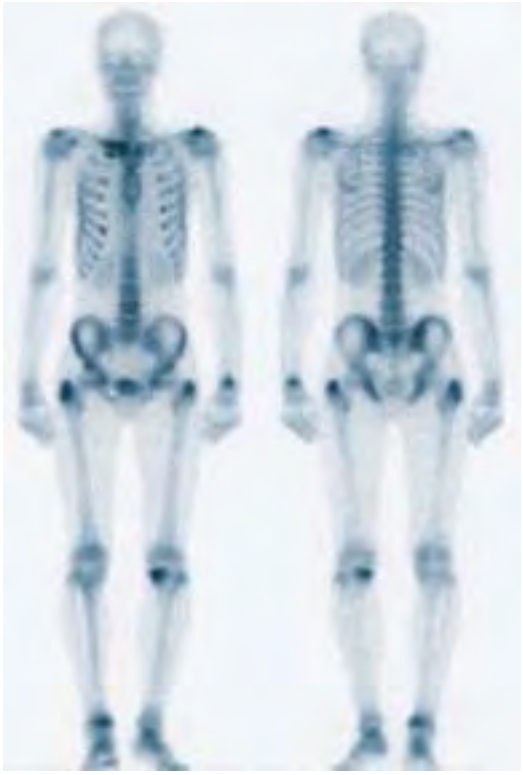

Figure 1. ^{99m}Tc-MDP bone scan showing intense tracer uptake in the right clavicle, both greater trochanters, the styloid process of the left radius, the medial condyle of the left tibia and the right medial malleolus

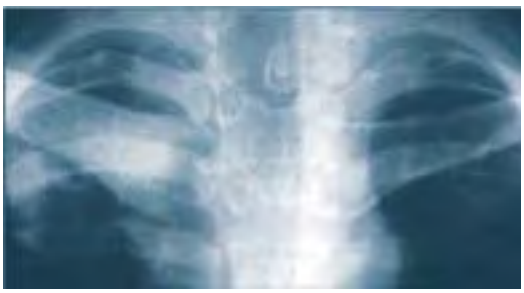

Figure 2. X-ray film of the clavicles showing right clavicle hyperostosis

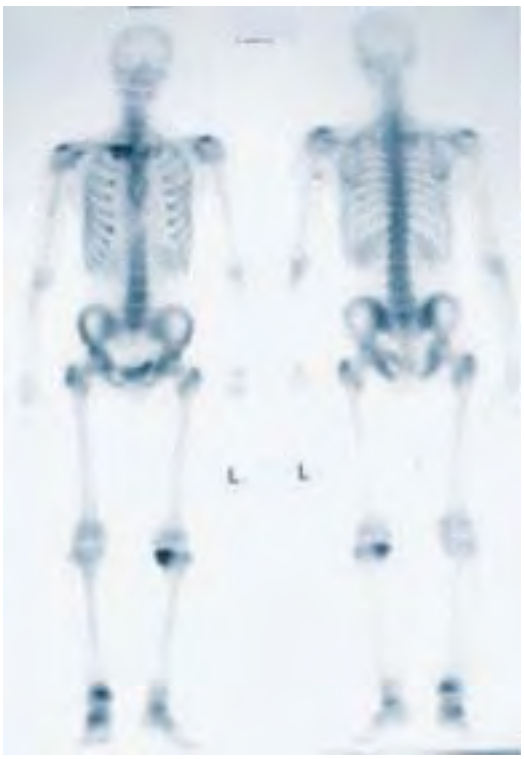

Figure 3. ^{99m}Tc-MDP bone scan showing decreased tracer uptake as compared to Figure 1 in the right clavicle as well as in both greater trochanters. The intense tracer uptake in the styloid process of the left radius has rather disappeared. Uptake of the radiotracer persists in the medial condyle of the left tibia and the right medial malleolus

Rheumatological and if necessary dermatological and clinical examination will support the diagnosis [3, 5]. ^{99m}Tc-MDP whole body bone scintigraphy is a very sensitive diagnostic test, while X-rays may be normal, or show osteosclerosis and hyperostosis of the affected bones [5]. Magnetic resonance imaging (MRI) may show inflammatory bone marrow oedema and synovial inflammation [10]. Synovial fluid is normal. Bone or synovial biopsy confirms the diagnosis, showing evidence of sterile plasma-cell sclerotic process and infiltration of non-infectious inflammatory cells (lymphocytes and plasma cells) [9, 11].

CRMO is recurrent and relapsing as is SAPHO syndrome. Cases with subacute courses, which recover after the first episode of the disease, have been reported [12]. Some chronic cases have also been reported with exacerbations and partial remissions [12, 13]. Duration of the disease is 2-20 years with an average of 4-5 years [12, 14]. In our case, a six months period free of symptoms after the first treatment, occurred .The patient remained free from symptoms at his last follow-up visit, four years after the initial diagnosis.

No specific treatment exists for SAPHO syndrome. NSAIDS and sulfasalazine are the cornerstones of treatment, which is symptomatic [3, 14]. Corticosteroids and immunomodulating drugs have been used. Azithromycin was also recommended as first-line treatment [15] and also calcitonin for the treatment of CRMO [16]. Recently diphosphonates (mainly pamidronate) have been suggested as a novel treatment for the bone, joint and skin involvement of SAPHO syndrome [17, 18].

In conclusion, we present a case of a 24-year old male with a possible enteropathic variant of SAPHO syndrome. The diagnosis was based on the bone scan and X-ray findings, clinical symptoms, negative blood tests, the therapeutic criterion, the exclusion of malignant or any other benign bone disease and the coexistence of chronic enteropathy.

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