

A Case of Sapho Syndrome Presenting with Positive HLA-B27 and Multiple Bone Involvement: Case Report

HLA-B27 Pozitifliği ve Birçok Bölgede Kemik Tutulumu Olan Bir Sapho Sendromu Olgusu

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ABSTRACT The SAPHO syndrome (synovitis, acne, pustulosis, hyperostosis and osteitis) is a rare syndrome with precise bone lesions and dermatologic manifestations. We report an unusual case of SAPHO syndrome with joint involvement preceding the appearance of psoriasis by years. Another unusual feature noted in our case was the multiple involvement of bone and joints. These patients can successfully be treated with steroids and methotrexate with a long-term remission. We present our case in the light of evidence obtained by an extensive review of the literature, to support the view that SAPHO may not be rare at all, but may easily be confused with seronegative spondyloarthropathy and/or psoriatic arthritis.

Key Word: Acquired hyperostosis syndrome; HLA-B27 antigen

ÖZET Sinovitis, akne, püstülozis, hiperostozis ve osteitis (SAPHO) sendromu kemik lezyonları ve dermatolojik bulguları olan ve çok nadir rastlanan bir sendromdur. Biz burada psöriazisi ve eklem tutulumu olan SAPHO sendromunun az rastlanan bir formunu sunmaktayız. Bir diğer nadir bulgu olgumuzda çok çeşitli kemik tutulumunun olmasıdır. Bu hastalar steroid ve methotrexate kullanılarak uzun süreli remisyon dönemleriyle tedavi edilebilmektedirler. Bu makalede, geniş bir literatür taramasıyla destekleyerek, aslında SAPHO sendromunun sanıldığı kadar nadir olmayıp kolaylıkla seronegatif spondilartropati veya psöriatik artrit ile karışabileceğini vurgulamak istedik.

Anahtar Kelimeler: SAPHO sendromu; HLA-B27

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The acronym SAPHO that includes synovitis, acne, pustulosis, hyperostosis and osteitis was first described in 1987 by Chamot.¹ Various forms of recurrent osteomyelitis accompanied by skin manifestations are characteristic in this syndrome. Skin manifestations accompany the bone and articular manifestations synchronously or appear after a long time after the bone lesions appear.² Types of chronic skin lesions consist of palmo-plantar pustulosis, severe acne, psoriasis and rarely hidradenitis suppurativa.³ Enlargement and osteosclerosis of the anterior chest wall may be present in most patients with SAPHO, which affects the sternoclavicular, upper costosternal and manubriosternal junction.⁴ Other axial bone lesions occur in the vertebrae, sacroiliac joints and mandibular bone. The common clinical manifestations of bone and articular lesions are pain and tenderness with or without swelling. This syndrome is considered a seronegative

spondyloarthropathy although HLA-B27 typing is rarely performed.⁵ We report an unusual case of SAPHO syndrome in which joint involvement preceded the appearance of psoriasis by years, thereby defying diagnosis. Our case was also unusual with multiple involvement of bones and joints. We will discuss our case in the light of the results of an extensive literature search, to help promote increased awareness of this not-so-rare entity that could easily be confused with seronegative spondyloarthropathy and/or psoriatic arthritis. Informed consent was obtained from the patients.

CASE REPORT

A forty-eight-year-old, white woman presented with severe swelling and pain of the left sternoclavicular joint, right shoulder and left wrist. She had difficulty opening her mouth. Her medical history revealed that she had suffered from an episode of sterile monoarthritis of the left wrist 5 years ago, which had resolved with non-steroidal anti-inflammatory agents (NSAI). Our patient did not report any other episodic attack of arthritis since her last presentation. Two years later, she had noted the appearance of widespread, scaly, pruritic skin lesions. Psoriasis was diagnosed and psoriatic lesions were palmoplantar pustulosis. Local glucocorticoid agents had been initiated.

On physical examination severe tenderness and local soft tissue swelling of the left sternoclavicular joint, the right shoulder, the left wrist and the temporomandibular joints were noted. Mouth opening was limited due to arthritis of the temporomandibular joint. Laboratory investigation revealed elevated CRP level (20 mg/L; normal range <6 mg/L) and normal sedimentation rate (17 mm/h); antinuclear antibodies (ANA) and anti-dsDNA and rheumatoid factor were negative. HLA-B27 typing of the patient was positive.

X-ray evaluation revealed erosive lesion on the distal ulna with soft tissue swelling (Figure 1). Computerized tomography examination showed increase in soft tissue thickness without erosive bone lesion in the anterior chest wall (Figure 2), unilateral sacroiliitis (Figure 3) and arthritis of the temporomandibular joint. Thoracic outlet syn-



FIGURE 1: X-ray evaluation revealed erosive lesion of the distal ulna. Erosive lesion is shown by the arrow.

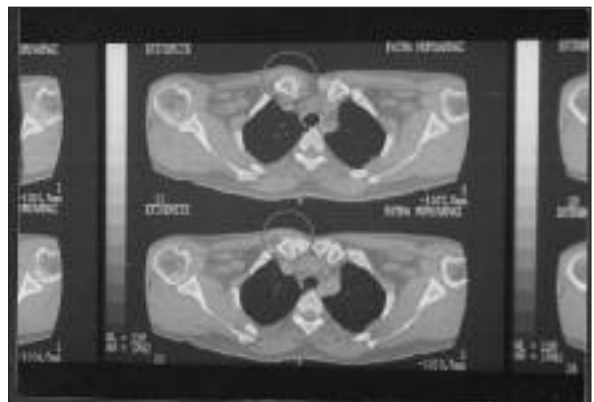


FIGURE 2: Computerized tomography examination showed increase in soft tissue thickness without erosive bone lesion in the anterior chest wall. Hyperosteoarthritis and soft tissue swelling of the sternoclavicular joint are shown by circles.



FIGURE 3: Computerized tomography examination showed unilateral sacroiliitis. Narrowing of the sacroiliac joint is shown by the arrow.

drome that is reported in the SAPHO syndrome was not detected in our patient.

The patient was initially treated with indomethacin 100 mg/day and sulfasalazine 2 g/day. After 30 days, repeated radiographs and physical examination showed that the patient did not respond sufficiently to those therapies; thus, oral corticosteroid was considered. Methyl-prednisolone 40 mg/day was administered for a week; thereafter, the dose was tapered as rapidly as the clinical situation permitted to a maintenance dose of 7.5 mg/day. The symptoms were relieved and the CRP level decreased to 12 mg/L. Therapy was maintained with methotrexate 7.5 mg/week for 4 years with complete remission of skin and bone-joint involvement.

DISCUSSION

The SAPHO syndrome is suggested to be a form of seronegative spondyloarthropathy, which is supported by its association with psoriasis, sacroiliitis, inflammatory bowel disease, and increased prevalence of HLA B27 in up to 30% of subjects in different Western studies.⁶ The presented case fulfilled the diagnostic criteria for the SAPHO syndrome. The patient presented with multiple bone involvement with positive HLA-B27 antigen. The most characteristic finding of the syndrome is inflammatory arthro-osteitis that is usually aseptic with a predominance of neutrophils. In a few patients, *Propionibacterium acnes*, a low-virulence organism was isolated.⁷ Bone involvement including the anterior chest wall, spine, and sacroiliac joint and peripheral bones is a component of the syndrome. Common lesions in the affected bones are erosions, sclerosis and periosteal reaction especially in the peripheral bones. Especially long bone involvement consists of osteosclerosis or osteolysis with periosteal new bone formation. Therefore, radiologically, osteosclerotic and erosive lesions may be easily misdiagnosed as bone tumor.⁵

Hayem et al in a group of 120 patients with SAPHO syndrome delineated its spectrum of skeletal involvement, with the anterior chest wall being the most frequently afflicted site, reported in 76 (63%) cases, followed by the sacroiliac joints,

the vertebrae, the mandible and pubic symphysis, in decreasing order of frequency.⁶ The results of Hayem et al point to the possibility of multiple skeletal site involvement in the SAPHO syndrome, as exemplified by our patient.⁶

X-ray imaging of the patient showed marked erosion in the distal part of the ulna and unilateral sacroiliitis. Reports indicate that 50% of patients with SAPHO syndrome present with unilateral sacroiliitis.⁸

In the SAPHO syndrome, the anterior chest wall is the major site of bone involvement and hyperostosis of the sternoclavicular joint is reported to be a frequent finding.⁹ In the present case, sternoclavicular joint involvement was already demonstrated. Thoracic outlet syndrome due to the compression of the subclavian vein was also reported in the SAPHO syndrome.⁴ Osteitis of the mandible extending to the temporomandibular joint may be seen in some cases.¹⁰ In the present case, bilateral temporomandibular joint involvement was detected. Marsot-Dupuch et al reported a case with SAPHO syndrome with temporomandibular joint involvement associated with sclerosing osteomyelitis of the mandible and the temporal bone, causing sudden deafness.¹¹ Temporomandibular joint involvement merits special attention, as it may prove to be another diagnostic clue for SAPHO syndrome. As no other disease is strongly correlated with mandibular osteitis and temporomandibular arthritis and rheumatoid arthritis being the only other disease associated with temporomandibular arthritis but not with mandibular osteitis, we suggest that the coexistence of mandibular osteitis and temporomandibular arthritis should indicate the SAPHO syndrome unless proven otherwise.

In a few cases, low virulence microbial agents were isolated from the lesions in the affected bones. Some reports suggest sustained response to doxycycline therapy in patients with SAPHO syndrome NSAID agents are suggested as first line treatment of the bone lesions. Disease modifying anti-rheumatic drugs such as sulfasalazine, methotrexate, cyclosporine and pamidronate were shown to be effective.¹²⁻¹⁴ A switch to corticosteroids is recommended when an NSAID agent is not effective in relieving symptoms. Infliximab is a

chimeric IgG1-kappa monoclonal antibody targeted against tumor necrosis factor- α was reported to be an effective agent in the treatment of psoriatic arthritis and in SAPHO syndrome.¹⁵⁻¹⁷ In parallel with van Doornum et al, we suspect that the SAPHO syndrome may not be rare but simply under diagnosed.¹⁴ We suggest that the SAPHO syndrome may prove to be more frequent than previously thought if a routine evaluation is done in patients with psoriasis and psoriasis-like disorders.

The diagnosis of the SAPHO syndrome appears to be largely dependent on clinical skills; on the other hand, it may be the first indicator of psoriasis or a psoriasis-like disorder with potential for multisystemic involvement and/or serious complications. In particular, it may be the harbinger of se-

ronegative spondyloarthropathy, with or without psoriasis. The presence of HLA-B27 in our patients supports this argument, as this antigen is characteristically associated with classical seronegative spondyloarthropathies.

The SAPHO syndrome, which is very rare, should be considered in the differential diagnosis of lytic, sclerotic, or hyperostotic lesions with various skin conditions but they do not necessarily accompany the bone manifestations. The present case report aims to underline the major clinical features of the SAPHO syndrome to avoid underdiagnosis. Early diagnosis may provide the means to control its progression, particularly with immunosuppressive treatment.

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