

SAPHO syndrome with acne fulminans and severe polyosteitis involving axial skeleton

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ABSTRACT

SAPHO syndrome (synovitis, acne, pustulosis, hyperostosis, osteitis), a rare inflammatory disorder, is an association of distinct skin disorders with pustules with osteoarticular inflammation. Its etiology remains unclear, and various treatment regimens frequently fail to control the disease. An 18-year-old male patient presented to the outpatient department with severe nodulocystic acne on the face with pain at both the wrists and lower back associated with high-grade fever and chills. On physical examination, he had severe tenderness at both wrist joints and lower back, along with swelling of right wrist. Magnetic resonance imaging revealed osteitis of the distal end of the right radius. Technetium-99m-MDP Whole Body Bone Scan revealed increased metaphyseal uptake in distal radius on both sides and prominent uptake at the sacroiliac joints, vertebral end plate, left 7th costo-vertebral joint and bilateral sternoclavicular joints and manubrium sternum (resulting in “bull’s head” sign, which is characteristic of SAPHO syndrome). He responded very well to a combination therapy of nonsteroid anti-inflammatory drugs, antibiotics, colchicine, and isotretinoin over a 12-week period.

Key words: Acne fulminans, bull-head sign, osteitis, SAPHO syndrome

INTRODUCTION

The SAPHO syndrome was first coined and introduced in 1987 by French rheumatologist Chamot to a symptom complex consisting of synovitis–acne–pustulosis–hyperostosis–osteitis, which till then was known by more than a dozen names over the previous 50 years. Although it can occur at any age, it commonly presents during childhood or middle age. The most common presentation is bone pain in a febrile patient associated with dermatological conditions such as pustular psoriasis, acne, and suppurative hidradenitis.^[1] Natural history of the disease is characterized by osteoarticular involvement and periodic exacerbations and remissions. At present, the exact pathogenesis is unclear.^[2] The treatment is difficult and often inadequate. Despite a good prognosis, involvement of multiple organ systems could complicate the disease course.

CASE REPORT

An 18-year-old male patient presented to our outpatient department with painful, nodulocystic

acne on the face since 9 months, severe pain in both wrist joints and lower back since 30 days, associated with bouts of chills and rigors, which made patient acutely ill. Patient’s elder sister had similar cystic acne lesions on the face, without bony pains or systemic symptoms. Physical examination revealed grade IV acne on face with multiple cysts, which were acutely tender discharging pus [Figure 1], associated with swelling of right wrist and tenderness over both wrist joints and lumbar spine, with restricted movements due to severe pain. The patient had high-grade fever of 102°F. Other physical findings were normal.

Complete blood picture showed mild leukocytosis (16,000 cells/mm³). Erythrocyte sedimentation rate

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Figure 1: Nodulocystic lesions on face before treatment

(ESR) was 130 mm/1st hour. C-reactive protein (CRP) levels are elevated at 24 mg/dL, (normal range <0.80 mg/dL). Rheumatoid Factor was negative and Liver function test results were normal. Blood and urine cultures showed no bacterial growth. Ultrasonography of abdomen was normal. Plain radiograph of the right hand showed evidence of a focal osteopenic area at the distal end of radius. Magnetic resonance imaging of the right wrist showed altered signal intensities, at distal metaphyses adjacent to physeal plate on the lateral side of the distal end of Radius, suggestive of osteitic lesions. To evaluate the skeleton, Technetium-99m-MDP Whole Body Bone Scintigraphy (WBBS) was done. Bone scintigraphy revealed increased metaphyseal uptake in distal radius at both wrists and prominent uptake at sacroiliac joints, vertebral end plates, left 7th costovertebral joint, and in addition, there was increased uptake at bilateral sternoclavicular joints and manubrium sternum, known as “bull’s head” or “bull-horn” sign, which is characteristic of SAPHO syndrome.

Initially, the patient was treated with nonsteroid anti-inflammatory drugs (NSAIDs), ceftriaxone and ampicillin–cloxacillin for 2 weeks with no significant relief of symptoms. Later cefpodoxime was started orally at the dose 200 mg twice daily, along with doxycycline 200 mg twice daily and colchicine 0.5 mg twice daily. Acne cysts on the face were drained weekly for 3 weeks, with two simultaneous sessions of intralesional injection of triamcinolone acetate (0.5 mL of 2.5 mg/mL). Clindamycin 1% was prescribed as a topical application, along with 2.5% benzoyl peroxide, for acne. The patient responded remarkably to the above treatment and his symptoms subsided in next 4 weeks. At this stage, isotretinoin 20 mg/day was introduced while continuing topical therapy and oral colchicine. By the end of 12 weeks, the lesions on the face flattened [Figure 2] and bone pains regressed completely. Leukocyte count, ESR and CRP returned to normal. Plain radiograph showed clearance of osteopenic area at the distal end of radius of right hand.

DISCUSSION

SAPHO syndrome is a complex disorder, characterized by a combination of bone lesions and inflammatory dermatosis associated with pustules, such as pustular psoriasis,



Figure 2: Improvement of facial acne after 12 weeks of treatment

palmoplantar pustulosis, fulminant acne, or suppurative hidradenitis. Patients typically present with musculoskeletal complaints, such as pain, swelling, and limitations of movement in the affected joints. In young and middle-aged adults the disease is more common in the sternoclavicular region (65%–90% of patients), but can also affect the spine (33%), pelvis (13%–52%), and long bones (30%),^[3] whereas the ilium and mandible are involved in less than 10% of cases. Patients with spinal involvement can present with numbness and radicular pain.^[4] In SAPHO syndrome axial skeleton and costo-sterno-clavicular region is more often affected, compared to localization of inflammation to acral skeleton in chronic recurrent multifocal osteomyelitis, a condition similar to SAPHO syndrome seen in children.^[5] SAPHO syndrome is associated with an elevated ESR and increased CRP values.^[6] The etiopathogenetic mechanism of SAPHO syndrome remains unclear, although several hypotheses have been proposed involving bacteriologic, immunologic, and genetic factors. By combining bacteriologic, immunologic, and genetic data, some workers consider SAPHO syndrome as a “reactive osteitis,” in which the opportunistic organism such as *Propionibacterium acnes* takes advantage of genetically determined deficiencies in antibacterial defense mechanisms and subsequently induces auto-amplification of the inflammatory response, possibly with an autoimmune component.^[2] This bone inflammation is usually sterile. Bacterial cultures are usually negative, with *P. acnes* being isolated rarely in deep bone biopsy specimens.

The diagnosis of SAPHO syndrome is based on history, characteristic scintigraphic and radiological results, and skin manifestations. Any one of the following criteria is regarded as sufficient to diagnose SAPHO syndrome:^[7] (1) Multifocal osteitis with or without skin lesions; (2) sterile acute, subacute, or chronic arthritis associated with pustular psoriasis, palmoplantar pustulosis, acne, or suppurative hidradenitis; and (3) sterile osteitis combined with one of the skin manifestations. However, the dermatological and skeletal conditions do not always occur in parallel, and they may be separated by a number of years.

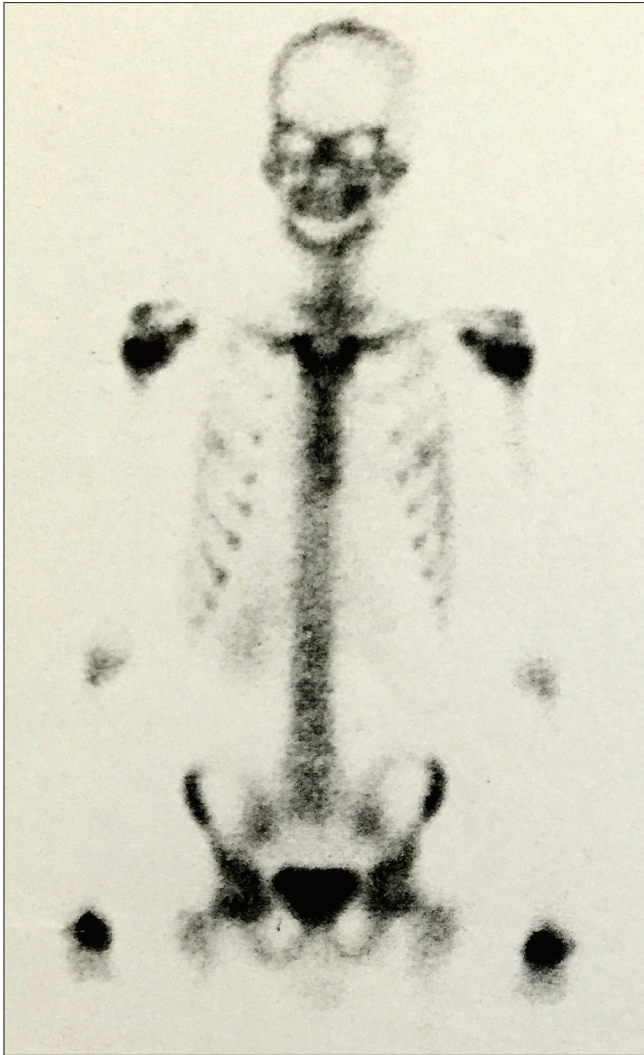


Figure 3: Technetium-99m-MDP Whole Body Bone Scintigraphy: Showing prominent uptake at bilateral sternoclavicular joints and manubriasterni (bull horn sign) and both wrist joints

Thus, diagnosing SAPHO syndrome is difficult in certain cases, particularly if the dermatological manifestations are absent.^[8] Our patient presented with pustular nodulocystic acne of face and systemic symptoms along with osteitis of multiple joints.

WBBS using 99m Tc-methylene-diphosphonate is a sensitive imaging modality that is able to identify its uptake in characteristic regions when changes in radiography are absent or subtly abnormal,^[9] is an important tool for the diagnosis of SAPHO syndrome, particularly for detecting multiple and early bone involvement. The sternoclavicular junction is the most common site of involvement in adults, followed by the spine and sacroiliac joints.^[6] The spinal involvement which was observed in this case along with sacroiliac joint involvement on scintigraphy, is generally reported to have a good prognosis and rarely cause neurological deterioration.^[7] High tracer uptake in the sterno-costoclavicular region yields the so-called “bull’s head sign,” with the manubrium sterni representing the upper

skull and the inflamed sterno-clavicular joint with the adjacent clavicae forming the horns.^[9] Our patient on scintigraphy demonstrated 'bull head' sign indicating increased uptake at these areas [Figure 3], characteristic of SAPHO syndrome.

Until now, there have been no uniform treatment guidelines for SAPHO syndrome. Current treatment of this illness is multimodal and empirical, and is mainly focused on relieving symptoms. Therapy is aimed at symptom relief and mainly includes NSAIDs and analgesics as firstline agents with or without antibiotics.^[10] Systemic corticosteroids, disease-modifying antirheumatic drugs, biologicals targeting tumor necrosis factor-alpha and interleukin-1, and bisphosphonates have all been beneficial in some patients, but ineffective in others, indicating poorly understood multifactorial pathogenesis of SAPHO syndrome.^[8] Bisphosphonates which inhibit bone resorption were observed to be of use in SAPHO syndrome. Several studies have supported the effectiveness of intravenous bisphosphonates as a treatment for SAPHO syndrome, as they exhibit a good response, due to their antiosteoclastic and anti-inflammatory effects that inhibit cytokine secretion by macrophages.^[10]

In the present case study, NSAIDs, oral cefpodoxime, doxycycline, colchicine, and intralesional steroids were prescribed simultaneously for first 6 weeks, followed by oral colchicine, isotretinoin, and topical therapy. Our patient responded remarkably to the above treatment and his nodulocystic acne, bony lesions and systemic symptoms subsided within 12 weeks.

CONCLUSION

This case presented with a rare combination of acne fulminans and osteitis of multiple joints of axial skeleton. Characteristic radiological features were noted on bone scintigraphy. Although it is considered that patients with SAPHO syndrome do not respond well to antibiotic therapy, our patient responded very well to therapy with cefpodoxime, doxycycline, colchicine, and cyst drainage followed by isotretinoin with significant clinical improvement in cystic acne and radiological clearance of osteopenic lesions.

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Conflicts of interest

There are no conflicts of interest.

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