CASE REPORT

SAPHO syndrome: A case report

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ABSTRACT

The present case is of SAPHO syndrome, which is a rare syndrome comprising of: synovitis, acne, pustulosis, hyperostosis and osteitis in 31 years old pregnant Saudi lady. Our patient suffered from skin lesion since 18 years of age till she was diagnosed 2 years back with sapho syndrome by serology blood work and magnetic resonance study of musculoskeletal system with multiple bone lesion, and was treated with methotrexate and adalimumab for 16 months with significant improvement. She is off treatment now because she is 17 week pregnant with no relapse.

The aim of this current study is to emphasize the importance for early diagnosis and treatment for positive outcome.

INTRODUCTION

Synovitis, acne, pustulosis, hyperostosis and osteitis (SAPHO syndrome) is a rare syndrome with no sufficient data on its prevalence, it is mainly reported in West and Japan.[1] It was first introduced by the rheumatologist Chamot in 1987, and it is characterized by a combination of skin and osteoarticular manifestation.[2] It is predominantly found in patient with average age of 30 and 50 years with female predominance.[3]

The pathogenesis of SAPHO is probably multifactorial, and it involves a combination of genetic, infectious, and immunological components.[4] Researchers have discovered that genes which seem to play a role in the SAPHO syndrome are located in the chromosome 18: LPIN2 and NOD2. LPIN2 encodes lipin 2, which is involved in modulating apoptosis of polymorphonuclear cells, and mutations of the NOD2 gene may lead to an abnormal immune response to bacterial peptidoglycans via activation of the proinflammatory transcription factor nuclear factor kappa B.[5]

There are also hypotheses of infectious cause, suggesting that bone lesions are caused by a low-virulence pathogen,[6] such as: *Staphylococcus aureus*,[7] *Haemophilus parainfluenzae,* and *Actinomyces,* as well as *Treponema pallidum*, *Veillonella,* and *Eikenella*.[8] The most important is *Propionibacterium acnes,* which were isolated from different bone lesion and skin pustules from multiple bone biopsies done by Assmann and Simon in their study of 21 SAPHO patients, where 67 % of them were positive.[6] It was supported by increasing circulating level of IgA seen in these patient. Since *P. acnes* is found in only two-thirds of biopsies at most and the treatment with antibiotics is effective only for as long as it is taken, it is considered that SAPHO cannot be classified among infections, even due to latent organisms.[9-11]

Also there is immune system dysfunction (humoral and cell mediated) either hypo - or hyper

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activation.[12] Assman and Simon[6] have shown that the proinflammatory response observed in SAPHO is mediated by the ability of P. acnes to trigger interleukin IL-1, IL-8, and IL-18 and TNFα release by monocytes, keratinocytes, sebocytes, and dendritic cells.

Sapho syndrome is benign but chronic disease with effective symptomatic treatment, early diagnosis and treatment can eliminate risk of complication and improve the patient quality of life.

CASE REPORT

A 31 years old Saudi lady 17 weeks pregnant presented with psoriatic plaque over lateral malleolus of left foot and bilateral great toe nail psoriasis for around 12 years.

Before she was suffering from severe psoriasis over the left big toe treated by many dermatologist with topical treatment with varying diagnosis ranging from eczema to fungal infection, but was never biopsied. She had variable response to treatment, but never cured completely.

Five years ago she started to feel fatigued and tired most of the time, with pain over sacroiliac region and back. She visited multiple orthopaedic clinic, but she was getting worse till she could not walk any more and became bed and wheel chair bounded. She was treated by orthopedic with intraarticular steroid injection with no improvement.

She never had severe acne, pustular lesion, eye or ear problem , no other joints were involved. Around that time she was pregnant but unfortunately she had intrauterine fetal death at 21 weeks gestation.

Eventually patient went to a rheumatologist, and he suspected SAPHO syndrome. She was treated with methotrexate and adalimumab with significant improvement.

No history of joint pain or morning stiffness, no history of similar illness in the family. She is the only child in her family with +ve consanguinity between her parents. No history of any drug use or smoking. She is married and she has a healthy 8 years old girl.

On examination: she had non tender, bilaterally enlarged protruding clavicles. (Fig. 1).

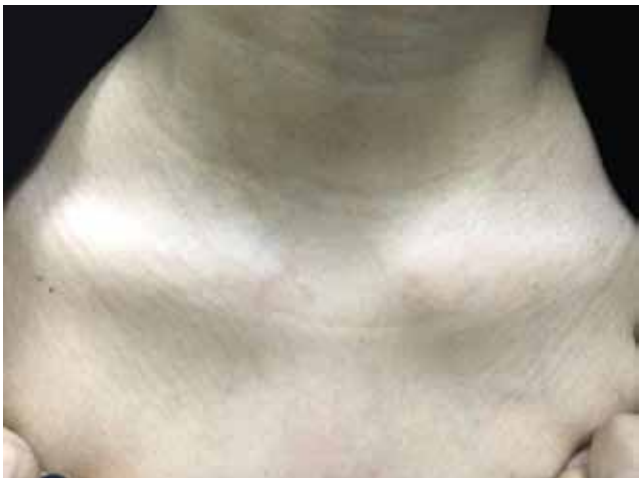

Fig. 1 Enlarged protruding clavicle bilaterally.

Single psoriatic plaque over left malleolus with minimal scaling with big toe nail trichorhexis bilaterally, and left second toe nail thickening. (Fig. 2).

She gave history of this finding since 5 years.

No other skin lesion, no hair, genital or finger nails lesion. No tenderness over joint, no signs of synovitis at the present.

Blood tests (Table 1), The rheumatoid factor and human leukocyte antigen B27 tests, antinuclear antibody, antidouble strand DNA, anticadiolipin and anti phospholipid were negative. The results for all other laboratory tests were within normal range.

Magnetic resonance imaging (MRI) scans of the sacroiliac joints demonstrated mild subchondral sclerosis with minimal bone marrow high signal intensity in both site suggestive of minimal

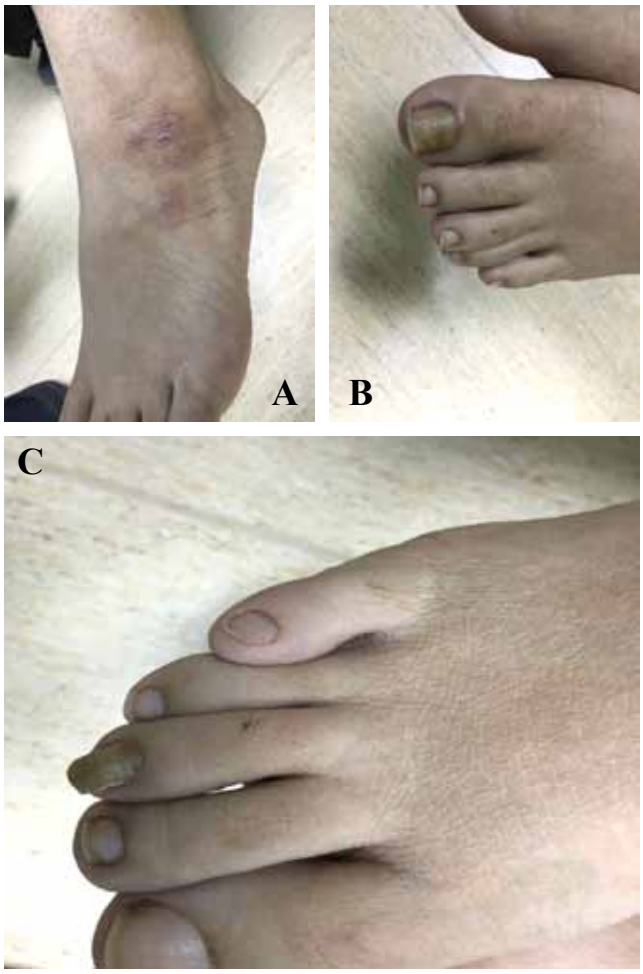

Fig. 2 Physical examination revealed (A) single psoriatic plaque over left malleolus with minimal scaling on (B) great toe nail trichorhexis bilaterally on (C) right third toe nail thickening.

Table 1 Patient's blood tests results

	Patient Result	Normal Range
ESR	15 mm/h	0–12mm/h
CK	22 U/L	0–170
CK-MB	8.8 U/L	0–25
Anti-Cardiac IgG	Negative <12.5 By Elisa	
Anti-Cardiac IgM	Negative <12.5 By Elisa	
Anti-Thrombin Iii	101 %	80–120
Lupus Anti-Coagulant	38	30.5–40.6
Protein C	90.523	70–130
Protein S	79 U/ML	60–140

inflammation. There was mild subchondral erosion more in the left side with no significant joint effusion. There was sacral bone marrow fatty infiltration near the lower portion of sacroiliac joint. There was general decrease in bone density of vertebral bodies and iliac bone with degenerative changes noted at lower end plate of L1, upper end plate of L4 and upper endplate of S1.

Both hips showed normal smooth articular surface of the femoral head and acetabulum, without erosions and mild joint effusion.

Patient refused to have any study with dye, or bone & skin biopsy.

Diagnosis of SAPHO syndrome was made by history and clinical presentation of psoriasis, osteoarticular manifestation and signs and MRI finding, accompanied with blood works.

DISCUSSION

Sapho syndrome has cutaneous and osteoarticular manifestations, and it needs a high level of suspicion to begin with.

There are several diagnostic criteria published to diagnose SAPHO syndrome only one inclusion criterion is needed to establish the diagnosis. The criteria suggested by Kahn and the other by Benhamou are the most frequently mentioned. All of them are preliminary and need further validation,[4] with respect to all of them this criteria made by Khan and modified at American College of Rheumatology 67th Annual Scientific Meeting 2003 is most precise one.[4] (Table 2)

The sternoclavicular junction is the most common site of involvement in adults, followed by the spine and sacroiliac joints.[13]

SAPHO syndrome is challenging disease to diagnose and treat. Several regimen were studied and published with reflecting result. Several

Table 2 Diagnostic criteria for SAPHO syndrome

Inclusion
Bone-joint involvement associated with PPP and psoriasis vulgaris
Bone-joint involvement associated with severe acne
Isolated sterile hyperostosis/osteitis (adults) (***Exception***: growth of *Propionibacterium acnes*)
Chronic recurrent multifocal osteomyelitis (children)
Bone-joint involvement associated with chronic bowel diseases
Exclusion
Infectious osteitis
Tumoral conditions of the bone
Noninflammatory condensing lesions of the bone

drugs has been used aiming to relieve symptoms mainly like: antibiotics especially macrolides, but unfortunately with high relapse rate after discontinuing the treatment,[14] non steroidal anti inflammatory drugs, both together or alone or in combination are the primary treatment.[15]

Bisphosphonates, which act as anti inflammatory against cutaneous and bone lesion with promising result mostly in combination with steroid and NSAIDs.[16] Methotrexate, cyclosporine, sulfasalazine, isotretinoin have been used with conflicting result.[17]

Anti tumor necrosis factor alpha such as etanercept and infliximab had been tried to relieve symptoms with variable result.

Our patient was treated by the rheumatologist with oral methotrexate 20 mg per week with daily folic acid supplement 1 mg tablet, and adalimumab 40 mg subcutaneous injection every other week for 16 months before she got pregnant. There was significant improvement noticed by the patient and by her rheumatologist regarding her hips pain and movement.

She started to move around without help, from being bed ridden after 3 months of treatment. But, the psoriatic plaque persisted, for which she used calcipitrol and betamethasone cream twice daily. She is off this regimen for 5 months now because of pregnancy. She is on aspirin 81 mg daily, folic acid 1mg daily, low molecular weight heparin 40 once daily. She is doing fine with no history of relapse. She is following with gynecological clinic monthly for check up.

SAPHO syndrome could be one of the disease that improves with the pregnancy.

CONCLUSION

SAPHO syndrome is a rare and challenging disease to diagnose and treat. Early diagnosis and treatment can eliminate risk of complication and improve the patient's quality of life.

Physicians and especially orthopedic surgeons should be aware of SAPHO syndrome because it needs a high level of suspicion to begin with.

Sapho syndrome could be one of the diseases that improves with the pregnancy.

ABBREVIATIONS

SAPHO syndrome = synovitis, acne, pustulosis, hyperostosis and osteitis.

P. acnes = *Propionibacterium acnes*

(MRI) = Magnetic resonance imaging

ESR = erythrocyte sedimentation rate

CK= creatine kinase

NSAIDs = non steroidal anti inflammatory drugs

PPP = Palmo-Plantar Pustulosis.

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