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CASE REPORT

Synovitis, acne, pustulosis, hyperostosis, and osteitis syndrome: a case report

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ABSTRACT

Synovitis, Acne, Pustulosis, Hyperostosis, and Osteitis (SAPHO) syndrome is an auto-inflammatory bone and skin disorders that is presented by dermatological manifestation such as palmoplantar pustulosis, pustular psoriasis, psoriasis vulgarism, severe acne, and hidradenitis suppurativa and joints and bones inflammation such as sacroiliac joint and vertebra. In this case report, a 16-year-old boy is presented that is suffering from low back pain, conglobata acne on trunk and face, and hidradenitis supportive (Dissecting Cellulitis) on the scalp. Diagnosis was based on clinical findings and laboratory tests. Treatment conducted by non-steroidal anti-inflammatory drugs and orally administered Isotretinoin. Dramatic improvement in low back pain was reported by patient in a few days. In follow-up examination of the patient after discharge from Hospital, we detected improving acne follicles and hidradenitis suppurativa on the scalp in clinic of rheumatology.

Key words: synovitis, acne, pustulosis, hyperostosis, and osteitis; (SAPHO) syndrome, chronic recurrent multifocal osteomyelitis (CRMO), non-infectious osteomyelitis, auto-inflammatory bone disorder

INTRODCTION

Synovitis, Acne, Pustulosis, Hyperostosis, and Osteitis (SAPHO) syndrome is characterized by synovitis, acne, pustulosis, hyperostosis, and osteitis. palmoplantar pustulosis, pustular psoriasis, psoriasis vulgarism, severe acne (conglobata), and hidradenitis Suppurativa are dermatological manifestations of SAPHO syndrome. Joints and bones could be involved in this syndrome such as sacroiliac joint and vertebra.[1]

In 1994, Chanot and Kahn suggested the acronym SAPHO in order to unify various conditions mainly involving skin, bone and joints.[2] SAPHO stands for synovitis, acne, pustulosis, hyperostosis and osteitis. Dermatological manifestations of SAPHO syndrome are palmoplantar pustulosis, acne Conglobata and hidradenitis suppurativa.[2]

The etiology of SAPHO syndrome is still unknown, but an association with infection by semi pathogenic bacteria such as Propionibacterium acnes has been suggested, but the role of these bacteria is discussed controversially.[3]

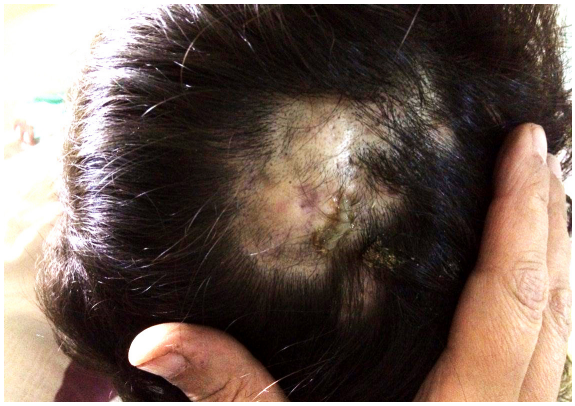

Figure 1, scalp produced a viscous, yellow to green colored pus.

Family-based observations and investigations of genetic variations gave rise to the hypothesis that genetic factors contribute to the development of disease. Genetic predisposition is more suggested by higher prevalence of HLA-B27 Antigen.[1]

SAPHO syndrome is an isolated auto-inflammatory bone disorder or may has overlap with several other rheumatologic disorders such as, ankylosing spondylitis, psoriatic arthritis, enteropathic arthritis, reactive

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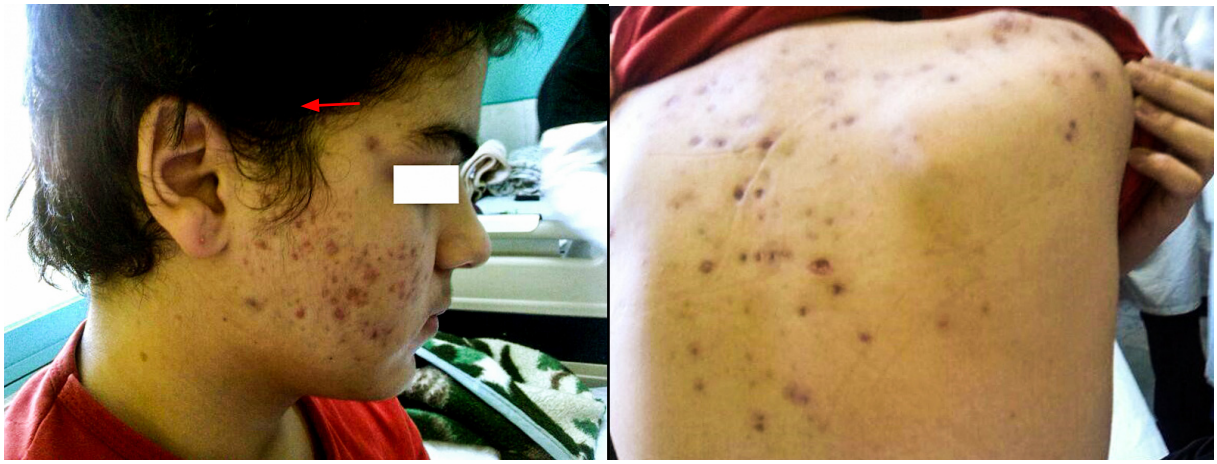

Figure 2, Severe fulminant pustular and cystic acne with deep scars on the face (left) and the trunk (right) (during remission phase).

arthritis and 13 - 52% of Sacroiliitis as in typical Ankylosing Spondylitis.[4,5,6,7]

This case report presents a case of SAPHO syndrome suffering from fulminant conglobata acne, hidradenitis suppurativa, and severe Low Back Pain.

CASE REPORT

A 16-year-old boy suffering from severs low back pain, fulminant conglobata acne and hidradenitis suppurativa was reffered to our tertiary rheumatologic clinic in Tehran. He complained of recent lack of ability to bend on sacroiliac and hip joint, with decreased range of flexion and extension as well as limited lateral rotation of pelvic girdle. There was no family history of rheumatologic diseases or evidence for (primary and/or secondary) immunodeficiency and no past history of any conditions justifiable by rheumatologic conditions. The patients was afebrile and skin lesions at the time of admission was several suppurative cysts on scalp with diameter of 1 to 1.5 centimeters. These lesions were examined by an expert Dermatologist and she confirmed them as hidradenitis suppurativa (dissecting cellulitis). These cysts on scalp produced a viscous, yellow to green colored pus (Fig. 1). Skin lesions on trunk (upper back and anterior part of chest) and face include severe fulminant pustular and cystic acne with deep scars (Fig. 2). There were some evidence for inflammation in laboratory investigation including: Leukocytosis (WBC= 12200, PMN: 78%), Platelet count: 465000, ESR= 99 and CRP: 160. Pus from suppurative cystic lesions on scalp (Dissecting cellulitis) was drained and evaluated by direct smear (gram stain) and culture. The result was positive gram cocci with many polymorphonuclear cells. The culture of skin lesion and blood culture were negative. HLA-B27 antigen was positive but other findings for autoimmune disorders didn't show any specific findings including: FANA: 1/80 (positive more than 1/80), Anti-ccp antibody, ANA profile and Anti-Ds DNA nucleosome were Negative. Liver function test, serum immunoglobulins and complements were within normal ranges.

Meanwhile, whole body 3-phasic bone scan with 99-technetium showed increased activity in the region of both knees (proximal portion of the tibia) more in the left side and also bilateral increased activity in both iliac bones more in the right side. No other abnormal activity was noted in other parts of the skeleton. It recommend suggestive of multiple active bony lesions (a systemic or infiltrative disorder, or multifocal osteomyelitis). The MRI of findings from hip showed a lesion in iliac bone without joint effusion and suggested an infectious or non-infectious inflammation in the iliac bone.

According to dermatological consult a skin biopsy for more evaluation of lesions was recommended. The result was neutrophilic pseudo-abscesses. Isotretinoin was prescribed in order to prevent further scaring by acne on skin.

Treatment with a non-steroidal anti-inflammatory drugs (NSAID) (naproxen 1500 milligram daily), Isotretinoin 20 milligram daily started. He revealed dramatic response to naproxen in 3 days duration. Low back pain and limitation in range of motion of sacroiliac joint improved in a few weeks. In outpatient follow-up, treatment was tapered after 2 month

Table 1, Modified diagnostic criteria for SAPHO syndrome

Bone +/- joint involvement associated with pustulosis palmoplantarisand psoriasis vulgaris
Bone +/- joint involvement associated with severe acne
Isolated sterile hyperostosis/osteitis§ (adults)
Chronic recurrent multifocal osteomyelitis (children)
Bone +/- joint involvement associated with chronic bowel diseases
Exclude:
Infectious osteitis
Tumoral conditions of the bone
Non-inflammatory condensing lesions of the bone

§ Exception: growth of Propionibacterium acnes.

and discontinue completely after 6 months. He was a mild skin lesion flare up and arthralgia after 6 months stop treatment. We had to start treatment again and his treatment continues for a period of 3 months again. In longtime follow-up, he is not under treatment for 3 years without any flare up.

DISCUSSION

In this report, we introduce a 16-year-old boy with SAPHO syndrome. Although he had excellent response to treatment with NSAID and Isotretinoin, he had flare up after 6 month cessation of treatment.

The SAPHO syndrome is a "skibo" (contraction of skin-bone), characterized by skin manifestations and osteoarticular involvement. Another synomim term for SAPHO is chronic recurrent multifocal osteomyelitis (CRMO). SAPHO and CRMO are more common term for autoinflamatory bone disorders in children. Although typical presentation of SAPHO syndrome have been reported in pediatric group, some authors believe it may well be the same disorder presenting in different age groups or same disorder with different clinical picture. So SAPHO syndrome is frequently utilized by adult rheumatologists, whereas the pediatric community has primarily utilized the term CRMO. Another group of authors utilize each term based on clinical picture. SAPHO syndrome utilize when we have auto-inflammatory bone disorder in conjunction with acne and pustulosis.[8, 9] In fact, the skin involvement in SAPHO syndrome is a neutrophilic dermatosis that can be seen in other auto inflammatory disorders.[8, 10] The etiology of SAPHO syndrome are unknown, but both CRMO and SAPHO syndrome have similar pathogenesis and dysregulation of innate immunity is predisposing of these disorders.[11] It seems CRMO is more severe than other than auto-inflammatory bone disorders such as SAPHO syndrome in clinical presentation and course.12 Due to the various clinical pictures, SAPHO cannot be caused by a single factor. However, it cannot be excluded that cutaneous lesions common to all patients are an etiologic component. Common genetic factors are still unclear. HLA-B27 antigen is not more prevalent than in average. Patients are often positive for HLA-B27 antigen and negative for other Rheumatologic factors; so, patients with sacroileitis according to many references considered as a subgroup of negative spondyloarthropathies.[1,13] Our patient has positive HLA-B27, but he didn't have positive family history for ankylosing spondylitis or psoriatic arthritis.

Pathogenesis is clearly of an enthesopathic nature and can be attributed to an auto-inflammatory and/or immunopathologic phenomenon. No infectious pathogen has been found in osteomyelitis of SAPHO syndrome, but propionibacterium acnes may play an important role, as a potential antigenic trigger.[13]

Although osteitis is main problem in SAPHO syndrome, arthritis has been seen frequently in this syndrome adjacent to active osteitis. Moreover, arthritis as well as sacroileitis can involve joints distant to the osteitis.

The diagnosis is proposed on clinical manifestations, supporting by para-clinical tests and imaging studies in favor of SAPHO syndrome.[14] Diagnostic criteria for SAPHO syndrome was described in 1994 by Kahn, but this criteria was modified in 2003 by American College of Rheumatology in Annual Scientific Meeting (Table 1).[14]

SAPHO syndrome must be suspected when a patient is affected by a pustularskin disease associated with Rheumatic pain. Before final diagnosis, some more common disorders should be ruled out especially infectious disease, but always these patients are missed by infectious osteomyelitis and they were treated several times for infectious osteomyelitis.[7] If examination demonstrates that the pains are produced by sterile inflammation of bones or joints, the hypothesis tends to be confirmed. The results of lab tests are uncharacteristic, with variable signs of inflammation with low activity. In our patient, infectious disease and immunodeficiency was ruled out by history, clinical symptoms (no fever) and negative blood and skin lesion and normal immunoglobulins.

Since 1986, two new diseases were described belonging to SAPHO syndrome: Pustulo-psoriatic hyperostotic spondyloathritis (PPHS) and CRMO.[15] SAPHO syndrome is clinically heterogeneous, covering several diseases. Definite diagnosis can be hard to establish. For each case, clinical, radiological and histopathological signs need to be taken in to account.

The main differential diagnosis of CRMO are acute (septic) osteomyelitis and possibly polyosteomyelitis, Langerhans cell histiocytosis, benign or malignant bone tumors (e.g Ewing's sarcoma), chronic polyarthritis, specially juvenile idiopathic arthritis, ankylosing spondylitis.[13]

Treatment of SAPHO is mainly symptom therapy. No specific drug exists for SAPHO syndrome and there is neither guidelines nor expert consensus on treatment of CRMO and SAPHO, although recently a suggested treatment protocol was published in Pediatric Drugs.[11] The first line treatment of SAPHO syndrome is NSAIDs but many authors believes NSAIDs could not cure SAPHO alone and about half patients didn't meet remission and/ or have flare disease after remission. So, other treatment such as corticosteroids and DMARDS usually use for long-term remission.[1,11,13] The second line drugs usually is prescribed if patient didn't have adequate reponse to NSAIDs after 4 weeks.[11, 13] Similar other auto-inflammatory bone diseases sometimes patients needs to other medication such as steroids, biologic agents, disease modifying anti-rheumatic drugs (Methotrexate, Hydroxychloroquine, Sulfasalazine, Azathioprine, Leflunomide), and Acitretin.[13, 16] Steroids should be prescribed only for a limited time period. In most cases, treatment with Methotrexate is given.[11, 17] It seems, bisphospho-

nates (especially pamidronate) have the benefit in treatment of CRMO as a second line drug and / or in combination with NSAIDs.[10, 11, 16, 18, 19]

Treatment of pustular skin disease, usually of psoriatic type, should be taken in charge go by dermatologists. This is also the case for the serious forms of acne, which favorably respond to retinoids administered orally or tropically.[13, 20] Acne fulminant can become a medical emergency.

The indication of interventional surgery is very limited in SAPHO syndrome such as recurrent osteomyelitis in spine, fracture and/ or for diagnostic biopsy. Nowadays, other surgical treatment have become obsolete.[20] Many cases of SAPHO syndrome have several remission and exacerbations course, so they require long term follow-up by an inter- disciplinary team including rheumatologist, dermatologist, physical therapist and sometimes orthopedics and /or neurosurgeon.[13,20] Our patient had a flare up during 6 months but in long term follow up, he was on remission without any treatment. All the patients with SAPHO benefit from physical therapy.

CONCLUSION

SAPHO syndrome should be considered in patients with musculoskeletal involvement and acne and hydradenitis suppurativa lesion. Our patient had dramatic improvement to Naprox and Isotretinoin. Flare-up of this syndrome is common during a few years.

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CONFLICT OF INTEREST

None.

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