SAPHO syndrome or psoriatic arthritis? A familial case study

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Abstract

Objective. To discuss the relationships between SAPHO (synovitis, acne, pustulosis, hyperostosis and osteitis) syndrome and the group of spondylarthropathies.

Methods. Few reports of familial SAPHO have been published. We describe three children, two sisters and one brother, whose clinical and radiological presentation was in accordance with SAPHO syndrome.

Results. Two children developed psoriasis, and one child palmoplantar pustulosis. Both sacroiliac and sternoclavicular joints were involved in these three cases. Some features in our observations are also common to psoriatic arthritis. No association was found with HLA antigens, but a history of trauma preceding the onset of symptoms was present in all three children.

Conclusions. We can consider that SAPHO is nosologically related to spondylarthropathies. Psoriatic arthritis could be the missing link between SAPHO and spondylarthropathies. It is likely that both genetic and environmental factors are involved.

Key words: SAPHO syndrome, Chronic recurrent multifocal osteomyelitis, Psoriatic arthritis, Spondylarthropathy.

The SAPHO (synovitis, acne, pustulosis, hyperostosis and osteitis) syndrome includes a group of disorders characterized by bone lesions most commonly involving the anterior chest wall, and sometimes associated with dermatological manifestations [1]. This syndrome is considered to be close to the group of seronegative spondylarthropathies [2, 3] and relationships with psoriatic arthritis (PsA) are also of interest [3, 4]. Few reports of familial occurrence of SAPHO syndrome have been published [5–9] and no clear association has been demonstrated with HLA histocompatibility antigens.

We report a new familial case of SAPHO with dermatological manifestations in three children. They concern two sisters and one brother of an Algerian family of 10 children. The parents and other children in the family were free of rheumatic or cutaneous disease.

Case 1

An 8½-yr-old girl presented to her local physician in March 1975 after a fall, with pain in her left lower extremity causing her to limp. Radiographs showed a large osteolytic lesion on the iliac side of the left sacroiliac joint. The erythrocyte sedimentation rate (ESR) was 25 mm/h. The sacroiliac joint was aspirated percutaneously, cultures were negative. Nevertheless, she was given antibiotic therapy. Two years following initial presentation, she was admitted to our institution with cervical pain, arthralgia in the shoulders, wrists, knees and sacroiliac joints, and a mildly elevated temperature. Ocular examination was normal and there was no aphthosis. X-rays revealed bilateral sacroiliitis with condensation of the adjacent bone and erosive lesions of the lower endplate of C5 and of the upper and lower endplate of C6 with osteosclerosing remodelling of the C6 vertebral body. ESR was 120 mm/h, haemoglobin 11.4 g/dl, white cell count (WCC) 9 × 10⁹/l and platelet count 170 × 10⁹/l. Other laboratory investigations were normal, including rheumatoid factor (RF) and antinuclear antibodies (ANA). HLA typing was A2 A28 B51 B57 BW4 CW6 CW14 DRB₁6 DRB₂3 DQB₁6 DQB₂2. Prednisone was started, 2 mg/kg/day, with a dramatic response. Three months after discharge, she developed guttate psoriasis of the legs and anterior chest wall. Symptoms tended to recur once the dose of prednisone was tapered below 20 mg on alternate days. At the age of 12 yr, she complained of swelling over the right sternoclavicular joint. Radiographs demonstrated an...
enlargement of the clavicle at its medial end. The course of the disease fluctuated, with intermittent courses of steroids. At age 16, after being on no treatment for 1 yr, she had a recurrent flare of pain in the right sacroiliac joint and right knee with a pustular rash on the right thigh (no histological examination was performed). One month later, she was reassessed in hospital after a fall on her left side and a lymphocyte-predominant exudative pleural effusion was diagnosed. Pleural RF was absent, cultures were negative and she had a good outcome with spontaneous remission in 2 weeks. The clinical course of skeletal disease was characterized by intermittent periods of exacerbation and improvement since her 18th year. In July 1997, at age 31, she complained of moderate chronic cervical and low back pain. Radiographs showed cervical bridging from C4 to C7 (Fig. 1) and fusion of sacroiliac joints. During the past few years, she had continued to have active skin involvement and examination revealed widespread psoriasis vulgaris.

Case 2

The brother was admitted to our institution in November 1976 aged 9 yr with pain in his left buttock and difficulty bearing weight on his left lower limb. He reported a trivial fall onto his back just prior to the onset of symptoms. Physical examination on admission revealed a tender swelling over the medial end of the left clavicle. Ocular examination was normal and there was no aphthosis. Radiographs demonstrated involvement of the left sacroiliac joint with periarticular sclerosis predominantly in the ilium, and enlargement of the sternal end of the left clavicle with osteolytic lesions. A technetium bone scan revealed increased uptake in the affected areas. ESR was 130 mm/h, haemoglobin 13.6 g/dl, WCC 7.6 × 10⁹/l and platelet count 300 × 10⁶/l. Tests for RF and ANA were negative. HLA typing was A2 B41 B51 BW4 BW6 CW14 CW17 DRB₁₁₁₅ DRB₁₁₁₆ DQB₁₁₅ DQB₁₁₆. An open biopsy of the left clavicle showed prominent subacute inflammation consisting primarily of plasmocytes and polymorphonuclear leucocytes, and some areas of focal osteonecrosis. There was also increased osteoblastic activity and periosteal new bone formation. Cultures were negative. Symptomatic relief was provided by prednisone 1 mg/kg/day, but symptoms tended to recur after stopping treatment. In the second year of the disease, he developed guttate psoriasis on the back and elbows. The course was fluctuating, with intermittent use of steroids. At the age of 15 yr, as prednisone was stopped for 1 yr, he complained of pain in the right elbow and radiographs revealed a lytic lesion with a fine sclerotic margin in the right epicondyle and 6 months later in the right olecranon. Repeat radiographs revealed healing of bone lesions. The clinical course was prolonged with remissions and relapses over several years. In July 1997, at age 30, he was free of symptoms without skin disease. Radiographs showed fusion of the left sacroiliac joint.

Case 3

The young sister was hospitalized in February 1981, age 7 yr, with a 3-month history of arthralgia in the ankles, knees, hips, sacroiliac and sternoclavicular joints. As for her sister and brother, a history of trauma onto her back immediately preceding the onset of symptoms was obtained. Ocular examination was normal and there was no aphthosis. X-rays showed right sacroilitis and a Te99m bone scan showed increased uptake in the right hip, right sacroiliac joint, right knee, right ankle and right sternoclavicular joint. ESR was 48 mm/h, haemoglobin 12.7 g/dl, WCC 6.8 × 10⁹/l and platelet count 290 × 10⁶/l. Serum RF and ANA were not present. HLA was A2 B41 B51 BW4 BW6 CW14 CW17 DRB₁₁₁₅ DRB₁₁₁₆ DQB₁₁₅ DQB₁₁₆. Aspirin, 1500 mg/day, allowed progressive improvement. At age 8, she was reassessed for a recurrent bout of pain accompanied by fever and, for the first time, vesiculopustular lesions of the palms and soles. Histological examination of skin biopsy revealed a non-specific sterile subcorneal pustule. Skeletal radiographs showed three lytic defects with surrounding sclerosis: in the distal left tibia close to the
epiphyseal cartilage plate, in the distal left fibula and in the distal right radius (Fig. 2). ESR was 125 mm/h. Aspirin gave no relief and prednisone 1 mg/kg/day was started with complete resolution of symptoms within 1 month. A few months later, radiographs showed sclerotic changes with disappearance of the lytic lesions. The patient was diagnosed as having chronic recurrent multifocal osteomyelitis (CRMO) associated with pustulosis palmoplantaris (PPP). She had intermittent joint pain and several flares of PPP. At age 12, she complained of painful swelling in the right ankle with corresponding new osteolytic defect in the right distal fibula. She was relatively well for the next few years. In July 1997, at age 23, she complained of some residual pain in the right ankle and right sternoclavicular joint with tumefaction of the medial end of the clavicle. Radiographs showed fusion of the sacroiliac joints.

Discussion

We describe three children, two sisters and one brother, whose clinical and radiographic presentation were in accordance with SAPHO syndrome. All three children developed sacroiliitis and sternoclavicular involvement during the course of observation. The first patient had a severely affected cervical spine with erosive and osteosclerosis vertebral lesions responsible for massive bridging from C4 to C7. Transient and migratory peripheral joint pain was present in all cases. None of them developed radiological evidence of peripheral erosive arthritis. In the third case, the bone lesions showed typical clinical and radiological features of CRMO. In all three children, skin lesions follow the complaints, guttate psoriasis in two cases, PPP in one case. They shared HLA phenotypes: A2, B51, BW4, CW14, DRB16, DQB5. The clinical course was marked by multiple remissions and exacerbations. They are currently still in remission with radiological sequelae, fusion of the sacroiliac joints in the three cases and cervical bridging in case 1.

In 1987, the concept of SAPHO was proposed to include a complex group of osteoarticular disorders [1]. Anterior chest wall involvement is the most characteristic feature of these conditions. The other sites are peripheral as well as axial. In some cases, the sacroiliac joints present a unilateral or bilateral involvement often characterized by juxta-articular bone sclerosis [2]. Erosive and sclerotic changes of the spine can also develop [10]. In most cases, spine lesions are segmental, involving several adjacent vertebrae, evolving with the years towards a vertebral fusion [2]. A non-erosive oligoarthritis may occur in ~30% of patients [11] and arthralgias are frequent. CRMO, first described by Giedion et al. in 1972 [12], is characterized by multiple sites of osseous involvement. Bony lesions usually occur in the metaphyseal region of long bones and are characteristically lytic in nature. Sites involved, in order of decreasing frequency, include the tibia, clavicle, fibula, femur and radius. The clinical course is marked by multiple remissions and exacerbations, but outcome is usually a permanent remission without major sequelae. CRMO primarily affects children and can be considered as the paediatric form of SAPHO syndrome [13]. The histological findings are non-specific inflammatory changes with acute inflammation and periosteal bone formation in the early stages [14].

These rheumatic conditions are closely associated with dermatological disorders including PPP, psoriasis and acne. Skin lesions are sometimes separated by a long time interval from osteoarticular manifestations [15]. Although the aetiology of PPP is unknown, it is thought by many authors to represent a variant of psoriasis vulgaris [16]. Apart from dermatological manifestations, extraskeletal manifestations are rare in SAPHO syndrome. Observations of lung infiltrate [17] and pulmonary nodules [18] have been described, suggesting that lung involvement may be associated with this syndrome. We have found no infective aetiology to explain pleural effusion in our first observation and the spontaneous remission, as for previous cases of parenchymal disease [17, 18], should be an argument to consider it as a manifestation of the disease.

The relationship of the SAPHO syndrome to PsA
remains unclear [19, 20]. Some features in our patients are common to PsA as well: thoracic involvement, sacroilitis, preferential location on the cervical spine. However, osteolytic foci in periarticular locations, as seen in two patients, are not described in PsA as defined by the classification by Moll and Wright [21]. In 1988, Laxer et al. [22] had already suggested that non-infectious inflammatory lesions of bone should be considered as another musculoskeletal manifestation of psoriasis. Recently, a new classification of PsA was made by Hellilwll et al. [4] which distinguishes three subgroups: peripheral arthritis, spondylarthropathy and a group of extra-articular manifestations including SAPHO syndrome. SAPHO syndrome should be classified as a seronegative spondylarthropathy [2, 3] and PsA could be the 'missing link' between this syndrome and spondylarthropathies [3].

PsA in childhood may be more common than previously described. Juvenile psoriatic arthritis (JPsA) precedes the cutaneous manifestations of psoriasis in half the cases [23]. Our two first cases fulfilled the Vancouver criteria of JPsA proposed by Southwood et al. [24]: juvenile arthritis persisting for at least 6 weeks associated, but not necessarily coincident, with typical psoriasis. Nevertheless, for some authors, JPsA does not appear to be a childhood spondylarthropathy, with a low frequency of sacroiliac involvement or enthesitis, a normal frequency of HLA-B27 antigen and a high frequency of ANA [25].

The pathophysiology of SAPHO syndrome remains unknown. No clear association has been demonstrated with HLA antigens, in particular the correlation with HLA-B27 phenotype appears to be weak [3]. Few cases of familial occurrence have been reported [5–9]. In our familial case, no patient carried the HLA-B27 antigen, or other phenotypes usually encountered in PsA. In PsA, it has been suggested that environmental factors could be important in precipitating arthritis in genetically predisposed individuals [26, 27]. We outline that a definite history of trauma preceded the onset of symptoms in all three children, as has already been described in other case reports of PsA [28] or CRMO [29–31]. Finally, organisms with low infectivity, mainly Propionibacterium acnes, have been isolated in a few cases from bone lesions in SAPHO syndrome [32].

This familial case study supports the hypothesis of a close relationship between SAPHO syndrome and PsA. As psoriasis vulgaris may be a skin component of SAPHO syndrome, could SAPHO syndrome be considered as a clinical subset of PsA [33]? In this familial case, like in previous studies, no clear association was found with HLA histocompatibility antigens. It is likely that both genetic and environmental factors are involved.

References

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Familial case study of SAPHO syndrome