Case Report

SAPHO Syndrome and Transient Hemiparesis in a Child: Coincidence or New Association?

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ABSTRACT. We describe a case of synovitis, acne, pustulosis, hyperostosis, osteitis (SAPHO syndrome) in an 8-year-old boy with an unusual presentation of acute transitory hemiparesis. SAPHO syndrome has been reported in association with inflammatory bowel diseases, chest complications, and pulmonary involvement. No patient with both SAPHO syndrome and neurologic complaints has been previously described. Further observations are needed to confirm if SAPHO syndrome and hemiparesis represent a coincidence or a new association. (J Rheumatol 2002;29:384–7)

Key Indexing Terms:
SAPHO SYNDROME
TRANSIENT HEMIPARESIS

The acronym SAPHO (synovitis, acne, pustulosis, hyperostosis, osteitis) was first introduced by Chamot in 1987[1] to designate patients with either musculoskeletal complaints combined with palmoplantar pustulosis and severe acne, or aseptic osteomyelitis preferentially localized to the anterior chest wall[2-9].

Common to all patients with this syndrome is an inflammatory aseptic osteitis. Bones around the anterior chest wall such as the clavicle and sternum are most commonly involved. Sacroiliac joints, mandible, long bones, and spine can also be affected[3,4,6,10,11]. The radiographic and histological features are similar in all patients, both with and without dermatosis.

Skin manifestations of SAPHO include palmoplantar pustulosis and pustulotic psoriasis, severe acne, and various patterns of psoriasis. These skin lesions may appear many years after the onset of bone lesions or may be totally absent, particularly in children[2-9,12].

Inflammatory bowel disease, thrombosis of the subclavian vein, thoracic outlet syndrome, and pulmonary involvement have been described in association with SAPHO[3,6,13-16].

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We describe a child with SAPHO syndrome with an unusual presentation of acute transitory hemiparesis. To our knowledge no patient with both SAPHO syndrome and primary neurologic complaints has been described previously.

CASE REPORT

An 8-year-old right handed boy was referred for evaluation of a right side flaccid hemiparesis. A painful mass over the right sternoclavicular joint (SCJ) had appeared suddenly one week earlier when he was on vacation in the Canary Islands. History included primary enuresis, urinary urgency and frequency, and occasional incontinence. There was also a history of learning disabilities and a mild speech disorder.

On admission, he did not appear sick and had no fever, but was limping. On examination there was a painful, swollen mass (6×5 cm) over the right SCJ, with warm and erythematous skin. Neurologic examination revealed flaccid weakness of the right lower extremity with decreased knee and ankle reflexes. Babinski reflex was diminishing. The strength and motility of the right upper extremity were also slightly impaired. Pain-thermal and light touch sensation were normal. On clinical followup, the right hemiparesis resolved within 2 weeks.

Laboratory tests showed an increase of erythrocyte sedimentation rate (40 mm/h), while C-reactive protein, C3, C4, antinuclear antibodies, rheumatoid factor, and coagulation tests, including anticardiolipin antibodies and lupus anticoagulant, were all normal. Serologic tests for viruses (cytomegalovirus, Epstein-Barr virus, adeno, herpes, echo, Coxsackie, influenza, parainfluenza) and blood cultures for aerobic and anaerobic bacteria were negative, as was the Tine test. Stool for occult blood was negative. Ophthalmologic evaluation was normal. Echocardiogram showed no cardiac abnormalities. He was HLA-B27 negative. Lumbar puncture with cerebrospinal fluid examination was not performed.

Standard radiograph of the SCJ was initially negative for bony lesions; 12 days after the onset, destructive changes with initial bone resorption were present; 3 months later, the clavicle appeared enlarged and sclerotic (Figure 1).

Total body ^{99}Tc scintiscan showed an isolated increased tracer uptake at the medial portion of the right clavicle. In the same area a computerized tomography (CT) scan showed extensive periosteal reaction and multiple areas of osteolysis and cortical destruction (Figure 2).

Cerebral CT scan and magnetic resonance imaging (MRI) performed at onset and one month later, respectively, were both negative, as were carotid

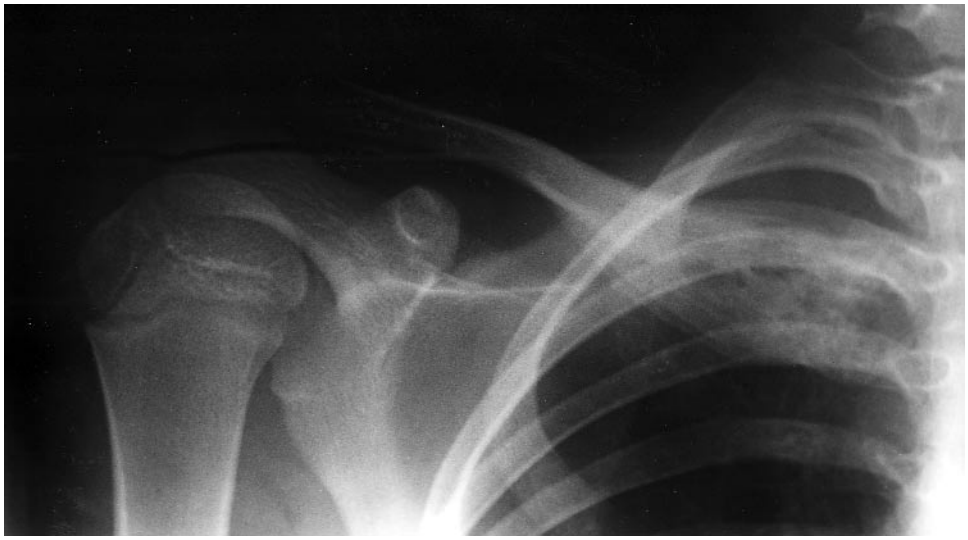

Figure 1. Standard chest radiograph 12 days after onset reveals destructive changes, with initial bone resorption of the right clavicle; the SCJ appears enlarged with increased bone density.

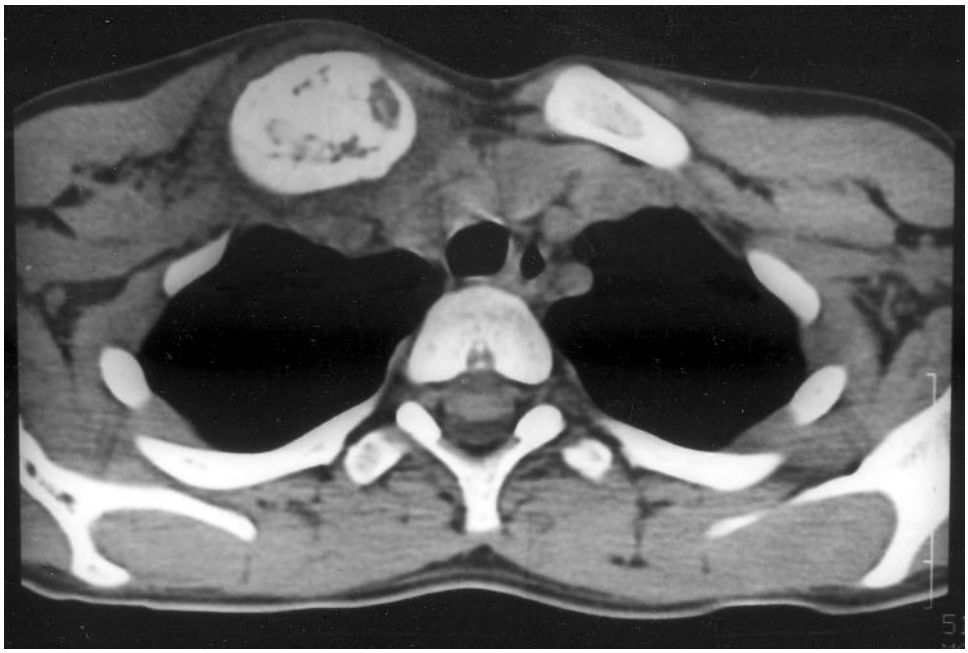

Figure 2. CT scan of the right SCJ region: extensive periosteal reaction of the medial portion of the clavicle with multiple areas of osteolysis and cortical destruction.

and subclavian artery echo Doppler. Gadolinium enhanced spinal MRI revealed a thoracic syringomyelic cavity between T5 and T11, which remained unchanged after 6 and 12 months.

An open biopsy of the medial portion of the right clavicle was performed 3 months after onset. The histological analysis showed osteitis with chronic inflammatory pattern with lymphocytes, plasma cells, and occasional giant cells. Vasculitis was absent. There was proliferation of mature enlarged fibroblast-like cells and apparent destruction of the bone, compatible with SAPHO syndrome. Microbiological cultures of bone and synovium for aerobic, anaerobic, and acid-fast organisms and fungi were negative.

To clarify the relationship between primary enuresis and syringomyelic cavity, further investigations were carried out. Lumbosacral radiograph and MRI were negative. Somatosensory evoked potential study evaluating the cervical, thoracic, and lumbar portions of the spinal cord was normal. A urodynamic study showed normal bladder sensibility and compliance, but decreased functional capacity and detrusorial lack of coordination.

On first admission to the hospital the boy was treated with oral and parenteral antibiotics for 14 days. The subsequent course was characterized by intermittent symptoms of pain and swelling, despite treatment with nonsteroidal antiinflammatory drugs.

DISCUSSION

We describe a child who developed an aseptic SCJ lesion, with acute transitory hemiparesis at onset and radiological

finding of syringomyelia. Infectious or tumoral conditions, suggested by the acute onset of the SCJ mass, were ruled out by negative microbiological cultures and histological examination. A diagnosis of neuropathic arthropathy was also considered on the basis of syringomyelia[17,18]. This entity is rarely observed in the pediatric age group and is usually associated with diseases involving peripheral nerves, such as tabes dorsalis, diabetes, syringomyelia, or myelomeningocele. In our patient, neuropathic arthropathy was excluded because the lesion was in an area supplied by the cervical cord whereas the syringomyelic cavity was in the thoracic cord. As well, the slight width of the cavity, the preservation of pain-thermal sensation and cutaneous trophism, and the rapid recovery suggested a lack of association with syringomyelia. Further, the histological picture of neuropathic arthropathy is characterized by large vascular channels intermixed with cartilaginous, bony debris and areas of immature cartilage and new bone formation. This was not the case in our patient.

On the other hand syringomyelia could explain the enuresis and altered urodynamic findings[19]. This hypothesis was also excluded on the basis of the normal somatosensory evoked potentials.

The diagnosis of SAPHO syndrome was established according to the criteria proposed by Benhamou, *et al* in 1988[2]. It was supported by the sternoclavicular involvement, with typical radiological and histological indications, and by the insidious clinical course.

Our patient did not have cutaneous involvement. However, SAPHO, particularly in children, may occur without skin manifestations[2-9].

SAPHO is rarely reported in pediatric age group[3,5-8], while chronic recurrent multifocal osteomyelitis (CRMO)[8,9] affects children almost exclusively. In recent years these 2 entities have appeared strictly related, but the nature of this relationship remains unclear. The insidious onset, the protracted course with intermittent exacerbations and remissions, and the failure to isolate pathogens from affected areas are common to both conditions. On the other hand, distinctive features of SAPHO are the age of presentation, the frequent involvement of the anterior chest wall, and the more relevant bony lesions. A recent study, including a large series of children with CRMO, has shown almost identical skeletal features in those with and without cutaneous involvement, justifying the use of the unifying acronym SAPHO for both entities[8].

Peculiar to this case and not previously reported is the temporal coincidence between the onset of SAPHO syndrome and acute transitory hemiparesis. The neurological motor deficit of both upper and lower right extremities excluded a peripheral nerve lesion. Cervical spinal cord involvement was ruled out by the asymmetrical weakness, the lack of sensorineural impairment, and the normal spinal MRI. Neurologic complications such as thoracic outlet syndrome[3,6], cervical spinal cord injury[11], and sudden deafness[10] have been described in SAPHO syndrome, but only in adults. These conditions are related to compression of vascular or nervous structures by expansive bone lesions. In our patient as well, this possible pathogenetic mechanism was ruled out.

The neurologic manifestation in our patient could be classified as a reversible ischemic neurologic deficit (RIND). This is a focal neurological deficit with rapid onset, duration of one to 21 days, and unusual permanent neurological impairment, due to a reversible cerebrovascular lesion[20,21]. In children this condition is very rare and is usually associated with systemic or vascular diseases, chemotherapy, or parenteral nutrition[22,23]. The diagnosis is essentially based on clinical course. As in our case, most of the patients have normal clotting tests, cerebral CT, and electroencephalogram results[21].

As the link between SAPHO and RIND is not clear, we speculate about a possible relationship between the 2 events. Infection with a microorganism of low virulence or an immune reactivity to such an infection has been suggested to be the triggering factor of SAPHO syndrome[3,5,8]. RIND can be the consequence of vascular insult due to different causes. Thus the "infectious hypothesis" could explain both the pathogenesis of the osteoarticular lesions and the start of a vasculitis-like process leading to the transient neurological deficit.

Associations of SAPHO syndrome with inflammatory bowel diseases[3,6,13,14], skin manifestations[1-6,12], and pulmonary lesions[15,16] suggest that this condition represents a systemic disease. Neurologic manifestations, as in this patient, could be part of this multiorgan involvement.

Despite our extensive investigations, the nature of the link between SAPHO and acute hemiparesis is not clear. Further observations and a better comprehension of this syndrome are needed to verify if they represent coincidental events or a new association.

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REFERENCES

1. Chamot AM, Benhamou CL, Kahn MF, Beraneck L, Kaplan G, Prost A. Le syndrome acne pustulose hyperostose osteite (SAPHO). Resultats d'une enquete nationale: 85 observations. Rev Rhum Mal Osteoartic 1987;54:187-96.
2. Benhamou CL, Chamot AM, Kahn MF. Synovitis-acne-pustulosis-hyperostosis-osteomyelitis syndrome (SAPHO): a new syndrome among the spondyloarthropathies? Clin Exp Rheumatol 1988;6:109-12.
3. Kahn MF, Khan MA. The SAPHO syndrome. Baillieres Clin Rheumatol 1994;8:333-62.
4. Maugars Y, Berthelot JM, Ducloux JM, Prost A. SAPHO syndrome: a followup study of 19 cases with special emphasis on enthesis

involvement. J Rheumatol 1995;22:2135-41.
5. Reith JD, Bauer TW, Schils JP. Osseous manifestations of SAPHO (synovitis, acne, pustulosis, hyperostosis, osteitis) syndrome. Am J Surg Pathol 1996;20:1368-77.
6. Hayem G, Bouchaud-Chabot A, Benali K, et al. SAPHO syndrome: a long-term follow-up study of 120 cases. Semin Arthritis Rheum 1999;29:159-71.
7. Letts M, Davidson D, Birdi N, Joseph M. The SAPHO syndrome in children: a rare cause of hyperostosis and osteitis. J Pediatr Orthop 1999;19:297-300.
8. Beretta-Piccoli BC, Sauvain MJ, Gal I, et al. Synovitis, acne, pustulosis, hyperostosis, osteitis (SAPHO) syndrome in childhood: a report of ten cases and review of the literature. Eur J Pediatr 2000;159:594-601.
9. King SM, Laxer RM, Manson D, Gold R. Chronic recurrent multifocal osteomyelitis: a noninfectious inflammatory process. Pediatr Infect Dis J 1987;6:907-11.
10. Marsot-Dupuch K, Doyen JE, Grauer WO, de Givry SC. SAPHO syndrome of the temporomandibular joint associated with sudden deafness. Am J Neuroradiol 1999;20:902-5.
11. Deltombe T, Nisolle JF, Boutsen Y, Gustin T, Gilliard C, Hanson P. Cervical spinal cord injury in SAPHO syndrome. Spinal Cord 1999;37:301-4.
12. Kahn MF, Bouvier M, Palazzo E, Tebib JG, Colson F. Sternoclavicular pustulotic osteitis (SAPHO). 20-year interval between skin and bone lesions. J Rheumatol 1991;18:1104-8.
13. Bognar M, Blake W, Aguledo C. Chronic recurrent multifocal osteomyelitis associated with Crohn's disease. Am J Med Sci 1998;315:133-5.
14. Murata I, Satoh K, Yoshikawa I, Masumoto A, Sasaki E, Otsuki M. Recurrent subcutaneous abscess of the sternal region in ulcerative colitis. Am J Gastroenterol 1999;94:844-5.
15. Vaile JH, Langlands DR, Prichard MG. SAPHO syndrome: a new pulmonary manifestation? J Rheumatol 1995;22:2190-1.
16. Ravelli A, Martini A. SAPHO syndrome and pulmonary disease. J Rheumatol 1996;23:1482-3.
17. Allman RM, Brower AC, Kotlyarov EB. Neuropathic bone and joint disease. Rad Clin N Am 1988;26:1373-81.
18. Sequeira W. The neuropathic joint. Clin Exp Rheumatol 1994;12:325-37.
19. Kothari MJ, Kelly M, Darbey M, Bauer S, Scott RM. Neurophysiologic assessment of urinary dysfunction in children with thoracic syringomyelia. J Child Neurol 1995;10:451-4.
20. Marshall J. The cause and prognosis of strokes in people under 50 years. J Neurol Sci 1982;53:473-88.
21. Taghavy A, Hamer H. Parenchymal "damage" in transient ischemic attacks and prolonged reversible ischemic neurologic deficits: the role of cranial CT and EEG. Int J Neurosci 1992;66:251-61.
22. Pascual Pascual SI, Pascual Castroviejo I, Velez A. Ischemic cerebrovascular accidents in childhood. An Esp Pediatr 1988;28:279-85.
23. Pihko H, Tyni T, Virkola K, et al. Transient ischemic cerebral lesions during induction chemotherapy for acute lymphoblastic leukemia. J Pediatr 1993;123:718-24.