Case reports

The SAPHO syndrome—a report of 2 patients

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Patient 1

A 44-year-old woman suffered from frequent episodes of bursitis-like complaints in several joints, backache and tiredness for more than 10 years. She lost all her teeth due to recurrent infections and had pain in the temporo-mandibular joints. Physical examination revealed no abnormalities, apart from pustulosis of the hands and feet (Figure 1).

C-reactive protein, ESR and the leucocyte differential count were normal and HLA-B 27 was negative. A technetium^{99} scan showed an increased uptake of isotope (Figure 2) in the sternum (Bull's head sign), both coracoid processes, the axial skeleton and symphysis, and the left temporo-mandibular joint. SAPHO (type III) was diagnosed on the basis of these findings.

Patient 2

A 30-year-old woman was referred because of fatigue and backache between the shoulder blades for 3 years. She had pustules and erythema on the soles of her feet and the palms of her hands, but no other abnormality.

Laboratory investigations were normal. Sclerosis of the thoracic spine was present (Figure 3) which, on MRI, was diagnosed as spondylodiscitis of Th5-7 vertebrae (Figure 4). A total body technetium^{99} scan showed multiple active locations including the anterior chest wall with a typical Bull's head sign. These findings established the diagnosis of SAPHO (type I).

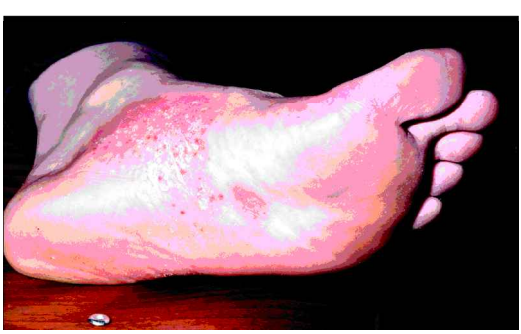


Figure 1. Left foot of patient 1, typical aspect of palmoplantar pustulosis.

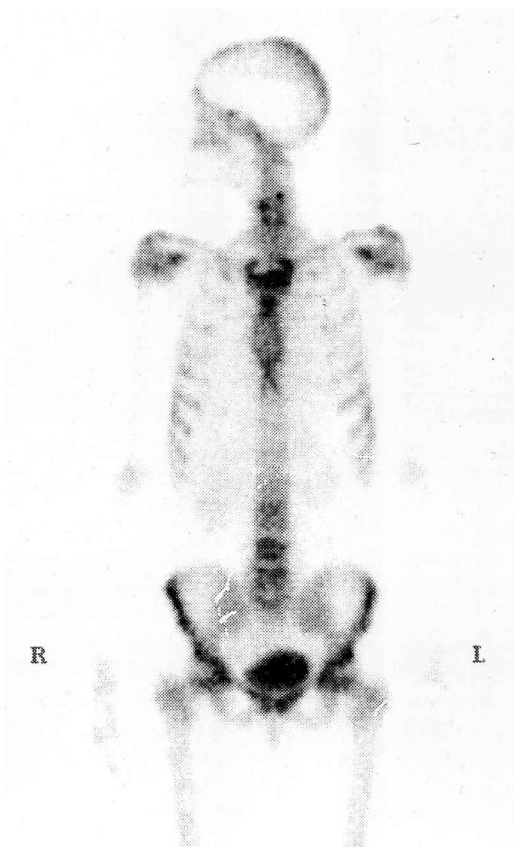
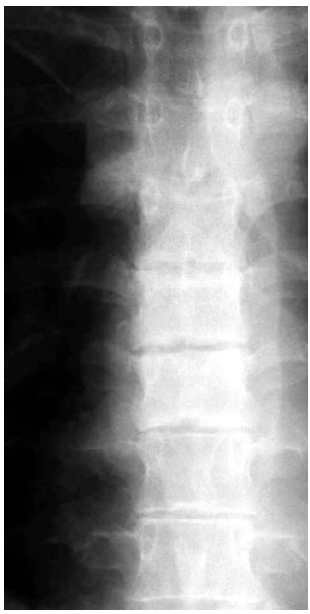


Figure 2. Technetium^{99} scan of patient 1 showing raised activity in anterior chest wall (Bull's Head sign) and both coracoid processes, lower cervical spine, both hips and symphysis.



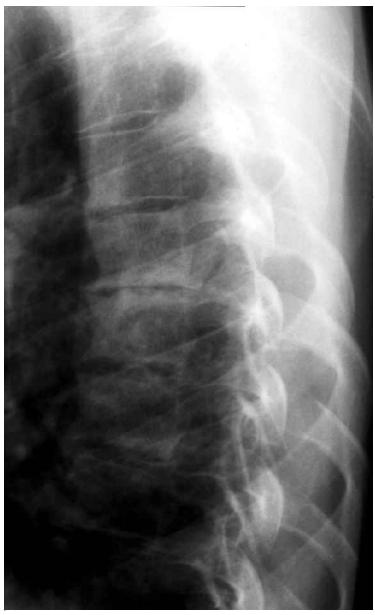


Figure 3. Patient 2 with sclerosis of vertebrae Th 5–7.

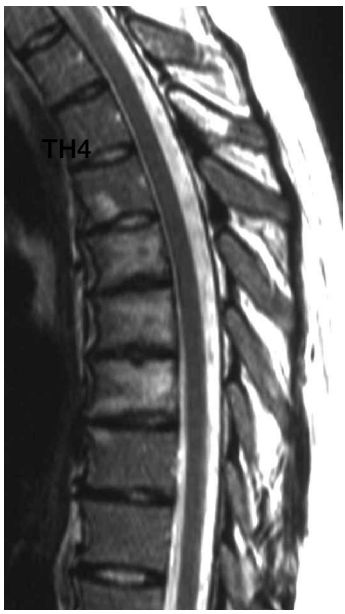


Figure 4. Patient 2. Mid-sagittal MRI scan of the thoracic spine with elevated signal in vertebrae Th 5–7, suggestive of spondylodiscitis.

Schilling and Kessler's (2000) classification of SAPHO syndrome

Group	Cluster of symptoms	86 patients
I	**Spondarthritis hyperostatica pustulo-psoriatica (SHPP)** A triad of 1. pustulosis palmo-plantaris (PPP) 2. sterno-costo-clavicular hyperostosis (SCCH) 3. 'productive' or active spondylopathy	31
II	**Sterno-costo-clavicular hyperostosis** Often associated with symptoms of group I, but incomplete triad	10
III	**Chronic recurrent multifocal osteomyelitis (CRMO)** Primarily non-purulent osteomyelitis of plasma cell sclerotic type Reactive inflammatory? 50% of patients showed PPP	25
IV	**Anterior chest wall** Inflammatory syndrome of the anterior chest wall, most likely CRMO limited to the sternal bone	15
V	**Osteoarticular symptoms in cases of acne pustulosa** Acne-associated spondarthritis and CRMO in the case of acne	5

Discussion

SAPHO, an uncommon chronic disease with a cluster of symptoms affecting the bones and skin, is an acronym for Synovitis (inflammatory arthritis), Acne (pustulosa), Pustulosis (psoriatic, palmoplantar pustulosis), Hyperostosis (abnormal osteogenesis) and Ostitis (osteomyelitis) (Sundaram et al. 1996, Schilling and Kessler 2000, VanDoornum et al. 2000).

Two types of the syndrome (Table) are more widely known as CRMO (Chronic Recurrent Multifocal Osteomyelitis) and SHPP (Spondarthritis Hyperostotica Pustulo-psoriatica).

SAPHO is a clinical diagnosis; no specific laboratory tests confirm its presence. A typical patient has pain and stiffness over the affected bone, backache and fatigue. SAPHO is characterized by skin lesions combined with exacerbations and remissions of osteomyelitis-like lesions at numerous sites. The anterior chest wall, spine and sacroiliac joints and the metaphysis of tubular bones are affected more commonly, but the skull bone and jaw may be affected as well. Knowledge of this disease may prevent repeated biopsies, unnecessary investigations and treatments (Schuster et al. 1996, Boutin and Resnick 1998, Hayem et al. 1999, Schilling et al. 2000, Roldan et al. 2001).

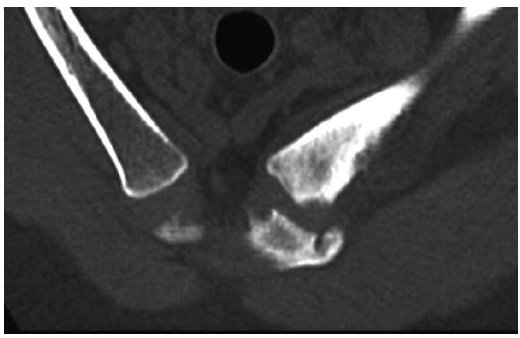


Figure 5. Patient 2. CT-scan through both clavicles. The left clavicle is irregular and sclerotic.

Skin lesions vary from common psoriasis, fulminant acne, palmo-plantar pustulosis and pustular psoriasis. The skin lesions may precede or follow bony involvement and may be absent at the time of presentation of other symptoms in 1/3 of patients (DiMeco et al. 2000, Schilling and Kessler 2000).

Laboratory investigations. The C-reactive protein and ESR are normal or slightly raised during exacerbations, but the white cell count is usually normal. Although HLA-B27 is usually negative, the frequency of the HLA-B27 phenotype and associated diseases (e.g., inflammatory bowel diseases) is slightly higher in persons suffering from the SAPHO syndrome than in the general population. Biopsy of a lesion usually does not reveal microorganisms (Kahn 1995, Jahangier et al. 1997, Hayem et al. 1999, Winchester 1999).

Microscopic features of the bony lesions vary with time. When biopsied early, a polymorphonuclear infiltrate is the main feature, and the findings are very similar to infectious osteomyelitis. Mononuclear cells characterize the main feature in the intermediate stage, while late lesions have enlarged sclerotic bone trabeculae with increased numbers of osteocytes and marrow fibrosis (Schilling and Kessler 2000, VanDoornum et al. 2000).

On plain radiographs, CT scan and MRI, typical findings consist of reactive sclerosis around lytic areas as in Paget's disease, and localized soft tissue swelling. The upper anterior chest wall is the site of predilection (Figure 5). In the spine, it mimics spondylodiscitis. MRI and CT are often helpful in establishing that the lesion is expanding, but can not distinguish between SAPHO lesions, osteomyelitis and malignancy (Sundaram et al. 1996, Jurik and Egund 1997, Girschick et al. 1998).

Total body technetium^{99} scintigraphy should be done early as it often shows clinically silent frequently bilateral, sites of involvement, as well as the typical 'Bull's head sign' (activity in the sternum and clavicle). The diagnosis of SAPHO is chiefly based on the clinical-radiological correlation, while the laboratory findings are invaluable in excluding other inflammatory or malignant conditions (Schuster et al. 1996, Boutin and Resnick 1998, Winchester 1999, Schilling et al. 2000).

Because of the slightly higher frequency of the HLA-B27 phenotype than in the general population, SAPHO is often regarded as a seronegative spondylarthropathy. However, it seems more likely that it is an autoimmune response, triggered by a microbial pathogen. Various mechanisms have been proposed, including the molecular mimicry hypothesis, which suggests that the immune system attacks normal osteoarticular tissue, mistaking it for structures or molecules of a microorganism. Another hypothesis suggests that the coupled product of an immunoglobulin and fragments from a microorganism is deposited in joints or bones, activating an inflammatory reaction (Boutin and Resnick 1998). The isolation of Propionibacterium acnes, recovered from biopsy specimens of SAPHO lesions (and lesions of severe acne), and experimental data on animals seem to support the autoimmune response theory (Kahn 1995, Schuster et al. 1996, Jahangier et al. 1997, Hayem et al. 1999).

A classification of SAPHO syndrome was proposed by Schilling and Kessler, who analyzed the clinical, radiological and histological/histopathological findings in 86 cases. They divided the patients into five groups according to their signs and symptoms (Table). Groups I (SHPP) and III (CRMO) are supposed to be well-defined diseases, while groups II, IV and V show various symptoms. We advocate the use of their classification, since SAPHO syndrome per se needs further differentiation (Schilling and Kessler 2000, Schilling et al. 2000).

To our knowledge, no controlled study on the treatment of SAPHO exists. Non-steroidal anti-inflammatory drugs are usually given, with satisfactory results. Patients who do not respond to NSAIDs are often treated with prednisone or methotrexate. Most authors claim that antibiotic

treatment is not indicated, but surprisingly, some still use it (Hayem et al. 1999, Rothschild et al. 2000, Schilling and Kessler 2000, Roldan et al. 2001).

The prognosis of SAPHO is good; it is usually a self-limiting disease. We conclude that knowledge of the SAPHO syndrome can avoid the use of numerous invasive procedures, such as repeated biopsies and unnecessary surgical interventions.

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