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Synovitis, acne, pustulosis, hyperostosis, and osteitis (SAPHO) syndrome — A challenging diagnosis not to be missed

Petra Zimmermann [a], **Nigel Curtis** [a,b,c,*]

[a] *Infectious Diseases Unit, The Royal Children's Hospital Melbourne, Parkville, Australia*
[b] *Department of Paediatrics, The University of Melbourne, Parkville, Australia*
[c] *Infectious Diseases & Microbiology Research Group, Murdoch Children's Research Institute, Parkville, Australia*

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Propionibacterium acnes

Summary SAPHO syndrome manifests as chronic inflammation of bones and joints, which may or may not be accompanied by skin changes. The term SAPHO is an acronym that stands for synovitis, acne, pustulosis (usually palmoplantar), hyperostosis and osteitis. The bones most commonly affected are those in the anterior chest wall (mainly the sternum, clavicles and sternocostoclavicular joints), the vertebrae and the sacroiliac joints, but peripheral and flat bones may also be involved, especially in children. There are no validated diagnostic criteria for SAPHO, and diagnosis is based on clinical and radiological findings. One of the main challenges in diagnosis is that the clinical features may occur many years apart. Additionally, patients may not develop all manifestations. Delayed diagnosis, as a result of a lack of awareness of SAPHO, can lead to patients suffering ongoing pain and disfiguring skin manifestations. One theory is that *Propionibacterium acnes* (isolated from bone biopsies in many SAPHO patients) triggers an auto-immune mediated chronic inflammation in genetically predisposed individuals. Treatment involves the use of nonsteroidal anti-inflammatory drugs, intra-articular steroids, bisphosphonates and biologicals. The course of SAPHO is often prolonged but, despite the challenges in diagnosis and treatment, the long-term prognosis is good.

Background

The term SAPHO is an acronym which stands for synovitis, acne (often severe forms like acne conglobata, acne fulminans or hidradenitis suppurativa), pustulosis (usually palmoplantar), hyperostosis and osteitis. It was introduced by Chamot in 1987 when the French Society of Rheumatology described 85 patients with this combination of manifestations.[1] Before this, the term chronic recurrent multifocal osteomyelitis (CRMO), was used to described

* Corresponding author. Department of Paediatrics, The University of Melbourne, The Royal Children's Hospital, 50 Flemington Rd, Parkville, 3052, Australia. Tel.: +61 3 9345 6366; fax: +61 3 9345 4751.
E-mail address: nigel.curtis@rch.org.au (N. Curtis).

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an auto-inflammatory disorder of bones manifesting with insidious onset of pain and swelling of affected bones and joints with or without fever.[2] After its initial description, many cases of CRMO in association with skin conditions, especially palmoplantar pustulosis (PPP), were observed and reported using up to 50 different names.[3] There is considerable confusion in the literature as these names are still sometimes used to report patients that would be better categorised as SAPHO. Previously it was thought that CRMO is the paediatric presentation of SAPHO. But skin manifestations have been underreported in children[4] and adults can also present solely with osteoarticular manifestations.[5,6] Therefore CRMO and SAPHO are now seen as part of a clinical spectrum of the same disease. Lately CRMO has been called chronic non-bacterial osteomyelitis (CNO), recognising the sometimes more chronic than recurrent course of the disease.[7]

Because of the frequent involvement of the axial skeleton (sacroileitis and spinal lesions), the occurrence of enthesitis and the associations with psoriasis and inflammatory bowel disease (reported in around 8% of SAPHO patients)[6,8] SAPHO sometimes gets classified as a seronegative spondyloarthritis.[9] But in contrast to seronegative spondyloarthropathies, sacroileitis in SAPHO is more frequently unilateral and associated with hyperostosis[10] and there is no clear association with human leukocyte antigen (HLA)-B27.[8,11,12]

Other related auto-inflammatory diseases are Majeed syndrome, which, in addition, to the inflammatory osteoarticular symptoms and skin changes, also presents with congenital dyserythropoietic anaemia (CDA) and DIRA (deficiency in interleukin-1 receptor antagonist) syndrome, a disease affecting young children, presenting with multifocal osteomyelitis and diffuse pustular rash. Further diseases overlapping with SAPHO are the autosomal-dominant inherited PAPA (pyogenic sterile arthritis, pyoderma gangrenosum and acne) syndrome, PASH (pyoderma gangrenosum, acne and hidradenitis suppurativa)

Table 1 Diagnostic criteria proposed for SAPHO syndrome.

Benhamou 1988[21]	Kahn 1994[3]	Kahn 2003[22]
Inclusion criteria 1 of the following 4:	**Inclusion criteria** 1 of the following 3:	**Inclusion criteria** 1 of the following 5:
Osteoarticular manifestations with acne conglobata, acne fulminans, or HS	Acute, subacute, or chronic arthritis associated with PPP, pustular psoriasis, or SA	Bone—joint involvement associated with SA
Osteoarticular manifestations with PPP	Any sterile osteitis associated with PPP, pustular psoriasis, PV or SA	Bone—joint involvement associated with PPP and PV
Hyperostosis (of the anterior chest wall, limbs, or spine) with or without dermatosis		Isolated sterile hyperostosis/osteitis (adults) (exception: growth of *P. acnes*)
CRMO involving the axial or peripheral skeleton with or without dermatosis	CRMO, usually sterile or with presence of *P. acnes*, spine might be involved, with or without skin condition	CRMO (children)
		Bone—joint involvement associated with chronic bowel diseases
Exclusion criteria Septic osteomyelitis with the exception of *P. acnes* Infectious ACW arthritis Infectious PPP Palmoplantar keratoderma (Vidal-Jacquet syndrome) Diffuse idiopathic skeletal hyperostosis (DISH), except for fortuitous association of this frequent condition Osteoarticular manifestations (mainly hyperostosis) of retinoid therapy		**Exclusion criteria** Infectious osteitis Tumoral conditions of the bone Non-inflammatory condensing lesions of the bone
Sometimes reported Possible association with psoriasis vulgaris Possible association with inflammatory enterocolopathy Features of ankylosing spondylitis Presence of low-virulence infections (*P. acnes)* in osteoarticular lesions Association acne vulgaris-ACW hyperostosis		