SAPHO and Mönckeberg's sclerosis: two rare diseases and one patient

Sirs,
We report medial arterial calcification (Mönckeberg's sclerosis) in a patient with SAPHO, an auto-inflammatory syndrome of unknown aetiology consisting of Synovitis, Acne, Pustulosis, Hyperostosis and Osteitis (1). He had no cardiovascular risk factors and his history was remarkable for past jaw osteomyelitis, depression, colonic diverticula, chronic anaemia, and claudicatio intermittens for which he was taking aspirin, citalopram, prednisone, pantoprazole, iron supplements, and ibandronic acid. SAPHO was diagnosed when he was 42 years old; ten years later, the patient underwent amputation of the right lower limb below the knee and of the first and second fingers of the left foot for septic gangrene. At that time, SAPHO was not active. At follow-up after six months, the patient was well and planar radiographs of the lower limbs showed severe and extensive calcification of iliac, femoral, tibial, and interdigital arteries with a "railroad track" pattern (Fig. 1); the abdominal aorta was not involved.
The patient fulfilled the Benhamou criteria for SAPHO. Furthermore, in the appropriate context, jaw osteomyelitis is now considered a SAPHO manifestation (2). The anterior chest wall is involved in most SAPHO patients and thrombosis is uncommon. There is no report of the association of SAPHO with arterial diseases. Fifteen cases of thrombosis of the subclavian and jugular veins and the superior vena cava have been reported; two patients also had iliac vein thrombosis and pulmonary embolism, and one case was diagnosed with the antiphospholipid antibody syndrome (3). At onset of thrombosis, all of them had mechanical entrapment, sheathing and obstruction of involved veins by a fibro-inflammatory plaque.
We provide the first evidence of the association of SAPHO with Mönckeberg's sclerosis. Medial calcification of small-to-medium-sized arteries with no intimal thickening is the hallmark of Mönckeberg's sclerosis (4, 5). It is associated with aging and is highly prevalent in type II diabetes and end-stage renal disease. Our case, however, was a relatively young man with no diabetes and normal renal-function tests. Patients are at risk for cardiovascular mortality, stroke and lower-limb amputation with an unpredictable although generally poor long-term outcome. Many cases have an indolent course, which could contribute to late detection and high mortality and complication rates.
The pathophysiology of Mönckeberg's sclerosis involves deposition of calcium phosphate in the extracellular matrix along the elastic lamina of arterial media (4, 5). As the lesion advances, media are filled with linear and parallel circumferential rings of calcium phosphate crystals, accounting for the "railroad track" radiographic pattern (6). These changes result in arterial stiffness, decreased compliance, and impaired perfusion leading to cardiovascular dysfunction. Calcification may not be restricted to arteries and soft tissues and other sites could be involved (7, 8).
Medial calcification is an active process (4, 5). Macrophages and vascular smooth muscle cells migrate and differentiate into osteoclast-like cells that initiate the process, however the underlying molecular and genetic pathways are poorly understood. Elevated blood calcium and phosphorus levels, suppressed parathyroid hormone, apoptosis, pro-inflammatory cytokines, reactive oxygen species, and lipid oxidation are all mechanistically implicated (4, 5).
It is unclear whether Mönckeberg's sclerosis and atherosclerosis are different diseases or represent a continuum of the same disease spectrum. Spotty calcified areas interspersed with non-calcified segments are found near branch points within the tunica intima of atherosclerotic large to medium-sized elastic proximal arteries. In contrast, calcification of Mönckeberg's sclerosis diffusely involves the deeper layers of smaller and distal muscular arteries such as the radial artery, intermammary arteries, and arteries in the ankle and foot. Furthermore, the intimal atherosclerotic calcification occurs near lipid or cholesterol deposits whereas medial calcIfication of Mönckeberg's sclerosis does not involve such deposits.
We cannot rule out a common pathophysiologic pathway between Mönckeberg's sclerosis and SAPHO, however if this association is clinically meaningful rather than due to chance is unclear. In the meanwhile, we suggest to screen SAPHO patients for vascular disorders and thrombosis.

G. Famularo[1], *MD, PhD*
F. Ceralli[2], MD
F. Sensi[1], MD
L. Gasbarrone[1], *MD*
G. Minisola[1], *MD*

[1]Internal Medicine and [2]Rheumatology, San Camillo Hospital, Rome, Italy.

Address correspondence to: Giuseppe Famularo, Internal Medicine, San Camillo Hospital, Circonvallazione Gianicolense, 00152 Rome, Italy.
E-mail: gfamularo@scamilloforlanini.rm.it

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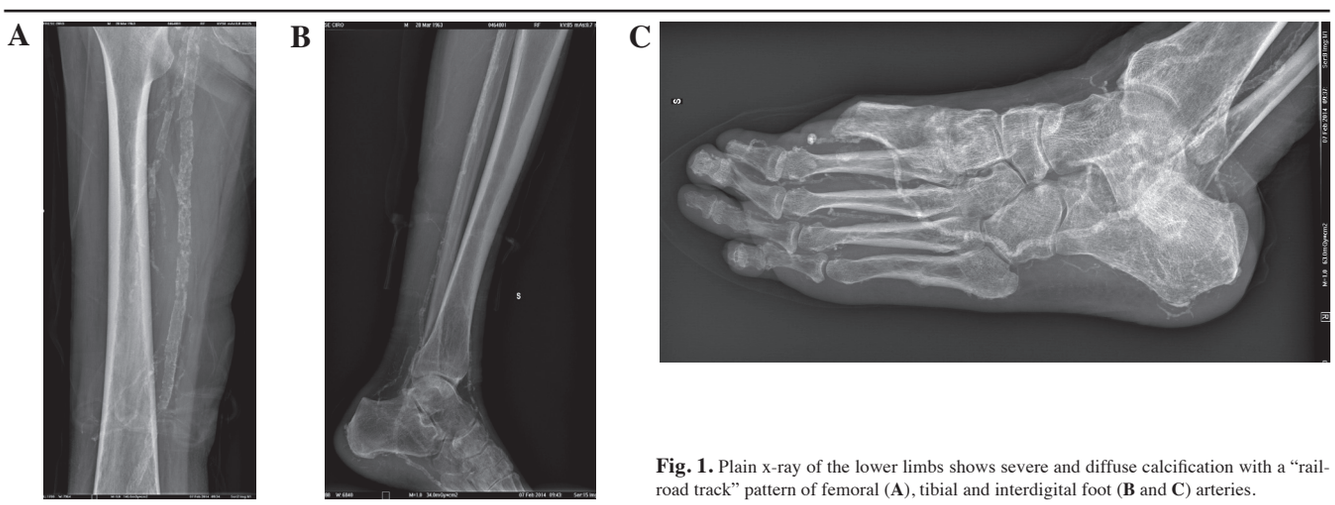

Fig. 1. Plain x-ray of the lower limbs shows severe and diffuse calcification with a "railroad track" pattern of femoral (**A**), tibial and interdigital foot (**B** and **C**) arteries.