Stress in a Case of SAPHO Syndrome

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In this article, we describe a case of seemingly stress-induced SAPHO (synovitis, acne, pustulosis, hyperostosis, osteitis) syndrome in a man who exhibited the central features of palmoplantar psoriasis and anterior chest involvement. We also review the etiology, pathogenesis, and treatment of SAPHO syndrome and emphasize the important differences between this syndrome and psoriatic arthritis.

In 1987, Chamot and Benhamou[1] coined the acronym *SAPHO* (synovitis, acne, pustulosis, hyperostosis, osteitis) to designate a clinicoradiologic entity with a combination of skin, bone, and joint manifestations. Since Sonozaki[2] first reported on SAPHO in 1981, the syndrome (under a variety of names) has been the subject of an increasing number of articles. The fundamental component of SAPHO syndrome is inflammatory osteitis, mainly on the anterior chest wall. The syndrome also may affect the axial skeleton (spine and sacroiliac joints) and peripheral joints and even flat bones such as the ilium and mandible.

Skin diseases are prominent in two thirds of patients with SAPHO syndrome. These diseases include, in decreasing frequency, pustulosis palmaris et plantaris, acne fulminans, acne conglobata, hidradenitis suppurativa, and various patterns of psoriasis. The skeletal and cutaneous manifestations of SAPHO syndrome are usually expressed simultaneously but can occur as much as 2 decades apart. Minor skin disease does not exclude the diagnosis of SAPHO syndrome.

To our knowledge, we were the first to report a case of SAPHO syndrome related to stress.[3,4] The patient was a young woman with classically presenting palmoplantar pustular psoriasis, acne, and sternoclavicular joint involvement.[3,4] In the present article, we report the case of a second patient—a man with SAPHO skin and bone manifestations apparently triggered partly or entirely by stress.

Case Report

A 45-year-old man of Yemenite origin presented to our outpatient clinic with a 2-month history of a palmoplantar pustular eruption and was hospitalized. Previous ambulatory treatment (topical steroids, tar preparations, acitretin tablets) was stopped after one week because of hyperlipidemia. Shoulder and anterior chest pain also developed at that time.

Ischemic heart disease was ruled out, and nonsteroidal anti-inflammatory drugs (NSAIDs) were begun (diclofenac suppositories, ibuprofen tablets). The patient's medical history included 40 pack-years of heavy smoking. There was no family history of psoriasis. The patient described having been forced to leave his job and being under severe emotional stress during the 3 months preceding his rash outbreak.

Results of the physical examination were normal except for tenderness on palpation of the sternum and on elevation of the right arm, symmetrical distribution of thick erythematous plaques with adherent white scales and small pustules merging into lakes of pus on the palms and soles (Figure 1), a single erythematous scaled lesion on the scalp, and fine pitting on several fingernails. Erythrocyte sedimentation rate was elevated (40 mm/h); blood count and blood chemistry results were normal, except for a finding of hypertriglyceridemia (305 mg/dL). Pus culture results were negative for bacteria, viruses, and fungi; results of blood and urine cultures were normal. Results were negative from serologic workups for collagen vascular diseases, human immunodeficiency virus, and human leukocyte antigen (HLA) typing for B27. Results of a histologic examination of an early pustular lesion showed psoriasiform epidermal hyperplasia with alternating parakeratosis and orthokeratosis (Figures 2 and 3), subcorneal infiltration of polymorphonuclear lymphocytes, widened dermal papillae, and an increased number of tortuous capillaries.

Results of radiographs of the chest, cervical and lumbar spine, and sacroiliac and acetabular joints

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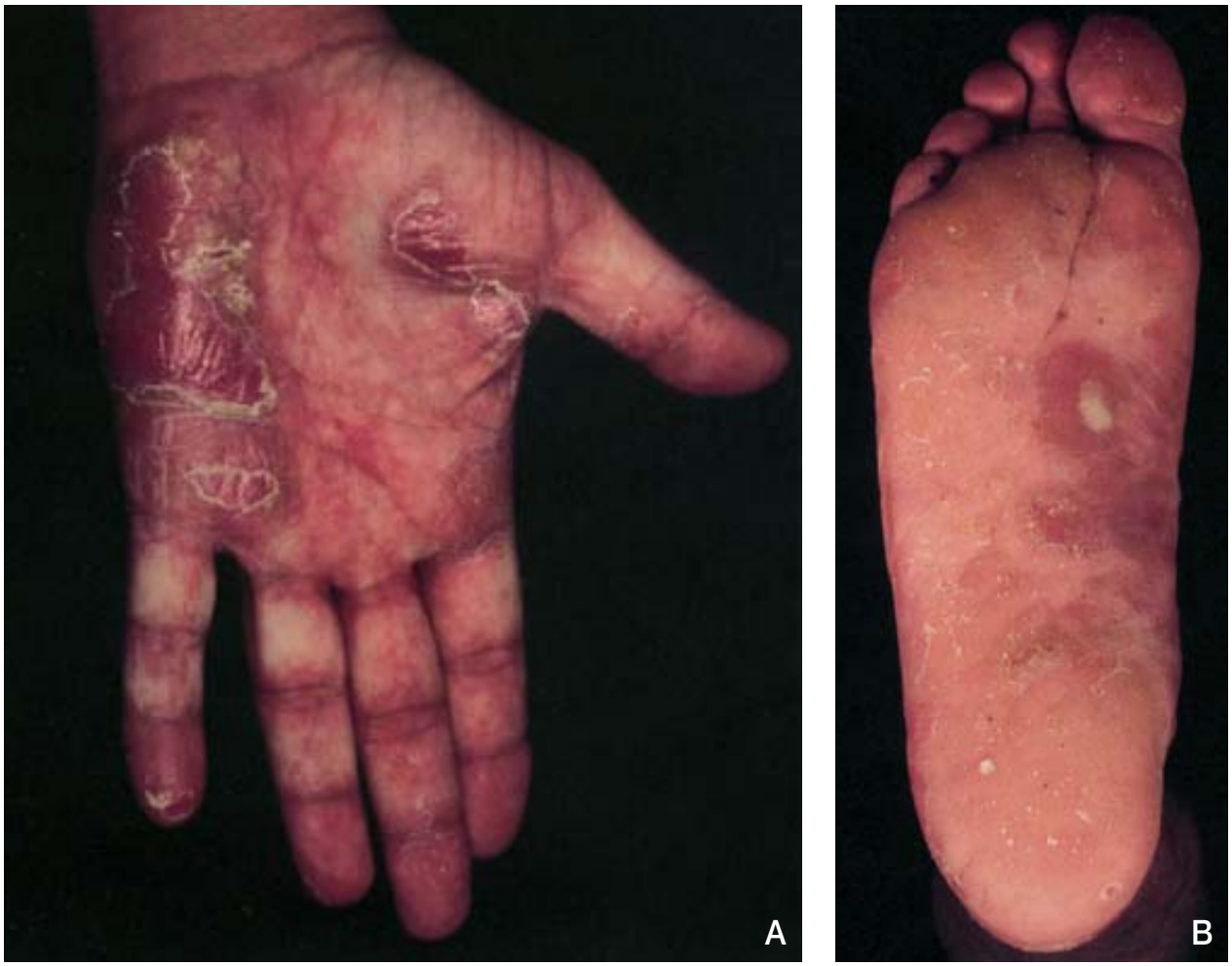

Figure 1. Pustular eruption on the palm (A) and sole (B) of a 45-year-old man.

were normal. A technetium-labeled bone scan image showed increased uptake in the sternal body and lateral third of the sternocostal joints (Figure 4).

SAPHO syndrome was diagnosed on the basis of the clinical and histologic skin findings, as well as the finding of multifocal osteitis on the bone scan. The patient was treated with a topical steroid, tar, and salicylic acid preparations and improved gradually. NSAID treatment was discontinued. The recommendation from a psychiatric consultation did not include anxiolytic or antidepressant treatment. New crops of pustules appeared on the palms and soles after the patient spent a weekend at home. A regular regimen of topical psoralen and phototherapy was started, the patient began a new job, and the eruption gradually cleared.

Comment

SAPHO syndrome includes a broad array of clinical patterns characterized by pseudoinfectious multifocal osteitis and past or current history of skin lesions with histologic evidence of neutrophil-rich aseptic infiltrations.[5] This syndrome primarily affects young adults but can occur and have the same manifestations in children.[6] In most series, females are affected more than males are; among patients with acne, the reverse is true.

In SAPHO syndrome, the main histologic inflammatory process is osteitis. Radiologic findings for osteitis are diverse, because manifestations change with lesion progression. Early lesions, in which polymorphonuclear cells dominate, can go undetected on plain radiographs; only a technetium-labeled bone scan image shows positive results at this stage. Later in the course of the disease, the inflammatory infiltrate consists mainly of monocytes and fibroblasts, and bone remodeling and bone marrow fibrosis have occurred; at this stage, sclerosis and hyperostosis are found on clinical and radiologic examination.[7]

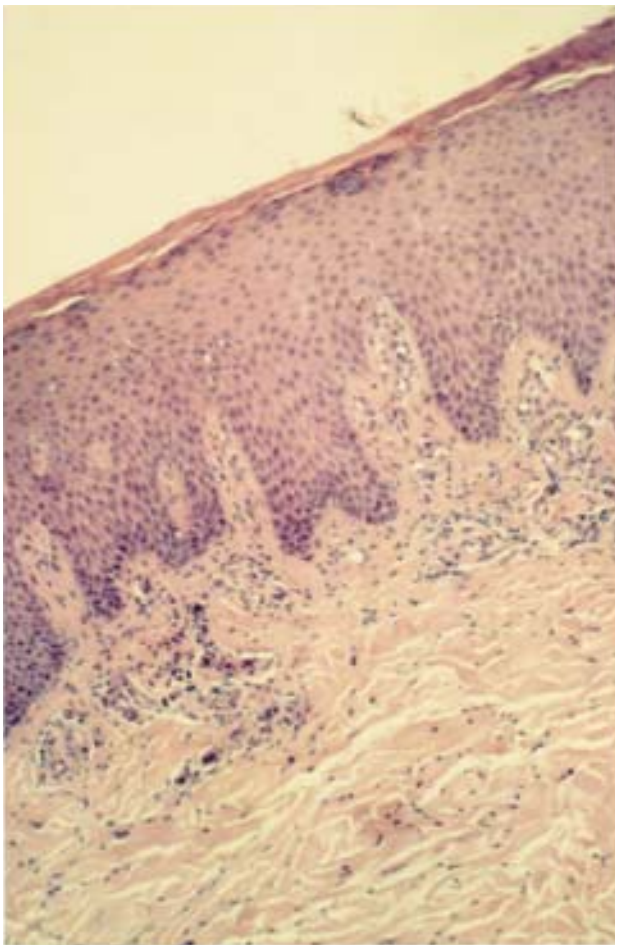

Figure 2. Results of a punch biopsy of a pustular lesion were positive for psoriasiform epidermal hyperplasia with alternating parakeratosis and orthokeratosis and showed an increase in the number of tortuous capillaries in the dermal papillae (H&E, original magnification ×100).

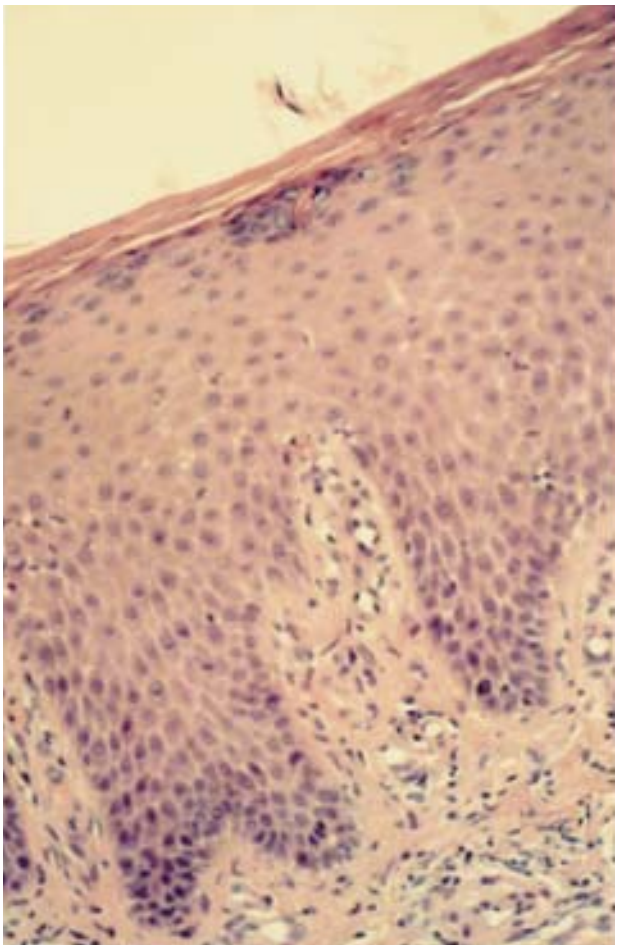

Figure 3. Subcorneal infiltration of polymorphonuclear lymphocytes (H&E, original magnification ×400).

Our patient presented with pustulosis palmaris et plantaris and anterior chest multifocal osteitis—features compatible with SAPHO criteria. We made the diagnosis early in the course of the disease, in the acute stage of osteitis, when only the bone scan image showed activity in the affected foci.

Although the etiology and pathogenesis of SAPHO syndrome remain unclear, they seem to mainly involve the immune system, with complex interactions occurring among superantigens, cytokines, and growth factors. Kahn and Kahn[5] suggested the presence of a specific gene associated with psoriasis-related conditions. *Propionibacterium acnes*, a common skin saprophyte, was isolated from some open bone biopsies in one study, but other specimens were sterile.[8] Hayen et al[9] speculated that SAPHO syndrome is a form of seronegative spondyloarthropathy—a suggestion supported by associations with psoriasis, sacroiliitis, inflammatory bowel disease, and increased prevalence of HLA B27 in as much as 30% of subjects in different Western studies.

Some of the skeletal components of SAPHO syndrome closely resemble psoriatic arthritis; distinguishing these 2 entities is mandatory because they differ in the pathologic process underlying bone changes and, more important, in natural history.[10] The main pathologic process in psoriatic arthritis is enthesopathy, which causes erosive skeletal lesions and mutilation. In SAPHO syndrome, osteitis is chronic but not mutilating. The high prevalence of the HLA B27 haplotype in both entities, however, may unite them in a single pathogenic spectrum.

Our patient had 3 factors known to induce or exacerbate SAPHO syndrome: heavy smoking (which correlates with developing pustulosis palmaris et plantaris), NSAID use, and severe stress. The patient's circumstances suggested that emotional

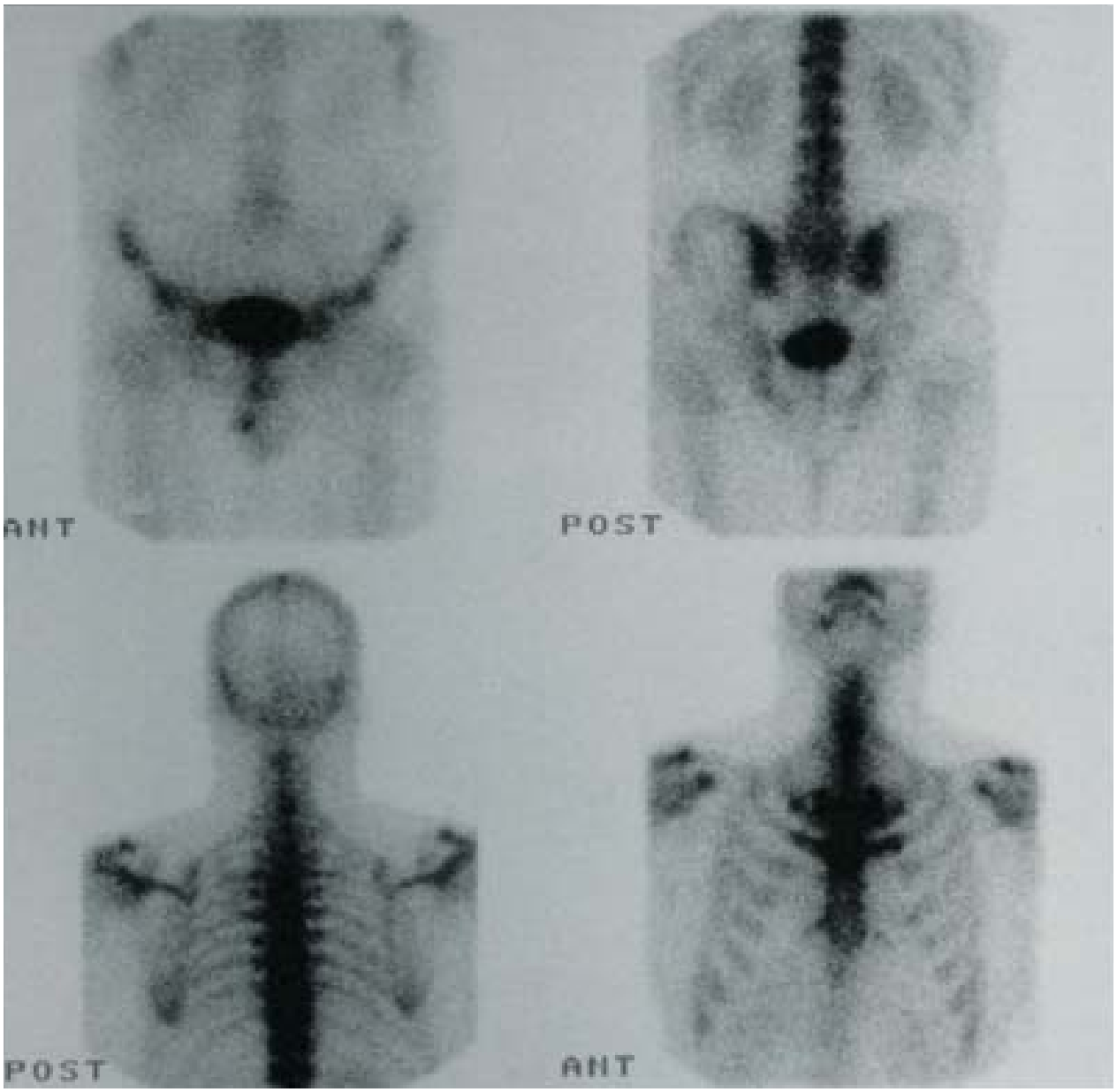

Figure 4. Bone scan image shows increased radioactive uptake in the sternal body and lateral third of the sternocostal joints.

stress was the major inducer of his skin disease and other components of the clinical picture. The role of stress in the development and progression of various dermatoses is well known, particularly in psoriasis.[11-13] Stress seems to induce an enhanced autonomic response and changes in pituitary–adrenal activity, which result in immunomodulation of natural killer cell activity. Stress also perturbs epidermal permeability barrier homeostasis in vitro, which links this mechanism with development of psoriasis.[14] Still more evidence for the effect of stress is provided by involvement of peptide β-endorphin in stress induction of flares in psoriasis. This peptide is believed to regulate expression of cytokeratin 16 in epidermal cultures of psoriatic skin—a known marker of hyperproliferative states, mainly psoriasis.[15] Although the connection between stress and psoriasis is well documented, the relation between stress and SAPHO syndrome has not yet been firmly established.

If nonorthopedic physicians are to take advantage of the relatively favorable prognosis for SAPHO syndrome and are to avoid unnecessary invasive diagnostic tests (eg, bone biopsies) that

add to patient stress, they need to know how to recognize this disease. For patients with SAPHO syndrome, dermatologists need to be able to offer treatment that is optimal for pain associated with rheumatic disease and that does not exacerbate skin disease.

Treatment of our patient's case posed a few problems. NSAIDs were discontinued, and smoking was discouraged. Retinoids, considered for controlling the skin disease, were ruled out because they cause hyperostosis and could have further impaired the patient's serum lipid profile. A regular regimen of topical psoralen and phototherapy, combined with topical steroid treatment, soon cleared the eruption but only slightly relieved the patient's chest pain. Both the eruption and the chest pain improved further when the patient began a new job.

Our patient's case underscores the stress component of the pathogenesis of SAPHO syndrome. Stress should be addressed in each case of this nonfatal but debilitating syndrome.

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