Letters to the Editor

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Psoriatic arthritis, nail disease and pustules following Hodgkin’s lymphoma

Sir, We refer to the association of pustules with arthritis both in the well-defined SAPHO (synovitis, acne, pustulosis, hyperostosis and osteitis) syndrome [1] and in relation to the evidence of an increased prevalence of arthritis in acne [2]. In the SAPHO syndrome, acne may evolve to guttate psoriasis [1]. The close association and overlap of psoriatic arthritis with the SAPHO syndrome is well recognized [3, 4].

A 37-yr-old Caucasian woman presented in August 1998 with a 3-yr history of pain and swelling of her right hand and feet. She also had a 6-yr history of a chronic generalized acneform rash affecting her trunk, arms and legs, including her palms and soles, relatively sparing her scalp and face. The pustules varied in size and were surrounded by bright red erythema. The nails of both hands and feet were dystrophic, with severe hyperkeratosis and onycholysis. She had tenderness and swelling of the proximal interphalangeal (PIP) and distal interphalangeal (DIP) joints of the right index finger and the PIP joint of her right middle finger. The right index finger had dactylitis. The left hand was uninvolved. She also had tender, swollen metatarsophalangeal joints and dactylitis of her toes. The clinical signs were typical of psoriatic arthritis. There was no evidence of sacro-iliitis and spinal movements were normal and pain-free.

She was treated with non-steroidal anti-inflammatory drugs and methotrexate 7.5 mg weekly and folic acid 5 mg for 3 months; however, her rash deteriorated, with enlargement of the pustules, increased erythema and discomfort. Treatment with flucloxacillin 500 mg q.i.d. on three separate occasions brought some relief. Methotrexate was discontinued and her second-line medication was changed to sulphasalazine 1 g b.d., but this failed to have any impact on either her skin or joint symptoms. She is now making excellent progress with tacrolimus 3 mg b.d., a better-tolerated alternative to cyclosporin [5]. Both joint and skin disease have markedly improved.

Her full blood count and renal and liver function were unremarkable. Her inflammatory markers were elevated, with an erythrocyte sedimentation rate of 81 mm/h and a C-reactive protein of 29 mg/l. A β-haemolytic streptococcus was isolated from the pustules on one occasion, in association with an exacerbation of the rash.

An autoantibody profile, including rheumatoid factor, antinuclear antibodies and extractable nuclear antigens, was negative. She had normal levels of complement components (C4, C3). Protein electrophoresis showed an elevated serum IgA of 7.5 gm/l (NI 0.9–3.4 g/l) and raised serum λ of 8.57 g/l (NI 2.9–5.8 g/l) with a compact band in β2–λ and no abnormality on immunofixation.

Lymphocyte phenotyping showed slightly reduced numbers of CD4+ 490 × 10^6 l⁻¹ (NI 500–1500) and relatively high numbers of CD8+ 830 × 10^6 l⁻¹ (NI 230–1100). She also had a significant double-negative population of T lymphocytes, which disappeared after treatment with tacrolimus.

X-ray of her hands and feet showed an asymmetrical erosive arthropathy affecting the DIP joints of her hands and feet, typical of psoriatic arthropathy.

Skin biopsy showed evidence of multiple cysts lined by squamous metaplastic epithelium with cholesterol

She had Hodgkin’s lymphoma in 1978 (nodular sclerosing type, stage I), and after a staging laparotomy and splenectomy underwent mantle radiotherapy. In 1987 she developed a localized recurrence on her left chest wall and was treated with chemotherapy (chlorambucil, vincristine, procarbazine and prednisolone).

On examination she had a severe generalized acneform pustular rash affecting her trunk, arms and legs, including her palms and soles, relatively sparing her scalp and face. The pustules varied in size and were surrounded by bright red erythema. The nails of both hands and feet were dystrophic, with severe hyperkeratosis and onycholysis. She had tenderness and swelling of the proximal interphalangeal (PIP) and distal interphalangeal (DIP) joints of the right index finger and the PIP joint of her right middle finger. The right index finger had dactylitis. The left hand was uninvolved. She also had tender, swollen metatarsophalangeal joints and dactylitis of her toes. The clinical signs were typical of psoriatic arthritis. There was no evidence of sacro-iliitis and spinal movements were normal and pain-free.

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Skin biopsy showed evidence of multiple cysts lined by squamous metaplastic epithelium with cholesterol
debris mixed with neutrophil polymorphs within the dermis. The superficial dermis showed a mild non-specific lymphocytic perivascular infiltrate, but the epidermis was normal. This is consistent with but not diagnostic of neutrophilic eccrine hidradenitis.

Musculoskeletal involvement in association with acne conglobata was first described by Windom et al. in 1961 [6], and this has been followed by over 50 reports of arthritis and bone lesions associated with pustular rashes, including the SAPHO syndrome [3, 7]. The pustular rashes include acne fulminans, acne conglobata, hidradenitis suppurativa, palmoplantar pustulosis and chronic pustular psoriasis; the last two may be the same entity. Nail dystrophy, markedly increased in psoriatic arthritis in comparison with psoriasis alone, may also be associated with palmoplantar pustulosis. The prevalence of psoriasis in the SAPHO syndrome is three times that in the general population [7]. The SAPHO syndrome has been classified as a clinical subset of psoriatic arthritis [8].

Neutrophilic eccrine hidradenitis is usually a transient benign dermatological disorder seen in patients receiving chemotherapy or treatment with granulocyte colony-stimulating factor [9, 10]. In our patient, the skin condition presented 6 yr after chemotherapy and developed into a chronic neutrophilic dermatosis with a relapsing and remitting course. Chemotherapy and biology are also known to cause an inflammatory arthritis [11]. Our patient’s background of Hodgkin’s lymphoma and subsequent radio- and chemotherapy and splenectomy may have changed the immunological milieu, reflected in the small depression of the CD4:CD8 ratio. It is well recognized that psoriasis and psoriatic arthritis may be fulminant in conditions with low CD4 counts, such as HIV infection. This could have been the predisposing factor to the development of the generalized pustular rash and psoriatic arthropathy. The excellent response of both to tacrolimus provides evidence that both the rash and arthritis in this case are T-cell driven.

This case illustrates the link between pustules and psoriatic arthropathy, and provides some clues to their aetiology. There is also a possible role of bacteria, such as *Streptococcus*, within the pustules in triggering or perpetuating the arthropathy. Both skin and joint manifestations may be a result of subtle immunological changes caused by chemotherapy, analogous to the link between psoriatic arthritis and HIV, and both skin and joint disease have responded to T-cell-modulating therapy.

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