Rheumatoid Neutrophilic Dermatitis as Presenting Sign of Seronegative Arthritis

Doreen Defaria[1] and George Kroumpouzos[2,3,4,5]
[1]Department of Internal Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA, [2]Division of Dermatology, Department of Medical Specialties, Worcester Medical Center, Worcester, MA and [3]Dermatology Clinic, South Shore Medical Center, Norwell, MA, [4]Department of Medicine, South Shore Hospital, South Weymouth, MA, and [5]9 Hawthorne Place, Suite 6D, Boston, MA 02 114, USA. E-mail: george.kroumpouzos@GKderm.com
Accepted October 6, 2003.

Sir,

Rheumatoid neutrophilic dermatitis (RND), first described by Ackerman (1), is a rare but distinctive manifestation of rheumatoid arthritis (RA) (2). Eighteen cases have been reported (3–14). RND typically develops in severe RA many years after the diagnosis of RA and has been associated with relatively high titres of rheumatoid factor (3, 5, 6). It manifests as symmetric erythematous papules, plaques and nodules and urticarial lesions over the trunk, shoulders, neck and extensor surfaces of the extremities (4, 9). Annular, vesicular or ulcerative lesions are less common (5, 7). There have only been 4 cases of RND associated with seronegative RA (11–14). We report here a unique case of RND in which the skin disease preceded the joint symptoms and diagnosis of RA, and was more severe than the joint involvement.

CASE REPORT

A 74-year-old man presented with an intensely pruritic eruption on his upper trunk and neck that had been worsening for 3 months. He noticed the skin lesions one month after starting a regimen of atenolol, ranitidine, fluvastatin, lisinopril, aspirin and clopidogrel. Two weeks prior to his visit to dermatology he was started on prednisone 10 mg day^{-1} for the eruption and all other medications were discontinued. There was no significant improvement of the eruption with prednisone therapy and discontinuation of other medications. Initial skin examination showed symmetric bright erythematous confluent lesions on the upper back, upper chest, shoulders and neck (Fig. 1). The patient was initially treated with a mid-potent topical steroid. Laboratory tests revealed a normal leucocyte count, mild anaemia, and a persistently elevated erythrocyte sedimentation rate (47 mm h^{-1}). The patient reported no febrile illness but complained of 6 kg weight loss over 3 months and worsening fatigue.

Two months later the patient was referred to rheumatology for several weeks of worsening arthralgias. There was no evidence of antecedent infection that could have caused a reactive arthritis. The diagnosis of RA was established based on the following criteria: morning joint stiffness, metacarpophalangeal and proximal interphalangeal joint involvement, soft tissue swelling of more than 3 joint areas, and symmetric arthritis (4 of 7 of the criteria established by the American Rheumatism Association in 1987)

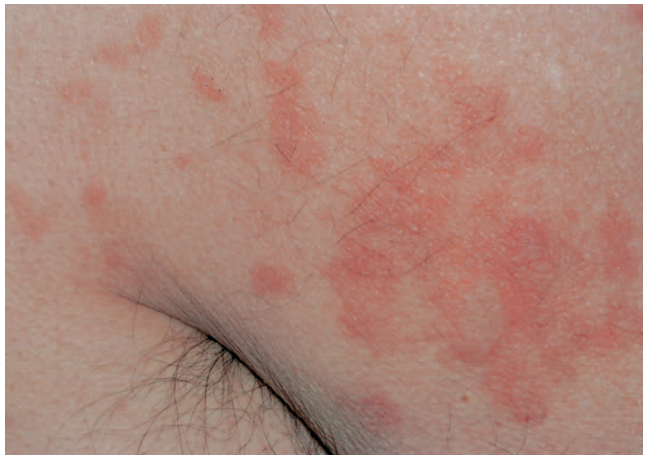

Fig. 1. Bright erythematous papules and plaques over the scapula. Some lesions are edematous and show microvesiculation, features also seen in Sweet's syndrome.

(15). The joint fluids were mildly inflammatory. Rheumatoid factor, antinuclear, Sm, double-stranded DNA, SSA, Jo-1 and Scl-70 antibodies were negative. Low-dose oral prednisone and hydroxychloroquine sulphate were started for the joint complaints. Although this regimen controlled the joint symptoms satisfactorily, the skin lesions would wax and wane and remain extremely pruritic. On visiting dermatology a month later, the eruption had started to remit on the upper back, neck and upper extremities but had spread onto the lower back. The patient was switched to a high potent topical steroid, prednisone was continued and hydroxychloroquine discontinued.

Skin examination 2 months later revealed further spread of the lesions onto the extensor surfaces of the extremities. Erythematous nodular lesions were noticed on the elbows and knees as well as involvement over the metacarpophalangeal joints. The dose of prednisone was increased with minimal change in the skin lesions. Laboratory tests showed a mild elevation of serum gamma globulin and a mild immunoglobulin G peak on serum protein electrophoresis. Multiple myeloma was ruled out by normal serum calcium, bone scans, and a bone marrow biopsy. A haematology consult was requested to determine the cause of elevated gamma globulin, which however was considered secondary to the inflammation of rheumatoid arthritis and not to paraimmunoglobulin. Computed tomography scan of the chest, abdomen and pelvis revealed no evidence of internal malignancy. The patient was then started on

 ISSN 0001-5555
DOI: 10.1080/00015550310007724

dapsone 200 mg day^{-1} with satisfactory preliminary response. The skin lesions, however, would recur every time dapsone was discontinued. The flares of skin lesions did not coincide with worsening of the articular disease that was well controlled with low-dose prednisone.

Two skin biopsies taken at different stages of the eruption revealed a dense neutrophil-rich dermal and perivascular inflammatory infiltrate. The infiltrate encompassed the entire dermis, and was composed predominantly of neutrophils with scattered eosinophils and lymphocytes. There was no evidence of vasculitis. Focal vacuolar change of the basal layer was noted as well as spongiosis and exocytosis of inflammatory cells. Immunofluorescence and special stains for microorganisms (Gram, Giemsa) were negative.

DISCUSSION

This case is unique in that the joint symptoms and diagnosis of seronegative RA were preceded by severe RND. Four cases of RND have been reported in seronegative RA (11–14). In these cases the diagnosis of RA was well established prior to the onset of skin lesions (11, 12, 14) and/or the joint involvement preceded the RND (13). This case is also distinctive in that a generalized very symptomatic RND contrasted with mild joint involvement. Fluctuations in the activity of skin lesions did not parallel the course of articular disease.

The following differential diagnoses were considered: (*i*) A drug eruption was ruled out because the lesions persisted and worsened despite discontinuation of medications. (*ii*) Our patient was not on any of the medications that can cause a Sweet's-like drug hypersensitivity (2). (*iii*) Negative immunofluorescence and absence of bullous lesions ruled out dermatitis herpetiformis, bullous lupus erythematosus, linear IgA bullous dermatosis and epidermolysis bullosa acquisita. (*iv*) Pyoderma gangrenosum, bowel-associated dermatosis-arthritis syndrome, and Behcet's disease were ruled out by history and absence of ulcerative or vesiculopustular lesions. (*v*) Erythema elevatum diutinum was ruled out by the absence of vasculitis.

Sweet's syndrome, which is well described by its original name, acute febrile neutrophilic dermatosis, is characterized by a variably extensive polymorphous skin eruption, histopathology of a dermal, non-vasculitic, neutrophilic infiltrate, leucocytosis, fever, and malaise in 78% of patients (2). Sixteen percent are associated with infection or an immunologic disease such as RA. While our case shows some clinical and histopathologic features of Sweet's syndrome, the absence of antecedent infection, fever and leucocytosis, and no response to corticosteroid therapy do not support the diagnosis of Sweet's syndrome.

RND is a rare manifestation of severe RA characterized by symmetric erythematous papules, plaques, nodules and urticarial lesions over the joints, extensor surfaces of the extremities and trunk that are often asymptomatic (4, 5). Differentiation of RND from Sweet's syndrome can be a challenge, since these entities share similar clinical and histopathologic features. Histologically, both Sweet's syndrome and RND show a predominantly neutrophilic infiltrate, may have prominent leucocytoclasia and lack areas of vasculitis (5, 9). Since both Sweet's syndrome and RND have been associated with RA, they may represent neutrophilic reactions mediated by common immunologic or other factors seen in RA (12).

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