Cutaneous Leukocytoclastic Vasculitis with Positive Anti-neutrophil Cytoplasmic Antibodies

Sir,

Anti-neutrophil cytoplasmic antibodies (ANCA) are useful diagnostic serological markers for systemic vasculitides. With indirect immunofluorescence, two distinct patterns are seen: a coarse granular, centrally accentuated cytoplasmic staining (c-ANCA) and a perinuclear staining (p-ANCA) on ethanol-fixed neutrophil cytocentrifuge preparations (1). c-ANCA is considered highly specific for Wegener's granulomatosis (WG) (2). Changes in titre often reflect changes in the disease activity. WG directly affects the skin in about 14% of patients (3). Purpura and petechiae on the lower extremities are the most common manifestations. These tend to occur early in the course of the disease and are frequently presenting signs. Histologically, leukocytoclastic vasculitis (LCV) is the most common pattern (3–5). We report here a patient who presented with LCV on the lower extremities and positive c-ANCA results, but with no evidence of systemic vasculitis. After 4 years of recurrent episodes of purpura, classic pulmonary WG developed.

CASE REPORT

A 64-year-old man was seen in March 1995 with purpuric and petechial eruptions on the lower extremities. The eruptions had been cyclical for the last 3 years, with episodes occurring every few months. The lesions had a tendency to resolve after a few days and were associated with symptoms of arthritis of the knees, elbows, ankles and shoulders. The patient's past medical history was significant for an episodic, non-deforming migratory arthritis. This was controlled using short courses of systemic corticosteroids and non-steroidal anti-inflammatory agents.

The following laboratory evaluations were either normal or negative at presentation: haematology group, chemistry group, urinalysis, total complement, C3, C4, serum protein electrophoresis and cryoglobulins. The erythrocyte sedimentation rate was 22 mm/h (normal, 0–22 mm/h). A chest radiograph showed fibrosis and linear atelectasis in both h t e c o u r s e o f t h e d i s e a s e a n d a r e f r e q u e n t y p r e s e n t i n g s i g n s . The patient's condition deteriorated despite treatment agents.

A diagnosis of cutaneous small vessel vasculitis with positive c-ANCA was made and treatment began with trimethoprim and sulfamethoxazole twice a day and continued with prednisone (15 mg/day). Skin eruptions continued to develop in association with arthritis, requiring higher doses of prednisone (60 mg/day) to control the symptoms. In March 1996, the patient was hospitalized for an exacerbation of vasculitis with bilateral pulmonary infiltrates not present on prior radiographs. The patient also complained of nasal congestion and crusting of nasal mucosa. The patient's condition deteriorated despite intravenous administration of antibiotics. Transbronchial biopsy was performed. The biopsy showed granulomatous vasculitis without evidence of infectious organisms. The c-ANCA titre remained increased, with negative findings for p-ANCA. A diagnosis of WG was made, and he was started on cyclophosphamide (100 mg/day) and prednisone (60 mg/day). At the last follow-up in September 1996, the patient was in remission on combination treatment with prednisone, cyclophosphamide, and trimethoprim and sulfamethoxazole.

DISCUSSION

Four similar patients (2 men and 2 women, aged 15–65 years) seen in our department between 1989 and 1995 with cutaneous LCV and positive c-ANCA and negative p-ANCA have developed WG. Skin was involved at presentation in all of these patients. Purpura and petechiae on the lower extremities were the most common signs. Pulmonary symptoms were noted at presentation or within the next few weeks of LCV, except in the one patient described above. The rheumatoid factor and the sedimentation rate were increased in all. Two had positive test for anti-nuclear factor. Our illustrative case had an unusual presentation, with recurrent episodes of LCV for 4 years before definitive systemic signs of WG developed. None of 54 patients with cutaneous LCV and negative c-ANCA results seen between 1994 and 1995 at our institution have developed WG.

ANCAs have been seen in association with systemic vasculitides, especially WG (3). It is proposed that several renal and pulmonary syndromes characterized by presence of ANCA be grouped under the term “ANCA-associated diseases” (6). They are characterized by vasculitis that affects many organs, including kidney, lung, joint, gastrointestinal tract, sinuses, muscles, skin and nerves. These ANCA-associated diseases could be mediated by c-ANCA or p-ANCA.

According to current classification schemes of WG (7), our patient and others who present with cutaneous vasculitis and progress to the classic WG would have remained unclassified, some of them for many years. We think that the spectrum of c-ANCA-associated vasculitides should be expanded to include patients with cutaneous LCV with positive c-ANCA results, similar to our group of patients. The use of the term “Wegener’s granulomatosis” would not be appropriate for this group of patients without systemic involvement. ANCA should be measured in all cases of cutaneous LCV where an aetiology is obscure, and cutaneous LCV should be included in the classification of ANCA-associated diseases, so that early detection of these patients can lead to early treatment.

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Naproxen-induced Lichen Planus Bullosus

Sir,

Certain drug provocations have been suggested in the aetiology of lichen ruber planus. We describe here a 46-year-old woman who has breast carcinoma with clinical and histological findings of bullous lichen planus, which was induced by naproxen.

CASE REPORT

A 46-year-old woman presented with a 2-month history of pruritic, violaceous maculopapular eruption. The lesions had started on her knees and elbows, then gradually spread all over the body. She had been using naproxen for osteoarthritis since 1 month before the beginning of her eruptions.

Dermatological examination revealed small, flat-topped, polygonal erythematous and violaceous papules and plaques on her trunk, arms and legs. Two weeks after the first examination, tense blisters began developing at the sites of pre-existing lesions (Fig. 1). General physical examination was normal. The patient had been diagnosed as having breast carcinoma 9 years previously. She had then undergone total mastectomy, chemotherapy and radiation therapy.

The result of laboratory tests, including urinalysis, complete blood cell count, biochemical analysis, AFP, CEA, CA-125, X-ray examination of the lung, ultrasonographic examination of abdomen, computerized tomography of the abdomen-chest and cranium, were normal. Erythrocyte sedimentation rate was 54 mm/h. Hepatitis markers and serological syphilis reactions were negative.

No casual or other provocative factors were detected other than naproxen.

A biopsy from 1 of the bullous lesions, which arose on an erythematous lesion, was taken. Hematoxylin-eosin staining showed compact orthokeratosis, epidermal hyperplasia, focal hypergranulosis, vacuolar degeneration of the basal layer, subepidermal vesicle formation and dense band-like infiltration of mononuclear inflammatory cells in the upper dermis. Direct immunofluorescence studies showed granular deposition of IgG, IgA, IgM and fibrinogen at the basement membrane zone.

Naproxen administration was stopped. She was then treated with topical corticosteroid and the lesions gradually disappeared. After the cessation of therapy, she was followed-up regularly (at 3, 6, 9 and 12 months) with no evidence of relapse.

DISCUSSION

The bullous form of lichen planus has been divided into 2 groups; lichen planus bullosus (or vesiculosus) and lichen planus pemphigoides. In the former group the blisters occur on pre-existing lichen ruber planus lesions. Conversely, the blisters appear on clinically normal skin as well as on lesional skin in the latter group. The clinical and histological findings for distinguishing bullous lichen planus and lichen planus pemphigoides are supported by immunohistological and immunobiochemical techniques (1).

Direct immunofluorescence findings of lichen ruber planus consist of deposition of IgM, IgG and C3 on colloid bodies. In contrast to bullous lichen planus, lichen planus pemphigoides shows clump-like inflammatory infiltrate, which may also contain eosinophils. Linear deposition of C3 and immunoglobulins at the dermoepidermal junction and colloidal bodies are detected by direct immunofluorescence microscopy (2). The clinical, histopathological and direct immunofluorescence findings of the case described here are consistent with bullous lichen planus.

The relationship between malignancy and some bullous dermatoses, such as pemphigus group, dermatitis herpetiformis and lichen planus pemphigoides, has been proposed for many years (2–4). Lichen ruber planus have also been reported in association with neoplasia (5). Although the case presented here also has a history of breast carcinoma, no relapses or metastasis were detected, so the patient is not fulfilling the reported paraneoplastic criteria (4).

Lichen planus caused by naproxen has rarely been reported (6, 7). To our knowledge this is the first case of lichen planus bullosus induced by this drug. It is reasonable to consider that any form of lichen planus might be possibly induced by naproxen.