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Cutaneous Vasculitis in Psoriasis

SAI-SIONG WONG and RONALD MARKS

Department of Dermatology, University of Wales College of Medicine, Cardiff, U.K.

Cutaneous vasculitis has been reported as a complication of pustular psoriasis but not of plaque type psoriasis. In the past 5 years we have observed 3 patients who in the course of their psoriasis developed cutaneous vasculitis. Two of these patients also had severe psoriatic arthropathy and were on etretinate during the onset of vasculitis. However, there was no deterioration or recurrence of vasculitis whilst the patients were maintained on the drug. The third patient with vasculitis had not received retinoids. No obvious causes of vasculitis were found in the 3 patients and the rash resolved spontaneously without any systemic complications though surgical amputation was necessary in one case. None of the cases required immunosuppressive therapy and the skin lesions mostly resolved spontaneously. The mechanisms that triggered off vasculitis in our patients are unknown but are likely to be immune-mediated.

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R. Marks, Department of Dermatology, University of Wales College of Medicine, Heath Park, Cardiff, CF4 4XN, U.K.

Cutaneous vasculitis has been reported with the use of retinoids in psoriasis (1, 2) and acne (2–5). We now report 3 cases of psoriasis presenting with vasculitis without a clear-cut relationship with the administration of retinoids, and we suggest that vasculitis is a rare complication of psoriasis unrelated to the use of these drugs.

CASE REPORTS

Case 1

A 75-year-old man presented with sero-negative arthropathy affecting his knees, lumbar spine and metacarpophalangeal joints in 1972. Ten years later, dystrophic nail changes and onycholysis were noted. In January 1988, he developed a scaly erythematous rash on the soles, hands, and elsewhere. Changes typical of psoriasis were seen on histological examination of a plaque. Radiographs of the sacro-iliac, knee and metacarpophalangeal joints were normal apart from changes of osteoarthrosis. A complete immunological screen was negative. His HLA B27 status was positive.

Etretinate 50 mg daily was commenced 3 months later because of progressing skin disease and disabling arthralgia. This had to be discontinued after 3 months of treatment because of intolerable xerosis, cheilitis and eye irritation. He was lost to follow-up until July 1990, when his psoriasis worsened considerably with loss of all his finger nails and evidence of distal phalangeal arthropathy.

Etretinate 30 mg daily was recommenced and his psoriasis improved. He developed an acute purpuric, palpable, papular rash affecting his legs and feet (Fig. 1), which was thought to be vasculitic in nature, 3 weeks after starting his treatment. It was accompanied by abdominal pain but there was no evidence of systemic vasculitis. There was no blood in his urine or faeces and his renal function and tests of immune function were all normal. Skin biopsy revealed classical leucocytoclastic vasculitis (Fig. 2*a*, *b*) with granular band of complement subepidermally on immunofluorescence. The rash and abdominal pain resolved with conservative treatment within 2 weeks. He remained on etretinate throughout this episode of vasculitis. On his last review at the outpatient clinic he remained well on etretinate with no further recurrence of vasculitis.

Case 2

A 54-year-old British Rail worker presented with patchy psoriasis affecting his elbows and knees since childhood. He had developed an acute eruption with purpuric papules characteristic of cutaneous vasculitis on his limbs in 1974 without deterioration of his psoriasis. There was no relevant drug history or past medical history. Examination revealed a well man with a purpuric papular rash on his limbs (Fig. 3) with stable chronic plaque psoriasis on the elbows and knees. Investigations including full blood count, blood cultures, viral studies, urine analysis, antistreptolysin titre, the erythrocyte sedimentation rate and a full immune screen were normal or negative. A skin biopsy from a resolving purpuric area on one leg showed accumulation of mononuclear cells as well as fragments of polymorph nuclei perivascularly and involving the endothelial walls of vessels in the upper dermis (Fig. 4). The rash resolved spontaneously without treatment in 5 weeks. He has had no recurrence of his rash and his psoriasis has been stable since.

Case 3

A 64-year-old man who had had widespread plaque psoriasis since 1975 developed arthropathy affecting his hands, feet and knees in 1978. Radiographs of the hands showed erosive changes compatible with psoriatic arthropathy. He was started on 75 mg daily of etretinate. He was hospitalized frequently from 1980–1985 with deteriorating psoriasis and arthropathy despite treatment with etretinate. He presented with an acute gangrenous big toe (Fig. 5) in July 1985. There was no evidence of emboli and his peripheral pulses were all normal. Blood sugar, blood cultures and tissue, antinuclear and organ specific antibodies were all negative. Amputation of the big toe was undertaken and subsequent histological examination of the amputated toe revealed evidence of severe vasculitis. His psoriasis remained unstable

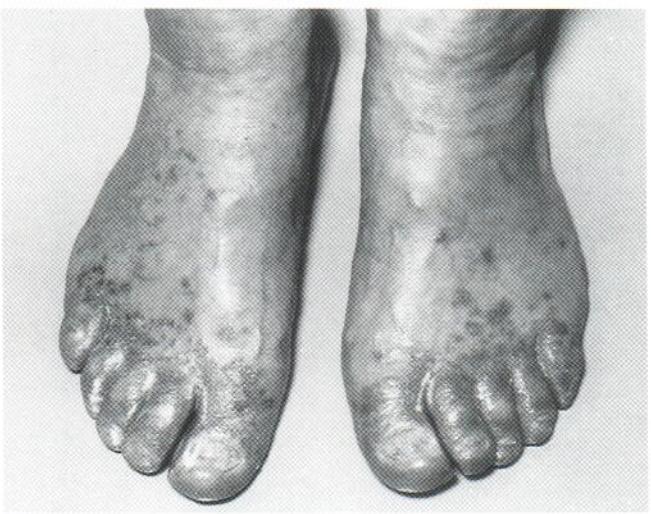

Fig. 1. Feet of patient 1. There are purpuric papules scattered over the dorsa of both feet.

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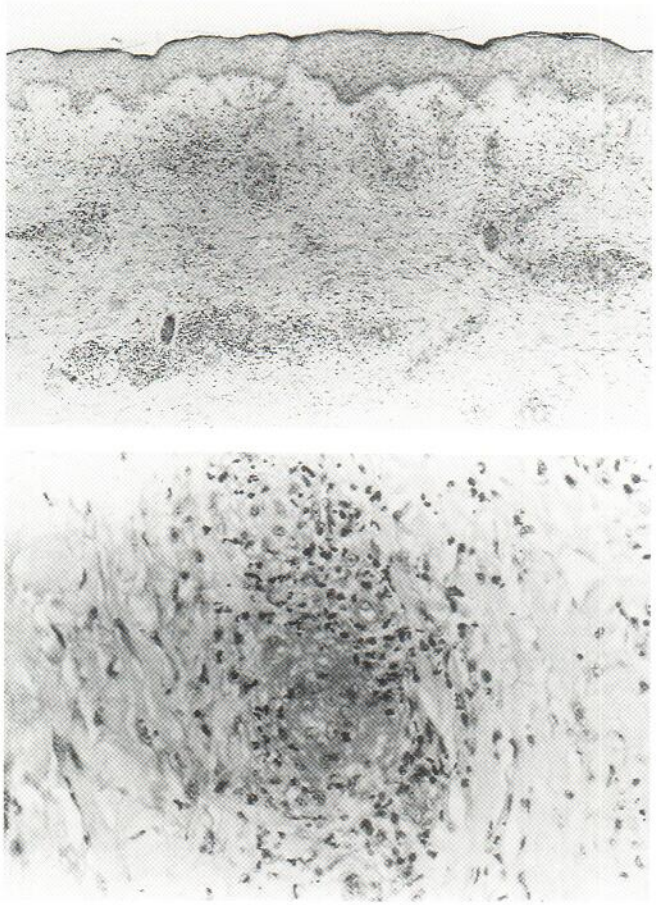

Fig. 2. (*a*) Photomicrograph of biopsy from patient 1, showing perivascular inflammatory cell infiltrate in the upper dermis (H&E × 48). (*b*) Detail showing degenerative changes in vessel wall and many fragmented nuclei interspersed in the perivascular inflammatory cell infiltrate (H&E × 250).

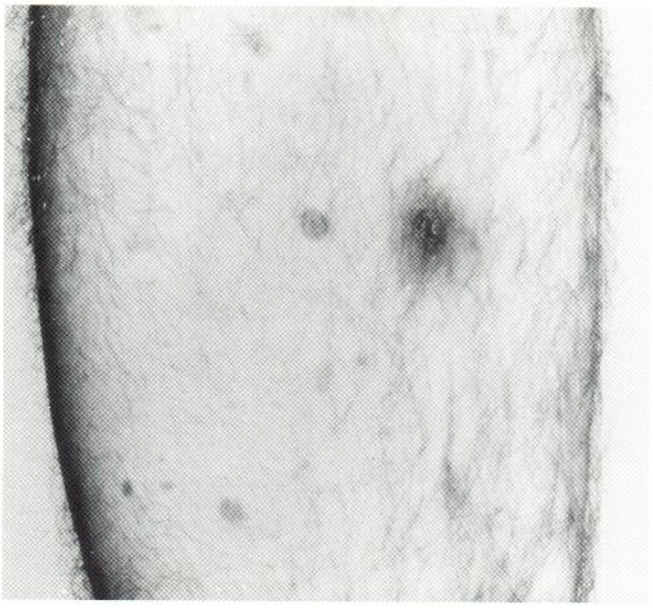

Fig. 3. Right lower leg of patient 2, showing purpuric lesions.

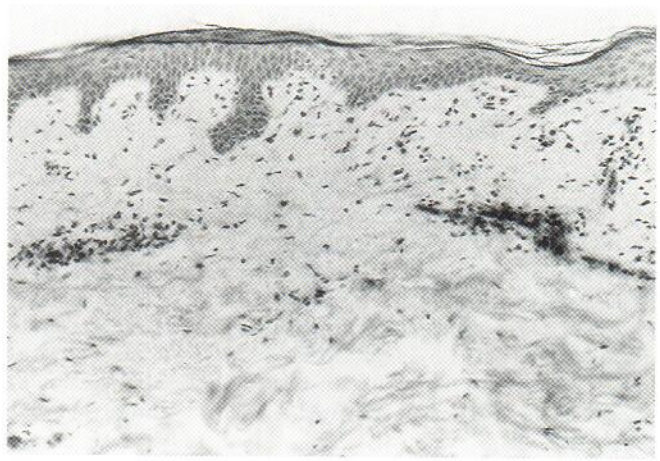

Fig. 4. Photomicrograph from resolving purpuric lesion of patient 2, 7 days after initial appearance. There is a perivascular cellular infiltrate with fragmented nuclei around the small blood vessels in the upper dermis (H&E × 45).

but without recurrence of purpuric lesions despite remaining on etretinate. He died suddenly in May 1988, but no post mortem was carried out.

DISCUSSION

There have been several reported cases of the occurrence of vasculitis with the use of synthetic retinoids (1–5). In several of these cases, the etiology of vasculitis could be explained by the presence of a pre-existing underlying vasculopathy such as Wegeners's granulomatosis, small vessel angitis and Henoch-Schönlein purpura (2–4). Furthermore, the rash persisted despite the cessation of retinoids and patients required aggressive immunosuppressive therapies.

In one series, 2 out of 5 psoriatic patients were judged to have had vasculitis associated with etretinate therapy (2). However, the remaining 3 patients had vasculitis unassociated with the use of etretinate but this was not included in the discussion. Some acne patients in this series also had vasculitis whilst on isotretinoin but they were either taking antibiotics in addition to retinoids or had infections, both of which are known to be associated with vasculitis. Some authors have

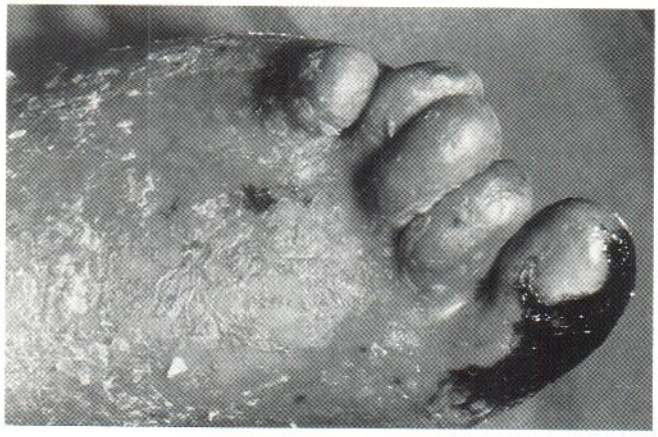

Fig. 5. Area of necrosis at medial side of left big toe (Patient 3).

proposed a direct toxic effect of retinoids causing vasculitis because the medication had been taken a few days before clinical manifestation (2). However, there has been a case of vasculitis reported that occurred in a psoriatic patient 4 months after treatment with etretinate (1) and the rash resolved spontaneously following the cessation of retinoids.

The only other reported case of vasculitis following isotretinoin was dismissed by others on the basis that the patient may well have had an underlying cause for the vasculitis (5, 6). No rechallenge with the drug was carried out in any of these reported cases to confirm the association.

Our patients differed from the reported cases in several respects. Case 1 showed improvement and resolution of the vasculitic rash and Case 3 developed no further vasculitic gangrene despite continuation of treatment with etretinate. The drug was not discontinued because it was felt that all other causes of vasculitis should be excluded first and the association between vasculitis and retinoids was weak. Furthermore, there was no recurrence or deterioration in the vasculitic rash in these 2 cases whilst they were maintained on etretinate. Case 2 developed vasculitis without the use of retinoids and no obvious cause was found. No systemic complications were present in any of the 3 cases and none of the patients required any systemic immunosuppressive therapy. We believe that in our patients it is unlikely that there is a true causal relationship between the vasculitis and the administration of etretinate and that it is more likely that the vasculitis is a complication of the psoriasis itself. In support of this, vasculitis has recently been reported in patients with pustular psoriasis (7). The patients reported were female, black South Africans whose lesions were pustular but dried to form a dark crust and had vasculitic features histologically. Circulating immune complexes in psoriasis have been reported several times previously but no clinical sequelae from these have been described (8–17).

Though the pathogenesis of psoriasis is still unknown, recent studies have attempted to determine the role of cell-mediated immunity in the disease, and it was proposed recently that immune mechanisms might be involved in the pathogenesis of the disease, with activation of helper T lymphocytes followed by production of keratinocyte stimulation factors by these cells (18). Immunohistological study also confirmed that plaques of chronic psoriasis have an infiltration of mostly helper T lymphocytes, without B lymphocytes and sometimes with granulocytes, macrophages and monocytes (19). Furthermore, cyclosporine, which acts principally by inhibiting the production of cytokines by helper T lymphocytes, has been shown to have a useful therapeutic effect in psoriasis (20). Psoriasis co-existing with bullous pemphigoid has also been described (21, 22), and the involvement of T lymphocytes in psoriasis was thought to predispose to the formation of autoantibodies causing bullous pemphigoid, which explained the immunological association between the two diseases (23). Similar considerations may apply to the production of vasculitic lesions. It is also of interest to note that rheumatoid factors of IgG and IgA isotype have been eluted from the scale in patients with psoriasis as well as detected in the serum (24).

What precipitated vasculitis in our psoriatic patients remains unknown, but in our view it seems possible that it is related to the immunopathogenesis of psoriasis. Of course we cannot exclude that the association of psoriasis with the vasculitis in our patients occurred by chance. However, the temporal relationship between the two disorders, the previous reports of "retinoid-induced vasculitis" and the absence of any other obvious cause for the vasculitis problem lead us to believe that the association is likely to be a real one. We suggest that awareness of the association may stimulate recognition of further examples and a more detailed study of the pathogenesis.

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