Ulcerated Atrophic Striae from Etretinate

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Oral retinoids such as etretinate and acitretin are commonly associated with dose-dependent, mucocutaneous side effects such as dryness, peeling, and fragility. Although these effects can be extreme in some patients and even require discontinuation of treatment, thinning of skin to the point of atrophy and ulceration has never been reported in the English literature. We present the case of a patient with psoriasis in whom ulcerated atrophic striae developed during etretinate therapy. After discontinuation of etretinate, all cutaneous ulcers resolved. Subsequently, the patient had a favorable response to oral calcitriol (1,25-dihydroxy vitamin D3), a novel therapy for psoriasis.

Oral synthetic retinoids are used in the treatment of a variety of proliferative and hyperkeratotic skin disorders. Dose-related side effects are common, and include cheilitis, palmar-plantar desquamation, conjunctivitis, hair loss, and nail changes. Skin fragility is a well-documented side effect of etretinate, an aromatic retinoid, and often limits its use. Blistering and frank ulceration are uncommon and have rarely been reported.[1,2] We present a case of ulceration of atrophic striae in a patient receiving etretinate. To our knowledge, this is the first such case to appear in the English literature.[3]

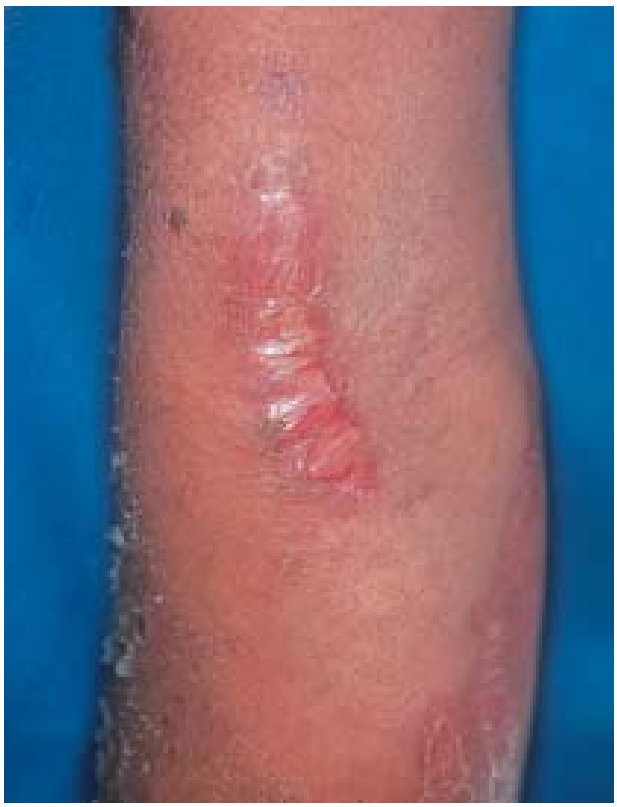

FIGURE 1. Shallow ulcerations developed within preexisting striae of the left arm.

Case Report

A 29-year-old black man with acquired immunodeficiency syndrome (CD4 count 1, human immunodeficiency virus-1 RNA viral load 396,152 copies), hepatitis B, glucose-6-phosphate dehydrogenase deficiency, and a 3-year history of psoriasis was admitted to the hospital for work-up of fever and perirectal abscess. Cultures from the abscess grew methacillin-sensitive *Staphylococcus aureus*, and the patient gradually improved with intravenous antibiotics. The patient's psoriasis worsened, despite continued treatment with 0.1% triamcinolone ointment. The patient denied prior systemic corticosteroid treatment and stated that stretch marks had appeared within the last year in areas where he had not applied topical corticosteroids. Prior to their development, he had taken etretinate for several months, but had discontinued it 6 months before admission.

Physical examination revealed a thin, chronically ill-appearing black man with extensive plaque-

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type psoriasis covering most of his body. We noted multiple atrophic striae extending from the axillae to the inner flexor aspects of the biceps, and on the flanks bilaterally.

Liver function tests and random cortisol gave normal results. We discontinued the triamcinolone ointment, and initiated treatment with etretinate, 25 mg daily, and 0.005% calcipotriene ointment to psoriatic plaques twice daily. The patient improved somewhat, but after 2 weeks, several shallow ulcers developed within the striae on his left arm (Figure 1), which were treated with 1% silver sulfadiazine twice daily. Porphyrin screen, anti-streptolysin O titer, and viral culture of the ulcer were negative. No further ulcers appeared after discontinuation of the etretinate, but the psoriasis became erythrodermic within several days. After a 24-hour urine test revealed normal calcium excretion, the calcipotriene ointment was discontinued and he began treatment with 0.25 mg calcitriol daily. The patient's psoriasis markedly improved, and the cutaneous ulcers resolved.

Comments

Increased skin fragility is common in patients treated with oral retinoids, but frank cutaneous ulceration is rare. Initially, it was thought that skin fragility was due to mucous metaplasia ("de-differentiation") of keratinocytes, resulting in an antikeratinizing effect. It was also suggested that fragility resulted from altered dermal connective tissue, since vitamin A affects acid mucopolysaccharide synthesis, and in pharmacologic quantities can stimulate breakdown of connective tissue. One study challenged this idea when it reported normal urinary hydroxyproline excretion (an index of collagen catabolism) in patients with retinoid-induced skin fragility.[4] The authors attributed skin fragility to active shedding of desmosomes in the stratum spinulosum and accumulations of amorphous material both intracellularly and extracellularly. A more recent study found enhancement of cellular differentiation and disappearance of parakeratosis in psoriatic skin. Measurement of Ki67 protein showed a 62% decrease in keratinocyte proliferation.[5] Increased corneocyte desquamation and near-elimination of the stratum corneum were believed to be the main cause of skin fragility.

Cutaneous ulceration, although rare, is important to recognize as a side effect of etretinate therapy. Skin fragility is dose related, but our patient experienced ulceration while on the low dose of 0.3 mg/kg daily, compared with 1 mg/kg in the only previously reported case.[3] Fortunately, we were able to discontinue the drug early and avoid potential extensive ulceration and possible secondary infection in this immunocompromised patient.

Oral calcitriol (1,25-dihydroxyvitamin D3), a novel therapy for refractory psoriasis, was very useful in our patient. Oral calcitriol inhibits proliferation of epidermal cells in a dose-dependent fashion, and induces terminal differentiation. Smith *et al*[6] showed these effects in keratinocytes cultured from patients with psoriasis, and documented clinical efficacy of oral calcitriol as monotherapy.

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