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Flegel's disease treated with psoralen ultraviolet A

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Summary Flegel's disease is an uncommon condition which causes asymptomatic keratotic papules on the limbs. It usually develops in the fourth or fifth decade. Therapeutic options are limited to emollients, topical 5-fluorouracil and retinoids, but none of these treatments is consistently helpful. We report a patient with Flegel's disease who responded to psoralen ultraviolet A treatment.

Key words: Flegel's disease, hyperkeratosis lenticularis perstans, keratinization, psoralen ultraviolet A

Hyperkeratosis lenticularis perstans is a rare disorder of keratinization first described by Flegel in 1958.[1] It is characterized by hyperkeratotic papules on the limbs, particularly on the dorsum of the feet, ranging from 1 to 5 mm in size. Onset is usually in the fourth or fifth decade. Flegel's disease has been reported more commonly in women than men. Autosomal dominant inheritance is likely because of the occurrence of the disease in two generations of several families.[2,3] Therapeutic options include emollients alone, topical 5-fluorouracil or retinoids, but these treatments are not consistently effective. We report a patient with Flegel's disease who responded to psoralen ultraviolet A (PUVA) treatment.

Case report

A 59-year-old woman, first seen in our department 20 years ago, developed asymptomatic, scaly, erythematous papules on the upper arms, which spread rapidly to the lower legs, from the dorsum of the feet to the upper thighs. The trunk, face and ears were clear. Lifting of the scale revealed pin-point bleeding. She was otherwise well and on no systemic medication. The possibility of Flegel's disease was considered, but initial biopsy of one of the scaly lesions was reported as being more consistent with pityriasis lichenoides.

She was treated for pityriasis lichenoides with topical tretinoin followed by a course of broad-band ultraviolet (UV) B, but the lesions remained unchanged. In 1986, she had a course of 8-methoxypsoralen (8-MOP) PUVA, after which her skin completely cleared. The normal psoriasis regimen at that time was used, with the starting dose based on skin type, followed by fixed incremental doses of 0·5 J/cm^2. For the next 7 years, the disorder was effectively controlled by the use of the patient's own sunbed and winter holidays in the sun. She presented again to the department in 1994 when these self-treatment measures were no longer controlling the problem. She had extensive scaly lesions on all four limbs, which remained asymptomatic but caused considerable cosmetic embarrassment. A biopsy from one of the scaly lesions on the lower leg showed lamellar hyperkeratosis with foci of parakeratosis, and a dermal infiltrate composed mainly of lymphocytes, confirming Flegel's disease. Review of the original histology showed similar features.

Narrow-band UVB was not tolerated because of burning, but a further course of 8-MOP PUVA cleared her skin completely. The skin remained clear for several weeks but the scaly lesions gradually returned. The following year, 8-MOP PUVA therapy was given to the patient's left leg only, to demonstrate objectively the response of this condition to PUVA and exclude the possibility of spontaneous resolution of the lesions in previous years. The normal psoriasis regimen was used, with the starting dose based on the minimal phototoxic dose and 20% increments depending on tolerance. After 11 treatments the treated leg was completely clear (Fig. 1a,b). The patient's left leg remained clear for 2 months

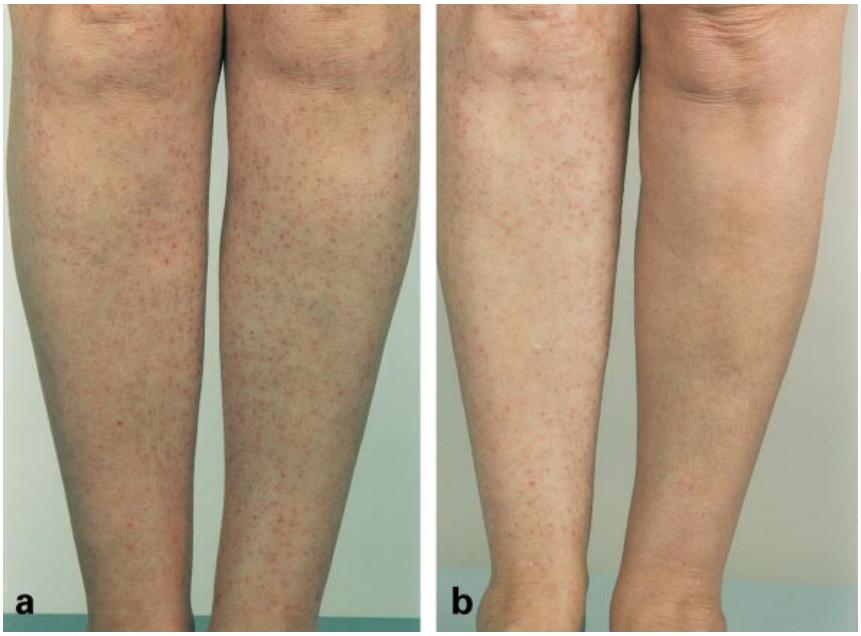

Figure 1. (a) Before psoralen ultraviolet A treatment, both lower legs showed extensive scaly lesions consistent with Flegel's disease. (b) Clearing is seen after a course of psoralen ultraviolet A to the left leg only.

but over the next 6 months the lesions gradually recurred.

Discussion

Flegel's disease or hyperkeratosis lenticularis perstans is an unusual dermatosis. In the St John's Institute review,[2] the dorsum of the feet was affected in all of 12 cases. Other affected sites were the thighs, upper arms and the pinnae in nine of the 12 cases. A genetic influence was suggested by the occurrence of the condition in sisters, plus a mother and daughter. The first to describe a genetic influence was Bean,[3,4] who reported the occurrence of the condition in two generations of one family and suggested an autosomal dominant inheritance. No candidate gene has yet been identified. Our patient remembers her father having similar lesions on his legs, but this had not been confirmed by a dermatologist.

Immunohistochemical and electrophoretic studies have shown that Flegel's disease is a disorder of keratinocyte proliferation and not a perforating disorder as once thought. Price *et al.*[2] found increased labelling of the monoclonal antikeratin antibody LMM3 on suprabasal keratinocytes, indicating epidermal hyperproliferation. The keratins found in the stratum corneum of Flegel's disease resemble those found in the normal upper spinous layer. This pattern is seen in any condition where the epidermis is hyperproliferating, e.g. in psoriasis, and provides further evidence of keratinocyte proliferation in Flegel's disease.

Management of this condition is difficult: a variety of different treatments has been tried, with varying success.[5] Simple moisturizers alone can be helpful.[2] Topical 5-fluorouracil[6,7] has been reported to be helpful. Topical retinoids[6] and betamethasone-17-valerate cream[8,9] have not been consistently effective. Systemic retinoids[10,11] are sometimes helpful but are difficult to justify for a benign asymptomatic condition. We found 8-MOP PUVA to be effective in our patient, and suggest PUVA as an additional short-term treatment option for this condition.

The mechanism of action of PUVA in Flegel's disease is unclear. There is an inflammatory infiltrate in the dermis in Flegel's disease. It is known that PUVA has some anti-inflammatory action. In addition, there is evidence of epidermal hyperproliferation in Flegel's disease. PUVA reduces cell turnover and is effective in psoriasis; thus, this action may be important in controlling the hyperproliferation seen in Flegel's disease.

There has been considerable debate in the literature as to whether Kyrle's and Flegel's diseases are similar or distinct entities.[12] We believe that Flegel's disease is a distinct dermatosis. Hyperkeratosis follicularis et parafollicularis in cutem penetrans, or Kyrle's disease, is one of the perforating collagenoses.[13] In this condition, characteristic keratin plugs are seen on biopsy. These are absent in our patient with Flegel's

disease and in all patients in the St John's series. A coalescence of lesions into larger plaques is seen in Kyrle's disease; this was absent in our patient.

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