

Dramatic Efficacy of Oral Aromatic Retinoid in Long-standing Hypertrophic Lupus Erythematosus

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Sir,

In 1940, Bechet described hypertrophic lupus erythematosus (LE) as a variant of discoid lupus erythematosus (DLE) characterized by erythematous verrucous plaques with indurated borders (1). Similar lesions were also described as verrucous LE (2, 3), or keratotic LE (4). Hypertrophic LE accounted for 2% of chronic LE (5). Various treatments have been tried including intralesional corticosteroids, hydroxychloroquine (2), retinoids (4, 6), thalidomide (7) and cryotherapy (8); however, hypertrophic LE is often resistant to these treatments. Here, we describe a patient with hypertrophic LE who was refractory to various treatments over a period of 24 years, but responded quickly to oral etretinate.

CASE REPORT

The patient is a 58-year-old Japanese woman. At the age of 28, she experienced a recurrent fever, malar erythema, photosensitivity, arthralgia, proteinuria and chilblain lupus and was diagnosed as having systemic LE (SLE). The activity of SLE was well controlled after systemic corticosteroid therapy was started and no systemic manifestations except arthralgia were observed. At the age of 34, 6 years after the onset of SLE, itchy hyperkeratotic plaques gradually appeared on her extremities. These lesions never disappeared despite dapsone, antihistamine, topical and occlusive corticosteroids and topical tacrolimus treatments, but were moderately controlled with 12.5–20 mg/day of prednisolone which was prescribed for almost 24 years. Several trials of tapering prednisolone below 10 mg/day always led to marked worsening of the skin lesions and especially the pruritus, which caused sleeping problems.

At the age of 58, she was admitted to hospital for a re-evaluation of her condition and for a new treatment trial.

Physical examination revealed red or depigmented hyperkeratotic nodules and plaques up to 8 cm in diameter on the extensor surface of the extremities, especially on the back of hands, elbows and knees (Fig. 1). The lesions were extremely itchy. Classical DLE lesions without any marked hyperkeratosis were also present on her back. A routine laboratory examination revealed that blood counts and liver function were within normal limits. The anti-nuclear antibody titre was positive at 1:160 and showed a homogeneous pattern. Anti-Ro/SSA antibodies and lupus anticoagulant were also positive. Anti-double strand DNA antibody, anti-RNP antibody, anti-La/SSB antibody, Sm antibody and anti-cardiolipin antibody titres were negative. Complement was within normal levels.

Histologically, the specimen taken from a hyperkeratotic nodule on the knee showed marked hyperkeratosis, irregular acanthosis and elongation of the rete ridge with a band-like mononuclear cell infiltrate in the upper dermis. Basement membrane thickening and hydropic degeneration of the basal keratinocyte layer was also observed. Direct immunofluorescence demonstrated a granular deposition of complement at the dermal-epidermal junction. These findings were consistent with hypertrophic LE. The specimen taken from the back with classic DLE characteristics showed the typical pathological features expected for DLE, including thinning of the epidermis, orthohyperkeratosis, follicular plugging, vacuolar degeneration and mucin deposition.

Due to the severe itching, etretinate 30 mg/day was added to the prednisolone dose (12.5 mg/day). Surprisingly, the intense pruritus showed a dramatic improvement over the next 4 days, and the hyperkeratosis associated with the hypertrophic LE also began to decrease. After 10 days, the hypertrophic LE lesions went into remission leaving depigmented maculas only. No major side effects were observed except for cheilitis, which cleared after the dose of etretinate was decreased to 10 mg/day. The DLE on the patient's back disappeared more gradually over a period of 6 months.

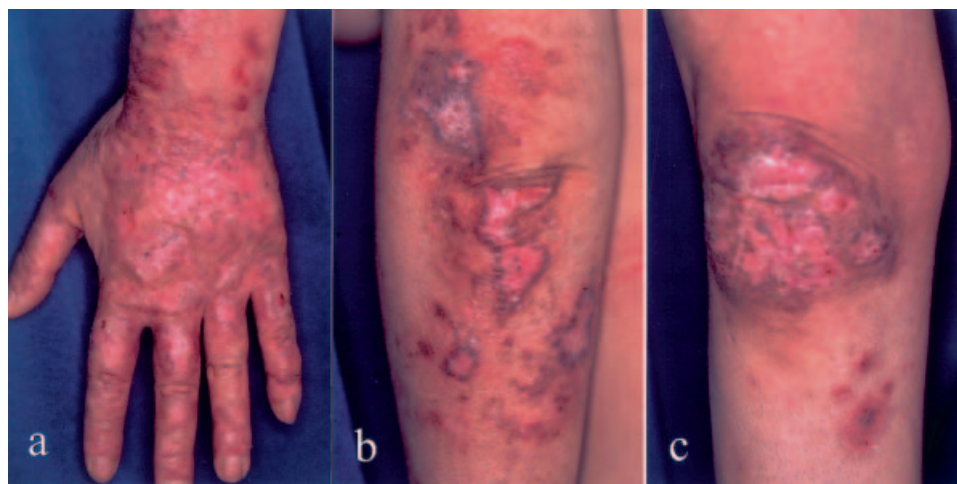


Fig. 1. The clinical appearance of hypertrophic lupus erythematosus on the hand (a), the elbow (b) and the knee (c) before etretinate therapy.

DISCUSSION

Hypertrophic LE histologically shows marked acanthosis, hyperkeratosis and hypergranulosis with a mononuclear cell infiltrate. The histological picture is variable and sometimes described as keratoacanthoma-like or hypertrophic lichen planus-like with a band-like mononuclear infiltrate (3). As in previous case reports (2, 3), our patient clinically showed typical DLE on her back in association with hypertrophic LE on the extremities. These lesions were refractory to various treatments including systemic prednisolone for more than 20 years; however, they showed a dramatic and complete response to etretinate.

According to a Medline search, only 50 cases of hypertrophic LE have been reported from 1963 to 2003. Of these, we reviewed 25 case reports where the treatment was described (2, 4, 6–13). Seventeen of the patients were women and the mean age at onset was 40.4 years. Hypertrophic LE usually occurred after a long previous history of cutaneous LE, although a few abrupt onsets were also reported. Only 5 of 25 patients with hypertrophic LE were diagnosed as suffering from SLE, i.e. fulfilling at least 4 of the American College of Rheumatology criteria (11, 12).

Various treatments have been tried for hypertrophic LE, such as antimalarial drugs, prednisolone, dapsone and intra-lesional corticosteroids. However, in the reviewed 25 cases the treatment did not always lead to any good results and was restricted by side effects and contraindications. Antimalarials and thalidomide are considered to be among the best systemic therapies for classic DLE but are not always effective for the hypertrophic LE forms (2, 7). Besides, antimalarials and thalidomide are not available in some countries, including Japan.

In the present case, the aromatic retinoid etretinate, which is still the only oral retinoid available in Japan, proved highly effective; the hyperkeratotic nodules and severe intolerable pruritus disappeared promptly with a low dosage. The efficacy of etretinate and its major metabolite, acitretin, has been studied in patients with cutaneous LE (14) but their efficacy in hypertrophic LE was only reported once before (15). Only rarely have topical tretinoin (6) and systemic isotretinoin (4, 12) been used in hypertrophic LE.

The exact mechanism of action of etretinate in hypertrophic LE is still unknown. The inhibition of epidermal proliferation by retinoids as well as the immunomodulatory effects (16) may be important in treating hypertrophic LE. Although the use of etretinate and acitretin is restricted for young women due to teratogenic effects, hypertrophic LE usually appears at

a higher age, following long-term classic DLE, thus obviating such contraindications.

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