Oral Alitretinoin in Lichen Planus: Two Case Reports

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Alitretinoin is an endogenous vitamin A derivative, 9-*cis*-retinoic acid. As a pan-agonist of both known nuclear retinoid receptor families (retinoic acid receptors (RAR) and retinoid X receptors (RXR)) it helps to regulate cell proliferation and promotes cell differentiation and apoptosis (1–2). Its anti-inflammatory and immune modulating efficacy results from controlling cytokine production in keratinocytes and leukocyte activity (3). In some European countries and in Canada alitretinoin (Toctino®, Basilea Pharmaceutica) is licensed for systemic therapy of severe chronic hand eczema that is refractory to potent topical steroids (4–6). Oral alitretinoin has a more favourable safety profile for mucocutaneous side-effects than do other vitamin A derivatives. Due to its dual receptor activity it may be argued that alitretinoin could also be more effective in retinoid-responsive dermatoses, such as lichen planus (LP), compared with acitretin or isotretinoin. Therapeutic use of systemic vitamin A derivatives is indicated in a variety of dermatological disorders, e.g. acne, psoriasis, ichthyosis, cutaneous T-cell lymphoma and LP. As all vitamin A derivatives are teratogenic the use of acitretin is sometimes problematic in women of childbearing age because a safe contraception has to be continued 2 years past treatment. With only one month prolonged contraception after therapy, alitretinoin might be a valuable alternative that is worth examining. Beyond chronic hand eczema this has not yet been investigated in clinical trials. We describe here two patients whose LP healed during combination treatment with alitretinoin.

CASE REPORTS

Patient 1

A 54-year-old man had developed itching, red, polygonal papules mainly affecting his trunk, back, legs and forearms approximately 7 months previously. Subsequently, blister formation and consecutive hyperkeratosis and fissures had emerged on his soles, with increasing itch. Skin biopsy specimens confirmed a diagnosis of lichen planus on the trunk. Although clinically compatible with LP, histology also showed signs of dyshidrosis on the soles. Tinea was excluded by mycological examination. Previous treatment courses, including topical steroids, had not led to a stable remission of the skin condition. His medical history included an episode of LP approximately 20 years previously. No pre-existing atopy or relevant contact allergies were reported. The patient was a heavy smoker.

A therapeutic regimen with systemic alitretinoin, 30 mg/day, was started, which was well-tolerated by the patient. Initially this was combined with topical therapy: silver nitrate for the fissures, steroids (e.g. betamethasonediproprionate) alone for the extra-plantar lesions, and a combination of steroids and salicylic acid for the soles.

The LP lesions on the trunk and the itch disappeared within 16 weeks. The plantar fissures, as well as the hyperkeratosis, also improved significantly, but more slowly, within a 6-month therapeutic course.

Patient 2

A 48-year-old woman presented with a one-month history of severely pruritic, palmoplantar skin lesions with polygonal red papules spreading to both wrists, hyperkeratosis and scaling (Fig. 1). Histological investigation of a skin biopsy confirmed the clinical diagnosis of lichen planus. Patch-testing revealed nickel allergy, mycological analysis did not show any infection. A gynaecological consultation found the patient to be post-menopausal. The patient was started on a therapeutic regimen combining systemic alitretinoin, 30 mg/day, and a course of cream-psoralen plus

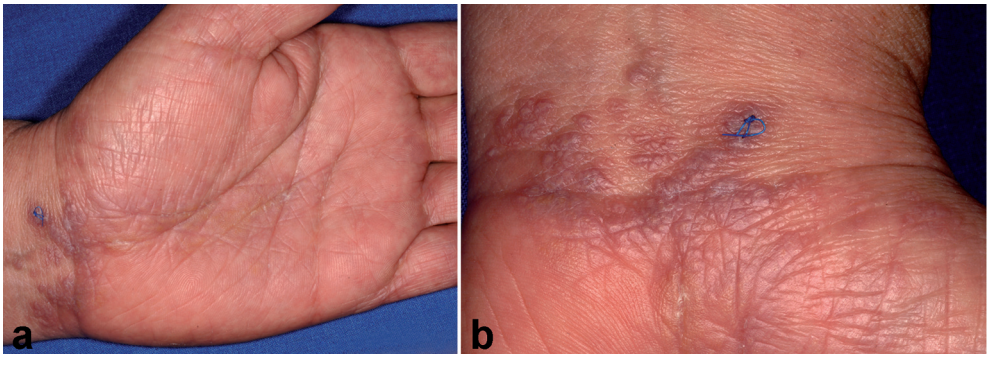

Fig. 1. (a and b) Severely pruritic, palmoplantar skin lesions with polygonal red papules spreading to both wrists, hyperkeratosis and scaling before treatment (patient 2). The suture indicates the biopsy site.

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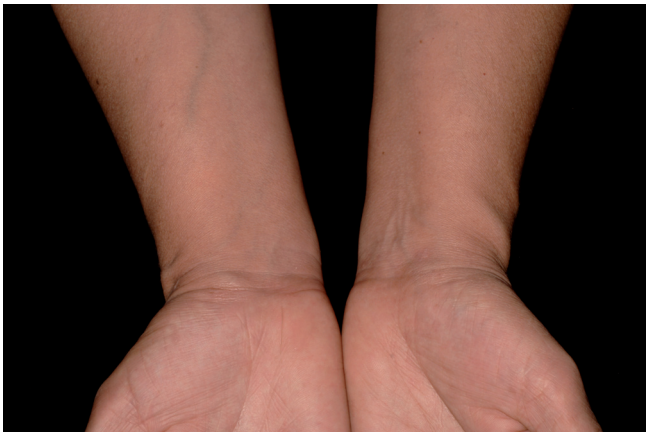

Fig. 2. Healing of the lichen planus lesions in patient 2 after a 5-month treatment course.

ultraviolet A (PUVA)-therapy, 3–4 times per week. This combination treatment was well tolerated without side-effects. As in patient 1, topical treatment had initially included a combination of salicylic acid and steroids (e.g. mometasonfuroate). The skin condition of the patient cleared over a period of 5 months (Fig. 2). An initial response became apparent after 1.5 months, whereas the palmar lesions improved more quickly than the plantar ones.

DISCUSSION

The use of systemic vitamin A derivatives in dermatology for diseases such as acne, psoriasis and LP is generally accepted. LP is a disease entity of unknown origin affecting the skin and mucous membranes. The manifold lesions are often accompanied by severe itch, which can severely impair patients' quality of life. Palmoplantar lesions are often problematic, as they can particularly affect everyday social and work activities of the individual patient. Although there seems to be a chance of spontaneous remission over a time course of one or 2 years, different treatment modalities are used and combined according to the clinical presentation: topical steroids, UV-therapy, extracorporeal photopheresis, systemic retinoids, cyclosporine A or topical calcineurin inhibitors (7). The benefit of systemic retinoids for LP is supposed to result from their anti-proliferative mode of action mediated by binding to nuclear receptors (RAR and RXR). The special receptor binding profile of alitretinoin, suggests not only anti-proliferative, but also increased anti-inflammatory efficacy (8). Acitretin and isotretinoin, mainly RAR agonists, are known treatment options for LP. Their efficacy is limited by mucocutaneous side-effects and laboratory changes of triglyceride or cholesterol values or liver enzymes.

The two patients with LP described here had severe palmoplantar hyperkeratotic and partly rhagadiform skin lesions, a condition in which systemic vitamin A derivatives, particularly acitretin, can be used therapeutically. In order to find a better tolerated and safe alternative to acitretin we decided to try alitretinoin in these two patients. Treatment with oral alitretinoin was beneficial for, and well-tolerated in, both patients and led to improvement, not only of their palmoplantar skin lesions. Our observations suggest that controlled clinical trials of alitretinoin may be warranted in LP.

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