Successful Treatment of Recalcitrant Prurigo with Alitretinoin

Karolina Gadaldi a  Yeliz Erdemoğlu b  Nikhil Yawalkar a

aDepartment of Dermatology, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland; bDepartment of Dermatology, School of Medicine, Acibadem University, Istanbul, Turkey

Abstract

Background: Chronic itch with secondary scratch lesions such as prurigo has a major impact on quality of life. Due to its relapsing nature and often unknown origin, its treatment is challenging. Objective: We sought to demonstrate that alitretinoin can be an efficacious and well-tolerated treatment in a patient suffering from chronic itch with concomitant prurigo and psoriatic lesions. Methods: Case report. Results: After 1 month of alitretinoin treatment (30 mg daily), itch as well as prurigo and psoriasis lesions decreased markedly. Three cycles of alitretinoin were administered, as each cessation of treatment led to relapse of the symptoms after 6–8 weeks. Tapering of the alitretinoin dose (30 mg every second day) after the third cycle allowed to maintain the effects for over 18 months. Conclusion: Treatment of refractory prurigo with alitretinoin might be an efficacious alternative to standard therapies. In case of relapse, retreatment with alitretinoin induces a further long-lasting response.

Introduction

Chronic pruritus presenting with secondary scratch lesions such as prurigo has been demonstrated to have a major impact on quality of life. Although the underlying origin is often unknown, it may be associated with numerous dermatological, systemic and/or psychological diseases. Given its chronicity and relapsing nature, treatment of chronic pruritus with prurigo can be challenging. Temporary relief can be achieved by use of corticosteroids, topical calcineurin inhibitors, menthol, capsacin creams or ultraviolet therapy. Treatment with oral agents such as ciclosporin, antibiotics, opiate receptor antagonists, thalidomide and gabapentin can be satisfactory; however, their pronounced toxicity prevents the long-term use of these drugs, and the severity of the disease often worsens markedly after treatment has been stopped. We present a case of a patient suffering from chronic itch with concomitant prurigo and psoriasis lesions successfully treated with alitretinoin.

Case Report

A 46-year-old Caucasian woman, with a history of plaque psoriasis of the elbows and knees, chronic alcohol abuse and depression was admitted to our outpatient clinic with severe, 5-year pruritus and secondary prurigo lesions on the extensor surface of her arms and legs (fig. 1a, b). Physical examination of the patient, blood chemistry test, chest X-ray, as well as direct and indirect immunofluorescence did not confirm any underlying systemic disease. Histological examination of a skin biopsy of a nodular lesion was consistent with prurigo.

Previous treatments including topical corticosteroids, topical tacrolimus, menthol, phototherapy, antihistamines, montelukast, doxepin and gabapentin did not provide healing of the lesions. Treatment with ciclosporin (200 mg daily) led to significant improvement of both prurigo and psoriatic lesions (body surface area: 3%), but due to a potential risk of long-term adverse reactions the treatment was interrupted after 1 year.

Eventually, successful treatment with alitretinoin (30 mg daily) was introduced. After approximately 1 month, pruritus deceased and both prurigo and psoriasis lesions (body surface area: <1%) improved significantly (fig. 1c, d). After 5 months, the skin lesions healed completely with some postinflammatory pigmentation and scars (fig. 1e, f). Consequently, alitretinoin was stopped. Altogether 3 cycles of alitretinoin were administered, as each cessation of retinoid treatment led to relapse of the symptoms after approximately 6–8 weeks. Tapering of the alitretinoin dose (30 mg every second day) after the third cycle allowed to maintain the therapeutic effect for over 18 months. In the last 3 months treatment with alitretinoin 30 mg was extended to every third day and no relapse has been observed so far. Treatment was well tolerated except for a slightly elevated level of nonfasting total cholesterol values (up to 7 mmol/l, normal value: <5.2 mmol/l).
Discussion

Alitretinoin (9-cis-retinoic acid) is a novel vitamin A derivate that binds to all 6 retinoid receptors (retinoic acid receptors RAR-α, -β, -γ and retinoid X receptors RXR-α, -β, -γ). The most frequent retinoid receptor in the skin is RAR-γ/RXR-α heterodimer [1]. Previously used retinoids (such as acitretin and etretinate) target mainly RAR receptors. Hence, alitretinoin is expected to act in a wider spectrum of diseases and on different pathways compared to the old retinoids. It has anti-inflammatory and immunomodulating effects and has been demonstrated to regulate the production of cytokine and leukocyte activity [2].

The most frequent adverse effects of alitretinoin include mucocutaneous dryness and headache [3]. The latter is dose dependent and often disappears with dose reduction. Laboratory abnormalities comprise the typical effects of retinoids such as increase in serum lipids and liver enzymes, as well as a reduced thyroid-stimulating hormone level. In our case, except for a slightly elevated level of nonfasting total cholesterol there was no change in the laboratory investigations, especially no increase in liver values was observed. Furthermore, the mood of the patient was not altered during the therapy.

Alitretinoin has been registered as a systemic treatment for severe chronic hand eczema unresponsive to potent topical corticosteroids [4, 5]. In addition to its approved use, alitretinoin has been reported to be beneficial also in refractory pityriasis rubra pilaris [6], lichen planus [7, 8], cutaneous lupus erythematosus [9], palmoplantar pustular psoriasis [10] as well as in mycosis fungoides [11], but it appeared to have a mixed effect in congenital ichthyosis [12]. Several studies have also been carried out with alitretinoin used in the treatment of AIDS-related Kaposi’s sarcoma [13].

The present report describes a case of chronic itch with secondary prurigo lesions and psoriasis successfully treated with alitretinoin (30 mg daily). After approximately 1 month of the therapy, pruritus decreased in our patient and both prurigo and psoriasis lesions improved. A significant decrease in intensity of itch after treatment with alitretinoin has already been demonstrated in the literature. A case report on 2 patients with mycosis fungoides described a cessation of pruritus after 2 months of alitretinoin treatment (30 mg daily), before improvement of the skin lesions [11]. Similarly, in 1 patient with lichen planus treated with alitretinoin (30 mg daily) pruritus disappeared after 4 weeks, before all skin lesions completely healed [8]. It is known that itch and subsequent repeated scratch-
mast cells exhibit in vitro the production of human IL-4 increases the production of IL-12p70 and tumor necrosis factor-α [18]. The latter and IL-12/IL-23 play an important role in the development of psoriasis [22, 23]. Hence, it can explain the positive therapeutic effect of altretinoin not only on prurigo, but also on psoriatic lesions in our patient. The positive effect of altretinoin in psoriasis has been described previously in only few reports. Irla et al. [10] observed 50% improvement in the Palmoplantar Psoriasis Area and Severity Index score in 100% of patients with palmoplantar pustular psoriasis (n = 7) treated with altretinoin 30 mg daily for 3 months. Moreover, they have also observed a significant decrease in itch intensity in all studied psoriatic patients.

After interruption of the therapy with altretinoin, prurigo lesions relapsed in our patient within 6–8 weeks. This phenomenon has already been observed in studies on hand eczema. The median time to relapse, defined as recurrence of 75% of initial signs and symptoms, was 5.5–6.2 months in the absence of other medications [4]. In our case the second and third therapeutic course of altretinoin (30 mg daily) was necessary to completely heal the skin lesions. This is consistent with the data from a recently reported trial on chronic hand eczema [3]. The authors of this study demonstrated that altretinoin at the dose of 30 mg daily reinduced response in the majority of patients who had relapsed within 6 months following successful treatment with an initial course of altretinoin.

In conclusion, our report shows that treatment of refractory prurigo with altretinoin might be an efficacious alternative to standard topical and systemic treatments. In case of relapse, retreatment with altretinoin reinforces a further long-lasting response. Further clinical studies are warranted to confirm efficacy and safety of altretinoin in this disease.

Disclosure Statement

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