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CONCISE COMMUNICATION

Ultraviolet A1 phototherapy for the treatment of localized scleroderma

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ABSTRACT

Ultraviolet (UV)A1 phototherapy is effective for T-cell-mediated skin diseases such as atopic dermatitis and mast cell-mediated skin diseases such as mastocytoma. UVA1 phototherapy is also effective against the sclerotic lesions of systemic sclerosis and morphea. Currently, in Japan, access to UVA1 phototherapy is limited because the UVA1 phototherapy device has not yet been approved. On the basis of our experience, we report three patients with localized scleroderma who responded successfully to UVA1 phototherapy. Efficacy was assessed by histological analysis and elastography. UVA1 successfully ameliorated sclerotic lesions, including morphea, linear scleroderma and morphea lesions in a patient with limited cutaneous systemic sclerosis. No side-effects were observed during UVA1 phototherapy.

Key words: localized, morphea, phototherapy, scleroderma, ultraviolet A1.

INTRODUCTION

Systemic sclerosis (SSc) is characterized by an excessive deposition of collagen and other connective tissue matrix proteins. We previously reported the effectiveness of 8-methoxypsoralen and ultraviolet A radiation (PUVA) therapy in a case of advanced SSc[1] as well as normalization of the collagen fibril size following PUVA therapy.[2] In another study, we reported that ultraviolet (UV)A1 (340–400 nm) was highly effective for scleroderma in SSc.[3] UVA1 irradiation phototherapy, in which lesional skin on the forearm was exposed daily to medium-dose ultraviolet radiation, induced marked softening of SSc lesions.[3] Histological evaluation of skin specimens obtained before and after UVA1 phototherapy revealed loosening of the collagen bundles and the appearance of small collagen fibers. These findings led us to further explore the applications for UVA1 phototherapy. In Japan, the access to UVA1 phototherapy is limited because the UVA1 phototherapy device has not yet been approved. On the basis of our experience, we report three patients with localized scleroderma who responded successfully to UVA1 phototherapy.

CASE REPORTS

Case 1

A 61-year-old Japanese woman first noticed edema on the posterior surface of her fingers. She gradually developed edema and sclerosis in her forearms and fingers, which was accompanied by Raynaud's phenomenon. She was referred to our dermatology clinic for evaluation of the sclerotic lesions. Clinical examination revealed sclerosis in her fingers and forearms, a shortened tongue corpuscle and a mask-like face. A biopsy specimen obtained from the forearm revealed a thickened dermis with collagen hyalinization. Her blood tests were positive for anticentromere antibody, and negative for anti-Scl-70, anti-DNA, anti-RNP and anti-Sm antibodies. On the basis of the clinical and laboratory data, we diagnosed her with limited cutaneous systemic sclerosis (lcSSc). Oral nicotinic acid, α-tocopherol and topical emollient were prescribed, but the patient developed sclerotic lesions on her abdomen with circumscribed, infiltrated erythema. The lesions gradually increased in size and she experienced an abdominal girdle sensation. A biopsy specimen from the abdominal lesion showed thickened and proliferated collagen fibers. The antinuclear antibody profile did not change. She was then diagnosed with morphea and lcSSc.

Ultraviolet A1 is effectively used to treat localized morphea[4] in other countries, and therefore we selected UVA1 to treat this case. The procedure was approved by the ethics committee of Nagoya City University Graduate School of Medical Sciences and the patient provided written informed consent. UVA1 was emitted by a metal halide lamp with a UVA1 filter and an infrared absorption filter (Sellamed; Sellas, Gevelsberg, Germany). The radiation wavelength was between 340 and 450 nm, with a peak at 365 nm.[3] UVA1 treatment (60 J/cm^2) was performed five times a week. The duration of UVA1 exposure for 60 J/

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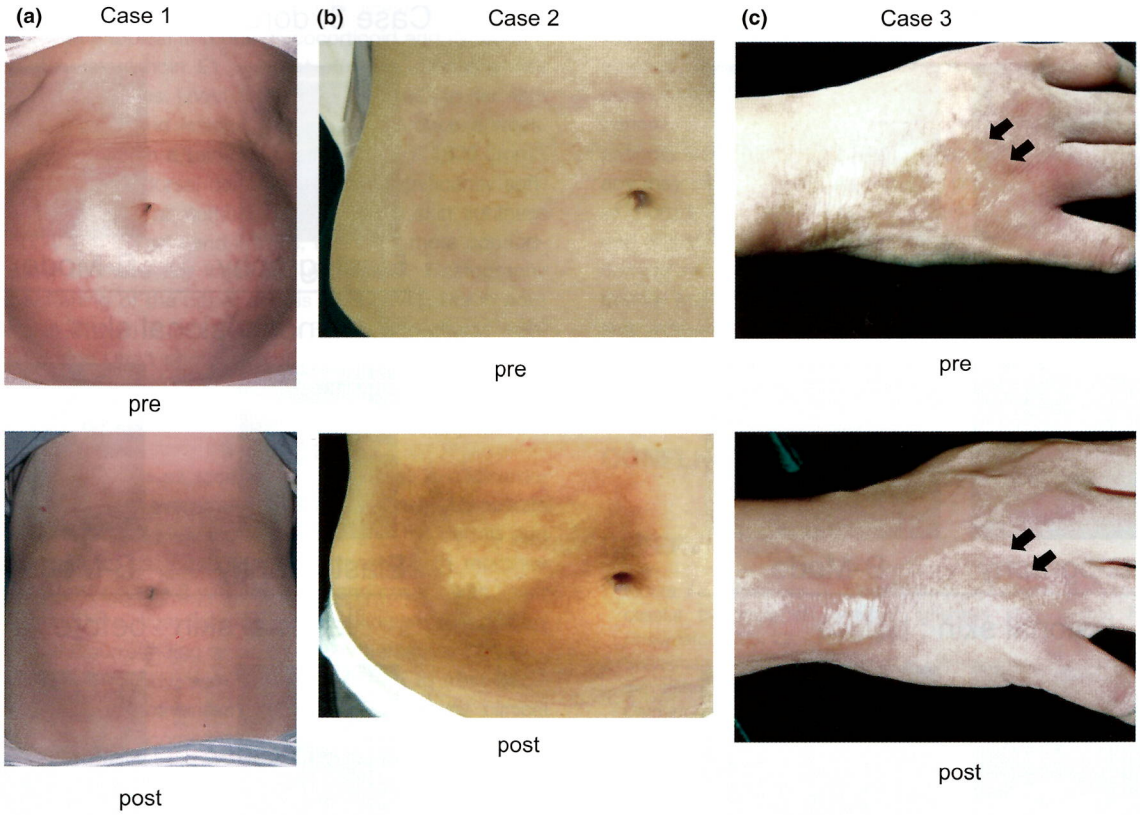
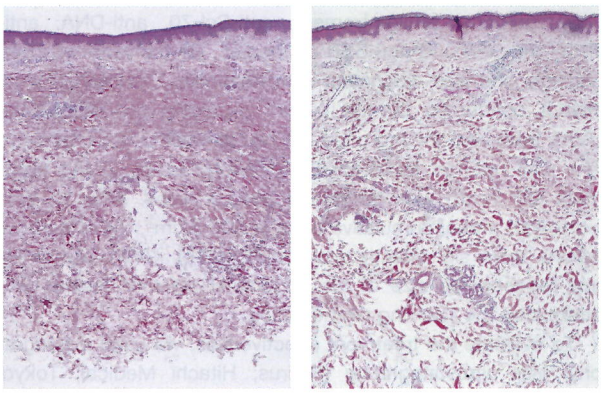


Figure 1. Efficacy of ultraviolet (UV)A1 phototherapy for treating morphea. (a) Marked skin tightening in the trunk before UVA1 phototherapy. Significant softening of the abdominal lesions was observed after nine sessions with 540 J/cm^2 UVA1 phototherapy. (b) Sclerosis with lilac ring on the patient's abdomen before UVA1 phototherapy. Significant reduction of the abdominal lesions was observed after 15 sessions with 600 J/cm^2 UVA1 phototherapy. (c) Edema and sclerosis in the dorsum of the right hand before UVA1 phototherapy. Significant softening of the lesions on the dorsum of the right hand was observed after 30 sessions with 1800 J/cm^2 UVA1 phototherapy.

cm^2 was approximately 16 min. After nine sessions with a total cumulative dose of 540 J/cm^2, the abdominal lesions had significantly softened but were highly pigmented (Fig. 1). UVA1 phototherapy reduced the skin tightness of the abdominal lesions. Abdominal lesion biopsy specimens obtained before and after UVA1 phototherapy revealed that the improvement was accompanied by concomitant histological changes (Fig. 2). The collagen bundles were decreased in size and released. Neither systemic side-effects nor overlapping collagen vascular disease were observed during UVA1 phototherapy.

Case 2

A 44-year-old US Caucasian woman first noticed a papule on her abdomen. She gradually developed erythema and sclerosis



Case 1

Figure 2. Histological appearance of systemic sclerosis in response to ultraviolet (UV)A1 phototherapy. Histological evaluation of site-matched skin biopsy specimens before and after. UVA1 phototherapy of the abdominal lesions. Pretreatment biopsy specimens demonstrate thickened and homogenous collagen bundles. Post-treatment biopsy specimens have a decreased collagen bundle size and delicate collagen fibers (hematoxylin–eosin, original magnification ×100).

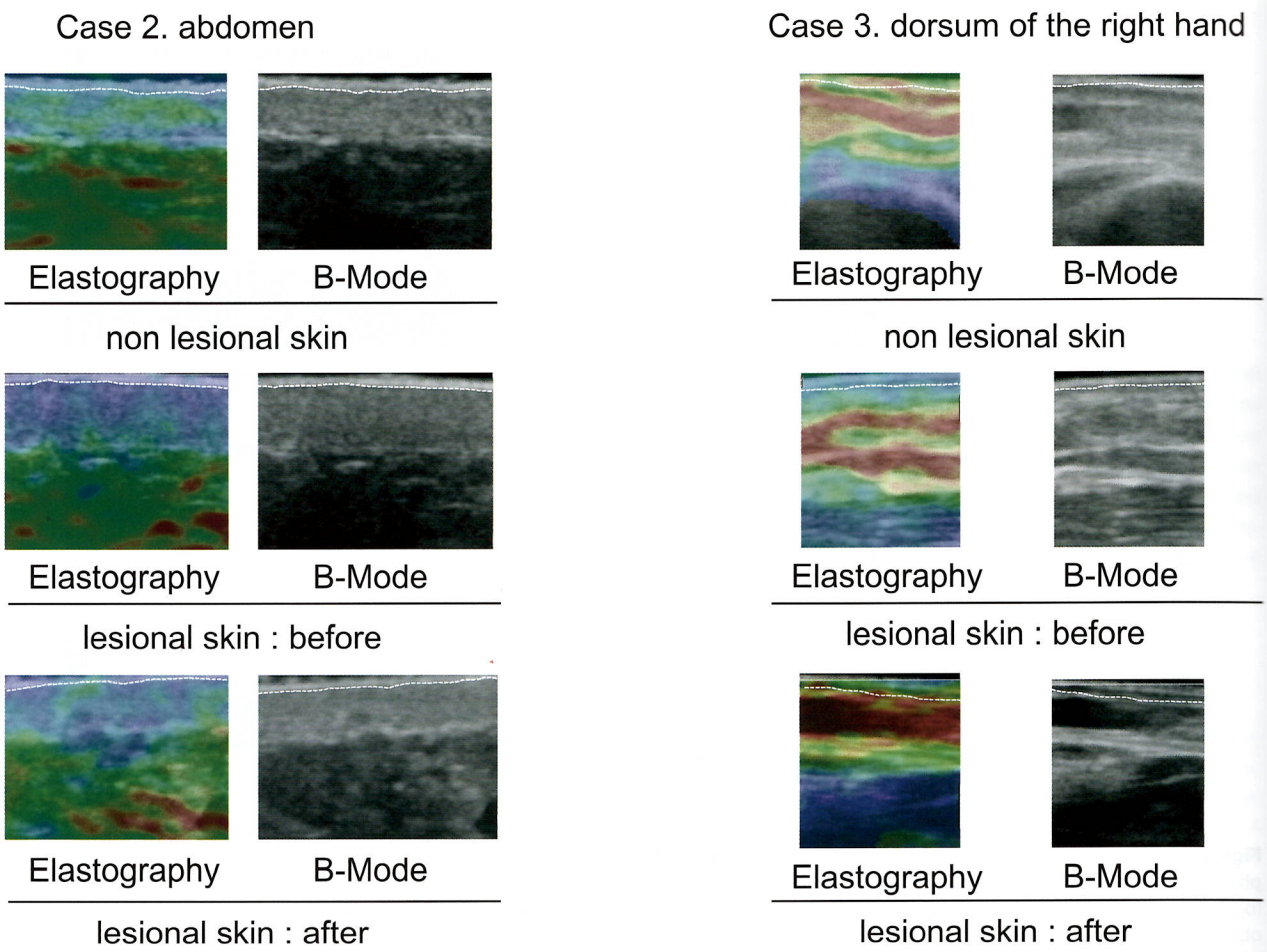


Figure 3. Elastography of the lesions of cases 2 and 3.

on the right side of her abdomen. She was referred to a dermatology clinic for evaluation of the sclerotic lesion. Clinical examination revealed a sclerotic plaque with a lilac ring on her abdomen. Her blood tests were negative for fluorescent antinuclear antibody, anticentromere, anti-Scl-70, anti-DNA, anti-RNP, anti-SSA and anti-SSB antibodies. On the basis of these findings, she was diagnosed with morphea. A published work search conducted by the patient regarding the efficacy of UVA1 treatment for morphea led her to seek UVA1 treatment. She was referred to us for UVA1 phototherapy. UVA1 treatment (60 J/cm^2) was performed once a week. After 15 sessions with a total cumulative dose of 900 J/cm^2, the abdominal lesions were significantly softened (Fig. 1b). UVA1 phototherapy reduced the size of the abdominal sclerotic lesions and attenuated the lilac ring pigmentation.

To evaluate the treatment effectiveness, we used elastography with ultrasonography (Preirus; Hitachi Medical, Tokyo, Japan). Elastography is an imaging technique used to visualize differences in tissue stiffness that are produced by compression and relaxation of the tissue. We used a conventional linear probe with a 13-MHz transducer (EUP-L65; Hitachi Medical). Areas of easily compressed tissue, such as adipose tissue, are shown as red pixels on the ultrasound viewing screen. Tissue areas that tend to compress to the same degree as benign tissue are shown as green pixels, while areas of hard or malignant tissue are shown as blue pixels. Before UVA1, the upper dermis was shown as blue in the elastogram. After UVA1, the area was shown as green in the elastogram, indicating that UVA1 phototherapy reduced the skin tightness (Fig. 3).

Case 3

A 36-year-old Japanese woman first noticed edema and sclerosis on her right arm. She gradually developed edema and sclerosis in her right elbow and dorsum of the right hand, Furthermore, she experienced restricted movement of her right wrist and ring finger. She presented to a dermatology clinic for evaluation of the sclerotic lesion. Clinical examination revealed sclerosis in her right arm, especially her elbow, dorsal hand and ring finger. Her blood tests were negative for fluorescent antinuclear antibody, anticentromere, anti-Scl-70, anti-DNA, anti-RNP, anti-SSA and anti-SSB antibodies. On the basis of

these findings, she was diagnosed with linear scleroderma. Treatment with a topical and oral glucocorticoid and i.v. administration of prostaglandin E1 was not effective, and she was therefore referred to us. UVA1 treatment (60 J/cm^2) to her right elbow and dorsal hand lesions was performed once a week. After 30 sessions with a total cumulative dose of 1800 J/cm^2, her right elbow and dorsal hand lesions had significantly softened (Fig. 1c). UVA1 phototherapy reduced the skin tightness of the elbow and dorsal hand lesions, making it more comfortable for her to move her wrist and ring finger. Elastography showed softening of the upper dermis after UVA1, like in nonlesional skin (shown in red in Figure 3). No side-effects were observed during UVA1 phototherapy.

DISCUSSION

Morphea, also known as localized scleroderma, is a disorder characterized by the overproduction of collagen by fibroblasts in the affected tissues, leading to thickening of the dermis and subcutaneous tissues. Case 1 was diagnosed with morphea lesions and lcSSc, case 2 with morphea and case 3 with linear scleroderma. The clinical features include skin sclerosis demarcated from the surrounding areas by an erythematous border.

In our previous study, we used topical PUVA to treat SSc.[1] The therapeutic effectiveness was demonstrated by clinical improvement and concomitant changes in the histological, laboratory and thermographic parameters. These changes most likely do not reflect spontaneous remission but rather improvement due to PUVA treatment. UVA1 phototherapy is also reported to be effective for the treatment of SSc.[3] According to previously described findings of the underlying mechanisms of phototherapy, UVA1 depletes skin-infiltrating T cells through the induction of T-cell apoptosis[5] and the upregulation of matrix metalloproteinase 1 (collagenase 1) expression in dermal fibroblasts, suggesting that UVA1 is beneficial for treating SSc.

In a previously reported phototherapy study, 17 patients with morphea were treated with UVA1 phototherapy.[4] In all patients, high-dose UVA1 therapy softened the sclerotic plaques and complete clearance was observed in four of 10 patients. In a case series report of generalized morphea,[6] four patients were given oral PUVA therapy. Oral PUVA phototherapy may offer an effective means of preventing the progression of morphea and reversing the inflammatory response. Symptom improvement, however, was observed only after a large number of treatment sessions. In our study, UVA1 successfully treated sclerotic lesions, including morphea, linear scleroderma and morphea lesions in a patient with lcSSc. We have been following the patients for a couple of years and there has been no recurrence.

CONFLICT OF INTEREST: None declared.

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