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Narrow-Band Ultraviolet B is a Useful Adjunctive Treatment for Atopic Dermatitis in Older Adults: Case Reports

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TO THE EDITOR

The prevalence of atopic dermatitis (AD) in elderly patients is gradually increasing in developed countries [1]. In this paper, we report cases of elderly Japanese patients with AD who were treated in our hospital with narrow-band ultraviolet B (UVB, wavelength: 311 ± 2 nm) phototherapy and discuss its utility as an adjunctive treatment for AD in older adults. We describe two instructive cases in detail, then summarize clinical characteristics of the AD and the efficacy of phototherapy for these cases and four additional cases in **Table 1.**

Phototherapy regimens consisted of intensive treatment (three to five irradiation sessions per week) and/or maintenance treatment (one irradiation session every one to four weeks). As a practical consideration, rather than measuring the minimal erythema dose (MED) in each case as is often done, we simply began the first irradiation treatment for each patient with a dose of between 0.30 and 0.40 Joule (J)/cm^2 (approximately half the value of the average MED in the Japanese population [2]), on only in a small area of the skin lesions. We then increased the dose by 0.05 J/cm^2 at each subsequent treatment until the optimal dose was achieved, as determined by effective therapeutic response without adverse effects (e.g., marked irritation). The assessment of therapeutic effects was defined as follows: clinical remission, disappearance of skin lesions in more than 95% of observed lesional areas for at least three months with standard treatments and maintenance treatment of narrow-band UVB; clinical improvement, disappearance of skin lesions in more than 95% of observed lesional areas for at least three months with standard treatments and maintenance treatment of narrow-band UVB *and* either oral corticosteroids (betamethasone, ≤0.5 mg/day) or cyclosporine (≤50 mg/day); minor improvement, mild to moderate improvement of lesional areas with standard treatments and narrow-band UVB (intensive and/or maintenance treatments), with or without oral corticosteroids/cyclosporine; and ineffective. The standard treatments comprised regular application of moisturizers and/or emollients in combination with topical corticosteroids and tacrolimus, as well as oral antihistamines/cytokine-inhibitors [3]. Topical tacrolimus was used for non-irradiated areas of skin lesions except for on the days of irradiation treatments.

Case 1: A 64-year-old man presented with refractory eczematous erythema on the face (atopic red face), and lichenified eczema with localized prurigo-forming papules on the trunk and extremities **(Figure 1a).** Serum laboratory tests revealed a prominent immunoglobulin (Ig) E-allergic status. A biopsy of the lichenified eczema revealed a chronic eczematous reaction with inflammatory cell infiltrates, including numerous IgE-positive mast cells (MCs), cluster of differentiation (CD) 11c+ dendritic cells (DCs), and CD1a+ DCs [4]. Previous treatments with standard therapies and oral corticosteroids had achieved only moderate improvements. We therefore administered narrow-band UVB phototherapy, which, after 12 irradiation sessions, resulted in clinical remission of his refractory AD (**Figure. 1b**), allowing for withdrawal of oral corticosteroids.

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Table 1. Cases treated with narrow-band ultraviolet B photo therapy as an adjunctive treatment for atopic dermatitis in older adults

Case No.	Clinical findings: Age/Sex Duration of AD Clinical types Skin manifestations Total IgE (IU/ml) Specific IgEs† Complications AD-associated Underlying disorders/ medical history	Narrow-band UVB phototherapy						
		Irradiation regimen Total number of irradiations Body areas of the irradiation	Irradiation dose (J/cm^2): Starting Maximum Total	Side effects	Efficacy	Severity of AD before and after the phototherapy: EASI§ Before After	Topical and oral anti-inflammatory treatments before and after phototherapy: Topical agent (dosage/week)¶ Oral medicine(dosage/day) Before	After
1	64-year-old/M Since childhood IgE-allergic AD Erythroderma/lichenified eczema/prurigo 8537 Class 6:*Der f* and HD; class 4, 3, and 2:other 6 allergens, AR ,BA Hypertension and hyperlipidemia	Approximately once every 4 weeks 12 times Trunk and extremities	0.40 0.60 5.45	Slight irritation after irradiation; mild solar lentigo on the upper back	Outcome: Discontinuation of phototherapy upon clinical remission; recurrence was not observed during the 18 months following cessation of phototherapy Therapeutic effect: Induction of clinical remission; induction of drug withdrawal and/or dose reduction	24.3 0.9	Corticosteroids 10g[#]; tacrolimus,3.3g and corticosteroids II, 16.7g[###] Beta methasone, 0.5mg; d-chlorpheniramine maleate,4mg; levocecetirizine hydrochloride, 5mg; sodium cromoglicate, 300mg; and suplatast tosilate,150mg;	Corticosteroids II, occasional use[###] Levocecetirizine hydrochloride, 5mg
2	76-year-old/M Since age 64 IgE-allergic AD Lichenified/nummular eczema 5489 Class 5:Cat; class 3:*Der f* and other 2 allergens; and class 2: other 7 allergens AR Hypertension and	Approximately once every 1-3 weeks 21 times Trunk and arms	0.40 1.00 14.75	Irritation after irradiation; worsening of eczema in exposure areas	Outcome: Discontinuation of phototherapy upon worsening of eczema in the irradiated areas Therapeutic effect: induction of clinical improvement at low UVB doses followed by	3.2 14.3	Tacrolimus, 2.5g[##]; Corticosteroids I, 1.9g[###]; and corticosteroids II, 9.4g[###] Levocecetirizine hydrochloride, 5mg; and	Tacrolimus, 5g[##]; Corticosteroids II, 25g[###]; and corticosteroids III, 50g[###] Levocecetirizine hydrochloride, 10mg; and bepotastine besilate, 20mg

	remission of hepatitis C				exacerbation AD at higher doses		cyclosporine 25-50mg	
3	60-year-old/M Since adolescence (asymptomatic during 20s - 40s, with recurrence in late 50s) IgE-allergic AD Lichenified eczema on the trunk and extremities and atopic red face 946 Class 6:*JC*;class3: cypress AR, BA Hypertension, chronic heart failure, renal dysfunction, diabetes mellitus, and old myocardial infarction	Once per week (first 35 times); once every 2-4 weeks (final 13 times) 48 times Face, trunk, and extremities	0.30 0.60 28.00	Mild solar lentigo on forearms	Outcome: Discontinuation of the phototherapy upon clinical remission; recurrence was not observed during the6 months following cessation of phototherapy Therapeutic effect: Induction of clinical remission; Induction of drug withdrawal and/or dose reduction	15.0 0.6	Corticosteroids III,8.3g[#]; corticosteroids IV, 1.7g[##]; and corticosteroids II,8.3g[###]	CorticosteroidsIII ,5.0g[#]; and corticosteroids III, 2.5g[###]
4	60-year-old/F Since adolescence IgE-allergic AD Lichenified eczema on the trunk and extremities and atopic red face 10436 Class 6: *Der f, JC*, HD and Cat; and class 5, 3 and 2: other 16 allergens AR and steroid phobia Hypertension	3 times per week (first 9 times); once every 2 weeks (final 9 times) 18 times Back and arms	0.65 0.70 12.43	Mild diffuse pigmentation on the back	Outcome: Discontinuation of phototherapy due to ineffectiveness as maintenance treatment Therapeutic effect: Induction of minor improvement by the initial intensive treatment	29.4 17.6	Tacrolimus, 50g[## and ###]; and white petrolatum,200 g[## and ###] Fexofenadine hydrochloride, 120mg;levocetirizinehydrochloride, 5mg; sodium cromoglicate, 300mg; and suplatast tosilate, 150mg	Essentially unchanged from pre-phototherapy regimen

5	78-year-old/M Since age 47 IgE-allergic AD Lichenified eczema on the trunk and extremities and atopic red face 28715 Class 6: *Der f*, *JC* and HD; class 3: other 2 allergens; class 2: other 16 allergens AR,BA Reflux esophagitis and spinal canal stenosis	5 times per week (first 5 times); once every 2-4 weeks (final 31 times) 36 times Trunk and extremities	0.40 0.45 15.35	None	Outcome: Continuation of photo therapy as maintenance therapy Therapeutic effect: Induction of minor improvement	24.1 5.7	Corticosteroids Ⅱ,10g[#]; tacrolimus, 2.5g[##]; and corticosteroids Ⅱ, 6.3g[###] Olopatadine hydrochloride, 10mg; hydroxyzine pamoate,25mg; d-chlorpheniramine maleate,4mg; sodium cromoglicate, 300mg; and suplatast tosilate,150mg	Essentially unchanged from pre-phototherapy regimen
6	67-year-old/M Since adolescence IgE-allergic AD Lichenified/nummular eczema on the trunk and extremities and atopic red face 4983 Class 6: *JC*; class 3:*Der f* and other 3 allergens; class 2: other 3 allergens AR Hypertension and colorectal polyp	Once every 2 weeks 10 times Face, trunk, and extremities	0.35 0.60 4.50	None	Outcome: Continuation of photo therapy as maintenance therapy Therapeutic effect: Induction of clinical improvement	13.2 1.1	Corticosteroids Ⅳ,5g[##]; and corticosteroids Ⅱ, 50g[###] Betamethasone, 0.5mg; d-chlorpheniramine maleate,4mg; Bepotastine besilate, 20mg; and suplatast tosilate,200mg	Essentially unchanged from pre-phototherapy regimen

Irradiation equipment: DERMARAY-400, Toshiba Medical, Tokyo, Japan.

Abbreviations: AD, atopic dermatitis; AR, allergic rhino-conjunctivitis; BA, bronchial asthma; Cat, cat dander; *Der f, Dermatophagoides farinae*; HD, house dust Ⅰ; IgE, immunoglobulin E;*JC, Japanese cedar*; UVB, ultraviolet B

†Specific IgEs against common environmental allergens were detected using the multiple antigens simultaneous test: MAST33 (BML, Tokyo, Japan): positive, class 6 (lumi count ≥160), 5 (lumi count 120-159), 4 (lumi count 58.1-119), 3 (lumi count 13.5-58.0) and 2 (lumi count 2.78-13.4); borderline, class 1 (lumi count 1.40-2.77); negative, class (lumi count <1.40)

§EASI, Eczema Area and Severity Index (maximum, 72) [7]

¶Topical agent: Rank of topical corticosteroids: corticosteroids Ⅰ, strongest; corticosteroids Ⅱ, very strong; corticosteroids Ⅲ, strong; and corticosteroids Ⅳ, medium [3]: Topical tacrolimus; Use for non-irradiated areas of skin lesions exclude the days of irradiation

[#]Topical treatment for scalp; [##]Topical treatment for face and neck;[###]Topical treatment for body and extremities

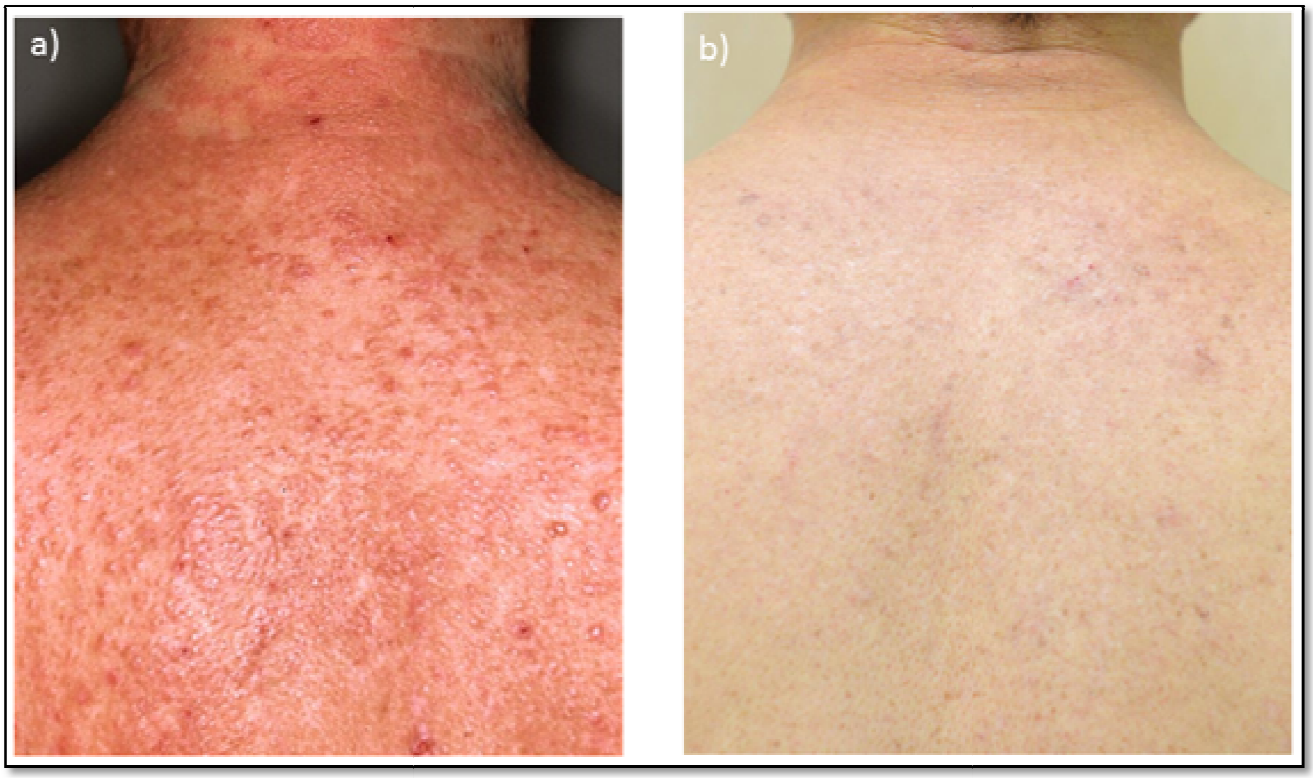

Figure 1. Clinical presentation of elderly patient with atopic dermatitis before (a) and after (b) narrow-band UVB phototherapy (case 1)

Case 2: A 76-year-old man presented with chronic eczema on the face and lichenified eczema and/or nummular-form eczema on the trunk and upper extremities. Laboratory data indicated IgE-allergic status. Skin biopsy showed allergic-type infiltration of the lichenified eczema by IgE+ MCs, IgE+ CD11c+ DCs, and IgE+ CD1a+ DCs. He had a history of hepatitis C, in remission since interferon therapy in his 50s. He had achieved moderate improvement of AD through standard treatments and oral corticosteroids or cyclosporine, but decreasing the doses of these resulted in AD relapse. We therefore administered narrow-band UVB phototherapy concomitantly with ongoing oral corticosteroids or cyclosporine. Clinical improvement of the AD was observed at least once following phototherapy (combined with standard treatments and occasional use of oral cyclosporine). However, when we increased the dosage of narrow-band UVB to 1.00 J/cm^2 (in an effort to achieve clinical remission without oral cyclosporine), the patient experienced marked deterioration at the areas of the phototherapy, with emergence of severe eczema. We therefore discontinued phototherapy.

Some older patients have difficulty managing AD using only standard treatments, as a diminishing ability to perform normal activities of daily living may inhibit adequate administration of topical medications. Therefore, for moderate to severe cases of AD, powerful anti-inflammatory treatments like oral corticosteroid or cyclosporine may be used in concert with the standard treatments [1]; however, underlying conditions (e.g., hypertension, renal dysfunction, and diabetes mellitus) in elderly patients with AD may preclude the use of such treatments.

In the presented cases **(Table 1),** we used narrow-band UVB phototherapy as an adjunctive treatment. Given its potent anti-inflammatory effects, we expected this treatment to provide substantial relief from, or even cure AD. Using phototherapy, we achieved a favorably therapeutic outcome for at least one in every six cases, and induced clinical remission in two (cases 1 and 3) of the six cases (33%). In these two cases, long-term clinical remission (≥6 months) was also observed after cessation of the phototherapy. One case (case 2) experienced a flare-up of eczema following the 1.00 J/cm^2 dose of narrow-band UVB, so we discontinued his phototherapy. This exacerbation was likely due to exceeding the patient's non-identified MED-dose, resulting in an irradiation-induced flare-up. Previous reports indicate that narrow-band UVB phototherapy is not effective for treating acute severe exacerbations of AD [5], so following this event, we only performed irradiation at doses over 0.70 J/cm^2 in a few select AD patients.

A recent study [6] demonstrated that the immunomodulatory effects of narrow-band UVB phototherapy for AD are achieved via suppression of the immune pathways of T-helper (Th)2, Th22, and Th1 cells and the associated decrease of inflammatory infiltrating cells such as CD1a+ DCs, CD11c+ DCs, and Fc epsilon receptor type 1 (FcεR1)+ cells in the lesional skin. In AD, complexes of IgE and FcεR1 on the surface of IgE+ MCs, IgE+ CD1a+ DCs, and IgE+CD11c+ DCs may capture large amounts of allergens resulting in induction of IgE-mediated immediate, late-phase, and even 'delayed-type' hypersensitivity [1]. Thus, we speculate that the efficacy of narrow-band UVB phototherapy for elderly patients with AD in our hospital is due to suppressions of both T-cell-activities and IgE-mediated allergic reactions in AD.

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