

of desmoglein, decreased local immuno-tolerance (reduced activity of T-suppressor lymphocytes) or release of antibodies via tumoral neo-antigens. ■

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Correlation between nocturnal scratch behavior assessed by actigraphy and subjective/objective parameters in patients with atopic dermatitis

Atopic dermatitis (AD) is a chronic relapsing inflammatory skin disorder caused by multiple factors. Pruritus, and consequent scratch behavior, is one of the major exacerbating factors of AD and is associated with the itch-scratch cycle [1]. Unconscious nocturnal scratch behavior induces sleep disturbance and symptomatic worsening, resulting in

a decreased quality of life [2]. Actigraphy is a non-invasive method of monitoring the human rest-activity cycle. Although several studies have used actigraphy to assess the relationship between pruritus and nocturnal scratch behavior [2-5], their endpoints have been limited. Therefore, in the present study, nocturnal scratch behavior was measured by actigraphy, and its correlation with subjective and objective parameters was investigated in patients with AD. After obtaining informed consent and approval by the institutional review board, 15 patients with AD (10 male, 5 female; mean age 34.3 ± 10.1 years) were enrolled in the study and received conventional interventions with or without antihistamine drugs, topical corticosteroids and moisturizer for 4 weeks. The following endpoints were investigated at the first and second visits: (1) clinical severity by the Severity Scoring of Atopic Dermatitis (SCORAD); (2) subjective symptoms by an average of first and latest 3 days of visual analogue scale (VAS), including sleep disturbance severity and itch severity during daytime and night-time; and (3) laboratory findings reflecting AD progression, including the number of eosinophils in peripheral blood, serum IgE, lactate dehydrogenase (LDH), and thymus and activation-regulated chemokine (TARC) levels. An actigraph ViM (MicroStone, Saku, Japan) was worn like a wristwatch on the non-dominant wrist during the first three and last three nights and collected on the second visit. The average percentage of nocturnal scratch behavior during sleep for each of the three days was calculated. The improvement rate of each parameter was compared with the rate of nocturnal scratch behavior as assessed by actigraphy and was statistically analysed with a Spearman rank-order correlation test. SCORAD, daytime itch, serum LDH, and TARC levels were found to correlate significantly with nocturnal scratch behavior (figure 1A), whereas night-time itch, sleep disturbance, number of eosinophils in peripheral blood and serum IgE levels showed no correlation (data not shown).

Next, we investigated if the level of nocturnal scratch behavior assessed by actigraphy indicates severity of pruritus and AD in the progression of AD treatment. Ten AD patients (6 male, 4 female; mean age 34.1 ± 3.6 years) who improved with the additional administration of 10 mg/day of the antihistamine drug olopatadine for 4 weeks, participated in the study. Each parameter was assessed before and after the intervention. Data was analyzed with the paired *t*-test. All subjective and objective parameters were in accordance with the decrease of nocturnal scratch behavior, including itch sensation, SCORAD, the number of eosinophils in peripheral blood, serum LDH and TARC levels except for serum IgE level, which does not reflect the rapid fluctuation of disease activity (figure 1B) [6].

Actigraphy has been used to assess sleep patterns and circadian rhythms in sleep disorders. It has been established that a wrist activity monitor can measure nocturnal scratch behavior in patients with AD [7]. Indeed, in our preliminary experiment, actigraphy was shown to correlate strongly with nocturnal scratch behavior when assessed using an infrared video camera (data not shown). In the first study, the improvement rate of nocturnal scratch behavior assessed by actigraphy correlated with daytime itch and SCORAD, although it did not correlate with ratings of night-time itch and sleep disturbance. This dissociation might be due to vague subjective endpoints such as night-time itch and sleep disturbance, which do not necessarily reflect disease severity.

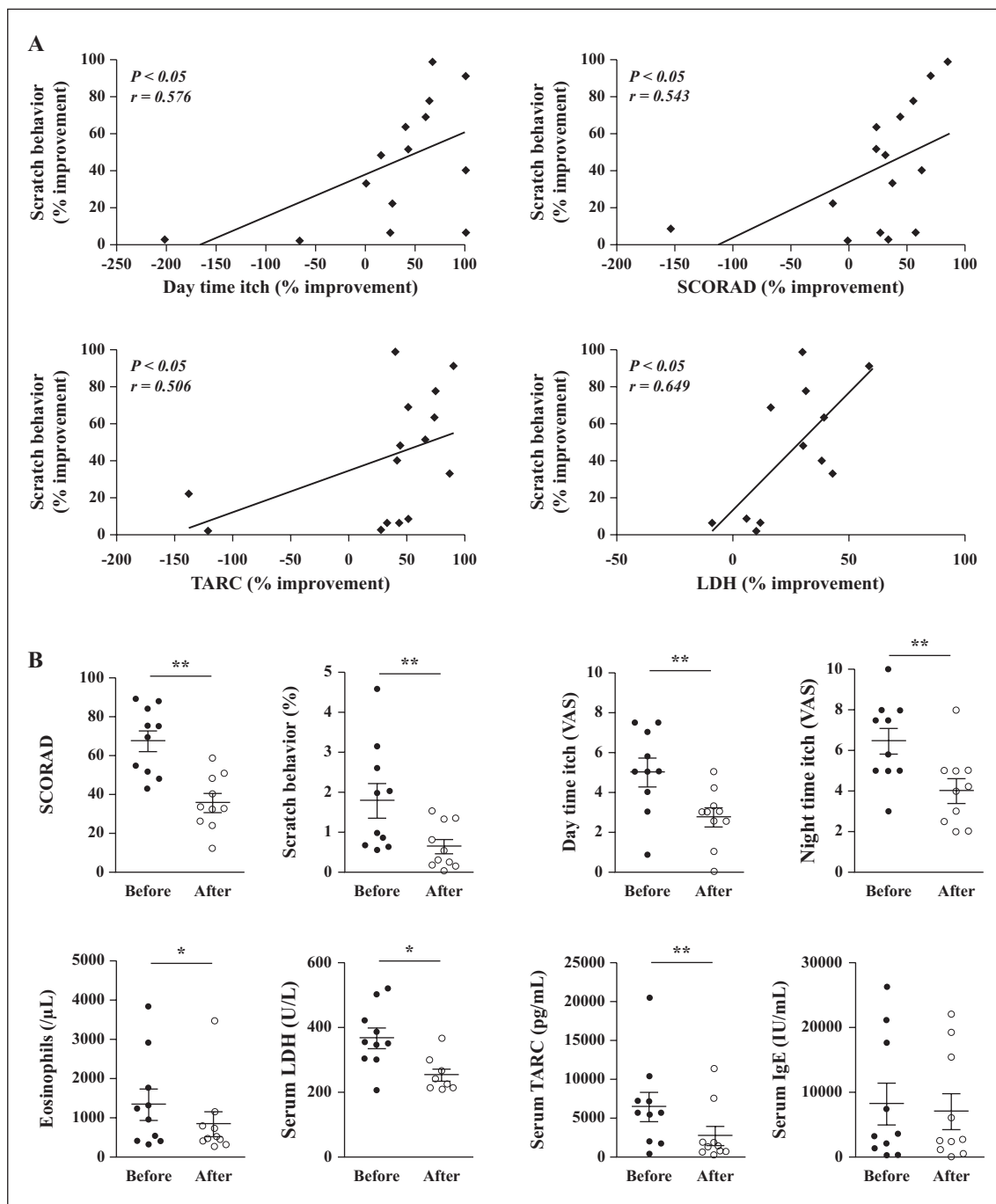


Figure 1. A) Correlation of improvement between nocturnal scratch behavior and each parameter. The horizontal axis shows the improvement rate of each parameter and the vertical axis shows that of nocturnal scratch behavior. The Spearman rank-order correlation test was used for the statistical analysis. **B)** The effect of antihistamine on AD associated parameters. Olopatadine was additionally administered for four weeks and each parameter was investigated before and after the medication. Data was analyzed with the paired *t*-test. Statistically significant at * $P < 0.05$ and ** $P < 0.01$.

ity, as reported previously [4]. In the second study, patients who received the additional intervention demonstrated a significant improvement of all subjective and objective AD parameters, except for serum IgE, accompanied with a decrease in nocturnal scratch behavior. Taken together, nocturnal scratch behavior assessed by actigraphy correlates with pruritus and AD severity in the progression of

AD treatment. The measurement of nocturnal scratch behavior using actigraphy seems to be useful for assessment of efficacy in the treatment of AD. ■

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Pachyonychia congenita in Japan: report of familial cases with a recurrent *KRT16* mutation

Pachyonychia congenita (PC) is a rare autosomal dominant keratinizing disorder showing nail changes. Besides hypertrophic nail dystrophy, the main clinical features include painful and highly debilitating plantar keratoderma, oral leukokeratosis and a variety of epidermal cysts. Classically, PC is classified into type 1 (PC-1) and type 2 (PC-2), depending on the distinct sets of clinical symptoms, primarily on the absence and presence of pilosebaceous cysts, respectively [1]. Since the causative genetic mutations were successively identified in four *Keratin (KRT)* genes in the mid 1990s, PC has been defined as the keratin disorder at the molecular level [2-4]. In correlation with the classical classification, mutations in the *KRT6A* or *KRT16* gene and those in the *KRT6B* or *KRT17* gene have been identified in PC-1 and PC-2, respectively.

A 32-year-old Japanese woman showing callus-like, painful, hyperkeratotic lesions on the soles was referred to our hospital in August 2011. She had repeatedly developed blistering on the soles after walking since 4 years of age, and the lesions gradually grew into the callus-like hyperkeratotic lesions. As her first son developed slightly hyperkeratotic lesions on the hands and feet after begin-



Figure 1. Clinical features of the proband (A-E) and her son (F), with the genetic feature (G). A) Symmetrical plantar keratoderma. B) Thick toenails with focal keratoderma. C) A pair of hand-made sandals adjusted for the focal keratoderma. D) Mild changes on the fingernails. E) Leukokeratosis of the tongue. F) Thick toenails. G) Electropherograms obtained by sequencing the *KRT16* gene for the genomic DNA samples from a control (left) and the proband (right).

ning walking, she consulted a dermatologist and then was referred to us. None of her relatives, except for her son, showed any similar symptoms. A physical examination revealed severe, callus-like, yellowish, symmetrical, hyperkeratotic lesions, mainly on the heels and the frontal areas of the soles, as well as the internal side of the first toes, the second and third digital pads and the tip of the fourth toes (figure 1A). Thickening and deformity of the first and the fourth toenails were also seen (figure 1B). To reduce the plantar pain, she used a pair of hand-made sandals whose soles were adjusted to reduce the pressure of the focal hyperkeratotic lesions (figure 1C). Although there were no hyperkeratotic lesions in the palms, hyperkera-