A Case of Nevoid Acanthosis Nigricans Successfully Treated with Topical Ketoconazole Plus Urea

Dear Editor,

Nevoid acanthosis nigricans (AN) is a rare form of benign AN that can be mostly found as a solitary lesion distributed along Blaschko's lines (1). It is not associated with any known syndrome, endocrinopathy, drugs, or internal malignancy. Treatments include retinoid, calcipotriol, and laser treatments (2). Herein we report a case of nevoid AN successfully treated with topical ketoconazole plus urea.

A 15-year-old woman presented with a 3-year history of asymptomatic plaques on her abdomen

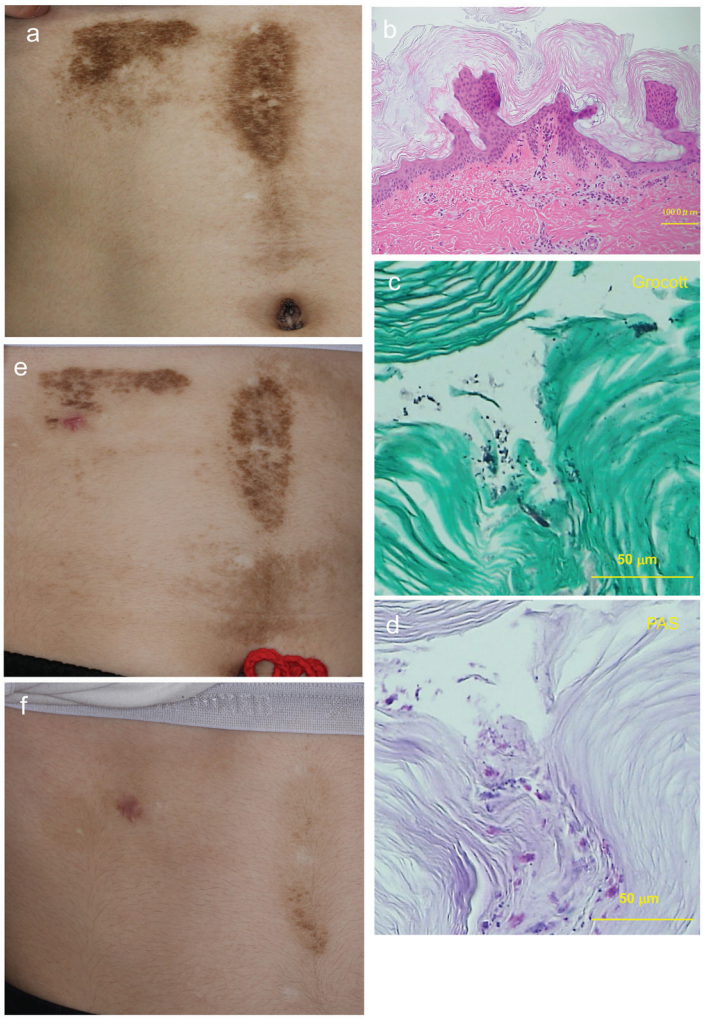

Figure 1. (a) Clinical manifestations in the patient at first visit. Dark-brownish pigmented plaques were observed on the midline and right side of the patient's abdomen. (b) Histological examination of skin biopsy showed hyperkeratosis and papillomatosis with minimal acanthosis and a mild perivascular lymphocytic infiltration in the superficial dermis. Hyphae and spores were confirmed by Grocott staining (c) and periodic acid-Schiff (PAS) staining (d). (e) One month after the application of ketoconazole cream. (f) Six months after the application of 20 % urea cream.

that were increasing in size. She had no medical history and no family history and was not obese. Physical examination revealed dark-brownish pigmented plaques on the midline and right side of her abdomen (Figure 1, a). Potassium hydroxide test was negative. Thyroid function test, antinuclear antibody test, and liver and renal function tests were within normal limits. Histological examination of skin biopsy showed hyperkeratosis and papillomatosis with minimal acanthosis and a mild perivascular lymphocytic infiltration in the superficial dermis (Figure 1, b). Some melanophages were observed in the superficial dermis. Based on the clinical features and these histological findings, a diagnosis of nevoid AN was established. Additionally, there were numerous hyphae and spores in the stratum corneum that were confirmed by Grocott staining (Figure 1, c) and periodic acid-Schiff staining (Figure 1, d). Fungal infection was suggested, and the result of a potassium hydroxide test was considered to be pseudo-negative. Topical ketoconazole cream was initially administrated for one month, and the rough surface was markedly improved (Figure 1, e). Subsequently, topical 20 % urea cream was used and the area of skin lesion decreased in size after 6 months (Figure 1, f). We discontinued ketoconazole cream after 2 months.

To the best of our knowledge, this is the first case of nevoid AN successfully treated with topical ketoconazole plus urea. Some cases of AN appear to have an associated endocrinopathy (1). However, genetic factors may also play a role in the pathogenesis of AN. It has been reported that mosaic mutation in fibroblast growth factor 3 (FGFR3) is associated with nevoid AN (3). All known mutations in FGFR3 are gain-of-function mutations, and the activity of the FGFR3 signal correlates with the severity of AN. Involvement of fungal infection has not been reported in the pathogenesis of nevoid AN. We did not identify the fungal species in our patient, but *Malassezia* infection was suggested. In general, potassium hydroxide test can reveal only yeast forms of *Malassezia*, and pseudo-negative results may often occur. The abundant hyphae and spores in the stratum corneum are a characteristic pathological feature of *Malassezia* infection, and the obvious effects of ketoconazole may support the *Malassezia* infection. Since *Malassezia* is known to promote cytokine production in human keratinocytes (4), an autocrine FGFR3 signal might accelerate the proliferation of keratinocytes such as myeloma cells (5). Urea is the most widely used moisturizer and keratolytic agent, and has been utilized for the treatment of various hyperkeratotic cutaneous diseases. We successfully treated nevoid AN with the combination of topical ketoconazole and urea. This combination therapy may have fewer side-effects than previous reported treatments and could be considered as an optional treatment.

Acknowledgment:

The patients in this manuscript have given written informed consent to publication of their case details.

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Ayaki Matsumoto, Kozo Nakai, Daisuke Tsuruta, Koji Sugawara

Department of Dermatology, Osaka City University Graduate School of Medicine, Osaka, Japan

Corresponding author:

Kozo Nakai, MD, PhD

Department of Dermatology, Osaka City University Graduate School of Medicine

1-4-3 Asahimachi, Abeno-ku, Osaka 545-8585, Japan

nakai.kozo@med.osaka-cu.ac.jp

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