

## LETTER TO THE EDITOR

# Case series of acanthosis nigricans treated with topical trifarotene cream

To the Editor,

Acanthosis nigricans (AN) is a pigmented dermatosis characterized by velvet-like, hyperpigmented, coarse plaques distributed in intertriginous areas. Due to aesthetic concerns, various methods including weight loss and topical agents are used for treatment.<sup>1</sup> Trifarotene is a fourth-generation retinoid used for the treatment of acne vulgaris, autosomal recessive congenital ichthyosis, and primary cutaneous T-cell lymphoma.<sup>2,3</sup> Retinoids have been used with success in the treatment of AN; however, no data are available for trifarotene. Here, we report three cases of AN and examine the efficacy and safety of topical trifarotene cream for AN.

An 18-year-old male was presented with brownish pigmentation on the neck. A coarse, hyperpigmented skin lesion in the extensor part of the neck was observed (Figure 1A). Dermoscopy demonstrated linear crista cutis and sulcus cutis with dispersed dark brown dots (Figure 1C). We diagnosed the patient as having AN and decided to apply topical 0.005% trifarotene cream 3 times a week. After 5 weeks, marked improvements were observed (Figure 1B,D).

In addition, a 14-year-old male and a 16-year-old male had dark patches on the skin with a thick, velvety texture either in the extensor part of the neck or both axillae, and they were both obese (Figure 1E,G). Dermoscopic findings of the patients were similar to that of an 18-year-old patient. There were no symptoms suggesting systemic disease or malignancy. Following a diagnosis of AN, they were both treated with the same regimen as above, and a significant improvement was observed (Figure 1F,H). All patients had no signs of skin irritation during the treatment.

All of the patients showed improved skin pigmentation until 3 months after treatment without any other treatment.

The prevalence of AN varies depending on comorbidities and other risk factors. Specifically, the incidence of AN increases with age, obesity, and darker skin.<sup>4</sup>

AN is diagnosed with histological examination characterized by hyperkeratosis, mild acanthosis, and papillomatosis of the epidermis.<sup>1</sup> However, AN can be diagnosed by specific clinical findings

with dermoscopic features, such as sulci cutis, and hyperpigmented dots.<sup>5</sup>

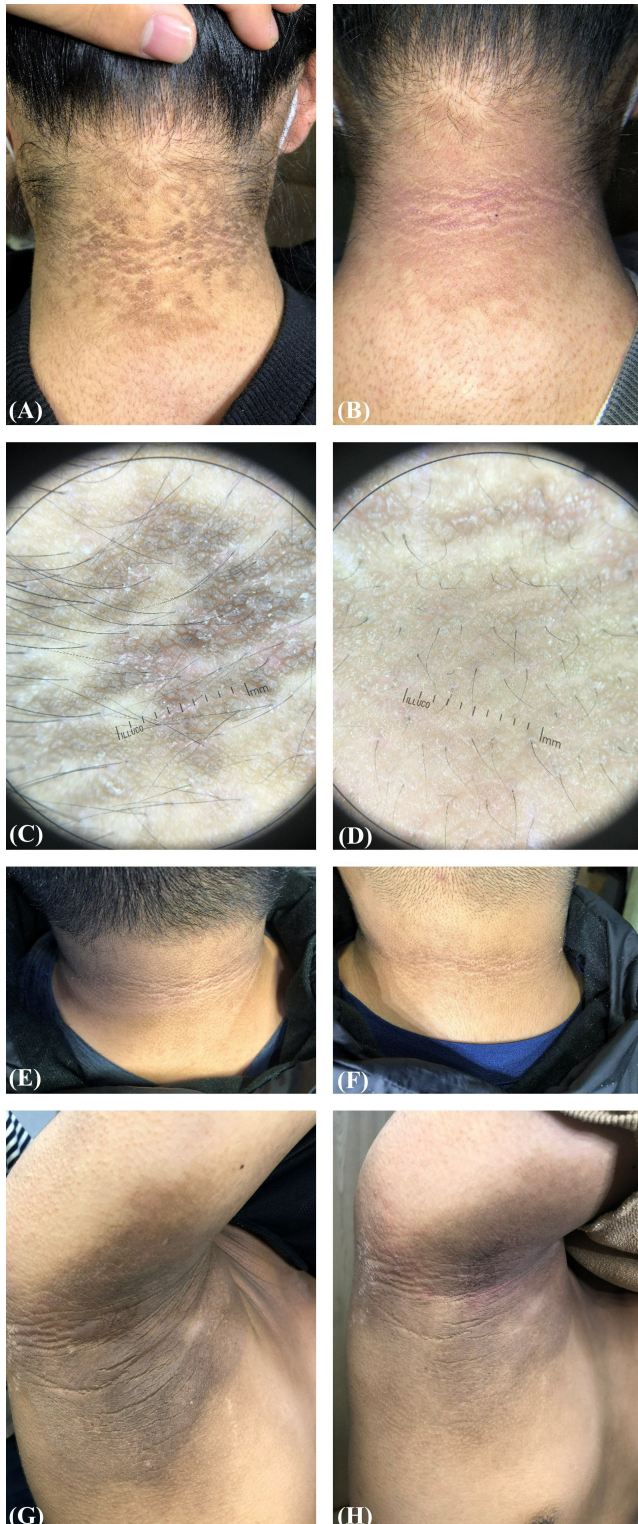
The pathophysiology of AN can be described as the proliferation of epidermal keratinocytes and dermal fibroblasts involving various mediators such as insulin, insulin-like growth factor (IGF), fibroblast growth factor receptors, and tyrosine kinase receptors including epidermal growth factor receptor. Insulin resistance might play a central role in AN as insulin at high concentrations could bind to the IGF-1 receptors of keratinocytes and fibroblasts.<sup>1,4</sup>

As most cases of AN are related to obesity, weight loss should be considered as the first-line treatment for AN.<sup>1</sup> Other conventional treatments for AN include topical and oral retinoids, topical vitamin D analogs, chemical peels, metformin, and rosiglitazone. Topical and oral retinoids reduce the stratum corneum replacement time, resulting in the correction of hyperkeratosis.<sup>2</sup> Topical vitamin D analogs suppress keratinocyte proliferation by increasing the intracellular calcium and cGMP levels of keratinocytes. Chemical peels necrotize the epidermis, resulting in re-epithelialization. Metformin and rosiglitazone reduce insulin levels by increasing insulin responsiveness.<sup>6</sup>

The fourth-generation retinoid trifarotene hydrates the skin by inducing peptidyl arginine deiminase 1 and aquaporin-3 channels. It also loosens the hemidesmosomes connection and intercellular adhesion. Trifarotene can improve skin texture by downregulating matrix metalloproteinases (MMPs).<sup>3</sup> Therefore, trifarotene may reduce fine wrinkling, roughness, and mottled hyperpigmentation in AN.

In our case series, weight loss was also recommended, but it was unsuccessful. Then trifarotene was applied and improved skin lesions. After treatment, the improvement was maintained, and no side effects were observed. However, histopathological improvement could not be confirmed because skin biopsy was not performed. Further long-term studies, clinical trials with more patients, and comparisons with other treatment regimens are needed.

In conclusion, topical trifarotene cream could be a novel, effective, and safe treatment option for AN.



**FIGURE 1** (A~D) Clinical and dermoscopic findings of an 18-year-old male with acanthosis nigricans. (A) Coarse, hyperpigmented skin lesion in the extensor part of the neck. (B) Improvement of skin lesion after applying topical trifarotene cream for 5 weeks. (C) Linear crista cutis and sulcus cutis with dispersed dark brown dots on dermoscopy. (D) Improvement of skin lesion on dermoscopy after treatment. (E, F) Clinical photographs of a 14-year-old male with acanthosis nigricans. (E) Thick, velvety skin lesion in the extensor part of the neck. (F) Significant improvement after treatment. (G, H) Clinical photographs of a 16-year-old male with acanthosis nigricans. (G) Darkish, coarse skin lesion in both axillae. (H) Marked improvement after treatment.

#### AUTHOR CONTRIBUTIONS

**WG Lee:** writing—original draft preparation; **YG Koh:** data collection; **SH Shin:** conceptualization and figure editing; **KY Park:** supervising, writing—review and editing; **HW Lee:** conceptualization, writing—review and editing.

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#### CONFLICT OF INTEREST STATEMENT

The authors have no conflict of interest to declare.

#### DATA AVAILABILITY STATEMENT

The data that supports the findings of this study are available in the supplementary material of this article

#### ETHICAL APPROVAL

None.

#### INFORMED CONSENT

The patients in this manuscript provided written informed consent for the publication of their case details and clinical pictures.

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