

Topical Therapy With Tretinoin and Ammonium Lactate for Acanthosis Nigricans Associated With Obesity

Steven H. Blobstein, MD, PhD

Acanthosis nigricans (AN) is a cutaneous marker of various underlying systemic conditions. To date, no satisfactory topical therapy for this cutaneous disorder has been described. The following is a report of the successful use of a combination of 12% ammonium lactate cream and 0.05% tretinoin cream to treat AN associated with obesity.

Acanthosis nigricans (AN) is classically considered a cutaneous marker of systemic disease.^{1,2} Several types of AN have been described (Table) that are associated with a variety of endocrinopathies, malignancies, syndromes, and drugs.¹ Therapy for the condition has generally been aimed at identifying and treating the underlying medical condition or eliminating the offending drug. I report on a topical regimen that has proved to be reproducible and helpful in improving AN associated with obesity.

Methods

Therapy consisted of applying 12% ammonium lactate (Lac-Hydrin[®] 12%) cream or lotion twice a day and tretinoin (Retin-A[®] Micro[®]) 0.05% cream once at night to the anterior neck. A small amount of tretinoin cream was applied nightly followed by the ammonium lactate cream. In the morning, only ammonium lactate was used.

Patients served as their own control in that they applied ammonium lactate alone to one side of the neck and tretinoin alone to the other side of the neck. In this small study, subjective evaluations, as well as baseline and follow-up photographs, were used to assess the outcome of the treatment.

Types of Acanthosis Nigricans

- Acral
- Benign
- Malignant
- Medication induced
- Mixed type
- Obesity associated
- Syndromic
- Unilateral

Case Report

One of the cases treated was an 18-year-old obese man who presented with a history of several months of discoloration of the neck (Figure, A). His weight had not changed recently. He had a history of borderline hypertension. There was no family history of hormonal problems or of a similar eruption. He had taken no medicine. Physical examination revealed velvety, hyperkeratotic, tannish-brown patches on the anterior neck, lateral neck, and axilla. Other significant findings were striae on the abdomen. Otherwise, the patient appeared healthy. He was evaluated by an endocrinologist and found to be normoglycemic but slightly hyperinsulinemic (insulin level, 33.5 U/mL [reference range, 0–30 U/mL]; fasting glucose, 78 mg/dL [reference range, 60–110 mg/dL]).

The patient was advised to lose weight. At the same time, the patient was given prescriptions for 12% ammonium lactate lotion twice a day and tretinoin 0.05% cream once at night. Within 6 weeks, improvement was noted, and by 4 months, a decrease in hyperkeratosis and hyperpigmentation was apparent (Figure, B). No tachyphylaxis was observed for 12 months after initiation of treatment.

Accepted for publication September 9, 2002.

From New York-Presbyterian University Hospital of Columbia and Cornell Department of Dermatology, New York Weill-Cornell Center, New York, and the Department of Medicine, Division of Dermatology, Coney Island Hospital, Brooklyn, New York.
Reprints: Steven H. Blobstein, MD, PhD, 1463 E 17th St, Brooklyn, NY 11230.



Neck of the patient before (A) and after 4 months of treatment with tretinoin and ammonium lactate (B).

Comment

In total, 5 patients were successfully treated with the regimen described. The combination therapy on the front of the neck was compared with the single-agent controls on the sides of the neck. Using either tretinoin or 12% ammonium lactate alone did not help the AN. Therefore, there seems to be a synergistic interaction between the ammonium lactate and the tretinoin. Generally, there was about an 85% to 95% improvement of the condition.

Regarding the mechanism of action of these 2 agents, the ammonium lactate used was a preparation of 12% lactic acid neutralized to a pH of 5.0.³ Lactic acid is an α -hydroxy acid that works effectively as a peeling agent.⁴ It has been used to treat a variety of ichthyotic disorders, as well as photodamaged skin.⁵ The mode of action of topical organic acids is thought to be via the release of desmogleins, indicating the disintegration of desmosomes. Retinoids such as tretinoin have a wide range of biological effects. Working via a nuclear receptor, retinoids affect cell growth, differentiation, and morphogenesis and alter cell cohesiveness.⁶ Because of these properties, retinoids as a class are used to treat a variety of different cutaneous disorders. They have been shown to be effective in the treatment of such diverse diseases as acne, ichthyosis, Darier disease, psoriasis, and pityriasis rubra pilaris.⁷

Obesity is one of a group of disorders associated with AN in which tissue resistance to the action of insulin is the common uniting factor.⁸ It appears that decreased insulin action, rather than insulin levels, is the best correlate with AN.⁹ Being that the underlying defect leading to the development of AN in this group of disorders remains to be elucidated, one cannot delineate the mechanism of action of these 2 agents in the treatment of this condition.

Further trials are needed to determine whether AN associated with other medical conditions and AN at body sites other than the neck will also benefit from this combination treatment. Furthermore, whether the use of other topical retinoids, such as adapalene or tazarotene, or oral retinoids will be as helpful or even more efficacious would prove of interest.

REFERENCES

1. Schwartz RA. Acanthosis nigricans. *J Am Acad Dermatol.* 1994;31:1-19.
2. Houpt KR, Cruz PD. Acanthosis nigricans. In: Freedberg IM, Eisen AZ, Wolf K, et al, eds. *Fitzpatrick's Dermatology in General Medicine.* 5th ed. New York, NY: McGraw-Hill; 1999:2121-2126.
3. Wehr R, Krochmal L, Bagatell F, Ragsdale W. A controlled two-center study of lactate 12 percent lotion and a petrolatum-based creme in patients with xerosis. *Cutis.* 1986;37:205-207, 209.
4. Van Scott EJ, Yu RJ. Control of keratinization with alpha-hydroxy acids and related compounds, I: topical treatment of ichthyotic disorders. *Arch Dermatol.* 1974;110:586-590.
5. Baden HP. Treatment of actinically damaged skin with a keratolytic gel. *Cutis.* 1978;21:563-564.
6. Mangelsdorf DJ, Umesono K, Evans RM. The retinoid receptors. In: Sporn MB, Roberts AB, Goodman DS, eds. *The Retinoids: Biology, Chemistry and Medicine.* 2nd ed. New York, NY: Raven; 1994:319-349.
7. Peck GL, DiGiovanna JJ. The retinoids. In: Freedberg IM, Eisen AZ, Wolf K, et al, eds. *Fitzpatrick's Dermatology in General Medicine.* 5th ed. New York, NY: McGraw-Hill; 1999:2810-2820.
8. Fleir JS. Metabolic importance of acanthosis nigricans. *Arch Dermatol.* 1985;121:193-194.
9. Dunaif A, Green G, Phelps RG, et al. Acanthosis nigricans, insulin action and hyperandrogenism: clinical, histological and biochemical findings. *J Clin Endocrinol Metab.* 1991;73:590-595.