

ACANTHOSIS NIGRICANS MANAGEMENT WITH NUTRITION SUPPLEMENTS

Acanthosis nigricans is a velvety, darkening of the skin that usually occurs in intertriginous areas. This hyperpigmentation has poorly defined borders, usually occurs in skin fold areas, such as the back of the neck, axilla, and groin, and may include thickening of the skin. ⁽¹⁾

Acanthosis nigricans is most commonly associated with diabetes and insulin resistance, but rarely it can be a sign of internal malignancy. It can also occur with hormone disorders, and with the use of certain medications like systemic glucocorticoids and oral contraceptives. ⁽²⁾

ETIOLOGY:

There are multiple factors involved in the development of acanthosis nigricans.

- Increased circulating insulin that activates keratinocyte insulin-like growth factor (ILGF) receptors, particularly IGF-1. At high concentrations, insulin may displace IGF-1 from IGF binding protein. Increased circulating IGF may lead to keratinocyte and dermal fibroblast proliferation.
- Hereditary variants are associated with fibroblast growth factor defects.
- Increased transforming growth factor (TGF) appears to be the mechanism for malignancy-associated acanthosis nigricans. TGF acts on epidermal tissue via the epidermal growth factor receptor. ⁽³⁾

TYPES OF ACANTHOSIS NIGRICANS:

- **Familial Acanthosis nigricans:** may arise as a result of an autosomal dominant trait, presenting at birth or during childhood. It occurs due to mutations in fibroblast growth factor receptor 3 (FGFR3). ⁽⁴⁾
- **Obesity-associated Acanthosis nigricans:** Obesity is one of the most common conditions associated with Acanthosis nigricans. Lesions are usually common in adulthood but can occur at any age. It was once labeled as “pseudoacanthosis nigricans”. It may be associated with insulin resistance. Treating obesity with diet, weight reduction or medications can result in revolvment of Acanthosis nigricans. ⁽⁵⁾
- **Medications associated Acanthosis nigricans:** Multiple medications have been linked to Acanthosis nigricans. These include the use of nicotinic acid, systemic glucocorticoids, diethylstilbestrol, combined oral contraceptive pill, growth hormone therapy, estrogen, protease inhibitors, niacin, injected insulin. Once the offending medication is stopped, acanthosis nigricans usually resolves. ⁽⁶⁾
- **Acanthosis nigricans associated with endocrine dysfunction:** It is more insidious in onset, less widespread, and patients are often obese. Insulin-resistance syndromes may be divided into type A (HAIR-AN) and type B syndromes. Type A syndromes present with hyperandrogenemia, insulin resistance, and Acanthosis nigricans. Type B syndrome usually occurs in females who have uncontrolled diabetes, ovarian hyperandrogenism or autoimmune disease like SLE, Sjogren's syndrome, scleroderma. Polycystic ovarian syndrome (PCOS) is associated with Acanthosis nigricans. Insulin resistance and hyperandrogenism are seen in patients with PCOS. ⁽⁷⁾
- **Acral acanthotic anomaly:** Refers to a variant of acanthosis nigricans limited to the elbows, knees, knuckles, and dorsal surfaces of the feet. It is common in individuals who have dark skin. ⁽⁸⁾

- **Malignant Acanthosis nigricans syndrome:** Is associated with gastrointestinal adenocarcinomas and genitourinary cancers such as prostate, breast, and ovary. Lung cancer and lymphoma rarely are associated with acanthosis nigricans. Malignant acanthosis nigricans may precede, accompany, or follow the onset of internal cancer. Malignancy-associated acanthosis nigricans usually has a rapid onset and is accompanied by skin tags, multiple seborrheic keratoses (sign of Leser-Trelat), or tripe palms. ⁽⁹⁾
- **Auto-immune Acanthosis nigricans:** Is associated with autoimmune disorders like SLE, Sjogren's syndrome, scleroderma or Hashimoto's thyroiditis. ⁽¹⁰⁾
- **Unilateral Acanthosis nigricans:** Also called as nevoid Acanthosis nigricans. It is very rare and is inherited in an autosomal dominant fashion. Lesions occur unilaterally. Lesions present at infancy, childhood or adulthood. ⁽¹¹⁾

DIFFERENTIAL DIAGNOSIS:

- Seborrhea
- Tinea
- Erythrasma
- Candidiasis
- Pellagra
- Ichthyosis
- Linear epidermal nevus
- Granular parakeratosis
- Cutaneous hyperpigmentation related to Addison's disease

TREATMENT:

Acanthosis nigricans is not treatable. It may fade over time by treating the cause, insulin resistance. Controlling blood glucose levels through exercise and diet often improves symptoms. Topical fade creams can lighten skin in less severe cases. Acanthosis nigricans malignant may resolve if the causative tumor is removed successfully.

The goal of treatment is to treat the underlying disease. In the majority of patients, the treatment is done only for aesthetic reasons. In some patients, weight loss and correction of insulin resistance lowers the burden of hyperkeratotic lesions. Acanthosis nigricans associated with insulin resistance can be treated with drugs such as metformin and rosiglitazone which are insulin-sensitizing agents.

All inciting agents and medications should be discontinued. One should make attempts to lower the lipid profile. Reports suggest that dietary fish and niacin may help.

Dermatologists sometimes prescribe keratolytics, such as topical retinoids (e.g. topical tretinoin 0.1% or combination of tretinoin 0.05% and 12% ammonium lactate) and podophyllin. Topical vitamin D analogs (e.g. calcipotriol (calcipotriene) 0.005%) act by decreasing keratinocyte proliferation and cause improvement of the Acanthosis nigricans lesions.

Supplementing zinc and vitamin D can also help in treating acanthosis nigricans

The success of these treatments is variable. Other agents that have been tried include metformin and etretinate. In one report octreotide also showed marked improvement in a patient with insulin resistance.

Melatonin can also improve cutaneous symptoms in obese patients with Acanthosis nigricans by improving the inflammatory status and insulin sensitivity.

Cosmetic treatments that have been tried include using alexandrite laser, dermabrasion, and chemical peels. Surgical removal is the main treatment for malignant lesions. ⁽¹²⁾

Food and Losing Weight

Losing weight will be an important part of your care plan. Here are a few tips you can use:

- Try to eat regular meals and eat when you are hungry.
- Try to eat a low fat diet: Trim the fat and skin from meats and chicken.
- Use low fat (1%) or skim milk instead of whole milk.
- Try to avoid eating fried foods like French fries, chips and chicken. Instead try to eat them baked.
- Try to eat a lot of fiber from whole grain foods like wheat bread instead of white bread.
- Eat a lot of fruits and vegetables. Besides having lots of vitamins and minerals, they are full of fiber, too.
- Drink water, water, and more water!

Patients with the benign form of acanthosis nigricans have few or no skin complications, good prognosis, and potential of resolution with treatment. Complications can stem from the underlying disease like diabetes and insulin resistance. Prognosis in patients with the malignant form of acanthosis nigricans is poor as the malignancy is advanced usually at the time of diagnosis in these patients.

REFERENCES:

1. Smid CJ, Modaff P, Alade A, Legare JM, Pauli RM. Acanthosis nigricans in achondroplasia. Am J Med Genet A. 2018 Dec;176(12):2630-2636.
2. Ozlu E, Uzuncakmak TK, Takır M, Akdeniz N, Karadag AS. Comparison of cutaneous manifestations in diabetic and nondiabetic

- obese patients: A prospective, controlled study. *North Clin Istanbul*. 2018;5(2):114-119.
3. Hermanns-Lê T, Scheen A, Piérard GE. Acanthosis nigricans associated with insulin resistance: pathophysiology and management. *Am J Clin Dermatol*. 2004;5(3):199-203.
 4. Fukuchi K, Tatsuno K, Matsushita K, Kubo A, Ito T, Tokura Y. Familial acanthosis nigricans with p.K650T FGFR3 mutation. *J Dermatol*. 2018 Feb;45(2):207-210.
 5. Ng HY. Acanthosis nigricans in obese adolescents: prevalence, impact, and management challenges. *Adolesc Health Med Ther*. 2017;8:1-10.
 6. Stals H, Vercammen C, Peeters C, Morren MA. Acanthosis nigricans caused by nicotinic acid: case report and review of the literature. *Dermatology*. 1994;189(2):203-6.
 7. Schmidt TH, Khanijow K, Cedars MI, Huddleston H, Pasch L, Wang ET, Lee J, Zane LT, Shinkai K. Cutaneous Findings and Systemic Associations in Women With Polycystic Ovary Syndrome. *JAMA Dermatol*. 2016 Apr;152(4):391-8.
 8. Anand V, Das A, Kumar P, Kumar R, Hassan S. Acral acanthosis nigricans (acral acanthotic anomaly). *Indian Dermatol Online J*. 2014 Dec;5(Suppl 2):S140-1.
 9. Liu XK, Li J. Hyperpigmentation in the skin folds. *BMJ*. 2018 Jan 18;360:j5729.
 10. Kondo Y, Umegaki N, Terao M, Murota H, Kimura T, Katayama I. A case of generalized acanthosis nigricans with positive lupus erythematosus-related autoantibodies and antimicrosomal antibody: autoimmune acanthosis nigricans? *Case Rep Dermatol*. 2012 Jan;4(1):85-91.
 11. Das A, Bhattacharya S, Kumar P, Gayen T, Roy K, Das NK, Gharami RC. Unilateral nevoid acanthosis nigricans: Uncommon variant of a common disease. *Indian Dermatol Online J*. 2014 Nov;5(Suppl 1):S40-3.
 12. Ghosh S, Roychowdhury B, Mukhopadhyay S, Chowdhury S. Clearance of acanthosis nigricans associated with insulinoma following surgical resection. *QJM*. 2008 Nov;101(11):899-900.