

ACANTHOSIS NIGRICANS- A CASE REPORT ON APPROACH TO EVALUATION AND MANAGEMENT

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ABSTRACT

Acanthosis nigricans is a skin disorder which characterized by dark, thick and velvety plaque of the skin which usually occurs in body folds but that may spread to other parts of the body. It could also be found on the elbow and knee and neck fold region. It is most likely caused by factors that stimulate epidermal keratinocyte and dermal fibroblast proliferation. The stimulating factor is probably insulin or an insulin like growth factor that copies the epidermal cell propagation. Hyperinsulinemia which activates the receptor result in hyperplasia of the skin. Treatment options for acanthosis nigricans is topical retinoids. However intermittent tretinoin was needed to maintain improvement as relapse was noted within a period of 4 weeks after discontinuation of treatment. The typical changes of hyperkeratosis and keratotic material between papillae were resolved on biopsy after 8 weeks of tretinoin application. Oral retinoids (isotretinoin), acitretin-0.8mg/kg(50mg) divided into two daily doses. After starting maintenance therapy of 25mg acitretin daily for 2 months lesions recovered that subsequently resolved with topical application of 0.1% retinoic acid can also be effective treatment options for acanthosis nigricans.^[1,2]

KEYWORDS: Acanthosis nigricans, dermatologic condition, pseudoacanthosis, tretinoin, topical therapy, insulin resistance.

INTRODUCTION

Acanthosis nigricans or otherwise known as monogenic obesity syndrome is a dermatological condition characterized by hyperpigmentation and thickening of the skin, which appears mainly in areas of the body with folds and wrinkles such as the elbows, armpits and neck region occurs pigmented skin. This pigmentation may vary in color from light brown to black and on rare cases may be accompanied by itching or have an unpleasant odor.

Under normal conditions, insulin facilitates the entry of glucose into the cells to be used as energy. In insulin resistance, this mechanism is compromised: the body's cells become less sensitive to the effects of insulin, leading the pancreas to produce and release increasing amount of this hormone to maintain metabolic balance.

One of most common cause is insulin resistance- a pre-diabetic condition that leads the body to produce more insulin than normal to compensate for the cells. Elevated insulin levels in the blood can stimulate the proliferation of keratinocytes and fibroblasts in the skin, overgrowth of which leads to the hyperpigmentation and thickening

of skin. Although insulin resistance is one of the most common causes, there are such conditions that trigger acanthosisnigricans.^[3]

EPIDEMIOLOGY

Acanthosis nigricans is much more common in people with darker skin pigmentation. The prevalence in whites is less than 1%. In Latinos, the prevalence in one study was 5.5% and in Africans Americans, the prevalence is higher at 13.3%. It varies from 7% to 74% in obese individuals.^[4]

PATHOPHYSIOLOGY

Acanthosis nigricans most likely is caused by factors that stimulate epidermal keratinocyte and dermal fibroblast proliferation. In the benign form of acanthosisnigricans, the factor is probably insulin or an insulinlike growth factor (IGF) that incites the epidermal cell propagation. Other proposed mediators include other tyrosine kinase receptors (epidermal growth factor receptor [EGFR] or fibroblast growth factor receptor [FGFR]).

At high concentrations, insulin may exert potent proliferative effects via high-affinity binding to IGF-1

receptors. In addition, free IGF-1 levels may be elevated in obese patients with hyperinsulinemia, leading to accelerated cell growth and differentiation.^[10] Familial and syndromic forms of acanthosis nigricans have been identified. Many syndromes share common features, including obesity, hyperinsulinemia, and craniosynostosis. These have been subdivided into insulin-resistance syndromes and fibroblast growth factor defects.

In malignant acanthosisnigricans, the stimulating factor is hypothesized to be a substance secreted either by the tumor or in response to the tumor. Transforming growth factor (TGF)-alpha is structurally similar to epidermal growth factor and is a likely candidate. TGF-alpha and epidermal growth factor have both been found in gastric adenocarcinoma cells, and EGFR expression has been identified in skin cells within acanthosisnigricans lesions. Reports of urine and serum TGF-alpha levels normalizing after surgical tumor removal exist, with subsequent regression of skin lesions.^[5,6]

TREATMENT

Oral retinoids (isotretinoin) can be the effective treatment options for acanthosis nigricans. Topical retinoids are considered as one of the first line treatment options for AN. Acitretin-0.8mg/kg (50mg) divided into two daily doses. After starting maintenance therapy 25mg acitretin daily 2 months lesions recovered that subsequently resolved with topical application of 0.1% retinoic acid.^[7,8,9]

CASE REPORT

A 12 year old male patient was admitted on pediatric department with complaints of cough for one week and shortness of breath for one week diagnosed as reactive airway disease with acute exacerbation. On his past history he had gained weight during covid time and his age was 8 year old. During that time the region in back side of the neck and elbows appears in blackish pigmentation and it has been diagnosed as monogenic obesity syndrome/ Acanthosis nigricans consulted in nearby pediatric care center and no further treatment was undertaken till now. His social history was intake of bakery items. His family history- mother having asthma on inhaler for one year on levolin 2 puff BD. Other relevant history- on Foracort and levolin MDI was used from 6 year old of his age whenever necessary at that time he had a breathing problem for 2-3 days and this both inhalers was used for one month back. Currently his BMI was 25kg/m². During the time of hospital stay he had consulted a pulmonologist and recommended him to continue Foracort MDI 400mcg BD for 2 weeks and also he consulted a dermatologist and recommended him to apply derma dew ointment for 1 week.

In this patient, during the time of admission period his vitals was checked according to follows as: Body temperature: 98.1°F (98.6°F), pulse: 94bpm (72bpm),respiratory rate: 24/min (28/min), blood pressure: 120/76 (92)mmHg (110/80mmhg), spo2: 98% (95-100%). According to laboratory investigation report due to initial period (Table 1).

Table 1: Laboratory investigations.

PARAMETERS	TEST VALUE WITH DATES	
	1/2/24	4/2/24
Hemoglobin	12.4	13.2
PCV	39.4	42.9
WBC	17230	11420
Polymorph	52.2	55.9
Lymphocytes	42	40
Eosinophils	0.2	0.4
Monocytes	5.2	3.4
ESR	20	30
PC	4.74	4.85
RBS	-	80
HBA1C	-	5.6
Urea	22	-
Creatinine	0.5	-
ALT	26	-
AST	21	-
Sodium	143	-
Potassium	4.2	-
Calcium	-	9.6
Phosphorous	-	5.7
Total. Cholesterol	-	162
TRG	-	274
LDL	-	65
HDL	-	42
VLDL	-	55

syndrome in pediatric patients.^[11,12] The thickening of the skin may be mild to moderate, but it is usually sufficient to give the affected areas a rough appearance and their distribution pattern is usually symmetrical, affecting both sides of the body equally.^[13]

Here is a case report of 12-year old male patient admitted on pediatric department with complaints of cough and breathlessness for 1 week and he consulted a dermatologist and recommended him to apply derma dew ointment for 1 week.

CONCLUSION

Acanthosis nigricans is a skin disorder which is characterized by dark, thick and velvety plaque of the skin which usually occurs in body folds but that may spread to other parts of the body. The stimulating factor is probably insulin or an insulin like growth factor that copies the epidermal cell propagation. There is a specific therapy according to this condition like topical and oral treatments are recommended in children. Shows dark pigmentation in skin can be controlled for further management. Here the patient was admitted with complaints of cough and breathlessness for 1 week. This patient was managed with macrolide antibiotics, corticosteroids, proton pump inhibitors, long and short acting beta-2 agonists.^[14]

For further management includes topical treatments like, Topical retinoids are considered as one of the first line treatment option for acanthosis nigricans. However intermittent tretinoin was needed to maintain improvement as relapse was noted within a period of 4 weeks after discontinuation of treatment. The typical changes of hyperkeratosis and keratotic material between papillae were resolved on biopsy after 8 weeks of tretinoin application.

Topical vitamin D analogs another topical treatment option for acanthosis nigricans is calcipotriene. It inhibits the keratinocyte proliferation and promotes differentiation by increasing keratinocyte intracellular calcium and cyclic GMP levels. It reduces the number of keratinocytes, it may minimize the cutaneous effects of insulin.

Oral treatments like,

Oral retinoids (isotretinoin) can also be effective treatment options for Acanthosis nigricans. Mechanism of action for this drug is to normalize epithelial growth and differentiation. Extensive Acanthosis nigricans associated with obesity. Few reports of Acanthosis nigricans treatment says that for generalized idiopathic Acanthosis nigricans experienced complete recovery after 45 days of acitretin -0.8mg/kg (50mg) divided into two daily doses. After starting maintenance therapy of 25mg acitretin daily for 2 months lesions recovered that subsequently resolved with topical application of 0.1% retinoic acid. Because of acitretin's longer terminal

elimination and fewer lipophilic properties, its use may be limited causing potential for early recurrence.

Other oral agents like combination of metformin with thiazolidiones that increase insulin sensitivity in peripheral muscles reported to have good results in patients with Acanthosis nigricans. The spontaneous regression of this condition has been reported after the addition of TZD pioglitazone and sitagliptin, a dipeptidyl peptidase 4 inhibitor which increases insulin secretion in an insulin resistant patient.

Other therapies which shows the improvement in Acanthosis nigricans according to reports includes fish oil that contains omega 3 fatty acids improved hyperpigmentation and skin texture. The use of alexandrite laser has been demonstrated one of cosmetic treatment option to be effective in improving Acanthosis nigricans lesions. This laser was to target melanin in hair and to improve the darkening of the skin in affected areas.^[15]

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