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Case Report

Generalised idiopathic benign acanthosis nigricans with onset during infancy: report of two patients

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ABSTRACT

Generalised acanthosis nigricans (AN) is usually seen in association with insulin resistance or internal malignancy in adults. Very rarely, this may occur in children without any evidence of systemic disease and runs a benign course. Its management requires only watchful waiting. Here, we report two children with benign AN who had onset of AN during infancy and showed spontaneous improvement during follow up for a mean duration of 7.7±0.14 years.

Keywords: Genaralised idiopathic benign acanthosis nigricans, Non-familial, Insulin resistance, Children

INTRODUCTION

Acanthosis nigricans (AN) is a skin condition characterized by areas of thickened, dark, velvety discoloration in body folds and creases.[1] Unlike adults where AN may signify several internal diseases including malignancies, its occurrence in children is usually associated with obesity and indicates the presence of insulin resistance.[2]

A rare form of AN occurs in children which shows a generalized distribution of skin lesions without any evidence of obesity or endocrinopathy.[2] The clinical course of this form of AN is benign but requires a close supervision for occurrence of any systemic manifestations. However, the reports on long-term follow up are scarce. In this report, we describe two children who developed generalized benign AN during infancy and started showing spontaneous improvement of skin lesions over a period of several years.

CASE REPORT

Patient 1

A 2 year old boy presented to the pediatric endocrinology clinic of our hospital with darkening of skin since 10 months of age. His mother had first noticed the darkening and roughening of skin around nape of the neck that gradually progressed to involve both underarms and flexural areas of upper and lower limbs. This was not associated with redness or pruritis. There were no other systemic complaints and family history did not suggest the occurrence of a similar disease in last three generations. He was born to non-consanguineous parents and his growth and development was normal. There was no history of any drug intake.

On physical examination, he was in good general health. His weight, height and body mass index were 11.2 kg (-1.16 z-score, WHO growth charts, 2007), 85 cm (-0.65 z-score) and 15.5 (-0.89 z-score) respectively. Blood

pressure was 90/60 mmHg (50th percentile for age and height). Skin examination showed thickened, dark and rough areas over nape of neck, chest, abdomen, cubital fossae, dorsum of hands, back, groin folds, and popliteal fossae (Figure 1). Roughening also involved lips, palms and external genitalia (Figure 1). However, mucosal areas, hair and nails were not involved. Rest of the systemic examination was unremarkable.

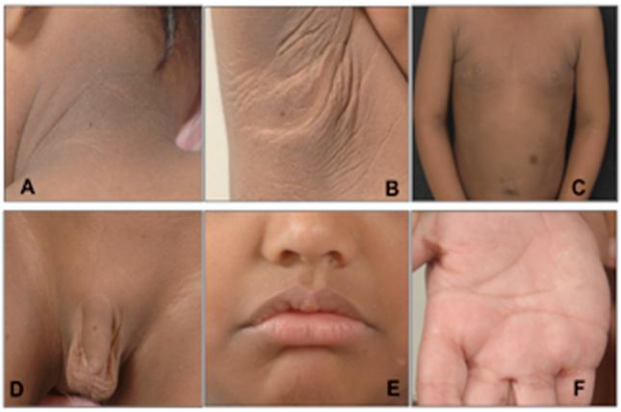

Figure 1: Clinical photographs of the 1st patient at 2 years age showing thickened, dark, velvety discoloration of skin over (A) neck, (B) right axilla, (C) chest and abdomen, (D) inguinal folds and external genitalia, (E) roughened lips and (F) roughened palm.

Patient 2

A 5 year old boy presented with progressive darkening and thickening of the skin first noticed at three months of age. Darkening of skin was first noted over the forehead, gradually progressed to involve nape of neck, both underarms and flexural areas of upper and lower limbs. He was born to non-consanguineous parents, with a normal pregnancy and delivery. He had no other medical issues. His parents and sibling had no skin or any other medical condition. His physical and mental development was normal. General physical examination was unremarkable. His weight was 19.2 kg (-0.38 z-score), height 114 cm (-0.02 z-score) and body-mass-index 14.8, (-0.5 z-score). His vital parameters including blood pressure (96/60 mmHg, 50th percentile for age and height) were normal. His skin was hyperpigmented, thickened and velvety over forehead, chin, nape of neck, axillae, cubital fossae, wrists, groin, buttocks, popliteal fossae and ankles (clinical photographs of the child at the time of initial presentation were not taken). The mucosal surfaces, lips, teeth, nails, hair and scalp were free of any lesions. System examination was within normal limits.

Both patients were extensively investigated for an underlying systemic disorder. Laboratory tests including a complete hemogram, liver function tests, serum electrolytes, blood urea, creatinine, serum calcium, phosphate, alkaline phosphatase, urinalysis, serum electrophoresis, serum immunoglobulins, thyroid function test, C-reactive protein, serum cortisol, growth hormone, insulin-like growth factor-1, fasting blood glucose, fasting lipid profile, glycosylated hemoglobin level, plasma insulin and C-peptide levels were within normal limits. Radiographs of chest were normal. Ultrasonography of the abdomen revealed no abnormality.

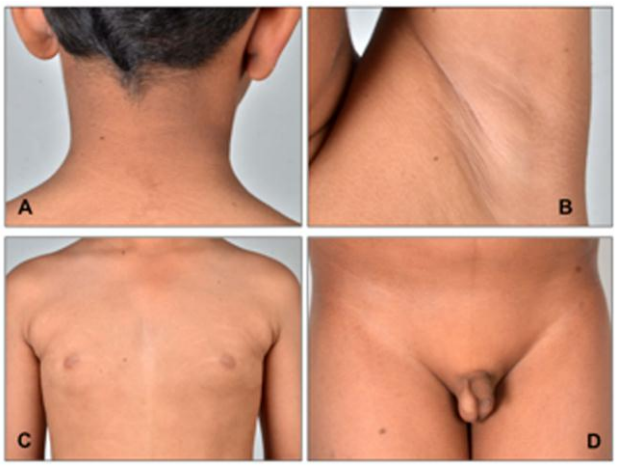

Figure 2: Clinical photographs of the 1st patient at 9 years of age showing fading of the skin lesions over (A) neck, (B) axilla, (C) chest (D) inguinal folds and external genitalia.

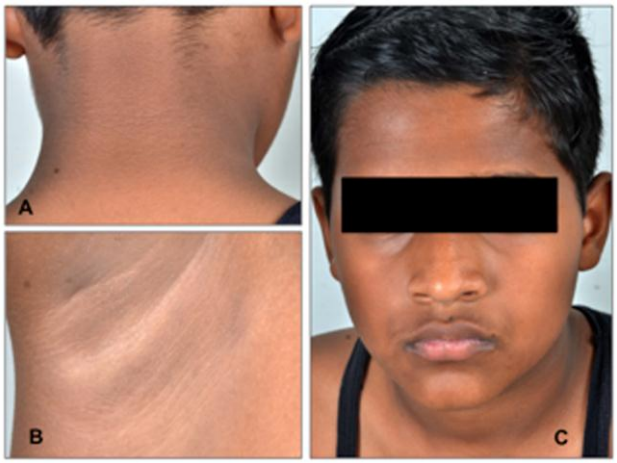

Figure 3: Clinical photographs of the 2nd patient at 12 years age showing minimal acanthosis over (A) neck, (B) axilla, (C) forehead and facial skin folds.

A final diagnosis of benign AN was made after thorough evaluation. No treatment was offered to the patients. Both patients were followed up at six monthly intervals with watchful expectancy for spontaneous resolution of skin lesions. At about four years of age in the first patient, parents started noticing fading of the lesions which first began in the less involved areas followed by improvement in lesions in the axillae and neck (Figure 2). Fading of lesions was also noted in the other patient

(Figure 3). Both patients have been followed for a mean duration of 7.7±0.14 years.

DISCUSSION

Acanthosis nigricans (AN) is symmetric velvety thickening and roughening of epidermis that involves the flexor areas of body.[1] In adults, AN may indicate the presence of internal diseases such as malignancies and scleroderma.[1] In children, several distinct forms of AN are described such as obesity associated, syndromic, malignant, acral, unilateral, drug-induced, mixed or benign.[2] The most common type is obesity related and often serves as a cutaneous marker of insulin resistance.[1] This is a harbinger of the future risk of cardiometabolic morbidity in children with simple obesity similar to several other risk factors.[3] A generalized form of AN occurs in children and runs a benign course.[4] There are only a few cases of this benign variety of AN reported in literature.[4-7] The salient clinical features of the previous reported patients are summarized in Table 1.

Table 1: Previously reported cases of benign acanthosis nigricans.

S. No.	Authors	Extent of involvement	No. of cases	Year of reporting
1.	Akovbyan et al[11]	Generalised	1	1994
2.	Skiljevic et al[12]	Entire integument	1	2001
3.	Uyttendaele et al[13]	Generalised	1	2003
4.	Inamadar et al[7]	Neck, axillae, groin, trunk, dorsum of hands, face	3	2004
5.	Ozdemir et al[14]	Generalised	1	2006
6.	Rai et al[15]	Generalised	1	2006
7.	Gonul et al[16]	Neck, perioral region, axillae, lateral region of the trunk, popliteal and antecubital regions	1	2009
8.	Mondal et al[17]	Back, sides of the neck, axillae, groins, dorsal hands and flexural areas of knees and elbows	1	2012
9.	Piccolo et al[2]	Neck, main folds, navel, upper and lower limbs	1	2013
10.	Denadai et al[6]	Perilabial areas, armpits, abdominal wall, antecubital fossae, neck, scapulae and lumbar regions	1	2013
11.	Das et al[5]	Neck, axillae, cubital fossae, wrists, groin, buttocks, knees and ankles	1	2014

This rare form of benign AN is considered a genodermatosis inherited as an autosomal dominant trait with variable penetrance.[2] However, a familial occurrence has been noted in only one of about 10 patients with benign AN where in the involvement was generalised.[7] Therefore, the generalised form has recently been considered a distinct entity with a proposed acronym of GIBAN which stands for generalized idiopathic benign acanthosis nigricans.[2] It should be considered in a child with generalised AN without association with obesity related insulin resistance or any systemic disease and in absence of a previous occurrence in the family.[2] Both our patients fit into the description of GIBAN, being the first occurrence in the family, generalized distribution of skin lesions, no signs of internal disease and a benign clinical course over a follow up period exceeding 7 years. This observation is similar to several other conditions where a long-term follow up is necessary to establish the benign nature of the disease.[8]

The diagnosis of AN is largely clinical, a skin biopsy is required only when the diagnosis is uncertain.[1,9] A long-term persistence of skin lesions has no physical adverse consequences and treatment is required only for cosmetic concerns or if there is associated pruritis.[2,5] The etiopathogenesis of GIBAN remains unclear. It is proposed that this variant is probably related to a new mutation occurring for the first time in a family, similar to familial occurrence of non syndromic AN due to mutation of fibroblast growth factor receptor-3.[10]

In conclusion, we report the occurrence of a benign form of AN with onset during infancy and a benign clinical course. The diagnosis is made after extensive evaluation aimed at excluding a number of systemic conditions associated with AN. Non-progression or spontaneous resolution of skin lesions is observed over a long follow up period.

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REFERENCES

1. Callen JP. Dermatologic manifestations in patients with systemic disease. In: Bolognia JL, Jorizzo JL, Rapini RP, editors. Dermatology. 2nd ed. Philadelphia; Mosby Elsevier; 2008: 76.
2. Piccolo V, Russo T, Picciocchi R, Errico M, Ametrano O, Moscarella E. Generalized Idiopathic

Benign Acanthosis Nigricans in Childhood. Annals of Dermatol. 2013;25:375-7.
3. Dayal D, Jain H, Attri SV, Bharti B, Bhalla AK. Relationship of high sensitivity C-reactive protein levels to anthropometric and other metabolic parameters in Indian children with simple overweight and obesity. J Clin Diag Res. 2014;8(8):5–8.
4. Sinha S, Schwartz RA. Juvenile acanthosis nigricans. J Am Acad Dermatol 2007;57:502-8.
5. Das D, Das A, Kumar D, Gharami RC. Generalized benign acanthosis nigricans in an infant. Indian Dermatol Online J. 2014;5:116-8.
6. Denadai R, Souto RM, Auada-Souto MP. Generalized acanthosis nigricans without systemic disease associated. Dermatol Online J. 2013;19:19614.
7. Inamadar AC, Palit A. Generalized acanthosis nigricans in childhood. Pediatr Dermatol. 2004;21:277-9.
8. Dayal D, Jayaraman D, Sankhyan N, Singhi P. Acute Painful Neuropathy in a Girl with Type 1 Diabetes: Long Term Follow-Up. J Clin Diagn Res. 2016;10(5):1-2.
9. Kutlubay Z, Engin B, Bairamov O, Tuzun Y. Acanthosis nigricans: A fold (intertriginous) dermatosis. Clin Dermatol. 2015;33:466-70.
10. Berk DR, Spector EB, Bayliss SJ. Familial acanthosis nigricans due to K650T FGFR3 mutation. Arch Dermatol. 2007;143:1153-6.
11. Akovbyan VA, Talanin NY, Arifov SS, Tukhvatullina ZG, Musabayev AN, Baybekov IM, et al. Successful treatment of acanthosis nigricans with etretinate. J Am Acad Dermatol. 1994;31:118-20.
12. Skiljevic DS, Nikolic MM, Jakovljevic A, Dobrosavljevic DD. Generalized acanthosis nigricans in early childhood. Pediatr Dermatol. 2001;18:213-6.
13. Uyttendaele H, Koss T, Bagheri B, Schneiderman P, Silfen ME, Gallagher MP, et al. Generalized acanthosis nigricans in an otherwise healthy young child. Pediatr Dermatol. 2003;20:254-6.
14. Ozdemir M, Toy H, Mevlitoğlu I, Demirkesen C. Generalized idiopathic acanthosis nigricans treated with acitretin. J Dermatolog Treat. 2006;17:54-6.
15. Rai VM, Balachandran C. Generalized acanthosis nigricans in childhood. Dermatol Online J. 2006;12:14.
16. Gönül M, Kiliç A, Cakmak SK, Gül U, Ekiz OD, Ergül G. Juvenile generalized acanthosis nigricans without any systemic disease. Pediatr Int. 2009;51:595-7.
17. Mondal A, Debbarman P, Kumar P. Generalized benign acanthosis nigricans. Indian Pediatr. 2012;49:853.

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