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ACANTHOSIS NIGRICANS IN SIBLINGS–A RARE CASE REPORT

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ABSTRACT
Acanthosis nigricans is an indicator of underlying medical disorders, most frequently linked with insulin resistance, although amongst elder patients acanthosis nigricans may occur as a paraneoplastic phenomenon.

INTRODUCTION

The primary changes in affected sites are grey–brown or black pigmentation and dryness and roughness of the skin, which is palpably thickened and covered by small papillomatous elevations, giving it a velvety texture. Acrochordons are a frequent associated with AN in the axillae and groin.

In children neck is the most common site affected (99%) when compared with axillae (73%). Eyelids, face, inner and outer surface of elbows and knees, dorsa of joints of hands, umbilicus, external genitalia, medial aspects of thighs and anus.

Acanthosis nigricans has two important categories, benign and malignant, although Schwartz [1] described eight types of acanthosis nigricans:

1.Benign : benign acanthosis nigricans is actually fairly common, especially in obesity or in individuals with insulin resistance, and is usually relatively mild; it has been documented in up to 7% of children, mainly in teenage years, and virtually all childhood cases are of benign type,

2. obesity-associated,

3. Syndromic (HAIR-AN syndrome: The triad of hyperandrogenism, insulin resistance and acanthosis nigricans in women) [2],

4. Malignant: malignancy-associated acanthosis nigricans is much less common than the non-malignancy-associated types. It may have a rapid onset and progression to produce, tripe palms manifesting as thickened skin of the palms and occasionally the soles, with an enhanced dermatoglyphic change, causing a velvety or, less commonly, a pitted honeycombed pattern of the hand. Most commonly the underlying tumour is bronchial or gastric, together accounting for over half of associated malignancy, but many sites is reported including tumours of genitourinary tract, breast and others [3, 4]

5. Acral,

6. Unilateral,

7. Medication-induced: especially nicotinic acid [5] and

8. Mixed types.

Histological findings are similar in all forms of AN: papillomatosis, hyperkeratosis and hyperpigmentation of the basal layer. There is an upward finger-like projection of the dermal papillae. The areas between papillae show mild acanthosis and are filled with keratotic material. The hyperpigmentation that is clinically seen is due to

hyperkeratosis and thickening, and not due to melanin.

Treatment of the type associated with malignancy consists of identifying and removing the primary tumor. The obesity associated AN usually improves with weight loss. If there is associated endocrinopathy (hyperandrogenism), it must be treated as well, supplementation with fish oil , oral retinoids [6] , metformin [7], topicals such as tretinoin, calcipotriol, urea, salicylic acid, and interventional therapies such as Co2 laser ablation, and long-pulsed alexandrite laser therapy have been implemented.

CASE REPORT

A 12 year old boy born out of consanguinity came with complaints of thick, dark skin lesions over the back, sides of the neck, face, armpits, groin, knuckles, between legs, elbows, over the abdomen for the past 1 yr. His younger brother aged 9 had similar complaints and was a diabetic, and was on treatment for the last two years. On general examination Hypertelorism & widely spaced nipples were two significant similar findings in both the siblings. On dermatological examination , the elder sibling had grey-brown/black pigmentation, dryness & roughness of skin, palpably thickened & covered by small papillomatous elevations, giving a velvety texture with prominent skin lines & mammillated surface over the face, axillae, back of neck, anogenital region, groin, all flexures, submammary region, umbilicus and knuckles. The younger sibling had dark, coarse and mildly thickened skin with a velvety texture, being symmetrically distributed on the neck, the axillae, ante-cubital and popliteal fossae, and groin folds, and knuckles (Figures 1 to 10). The HOMA-IR , The calculated model which provided equations for estimating IR and β-cell function from simultaneous fasting measures of glucose and insulin levels . The formula used to estimate is ,HOMA-IR = Fasting glucose (mmol) × Fasting insulin (uU/mL)/ 22.5. IR is diagnosed when the result is >2.71.In our case, for the elder sibling HOMA-IR was 19.24 and for the younger sibling was 82.54. On histopathological examination sections from the skin showed hyperkeratosis and papillomatous epidermis enclosing keratin cysts and increased pigmentation in the basal layer .Dermis showed lymphocytic infiltration and areas of hemorrhage (Figures 11 and 12). A diagnosis of acanthosis nigricans was made based on the clinical and histopathological features and the HOMA-IR values.

Figure 1. Clinical photograph showing younger and elder sibling frontal view

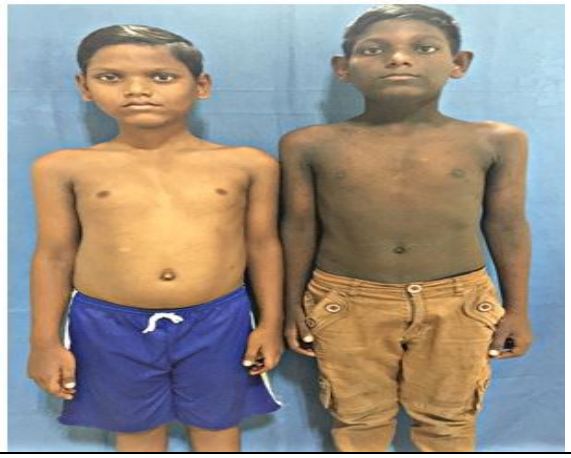

Figure 2. Clinical photograph showing younger and elder sibling back view

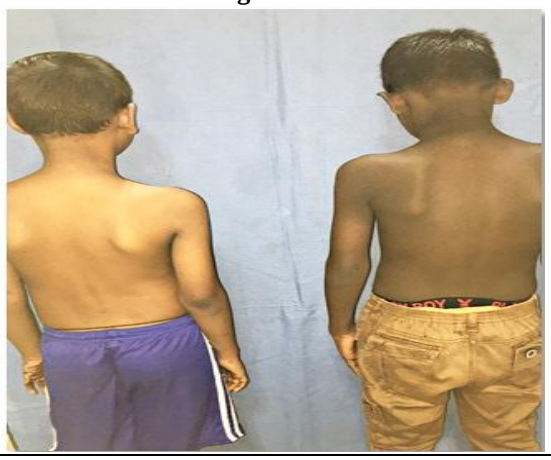

Figure 3. . Clinical photograph showing dark coarse thickened skin over the sides of the neck in the elder sibling

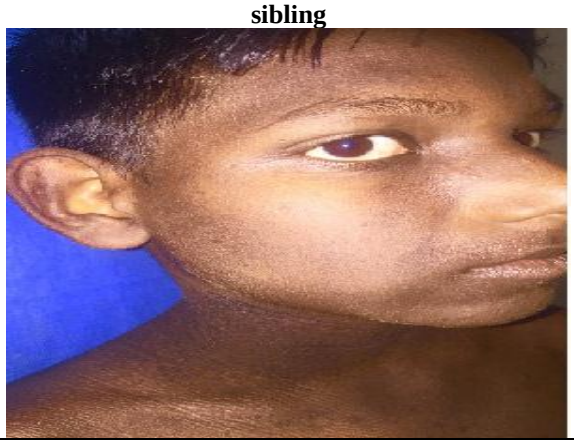

Figure 4. Clinical photograph showing brownish pigmentation and dryness over the sides of the neck in the younger sibling

Figure 5. . Clinical photograph showing dark coarse thickened skin over the chest, abdomen, cubital fossa in the elder sibling

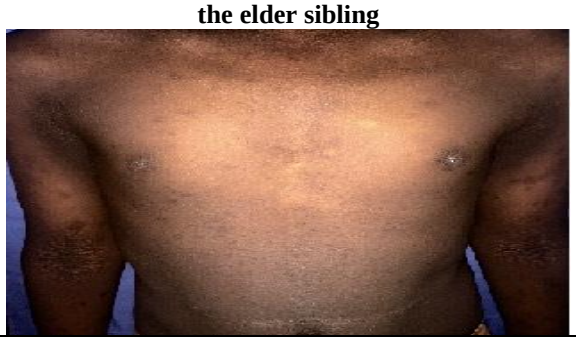

Figure 6. . Clinical photograph showing brownish pigmentation and dryness over the chest, abdomen, cubital fossa in the younger sibling

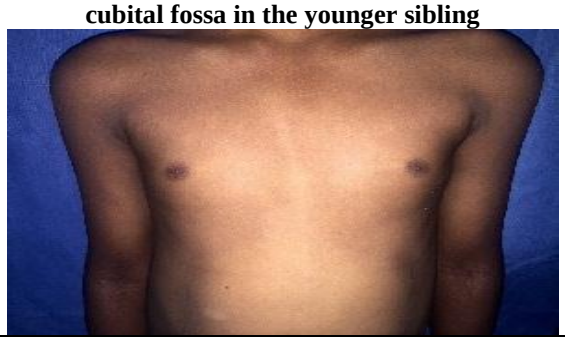

Figure 7. . Clinical photograph showing dark coarse thickened skin over the dorsal aspect of hands in the elder sibling

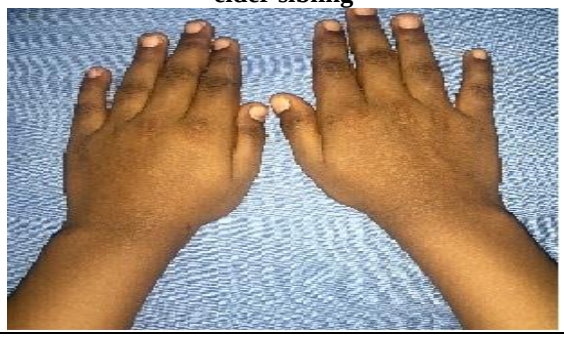

Figure 8. . Clinical photograph showing brownish pigmentation and dryness over the dorsal aspect of hands in the younger sibling

Figure 9. Clinical photograph showing dark coarse thickened skin over the dorsal aspect of feet in the elder sibling

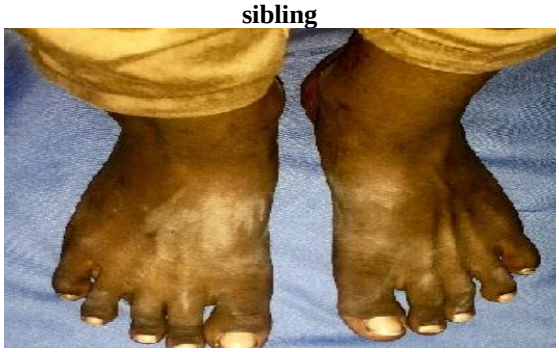

Figure 10. . Clinical photograph showing brownish pigmentation and dryness over the dorsal aspect of feet in the younger sibling

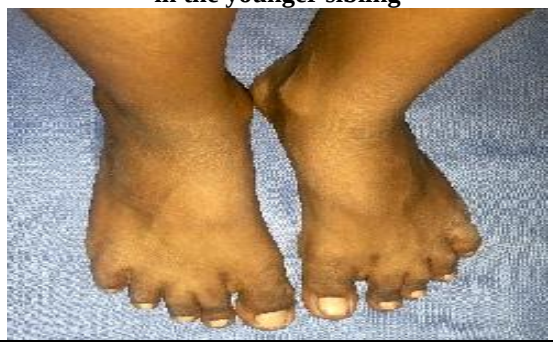

Figure 11. Histopathology slide under low power showing hyperkeratosis and papillomatous epidermis enclosing keratin cysts and increased pigmentation in the basal layer .Dermis showed lymphocytic infiltration and areas of haemorrhage

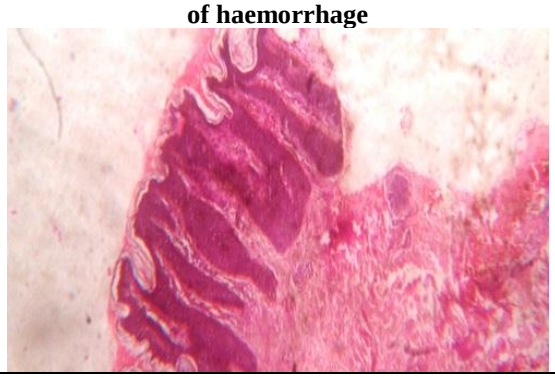

Figure 12. Histopathology slide under high power microscopic view

DISCUSSION

Insulin resistance (IR) refers to a reduced biological response (glucose clearance) of peripheral tissues to circulating insulin. The diminished peripheral response to circulating insulin results in compensatory hypersecretion of insulin to maintain normal blood glucose levels.). Obesity is now the most common cause of insulin resistance in children and adolescents. The characteristic findings of IR are AN in both sexes.AN has been called a clinical surrogate to hyperinsulinemia determined by other laboratory investigatory methods. All most all, if not most, patients with acanthosis nigricans may have either clinical or subclinical insulin resistance, and patients should have a glucose and insulin level drawn simultaneously. Childhood benign AN, increases the risk for type 2 diabetes, hypertension and AN may be used as reliable index of IR [8]. Insulin has been demonstrated to easily pass over the dermoepidermal junction to reach keratinocytes. At normal or low concentrations, insulin regulates lipid, protein and carbohydrate metabolism and can mildly promote growth by binding to insulin receptors. At increased levels , insulin can exhibit more aggressive growth-promoting effects by attaching to insulin-like growth factor 1 receptors (IGF-1Rs) that are clones in size and structure to insulin receptors, but bind IGF-1 with 1000 times greater affinity than insulin. This stimulates increased proliferation of keratinocytes and fibroblasts, leading to AN [9]. One of the most important indicator of IR than AN is obesity, hence AN should not be used as the only marker for IR. This case is being presented for its rarity , wherein two non obese siblings presenting with acanthosis nigricans as a common feature and marker of insulin resistance , one sibling having type 1 diabetes and the other though presently at a euglycemic state , can evolve into type 2 diabetes.

CONCLUSION

Acanthosis nigricans was proposed as an insulin resistance marker and an independent risk factor for type 2 diabetes. A number of studies had associated Acanthosis nigricans with insulin resistance and much higher prevalence of type 2 diabetes in childhood

Although children with AN are often obese , in non obese children with AN, it is an outward sign that they are insulin resistant , and further investigations to rule out childhood type 2 diabetes should be carried out.

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CONFLICT OF INTEREST: NIL

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