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Case Report

Obesity and Acanthosis Nigricans as the Clinical Markers of Insulin Resistance and Type-2 Diabetes Mellitus in Young Patients; A Case Report of Two Cases

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ABSTRACT

Two young girls, aged 11 and 12 years, presented with obesity and Acanthosis Nigricans. They were found to have severe insulin resistance and type-2 diabetes mellitus. Anti-glutamic acid decarboxylase and anti-islet cell antibodies were negative. Tests for hypothyroidism and Cushing's syndrome were negative. They were managed with lifestyle modification and metformin.

Keywords: Child, Diabetes mellitus, Type 2, Anti-GAD65 autoantibody, Islet cell antibodies, Hypothyroidism, Cushing syndrome, Diabetes mellitus, Insulin-resistant, Acanthosis Nigricans.

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INTRODUCTION

The prevalence of type-2 diabetes in children and young adults has risen considerably all over the world and is strongly related to the rise in childhood obesity.[1] The development of complications due to type-2 DM is more rapid and aggressive in children as compared to adults.[2] Acanthosis Nigricans (AN) is a dark brown velvety pigmentation of the skin typically presenting on the back of the neck and the axillae. Acanthosis Nigricans is strongly associated with obesity, hyperinsulinism and insulin resistance. Obese people with AN are at an increased risk of developing type-2 DM.[3] A study of children and adolescents suggested a strong association between AN and hyperinsulinemia with a positive predictive value (PPV) of 39%, and this PPV increased to 47% when obesity was also taken into account.[4]

We are presenting here case report of two girls who developed type-2 DM at a very young age to highlight the importance of obesity and AN as clinical biomarkers of severe insulin resistance.

CASE 1

An eleven-year-old girl presented with polyuria and polydipsia. There was no history of abdominal pain, vomiting or any significant weight loss. There were no visual complaints or deafness. She was born full-term through spontaneous vaginal delivery with no history of gestational diabetes in the mother. Developmental milestones were normal. Her father developed diabetes at the age of 40 years, and many of his near relatives had diabetes. There was no history of the development of diabetes at a young age in her first and second-degree relatives. On examination, she was an obese child with uniformly distributed excess weight. Her weight was 63 kg, and her BMI was 33 kg/m^2. Her blood pressure was 110/70 mm Hg, pulse was 78 bpm, and respiratory rate was 16 per minute. She had dark brown velvety pigmentation at the back of her neck and axillae (Figure-1).

Figure-1: Acanthosis Nigricans at the Back and Sides of Neck in 11 Year Old Girl

Systemic examination was unremarkable. Plasma fasting glucose was 7.5 mmol/l, HbA1c 10.1%, urine ketones nil, serum C-peptide (fasting) 3.5 ng/ml (ref range: 1.0–6.8) and serum Insulin (fasting) 22.4 uIU/ml (ref range: 2–25). HOMA-IR index was 7.47. Serum Anti glutamic acid decarboxylase (Anti GAD) and anti-

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Islet cell antibodies were negative. Serum TSH was 2.5 mIU/ml, and 24 hours of urine-free cortisol was within normal limits. She was advised lifestyle modification (dietary control and regular exercise) and oral metformin. She responded well, and on a follow-up visit after four months, she had reduced weight by 4 kg and HbA1c was 6.7%.

CASE-2

A twelve-year-old girl presented with excessive weight gain for the last two years. The mother said that her daughter snores a lot and has been passing urine more frequently for the last few months. She had an unremarkable birth and developmental history. There were no vision or hearing abnormalities. There was no history of gestational diabetes in the mother. Both of her parents were obese; her mother had diabetes, and her father had pre-diabetes, but no near relative developed diabetes at a young age. On examination, she was an obese child with no dysmorphism in appearance. Her weight was 66 kg, and her BMI was 32.2 kg/m^2. Her blood pressure was 110/80 mm Hg, pulse was 80 bpm, and respiratory rate was 14 per minute. Dark velvety pigmentation was at the back of the neck and axillae (Figure-2). There were few pale stretch marks but no wide purplish striae of Cushing's syndrome.

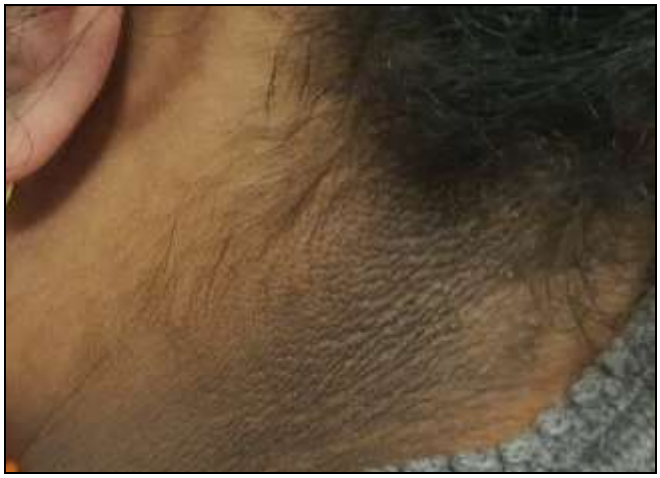

Figure-2: Acanthosis Nigricans at the Back and Sides of Neck in 12 Year Old Girl

Systemic examination was unremarkable. Plasma fasting glucose was 8.3 mmol/l, HbA1c 10.9%, urine ketones nil, serum C-peptide (fasting) 3.2 ng/ml (ref range: 1.0–6.4) and serum Insulin (fasting) 17.2 uIU/ml (ref range: 2–25). HOMA-IR index was 6.4. Serum anti-GAD and anti-Islet cell antibodies were negative. Serum TSH was 1.7 mIU/ml. Twenty-four hours of urine-free cortisol was within normal limits, and overnight, the dexamethasone suppression test showed normal suppression of serum cortisol. She is also doing well on lifestyle modifications and oral metformin. Due to her snoring, a sleep study was planned in future if it does not improve with lifestyle modification and weight reduction.

DISCUSSION

As noted in our patients, most of the cases of Acanthosis Nigricans are associated with obesity and insulin resistance. Evidence indicates that Acanthosis Nigricans is a useful clinical marker for the identification of obese and overweight children and adolescents with insulin resistance who are susceptible to type-2 DM and metabolic syndrome.[5] A study with obese children (n=145) suggested a strong link between Acanthosis Nigricans and hyperglycemia, even after adjusting for BMI.[6] Burke *et al.* suggested that people with Acanthosis Nigricans had higher fasting insulin and glucose levels than those without AN. They also reported that the severity of Acanthosis Nigricans was directly linked to the degree of insulin resistance.[7] Our cases also had severe AN, which correlated with their high HOMA-IR values. Ethnicity is important in the evolution of AN.[1] In a study at Yorkshire and Humber, the authors noted that AN was more common in people with dark skin. People of Pakistani origin constituted about 23.4% of the subjects with AN, while they represented only 4.5% of the population of that area. The people with AN had higher fasting plasma glucose and serum Insulin levels and high HOMA-IR index values.[8] A strong genetic predisposition is an important factor for developing type-2 DM. Diabetes in parents is also a risk factor for the development of type-2 DM in young adults.[9] Our cases have also shown a strong family history of type-2 DM. It is more common among children in the age group between 10 and 19 years, probably due to the hormonal dynamics of puberty. Girls are more likely to develop type-2 DM than boys.[10]

Studies have suggested that Acanthosis Nigricans in childhood and adolescence can be used as a clinical marker for the future development of diabetes and other non-communicable diseases, and it can be reduced by enhancing physical activity and dietary modification during childhood.

Conflict of Interest: None.

Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

MA & WA: Conception, data acquisition, drafting the manuscript, critical review, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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