The Role of Acanthosis Nigricans in Identifying Clinical and Metabolic Features of the Metabolic Syndrome in Obese Children

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Background: Acanthosis nigricans (AN) is a dermatologic marker of hyperinsulinemia and has been linked with metabolic syndrome in adults. In children, the relationship between AN and different components of the metabolic syndrome has received mixed research results. We investigated whether the clinical and metabolic profile of obese children with AN was different from those without AN.
Material and methods: We studied retrospectively the observation charts of children who were evaluated in our clinic for obesity and/or anomalies of glucose metabolism from January 1st 2005 to December 31st 2009. The study population consisted of 52 children. The analyzed data included: age, sex, body mass index (BMI), the presence or absence of AN, systolic and diastolic blood pressure, the results of the oral glucose tolerance test, triglycerides and high-density lipoprotein (HDL) cholesterol levels, baseline insulin, the homeostatic model assessment: insulin resistance (HOMA-IR), glicated hemoglobin. We divided our study population into two groups according to the presence or absence of AN. We used One-Way ANOVA to evaluate the clinical and metabolic differences between the two study groups.
Results: We found significant differences between the two groups for BMI, systolic and diastolic blood pressure, triglycerides, HDL cholesterol, baseline insulin and HOMA-IR.
Conclusions: Our study shows that AN seems to be linked with most of the features of the metabolic syndrome in children. The relationship of AN and anomalies of glucose metabolism need further testing.

Keywords: acanthosis nigricans, metabolic syndrome, children, obesity

Introduction

Acanthosis nigricans (AN) is a usually asymptomatic dermatosis characterized by velvety, papillomatous, brownish-black, hyperkeratotic plaques, typically of the intertriginous surfaces and neck [1,2,3,4]. The general prevalence of AN varies with age, sex, race [1,2,4]. Although the cause of AN appears to be related to insulin resistance, the true pathogenesis of AN is likely to be more complex [1,2]. AN is considered a dermatologic marker of hyperinsulinemia, features of the metabolic syndrome, polycystic ovary syndrome or malignancy in adults [1,2,4]. Needless to say, early recognition of these conditions is essential for prevention of disease progression. In children, however, the relationship between AN and different components of the metabolic syndrome has received mixed research results [2]. We investigated whether the clinical and metabolic profile of obese children with AN was different from those without AN.

Material and method

We studied retrospectively the observation charts of the children that were evaluated in our clinic for obesity and/or anomalies of glucose metabolism from January 1st 2005 to December 31st 2009. Further data was registered if insulin levels were tested and the body mass index (BMI, weight in kilograms divided by the square height in meters) was above the 97th percentile for age and gender according to the World Health Organization (WHO) growth charts. Exclusion criteria were the known presence of malignancy, diabetes, diseases associated with insulin resistance, the use of medication that alters blood pressure, glucose or lipid metabolism. The study population consisted of 52 children.

Data obtained from the observation charts included: age, sex, weight, height, systolic and diastolic blood pressure, the presence or absence of AN, the results of the oral glucose tolerance test (1.75 g of glucose per kilogram of body weight; maximal dose, 75 g), baseline insulin, glicated hemoglobin (HbA1c), triglycerides and high-density lipoprotein (HDL) cholesterol levels. We calculated the homeostatic model assessment: insulin resistance (HOMA-IR) as the baseline glucose in millimoles per liter multiplied by the baseline insulin in microunits per milliliter, divided by 22.5.

We divided our study population into two groups according to the presence or absence of AN: children that had AN (AN+) and children without AN (AN–).

The data are expressed either as frequencies or as means ± standard deviation. For each variable, we used Lavene's test for evaluating the equality of variances between groups and since the groups were almost equal we used One-Way ANOVA (with a confidence interval of 95 percent) to evaluate the clinical and metabolic differences between the two study groups and across gender categories. In case of missing values, the cases were excluded analysis by analysis. All analyses were performed with the use of SPSS Statistics Software (version 17, IBM Company).

Table I. Clinical and Metabolic Characteristics of the Study Groups[1]

	AN+ Mean (SD)	AN– Mean (SD)	Study group (n = 52)	Missing values no (%)	p value[1]
Gender no (%)					
Male	10 (41.67)	17 (60.72)	27 (51.93)	0	0.17
Female	14 (58.33)	11 (39.28)	25 (48.07)	0	0.17
Age (yrs)	13.20 (3.12)	11.11 (3.76)	12.12 (3.59)	0	0.03
BMI (kg/m^2)	34.62 (5.72)	26.94 (5.36)	30.71 (6.72)	0	0.00
Systolic blood pressure (mmHg)	121.50 (13.05)	109.14 (10.88)	115.73 (13.48)	7 (13.5)	0.00
Diastolic blood pressure (mmHg)	75.79 (10.84)	68.76 (9.89)	72.51 (10.88)	7 (13.5)	0.02
Baseline glucose (mmol/l)	4.37 (0.73)	4.58 (0.82)	4.48 (0.78)	0	0.34
2 hours glucose	5.54 (1.78)	5.43 (1.24)	5.48 (1.49)	6 (11.5)	0.80
Baseline insulin (µui/l)	17.80 (12.45)	10.72 (7.13)	14.12 (10.56)	0	0.01
HOMA-IR	3.40 (2.33)	2.28 (1.82)	2.82 (2.13)	0	0.05
HbA1c	5.55 (0.47)	5.53 (0.49)	5.54 (0.47)	35 (67.3)	0.94
Triglycerides (mmol/l)	1.44 (1.08)	0.88 (0.41)	1.18 (0.88)	9 (17.3)	0.03
HDL cholesterol (mmol/l)	0.97 (0.35)	1.22 (0.25)	1.10 (0.32)	24 (46.2)	0.04

SD = standard deviation, BMI = body mass index, HDL = high-density lipoprotein, HOMA-IR = homeostatic model assessment: insulin resistance.
[1] p value when comparing the AN+ and the AN– groups.

Results

Clinical and metabolic characteristics of the study groups are shown in Table I. We found significant differences between the two groups for BMI, systolic and diastolic blood pressure, triglycerides, HDL cholesterol baseline insulin and HOMA-IR. We did not found significant differences between the two groups for baseline glucose, 2 hours glucose and HbA1c. We found significant differences for age, BMI and baseline insulin levels across gender categories as shown in Table II. We did not find significant differences for the rest of the variables (data not shown).

Discussions

Our findings show that AN is linked with most of the components of the metabolic syndrome in children.

Children with AN had significantly higher BMIs and systolic and diastolic blood pressures than those without AN. Although we also found significant age differences between groups, we believe they are related with the fact that the prevalence of AN rises with age and it is higher during puberty, when a physiological resistance to insulin exists [1,2,4,5]. Larger international studies found that AN is associated with higher BMI independent of age [4–10]. In addition, mean age, BMI and baseline insulin levels were significantly higher in females, gender associated with higher AN prevalence rates in international studies [1,2,5]. In our study, the number of girls with AN was higher than of boys with AN, but this was not statistically significant.

Children with AN had significantly higher triglycerides levels and significantly lower HDL cholesterol levels. Both markers are key components of most metabolic syndrome definitions. Our results are supported by international larger studies [4,8]. A study that included 236 children with AN, found a prevalence for dyslipidemia of 27% in the AN group [5].

Table II. Age and BMI across gender categories

	Male (n = 27)	Female (n = 25)	p value[1]
Age (yrs)	11.00 (4.12)	13.42 (2.32)	0.01
BMI (kg/m^2)	29.02 (7.42)	32.75 (5.20)	0.04
Baseline insulin (µui/l)	11.48 (7.57)	17.21 (12.71)	0.05
HOMA-IR	2.39 (1.84)	3.32 (2.38)	0.12

[1] p value when comparing ages and BMIs between gender categories

As we expected, baseline insulin levels were significantly higher in the AN+ group. Because of the age differences between groups, puberty could have influenced these results. In addition, HOMA-IR was significantly higher in children with AN while baseline glucose was not, suggesting that HOMA-IR is a marker of insulin resistance in our group of obese children. Larger studies proved that AN is indeed a marker of hyperinsulinemia and insulin resistance in children [4,5,8,11].

Our study did not find a relationship between AN and markers of the glucose metabolism used in defining the metabolic syndrome. More so, baseline glucose and 2 hours glucose means were below the international cut-offs that define anomalies of the glucose metabolism [12,13]. International data is conflicted: there are studies that show a relationship between AN and abnormal glucose metabolism [3,11], but also studies that fail to identify such a relationship [4,8]. When we analyzed HbA1c levels, they were not significantly higher in AN+ children, maybe due to the small number of children that had their HbA1C levels tested. Still, the HbA1c mean of the AN+ group was slightly higher than the mean of the AN- group. Interestingly, both are close to the lower limit (5.6%) used by the American Diabetes Association to define adults at risk for type 2 diabetes [13].

Some studies suggest that HbA1c may be a better way of evaluating the glucose metabolism in defining the metabolic syndrome in adults [14,15]. Other studies, including findings from the Bogalusa Heart Studies, show the potential value of HbA1c as a marker of the metabolic syndrome [16,17,18]. Our findings may reflect the need to reevaluate our means of identifying children with anomalies of glucose metabolism.

The limitations of the present study are those of a retrospective study: we lost a lot of possible subjects due to incomplete data and our study group was small.

Conclusions

Our study shows that, in obese children, AN is linked with higher BMI and higher systolic/diastolic blood pressure. The presence of AN is associated with higher triglycerides levels, lower HDL cholesterol levels and higher HOMA-IR values. The relationship between AN and anomalies of glucose metabolism needs further testing.

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