Acanthosis nigricans as a presentation of severe insulin resistance in obese children
- a case report -

Maria Krajewska, Jędrzej Nowaczyk, Dominika Labochka, Anna Kucharska, Beata Pyrżak
Department of Paediatrics and Endocrinology, Medical University of Warsaw, Poland

Acanthosis nigricans

- Acanthosis nigricans is well known as the skin symptom of insulin resistance, nevertheless children with such skin disorders usually undergo a long way until they are properly diagnosed.
- We would like to present the history of two young patients with severe acanthosis nigricans combined with insulin resistance of major grade.

Patient 1

A 13-year-old boy referred to the Clinic by dermatologist due to acanthosis nigricans and obesity.

Medical history:

- born from uncomplicated pregnancy with the forces of nature, 38 weeks, body weight 3100g, length 51 cm, in infancy fed with modified milk, negative history of chronic diseases and taking medications
- excessive body weight from the age of five:
  frequent and irregular eating, large amounts of sweets and sweet drinks (up to 4-5 liters per day), insufficient physical activity;
  acanthosis nigricans was noticed at the age of 12 years.
- family history: grandfather suffers from type 2 diabetes and hypertension, negative history of familial acanthosis nigricans and obesity

Physical examination:

- Obesity: BMI 32,6 kg/m2 (>97 pc) (height 170cm= 85 pc, weight 94,3 kg= >97 pc, due body weight 60kg (+/- 10%), fat percentage 38%)
- acanthosis nigricans on the neck, elbows, knees and knuckles of the hands, behind the ears, in the axillae, genital region, inguinal and abdominal skin folds (Photo 1)
- pink stretch marks around the abdominal region
- Steatomastia and gynecomastia
- Secondary sex characteristics inTanner scale: G III, P III

Laboratory tests:

- Normal function of thyroid, liver and kidneys, hypercortisolemia was excluded, HDL 42 (norm > 45 mg/dl), no other lipid disorders, normal: morphology, ions and IGF1, low concentration of vitamin D= 8,9 ng/ml
- OGTT- hyperglycaemia and extremely high hyperinsulinemia (Table 1)
- HbA1c= 6% (norm 4,5-6,2%)
- Glycemia profile: before and 2 hours after meals (for 6 days)- fasting glucose max 106 mg%, after meals- within the norm

Intervention:

- Dietary management, increased physical activity

Control laboratory tests after weight loss 3,5 kg (Table 3)

Additional blood tests:

- Elevated C-peptide 9,44 (norm 1,06-3,53 ng/ml)
- Anti-GAD, anti-IA-2 and ICA within the normal values, genetic tests for monogenic diabetes (results remain in the study)

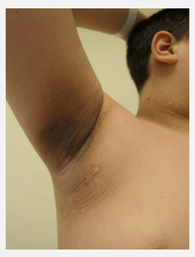
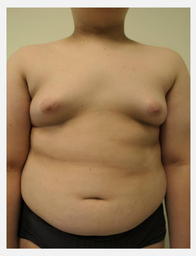
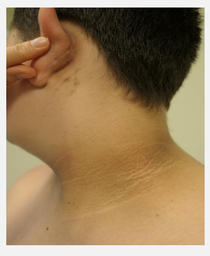
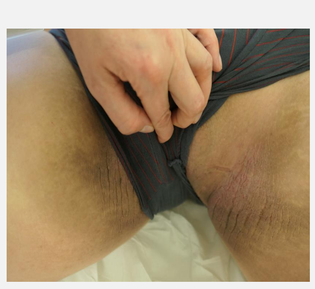
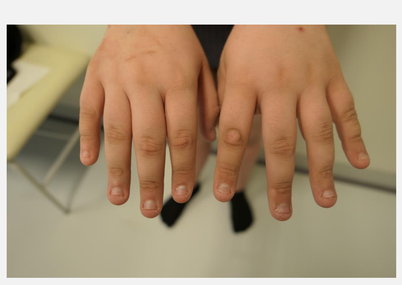
Diagnosis: diabetes mellitus type 2

Treatment: metformin, behavioral therapy: diet, regular physical activity

Table 1. Patient 1- OGTT, HOMA IR= 76,52, QUICKI= 0,22

OGTT	0’	30’	60’	90’	120’	150’	180’
Glucose (mg/dl)	104	206	232	247	233	224	203
Insulin (uIU/ml)	298	472	1110	1135	1489	1419	1561

Photo 1. Patient 1- acanthosis nigricans

Patient 2

A 14-year-old boy referred to the Clinic by general pediatrician due to acanthosis nigricans and obesity.

Medical history:

•born with the forces of nature, from uncomplicated pregnancy, 40 weeks, with body weight 2700g. Delayed psychomotor development since the infancy period. Negative history of chronic diseases and taking medications

•excessive body weight from the early childhood:
frequent and irregular eating
insufficient physical activity

•family history: grandmother suffers from type 2 diabetes, brother is suffering from autism, negative history of familial acanthosis nigricans and obesity

Physical examination:

•obesity BMI 32,8 kg/m2 (>97 pc) (height 168,5cm= 50 pc, weight 93,3 kg= >97 pc, due body weight 54kg (+/- 10%), fat percentage 38,7%)

•acanthosis nigricans on the neck, in the skin folds, the upper chest, arms, axillae and genital region (Photo 2)

•Steatomastia

•Secondary sex characteristics in Tanner scale: G IV, P V

Laboratory tests:

•Normal function of thyroid, liver and kidneys, hypercortisolemia was excluded, HDL 35 (norm > 45 mg/dl), no other lipid disorders, normal: morphology, ions and IGF1, low concentration of vitamin D= 7,1 ng/ml

•OGTT- normal glycemia and extremely high hyperinsulinemia (Table 2)

•HbA1c= 5,5% (norm 4,5-6,2%)

Intervention:

•Dietary management, increased physical activity

Control laboratory tests after weight loss 7,3 kg/1,5 month (Table 3)

Diagnosis: obesity, severe insulin resistance

Treatment: diet, regular physical activity, metformin- discontinued due to digestive tract problems

Table 2. Patient 2- OGTT, HOMA IR= 62,22, QUICKI= 0,23

OGTT	0’	30’	60’	90’	120’	150’	180’
Glucose (mg/dl)	84	120	129	110	100	78	47
Insulin (uIU/ml)	300	620	971	875	738	400	249

Photo 2. Patient 2- acanthosis nigricans

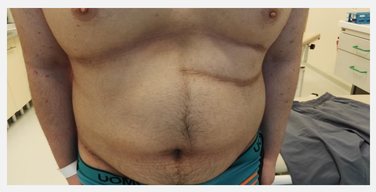
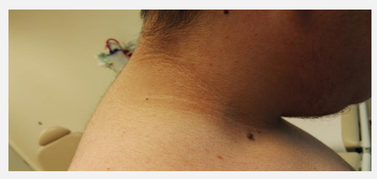
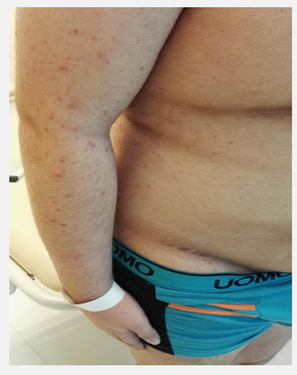




Table 3. Laboratory tests and HOMA index- before and after weight loss

	Before weight loss	After weight loss	Degree of weight reduction
Patient 1	Glucose 104 mg/dl Insulin 298 uIU/ml HOMA-IR 76,52 QUICKI 0,22	Glucose 71 mg/dl Insulin 42,4 uIU/ml HOMA-IR 7,43 QUICKI 0,29	-3,5 kg / 7 days Δ BMI = -1,2 / 7 days Clinically: systematic reduction of the severity of acanthosis nigricans
Patient 2	Glucose 84 mg/dl Insulin 300 uIU/ml HOMA-IR 62,22 QUICKI 0,23	Glucose 73 mg/dl Insulin 28,6 uIU/ml HOMA-IR 5,16 QUICKI 0,3	-7,3 kg / 1,5 month Δ BMI = -2,5 / 1,5 month Clinically: systematic reduction of the severity of acanthosis nigricans

Conclusions:
Acanthosis nigricans should always be considered as a symptom of systemic abnormalities.
It strongly suggests insulin resistance. But it should also be diagnosed in familial acanthosis nigricans (connected with mutations in FGFR3) and some malignant states (for example Wilm’s tumor, osteogenic sarcoma or gastric adenocarcinoma).
In our first patient we diagnosed diabetes mellitus type 2.
Patient 2 has the diagnosis of obesity and severe insulin resistance.
In short time after weight loss in both patients we observed improvement in HOMA-IR and QUICKI followed by systematic reduction of skin symptoms. This fact shows, that in obese children severe insulin resistance as well as acantosis nigricans can be reversible after the diet and behavioral therapy.

▪Literature: Inbal Sander, Jeffrey Callen, Abena O Ofori: Acanthosis nigricans. UpToDate, 15.03.2018