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

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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: 3010g, 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 noted 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 93.3 kg, >97 pc, due body weight 54kg (10%), fat percentage 38,7%)
- Frequent and irregular eating, large amounts of sweets and sweet drinks (up to 4-5 liters per day), 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:
- Obese: BMI 32.6 kg/m2 (>97 pc) (height 170cm, 85 pc, weight 93.3 kg, >97 pc, due body weight 54kg (10%), fat percentage 38,7%)
- Acanthosis nigricans on the neck, elbows, knees and inulae of the hands, behind the ears, in the axilla, genital region, inguinal and abdominal skin folds.
- Pectus carinatum.
- Secondary sex characteristics in Tanner scale: G III, P III.

Laboratory tests:
- Normal function of thyroid, liver and kidneys, hypercholesterolemia was excluded. HDL 42 (norm > 45 mg/dl), no other lipid disorders, normal morphology, ions and IGF1, low concentration of vitamin D 6.9 ng/ml.
- OGTT: hyperglycaemia and extremely high hyperinsulinaemia (Table 1).
- HbA1c 4% (norm 5-6,2%).
- Glycemic profile: before and 2 hours after meal (for 6 days) - testing glucose max 106 mg%. after meal - 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 1.06-2.53 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.

Patient 2
- A 14-year-old boy referred to the Clinic by general practitioner due to acanthosis nigricans and obesity.
- Medical history:
  - Born from 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:
- Obese: 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, axilla and genital region (Photo 2).
- Secondary sex characteristics in Tanner scale: G IV, P V.

Laboratory tests:
- Normal function of thyroid, liver and kidneys, hypercholesterolemia was excluded, LDL 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 glycaemia and extremely high hyperinsulinaemia (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/1.2 month (Table 3).

Diagnosis: obesity, severe insulin resistance.

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

Table 1. Patient 1 - OGTT, HOMA-Ir, 75,52, QUICKI 0.22

<table>
<thead>
<tr>
<th>OGTT</th>
<th>0</th>
<th>30</th>
<th>60</th>
<th>90</th>
<th>120</th>
<th>150</th>
<th>180</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose (mg/dl)</td>
<td>104</td>
<td>239</td>
<td>232</td>
<td>247</td>
<td>232</td>
<td>204</td>
<td>253</td>
</tr>
<tr>
<td>Insulin (uIU/ml)</td>
<td>238</td>
<td>472</td>
<td>1110</td>
<td>1335</td>
<td>1489</td>
<td>1419</td>
<td>1531</td>
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Table 2. Patient 2 - OGTT, HOMA-Ir 0.22, QUICKI 0.23

<table>
<thead>
<tr>
<th>OGTT</th>
<th>0</th>
<th>30</th>
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<th>90</th>
<th>120</th>
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<th>180</th>
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</thead>
<tbody>
<tr>
<td>Glucose (mg/dl)</td>
<td>54</td>
<td>129</td>
<td>129</td>
<td>115</td>
<td>110</td>
<td>71</td>
<td>47</td>
</tr>
<tr>
<td>Insulin (uIU/ml)</td>
<td>393</td>
<td>682</td>
<td>571</td>
<td>575</td>
<td>756</td>
<td>405</td>
<td>210</td>
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</table>

Table 3. Laboratory tests and HOMA Indexes before and after weight loss

<table>
<thead>
<tr>
<th>Degree of weight reduction</th>
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<th>After weight loss</th>
<th>Degree of weight reduction</th>
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<tbody>
<tr>
<td>Patient 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucose 104 mg/dl</td>
<td>HbA1c 4.5%</td>
<td>HbA1c 4.4%</td>
<td>HOMA-Ir 75,52</td>
</tr>
<tr>
<td>Insulin 222 uIU/ml</td>
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<td></td>
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<tr>
<td>Patient 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glucose 71 mg/dl</td>
<td>HbA1c 5.1%</td>
<td>HbA1c 5.1%</td>
<td>HOMA-Ir 5.1</td>
</tr>
<tr>
<td>Insulin 222 uIU/ml</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 4. Treatment and HOMA Indexes before and after weight loss

<table>
<thead>
<tr>
<th>Degree of weight reduction</th>
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<th>After weight loss</th>
<th>Degree of weight reduction</th>
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Conclusion:
- 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 Wilms’ 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 acanthosis nigricans can be reversible after the diet and behavioral therapy.