Monogenic obesity in children: focusing on SH2B1 deletion

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INTRODUCTION

Genetic obesity is rare, and quite challenging for pediatricians in terms of early identification. SH2B1 is an important component in the leptin-melanocortin pathway and is found to play an important role in leptin and insulin signaling, and therefore in the pathogenesis of obesity and diabetes. Microdeletions in chromosome 16p11.2, encompassing the SH2B1 gene, are known to be associated with obesity, insulin resistance, hyperphagia and developmental delay.

AIM

Aim of our study is to report on a case series of young individuals with 16p11.2 microdeletions, including the SH2B1 gene, and provide detailed information on BMI development and obesity-associated comorbidities.

In this way, we want to raise awareness of this syndromic form of obesity as a differential diagnosis of genetic obesity.

METHOD

- Inclusion criteria:
  - obesity (≥ 97th percentile for age and sex*) and 16p11.2 deletions, including the SH2B1 gene, detected by MLPA
- Phenotype of 7 children
  (5 male; age range: 2.8 – 18.0 years)
- BMI-trajectories from birth onwards
- Screening for obesity-associated comorbidities

CONCLUSIONS

Chromosomal microdeletions in 16p11.2, including the SH2B1 gene, in children are associated with severe, early-onset obesity and comorbidities associated with insulin resistance.

Early genetic testing in suspicious patients and early screening for comorbidities is recommended.

REFERENCES


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CONTACT INFORMATION

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Table 1. Laboratory findings in patients with microdeletions in chromosome 16p11.2, encompassing the SH2B1 gene.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (years)</th>
<th>Sex</th>
<th>LEP (µg/L) (SDS)</th>
<th>bioLEP (µg/L)</th>
<th>Fasting insulin (mU/L)</th>
<th>Fasting C-peptide (µg/L)</th>
<th>Hba1c [%]</th>
<th>Insipid status</th>
<th>Cholesterol (mmol/L)</th>
<th>Triglycerides (mmol/L)</th>
<th>HDL (mmol/L)</th>
<th>LDL (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.8</td>
<td>male</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>normal</td>
<td>153.0</td>
<td>291.0</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>2</td>
<td>18.5</td>
<td>female</td>
<td>64.8 (-2.5)</td>
<td>69.3</td>
<td>30.0</td>
<td>3.9</td>
<td>5.4</td>
<td>normal</td>
<td>143.1</td>
<td>96.3</td>
<td>46.4</td>
<td>96.7</td>
</tr>
<tr>
<td>3</td>
<td>7.7</td>
<td>female</td>
<td>66.8 (+1.1)</td>
<td>57.6</td>
<td>20.0</td>
<td>3.4</td>
<td>5.6</td>
<td>NAFLD</td>
<td>204.0</td>
<td>152.6</td>
<td>69.6</td>
<td>120.0</td>
</tr>
<tr>
<td>4</td>
<td>12.6</td>
<td>female</td>
<td>56.5 (+1.1)</td>
<td>51.4</td>
<td>78.0</td>
<td>6.2</td>
<td>8.4</td>
<td>NAFLD</td>
<td>143.0</td>
<td>114.0</td>
<td>43.0</td>
<td>97.0</td>
</tr>
<tr>
<td>5</td>
<td>16.8</td>
<td>female</td>
<td>62.9 (-2.6)</td>
<td>83.7</td>
<td>40.0</td>
<td>6.3</td>
<td>5.2</td>
<td>NAFLD</td>
<td>186.0</td>
<td>105.0</td>
<td>43.0</td>
<td>112.0</td>
</tr>
<tr>
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<td>46.94 (+0.7)</td>
<td>42.17</td>
<td>39.9</td>
<td>4.0</td>
<td>5.5</td>
<td>NAFLD</td>
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<td>132.0</td>
<td>46.4</td>
<td>92.8</td>
</tr>
<tr>
<td>7</td>
<td>5.9</td>
<td>male</td>
<td>71.0 (+0.5)</td>
<td>5.0</td>
<td>n/a</td>
<td>5.3</td>
<td>normal</td>
<td>168.0</td>
<td>55.0</td>
<td>50.0</td>
<td>103.0</td>
<td></td>
</tr>
</tbody>
</table>

*suspected NAFLD as assessed by liver enzymes and/or liver ultrasound

LEP: leptin, bioLEP: biologically active leptin, Hba1c: glycated haemoglobin A1c, NAFLD: non-alcoholic fatty liver disease, HDL: high-density lipoprotein, LDL: low-density lipoprotein, n/a: not available.