Hypertriglyceridemia in a boy with Bardet-Biedl Syndrome – Case Report

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Introduction

Bardet-Biedl syndrome (BBS) is a rare autosomal recessive ciliopathy characterized by retinal dystrophy, obesity, post-axial polydactyly, renal anomalies, mental retardation and hypogonadism. BBS diagnosis is confirmed by sequencing of 16 known BBS disease-causing genes, which encode proteins responsible for formation of BBSome and chaperonin complex, which interact with BBS3 (a GTPase) to mediate ciliogenesis and organization of the cilia. Defective immotile cilia possess a “9+0” configuration resulting in left-right asymmetry, which is caused by disturbed bidirectional interflagellar transport of particles required for cilia maintenance and developmental cell signaling including Wnt and hedgehog pathways leading to BBS (Fig.1).

Patient

INITIAL PRESENTATION

Male patient admitted at the age of 16 months
Physical Examination:
- upper and lower extremities polydactyly
- current severe central obesity (BMI 28 kg/m2)
- recurrent upper airway infections
- psychomotor retardation
- severe gastroesophageal reflux disease

Initial Diagnosis: Bardet-Biedl syndrome type 2

EVALUATION AND DIAGNOSIS

Genetic examination: 46, XY karyotype
Psychiatric examination:
- severe mental retardation
- no speech development until 10 y/o
- mental development of 2 y/o at the age of 9.5 y/o
- no reaction to vocal and visual gestures at 9 y/o
- partial deafness in the left ear

<table>
<thead>
<tr>
<th>16 months/o</th>
<th>11 years/o</th>
<th>8 weeks post fenofibrate</th>
</tr>
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<tbody>
<tr>
<td>TGL 3.01 mmol/L</td>
<td>8.41 mmol/L</td>
<td>1.82 mmol/L</td>
</tr>
<tr>
<td>LDL cholesterol 3.11 mmol/L</td>
<td>2.13 mmol/L</td>
<td>3.31 mmol/L</td>
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<tr>
<td>HDL cholesterol 0.94 mmol/L</td>
<td>0.70 mmol/L</td>
<td>4.6 mmol/L</td>
</tr>
<tr>
<td>AST 36 U/L</td>
<td>29.7 U/L</td>
<td>22.7 U/L</td>
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<tr>
<td>ALT 20 U/L</td>
<td>34.1 U/L</td>
<td>30.4 U/L</td>
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<tr>
<td>TSH 2.56 μIU/mL</td>
<td>2.44 μIU/mL</td>
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</tr>
<tr>
<td>Cortisol at 8 a.m. -</td>
<td>5.6 ng/mL</td>
<td></td>
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<tr>
<td>Fasting serum glucose 4.4 mmol/L</td>
<td>4.4 mmol/L</td>
<td></td>
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<tr>
<td>Fasting serum insulin 2.13 μIU/mL</td>
<td>9.8 μIU/mL</td>
<td></td>
</tr>
<tr>
<td>Serum glucose (120) -</td>
<td>4.9 μIU/mL</td>
<td></td>
</tr>
<tr>
<td>Serum insulin (120) -</td>
<td>58.9 μIU/mL</td>
<td></td>
</tr>
</tbody>
</table>

Table 1. Selected results of the biochemical tests

Fig. 1. Structure of BBSome forming cilia (Adapted from Baker et al 2009).

Fig. 2. Images of patient presenting dysmorphic features of BBS. (A) demonstrates typical facial features: low-set ears, flat nasal bridge, deep set eyes. (B-C) deformed phalanges including the brachydactyly and scars from excision of accessory phalanges.

Fig. 3. Patient’s growth charts

DIAGNOSIS

Severe hypertriglyceridemia typically results from genetic origin. Family history was negative therefore familial and secondary hypertriglyceridemia were excluded. The increased TG levels in this patient cannot be a result of typical endocrinopathies due to correct hormone levels. The combination of central obesity, high TG and decreased HDL suggests occurrence of metabolic syndrome although insulin levels are within range (Tab.1).

TREATMENT

Low fat diet was unsuccessful with resulting permanent severe elevated TG level (8.41 mmol/L). Administration of fenofibrate resulted in significant decreased of TGL (1.82 mmol/L) after 2 months. No adverse effects of fenofibrate have been noticed.

Conclusion

This case study describes the first case of BBS with hypertriglyceridemia which is a novel sign to the syndrome that cannot be explained by accompanying diseases, diagnosed up to date. Treatment with fenofibrate in BBS patients may be effective and safe.