Congenital Generalized Lipodystrophy
A Case Presentation
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Disclosures

• Neither presenter has any financial disclosures
• Neither presenter has any conflicts of interest

Cardiovascular Health and Risk Prevention Program

• Purpose:
  – Better understand the cause(s) of premature CVD, including genetic and acquired health risks;
  – Develop effective means of prevention through public and professional health education;
REACH – Risk Evaluation to Achieve Cardiovascular Health

- 2 pediatric endocrinologists
- 1 pediatric geneticist
- 2 registered nurses
- Registered dietitian
- Social worker
- Psychologist
- Child life specialist
- Research project manager

Objectives

- Identify clinical features
- Describe treatment
- Explain Complications

Case Report

- 2 Mexican - American siblings
- 19 yo male, 8 yo female
- 4 healthy siblings
- Abnormal clinical findings
- Birth history
Assessment Findings

<table>
<thead>
<tr>
<th>Clinical finding</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>No subcutaneous fat</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Abnormal lab results</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Muscle manifestations</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Dysmorphic features</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Cardiac manifestations</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Failure to thrive</td>
<td></td>
<td>✓</td>
</tr>
</tbody>
</table>

Case Report

Case Report

Case Report
Test Your Knowledge

Which of the following laboratory results are commonly found in a patient with CGL?
A. Elevated leptin level
B. Decreased cortisol level
C. Elevated creatine kinase level
D. Decreased blood glucose level

Laboratory Findings

<table>
<thead>
<tr>
<th></th>
<th>TChol mg/dl</th>
<th>TG mg/dl</th>
<th>HDL mg/dl</th>
<th>A1C %</th>
<th>FBG mg/dl</th>
<th>CK Total U/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>260</td>
<td>2034</td>
<td>&lt;10</td>
<td>5.1</td>
<td>85</td>
<td>983</td>
</tr>
<tr>
<td>Female</td>
<td>160</td>
<td>616</td>
<td>19</td>
<td>5.0</td>
<td>84</td>
<td>2914</td>
</tr>
<tr>
<td>Goal</td>
<td>&lt;200</td>
<td>&lt;150</td>
<td>≥40</td>
<td>&lt;5.7</td>
<td>65-99</td>
<td>&lt;143</td>
</tr>
</tbody>
</table>

Test Your Knowledge

If both parents are carriers, what is the probability of a child being born with an autosomal recessive disorder?
A. 75%
B. 100%
C. 50%
D. 25%
**Acquired Lipodystrophy**

1) HIV  
   - Long term antiretroviral therapy
2) Partial  
   - 250 patients identified
3) Generalized  
   - 80 patients identified
4) Localized  
   - Various causes

**Congenital Lipodystrophy**

1) Autosomal recessive
2) Four types  
   - Type 1 – AGPAT2  
   - Type 2 – BSCL2  
   - Type 3 – CAV1  
   - Type 4 – PTRF

**CGL Clinical Features**

- Muscular appearance
- Accelerated growth
- Hyperphagia
- Hepatomegaly
- Mild hirsutism in females
- Irregular menses with PCOS
Test Your Knowledge

Leptin is also known as the ______ hormone.
A. Synthesis
B. Satiety
C. Thyroid
D. Growth

Leptin and It’s Role in CGL

Food is eaten
Fat stores release leptin
Hypothalamus sees leptin levels rising
Hypothalamus signals brain to stop eating
Leptin levels decrease and hypothalamus signals brain to eat

Leptin and It’s Role in CGL

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CGL Type 4

Type 4 confirmed by genetic testing - 30 patients
1) Progressive fat loss
   – During infancy
2) Congenital myopathy
   – CK levels and arrhythmias
3) Cardiac arrhythmias
   – Catecholaminergic polymorphic ventricular tachycardia (CPVT)
4) Other clinical findings

CGL Clinical Features

TG use/storage; normal vs CGL
Metabolic Complications

- Lack of adipose tissue
- Excess triglycerides
- Profound hypoleptinemia
- Hyperinsulinemia
- Acanthosis nigricans
- Diabetes mellitus

Management of Complications

1) Medications
   - Fenofibrate
   - Fish oil
   - Gemfibrozil
   - Vitamin D3
   - Atenolol
   - Metreleptin

2) Dietary Modifications

Management of Complications cont.

1) Cardiac manifestations
   - Defibrillator
   - 2 episodes of cardiac arrest
   - Cervical sympathectomy
Metreleptin

- Metreleptin replaces leptin
  - In conjunction with a recommended diet
    - Lower triglyceride levels
      - Average reduction 184 mg/dL
    - Lower blood sugar levels
      - Average reduction 49 mg/dL
    - Lower A1c levels
      - Average reduction of 2%

More on metreleptin

Side Effects & Adverse Reactions
- Headache
- Weight loss
- Abdominal pain
- Hypoglycemia
- Anti-metreleptin antibodies

Test Your Knowledge

What type of diet would you recommend for a patient with CGL?

A. Low fat diet
B. Ketogenic diet
C. Low residue diet
D. Low sodium diet
A Word About Diet Modifications

- Limited research on most effective diet for patients
- Recommended Diet:
  - Calorically balanced, low fat diet (15-20% daily Calories from fat)
  - No concentrated sweets (Ex: Sweets/Desserts, Sugary Beverages)
- Goal of total caloric intake matching expenditure

Diet Modifications

<table>
<thead>
<tr>
<th></th>
<th>Estimated kcal needs</th>
<th>Fat intake recommended (15-20% daily kcal)</th>
<th>Fat intake recommended for healthy individuals (25-30% daily kcal)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>2450 kcal/day</td>
<td>&lt;36-48g/day</td>
<td>61-73g/day</td>
</tr>
<tr>
<td>Female</td>
<td>1600 kcal/day</td>
<td>&lt;25-33g/day</td>
<td>42-50g/day</td>
</tr>
</tbody>
</table>

Challenges with diet
- Miscommunication with Women Infants and Children program
- Hyperphagia
- Compliance with diet
- Lack of data/research
In Summary


References

Questions?