10 year old girl with elevated triglycerides

Katie Stanley, MD
March 28, 2013
10 year old girl with aplastic anemia undergoing preparation for SCT found to have elevated triglycerides

Failed immunosuppressive therapy for aplastic anemia so admitted 11/18 to prepare her for stem cell transplant starting with 2 weeks of desensitization and plasmapheresis
HPI

- Two weeks into her admission, CBC noted to be lipemic
- Lipid panel then sent which showed elevated triglycerides
- Lipid panel repeated fasting the next morning showed similar results
- No known prior lipid panels
- No prior CBCs were lipemic (last one had been 3 days prior)
Review of Systems

- Constitutional: Negative for fever, appetite change and unexpected weight change.
- Eyes: Positive for visual disturbance (legally blind).
- Respiratory: Positive for cough.
- Cardiovascular: Negative for leg swelling.
- Gastrointestinal: Negative for nausea, vomiting and abdominal pain.
- Skin: Negative.
- Musculoskeletal: Negative for weakness.
- Hematological: Bruises/bleeds easily.
Past Medical History

- Aplastic anemia
  - Idiopathic aplastic anemia diagnosed April 2007; complications include recurrent epistaxis and recurrent vitreous hemorrhage into (unrelated) retinal vascular malformations
- AVM (congenital arteriovenous malformation)
  - Retinal AVM's, likely congenital and hereditary (mother has a history of similar retinal lesions)
- Recurrent vitreous hemorrhages into AVMs leading to blindness in both eyes
- Hemochromatosis due to repeated red blood cell transfusions
- PRES (Posterior reversible encephalopathy syndrome)
  - 8/2012, likely related to cyclosporine
Medications

- Amlodipine
- Brimonidine eye drops
- Ceftriaxone
- Deferoxamine MWF
- Hydrocortisone 50 mg IV prn with transfusions
- Immune globulin MWF
- Lansoprazole
- Latanoprost eye drops
- Levetiracetam (Keppra)
- Mycophenolate Mofetil (Cellcept)
- Rituximab qwk
- Sirolimus
- Sulfamethoxazole-trimethoprim

- Chlorhexidine Towelette
  - Rash
- Propofol
  - Angioedema and Rash
- Deferasirox
  - Angioedema
- Cyclosporine
  - Diarrhea and Hives, possible PRES
- Dorzolamide-Timolol
  - Hives and Pruritis
- Fish Product Derivatives
  - Hives
- Iv Dye, Iodine Containing Contrast Media
  - Hives
- Metipranolol
  - Local eye swelling after eyedrops
- Phenazopyridine
  - Transient numbness of tongue
Family History

- Hypertension
  - Maternal Grandmother

- Heart Disease
  - Maternal Grandfather died of MI in 40s
  - Multiple other relatives with CAD on MGF’s side

- Diabetes
  - Negative
Physical Exam

- Vital signs: Wt 53.5 kg (97.8%), Ht 143.5 cm (74.6%), BMI 25.9 (>95%), T 37.5, HR 94, RR 22, BP 116/62, 100% RA
- Constitutional: She appears well-developed and well-nourished. She is active. No distress.
- Head: Atraumatic.
- Nose: Nose normal. No nasal discharge.
- Mouth/Throat: Mucous membranes are moist.
- Eyes: Bilateral vision loss.
- Neck: Normal range of motion. No thyromegaly.
- Cardiovascular: Normal rate, regular rhythm, S1 normal and S2 normal. No murmur heard.
- Pulmonary/Chest: Effort normal and breath sounds normal. There is normal air entry. No respiratory distress.
- Abdominal: Soft. Bowel sounds are normal. She exhibits no distension. There is no tenderness. There is no guarding.
- Musculoskeletal: Normal range of motion.
- Neurological: She is alert. She exhibits normal muscle tone.
- Skin: Skin is warm and dry. No xanthomas or xanthelasmas
<table>
<thead>
<tr>
<th>Date</th>
<th>Total</th>
<th>HDL</th>
<th>LDL</th>
<th>Direct LDL</th>
<th>TGs</th>
</tr>
</thead>
<tbody>
<tr>
<td>12/3</td>
<td>164</td>
<td>33</td>
<td>Incalc</td>
<td>N/A</td>
<td>1579</td>
</tr>
<tr>
<td>12/4</td>
<td>140</td>
<td>18</td>
<td>Incalc</td>
<td>&lt;3</td>
<td>1810</td>
</tr>
</tbody>
</table>
Differential Diagnosis

- **Primary disorders**
  - Familial chylomicronemia
    - Apo E4
  - Familial dysbetalipoproteinemia
    - Apo E2
  - Familial hypertriglyceridemia
    - LPL
  - Familial combined hyperlipidemia
    - Apo B100 (overproduction)

- **Secondary**
  - Obesity
  - Poorly controlled DM
  - Hypothyroidism
  - Nephrotic syndrome
  - Renal failure
  - Medications: Cyclosporine, mTOR inhibitors, retinoids, glucocorticoids, antiretrovirals, beta blockers
Sirolimus and Hyperlipidemia

- 40% of pediatric renal transplant patients
- Dose dependent
- Reversible
- Findings
- Mechanisms
Sirolimus vs. Everolimus
Tacrolimus/Sirolimus vs. Tacrolimus/MMF

12 hospitalizations for cardiovascular events in tacro + siro group vs. tacro vs. MMF group

### Table 4. Cardiovascular risk status at 6 months

<table>
<thead>
<tr>
<th></th>
<th>Tacrolimus + sirolimus (n = 186)</th>
<th>Tacrolimus + MMF (n = 176)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean serum lipid levels (mg/dL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>217.6 ± 60.5</td>
<td>191.7 ± 39.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mean LDL cholesterol</td>
<td>111.4 ± 37.0</td>
<td>98.4 ± 33.0</td>
<td>0.006</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>248.4 ± 169.4</td>
<td>196.4 ± 136.3</td>
<td>0.0015</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>54.2 ± 15.1</td>
<td>52.5 ± 19.6</td>
<td>0.075</td>
</tr>
<tr>
<td>Hyperlipidemia (% patients)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cholesterol &gt;200 mg/dL</td>
<td>56.5%</td>
<td>37.4%</td>
<td>0.0001</td>
</tr>
<tr>
<td>Total cholesterol &gt;240 mg/dL</td>
<td>29.3%</td>
<td>12.2%</td>
<td>0.0003</td>
</tr>
<tr>
<td>LDL-cholesterol &gt;130 mg/dL</td>
<td>31.5%</td>
<td>13.3%</td>
<td>0.001</td>
</tr>
<tr>
<td>LDL-cholesterol &gt;100 mg/dL</td>
<td>54.1%</td>
<td>49.6%</td>
<td>0.50</td>
</tr>
<tr>
<td>HDL-cholesterol &lt;40 mg/dL</td>
<td>14.8%</td>
<td>26.4%</td>
<td>0.02</td>
</tr>
<tr>
<td>Triglycerides &gt;200 mg/dL</td>
<td>55.6%</td>
<td>38.0%</td>
<td>0.004</td>
</tr>
</tbody>
</table>
Fish oil for sirolimus-induced hypertriglyceridemia
Recommendations

- Fibrate?
  - Total cholesterol: TG
- Dietary changes
  - Very low fat
- Medication change
  - Tacrolimus or everolimus
### Lipoprotein Profile 12/7/12

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
<th>Status</th>
<th>Remark</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDL-P (total) 25.0 umol/L</td>
<td></td>
<td>Low Risk: &gt;34.9</td>
<td>Insulin Sensitive: &gt;21.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Intermediate: 34.9 - 26.7</td>
<td>Insulin Intermediate: 21.2 - 29.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High Risk: &lt;26.7</td>
<td>Insulin Resistant: &lt;20.4</td>
</tr>
<tr>
<td>HDL-P (total) 25.0 umol/L</td>
<td></td>
<td>Low Risk: &gt;21.2</td>
<td>Insulin Sensitive: &gt;3.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Intermediate: 9.6 - 8.9</td>
<td>Insulin Intermediate: 7.6 - 8.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High: &gt;8.5</td>
<td>Insulin High: &gt;52.5</td>
</tr>
<tr>
<td>LDL Particle Number 717 nmol/L</td>
<td></td>
<td>Low: &lt;1000</td>
<td>LP-IR Score (0-100) 75</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Moderate: 1000 - 1299</td>
<td>- REFERENCE VALUE --</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Borderline-High: 1300 - 1599</td>
<td>- REFERENCE VALUE --</td>
</tr>
<tr>
<td></td>
<td></td>
<td>High: 1500 - 2000</td>
<td>- REFERENCE VALUE --</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Very High: &gt;2000</td>
<td>- REFERENCE VALUE --</td>
</tr>
<tr>
<td>Large VLDL-P 25.7 nmol/L</td>
<td></td>
<td>Low Risk: &gt;1000</td>
<td>Small LDL-P 717 nmol/L</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Intermediate: 717 - 526</td>
<td>- REFERENCE VALUE --</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Borderline: 527 - 639</td>
<td>Insulin Sensitive: &lt;117</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Insulin Resistant: &gt;839</td>
<td>Intermediate: 117 - 526</td>
</tr>
<tr>
<td>Small LDL-P 717 nmol/L</td>
<td></td>
<td>Low: &lt;1000</td>
<td>Borderline-High: 1300 - 1599</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Moderate: 1000 - 1299</td>
<td>High: 1500 - 2000</td>
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<tr>
<td>Large HDL-P 3.4 umol/L</td>
<td></td>
<td>Low Risk: &gt;3.4</td>
<td>HDL-C 36 mg/dL</td>
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<tr>
<td></td>
<td></td>
<td>Intermediate: 3.4 - 3.1</td>
<td>- REFERENCE VALUE --</td>
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<tr>
<td></td>
<td></td>
<td>Insulin Resistant: &gt;3.4</td>
<td>Desirable: &gt;= 40</td>
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<tr>
<td>VLDL Size 80.8 nm</td>
<td></td>
<td>Low Risk: &gt;159</td>
<td>Triglycerides 364 mg/dL</td>
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<tr>
<td></td>
<td></td>
<td>Intermediate: 129 - 159</td>
<td>- REFERENCE VALUE --</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Insulin Resistant: &gt;159</td>
<td>Desirable: &lt;150</td>
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<tr>
<td>Total Cholesterol 115 mg/dL</td>
<td></td>
<td>Low Risk: &gt;159</td>
<td>Total Cholesterol 115 mg/dL</td>
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<tr>
<td></td>
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<td>Intermediate: 129 - 159</td>
<td>- REFERENCE VALUE --</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Insulin Resistant: &gt;159</td>
<td>Desirable: &lt;= 200</td>
</tr>
</tbody>
</table>

**LDL Size 19.5 nm**
- REFERENCE VALUE --
Insulin Sensitive: >21.2
Intermediate: 21.2 - 29.4
Insulin Resistant: <20.4

**HDL Size 8.8 nm**
- REFERENCE VALUE --
Insulin Sensitive: >3.6
Intermediate: 9.6 - 8.9
Insulin Resistant: <8.9

**LDL-C (calculated) <10 mg/dL**
- REFERENCE VALUE --
Optimal: <100
Near or above optimal: 100 - 129
Borderline-High: 130 - 159
High: 160 - 190
Very High: >190

**HDL-C 36 mg/dL**
- REFERENCE VALUE --
Desirable: >= 40

**Triglycerides 364 mg/dL**
- REFERENCE VALUE --
Desirable: <150
Basis of LP-IR score
Follow-up

- Changed from sirolimus to tacrolimus on 12/6
- CBC no longer lipemic the following morning
- Triglycerides 12/10: 650
- Lipid panel 12/12: Total cholesterol 142, HDL 41, calc LDL 60, direct LDL 82, TG 207
References