28 Year-old Male w/ Uncontrolled Type 2 Diabetes, Bipolar Disorder Presents with Epigastric Pain

Jess Hwang
9/27/12
HPI

- Presented to an OSH with epigastric pain, diarrhea.
- + fevers up to 104.9
- 1 year ago had a similar presentation, was found to have pancreatitis from elevated hypertriglyceridemia
- Transferred to UCMC because he had a CT concerning for possible fluid collection
Diabetes history

- Diagnosed 2 years ago
- Was supposed to be taking insulin but stopped this over a year ago, does not remember his regimen
- Never checks blood sugars at home
Bipolar history

- Diagnosed 15 years ago when parents got divorced
- Last major manic episode was in 2009 was when he took a hammer to a car that was not his
PMHx
- Bipolar disorder
- HTN

SHx
- Tobacco - 2 cigs/day
- Marijuana
- EtOH - 1 beer/wk

FHx
- No dyslipidemia
- No heart disease
- No diabetes

Meds
- Depakote 1000mg qAM
- Depakote 1250mg qPM
- Lithium 600mg BID
- Thorazine 100mg qAM
- Thorazine 200mg qPM
Physical Exam

Vitals: 102.2 280lb 146/90, 119, 20, 95%

HEENT: PERRLA, EOMI

Neck: no thyromegaly or nodules

CV: tachycardic, regular rhythm, no murmurs

Resp: no rales or rhonchi

GI: epigastric tenderness, no rebound or guarding

Skin: papular lesions c/w xanthomas

Psych: normal mood, affect
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDL</td>
<td>72 (40-100)</td>
</tr>
<tr>
<td>Non-HDL</td>
<td>1092 (RR 0-159)</td>
</tr>
<tr>
<td>TSH</td>
<td>4.0, FT4 1.26 (0.9-1.7)</td>
</tr>
<tr>
<td>HbA1c</td>
<td>11.2 %</td>
</tr>
<tr>
<td>Lipase</td>
<td>988 (13-60)</td>
</tr>
<tr>
<td>TG</td>
<td>8590 (0-149)</td>
</tr>
</tbody>
</table>

**Initial Labs HD #1**
### DDx for Hypertriglyceridemia

#### TABLE 2. Causes of hypertriglyceridemia

<table>
<thead>
<tr>
<th>Category</th>
<th>Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary hypertriglyceridemia</td>
<td>FCHL&lt;br&gt;FHTG&lt;br&gt;Familial dysbetalipoproteinemia&lt;br&gt;FHA&lt;br&gt;Familial chylomicronemia and related disorders</td>
</tr>
<tr>
<td>Primary genetic susceptibility</td>
<td>Metabolic syndrome&lt;br&gt;Treated type 2 diabetes</td>
</tr>
<tr>
<td>Secondary hypertriglyceridemia</td>
<td>Excess alcohol intake&lt;br&gt;Drug-induced (e.g. thiazides, β-blockers, estrogens, isotretinoin, corticosteroids, bile acid-binding resins, antiretroviral protease inhibitors, immunosuppressants, antipsychotics)&lt;br&gt;Untreated diabetes mellitus&lt;br&gt;Endocrine diseases&lt;br&gt;Renal disease&lt;br&gt;Liver disease&lt;br&gt;Pregnancy&lt;br&gt;Autoimmune disorders</td>
</tr>
</tbody>
</table>

The Endocrine Society 2012 Guidelines on Hypertriglyceridemia
CT abdomen/pelvis

Day #1: Acute pancreatitis. Hazy appearance around pancreatic body and tail. Hepatomegaly with fatty infiltration noted.

Day #5: Severe inflammation of the pancreatic tail c/w acute pancreatitis. Fluid collection adjacent to the pancreatic tail measuring 21 x 9 x 12 cm. Consolidation LLL lung, atelectasis vs infiltrate.
<table>
<thead>
<tr>
<th></th>
<th>9/3</th>
<th>9/4</th>
<th>9/5</th>
<th>9/11</th>
</tr>
</thead>
<tbody>
<tr>
<td>TG</td>
<td>8590</td>
<td>P L A S M A P H E R E S I S</td>
<td>1213</td>
<td>161</td>
</tr>
<tr>
<td>Lipase</td>
<td>988</td>
<td>29</td>
<td>29</td>
<td></td>
</tr>
<tr>
<td>Amylase</td>
<td></td>
<td>14</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Hypertriglyceridemia
Pancreatitis

- Hypertriglyceridemia- 1º vs 2º
- 1-4% of cases of acute pancreatitis
- Risk is related to degree of elevation (usually > 1000 mg/dL)
- Pathogenesis
  - TG+Lipase → FFA formation
  - Chylomicrons → pancreatic capillary congestion
Clinical Questions

- Antipsychotics/Bipolar medications causing metabolic syndrome?
- Plasmapheresis in hypertriglyceridemia pancreatitis?
- Combination therapy with fibrates and statins in hypertriglyceridemia and T2DM?
Antipsychotics & Metabolic Disturbances

H1 receptor blockade
5HT2C receptor blockade
M3 cholinergic receptor antagonism

## Antipsychotics & Metabolic Disturbances

<table>
<thead>
<tr>
<th>Antipsychotic</th>
<th>Risk for weight gain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clozapine</td>
<td>+++</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>+++</td>
</tr>
<tr>
<td>Risperidone†</td>
<td>++</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>+</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>±</td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>±</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Antipsychotic</th>
<th>Expert consensus</th>
<th>CATIE</th>
<th>FDA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clozapine</td>
<td>Definite risk</td>
<td>ND</td>
<td>Diabetes warning</td>
</tr>
<tr>
<td>Olanzapine</td>
<td>Definite risk</td>
<td></td>
<td>Diabetes warning</td>
</tr>
<tr>
<td>Risperidone†</td>
<td>Inconclusive</td>
<td>Intermediate</td>
<td>Diabetes warning</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>Inconclusive</td>
<td>Definite risk</td>
<td>Diabetes warning</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>±Limited data</td>
<td>Low risk</td>
<td>Diabetes warning</td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>±Limited data</td>
<td>ND</td>
<td>Diabetes warning</td>
</tr>
</tbody>
</table>

Bipolar Disorder & Metabolic Disturbances

- Kemp et al. looked at 2 studies exploring the relationship between lithium and valproic acid to metabolic disorders. Conclusion - BMI was a significant predictor of non-remission.
- Biological mechanisms common to bipolar and metabolic syndrome:
  - Abnormal glucocorticoid signaling, oxidative stress, altered energy biosynthesis, autonomic nervous system dysfunction
  - Implications for future avenues of treatment
Triglyceride improvement w/plasmapheresis

Our patient

J Clinical Apheresis 2010; 25:229-234.
Table 1. Apheresis in hypertriglycerideridemic pancreatitis (reports with five or more patients)

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of patients</th>
<th>No. of patients with complete recovery (%)</th>
<th>Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chen et al. (56)</td>
<td>20</td>
<td>0 (100)</td>
<td>0</td>
</tr>
<tr>
<td>Yeh et al. (64)</td>
<td>17</td>
<td>13 (76.5)</td>
<td>2 (11.8)</td>
</tr>
<tr>
<td>Kyriakidis et al. (61)</td>
<td>10</td>
<td>9 (90)</td>
<td>1 (10)</td>
</tr>
<tr>
<td>Kadikoylu et al. (59)</td>
<td>7</td>
<td>7 (100)</td>
<td>0</td>
</tr>
<tr>
<td>Lennertz et al. (62)</td>
<td>5</td>
<td>5 (100)</td>
<td>0</td>
</tr>
</tbody>
</table>

AJG 2009; 104:984-991.
Fibrate + Statin Combination Therapy

- Additions to Endo Society Guidelines 2012
  - Addition of statins in mild-mod hyperTG (150-1000) and high non-HDL cholesterol
- ACCORD-Lipid trial 2010
  - General diabetics: no benefit from combination therapy
  - Sub analysis supports combination therapy in hypertriglyceridemia (TG > 204 mg/dL) and low HDL (HDL < 34 mg/dL)
Fibrate + Statin Combination Therapy

If triglycerides 200-499 mg/dL after LDL goal is reached, consider adding drug if needed to reach non-HDL goal:

- intensify therapy with LDL-lowering drug, or
- add nicotinic acid or fibrate to further lower VLDL.

If triglycerides ≥500 mg/dL, first lower triglycerides to prevent pancreatitis:

- very low-fat diet (≤15% of calories from fat)
- weight management and physical activity
- fibrate or nicotinic acid
- when triglycerides <500 mg/dL, turn to LDL-lowering therapy.

ATP III Guidelines 2001
Hospital Course

- Follow-up appointments
  - Psych: bipolar therapy
  - GI: repeat CT abdomen
  - Endo: hyperTG w/u, DM management

- Discharged home on:
  - Tricor 145 mg daily
    - Lantus 33U qHS, Novolog correction factor
Take Home Points

- Management of hypertriglyceridemic pancreatitis including plasmapheresis for severe cases
- Antipsychotic/Bipolar therapy and metabolic syndrome risk
- Indications for combination statin/fibrate therapy
References