79 year-old Man with Hypoglycemia

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Endorama
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79-year-old man with past medical history significant for coronary artery disease, ischemic cardiomyopathy, peripheral vascular disease, and hypertension who initially presented to Morris Hospital with confusion and slurred speech.

- Sudden onset of lightheadedness, generalized weakness, and diaphoresis.
- EMS found him with a blood sugar of 22.
- No other similar episodes prior but had episodes of diaphoresis for the 3-4 days prior to admission.
- Lost 40 lbs in the last 2 months, intentionally with diet and exercise to help with his cardiac issues.
- Wife seemed to think his appetite was poor; he denied this.
- Wife has diabetes mellitus type 2, treated with metformin only.
Morris Hospital course

- Required D20 gtt.
- Cort stim: 6 → 21.8 → 27.
- CT abdomen/pelvis showed no evidence of malignancy, normal pancreas.
  - Per notes, ?small mass on the pancreas.
- Colonoscopy unrevealing.
- PSA 3.8.
- Endocrine consult:
  - C-peptides of 12.5, 11.3, 17.3, no corresponding glucose readings.
  - Proinsulin 60.
  - Negative sulfonylurea screen.
- Started hydrocortisone 100 mg IV BID.
- Transferred for further work-up of insulinoma.
Past Medical History

- Coronary artery disease:
  - s/p CABG x 7 in 1997
  - Cardiac cath on 9/1/11 with drug eluting stent to saphenous right vein graft to the right coronary artery
- Ischemic cardiomyopathy, EF 35→65%
- Hypertension
- Dyslipidemia
- Peripheral vascular disease
- Moderate aortic stenosis
- Carotid stenosis
- Diverticulosis

Allergies: NKDA

Medications:
- Hydrocortisone 100 mg BID
- Atenolol 50 mg daily
- Amlodipine 5 mg daily
- Aspirin 81 mg daily
- Clopidogrel 75 mg daily
- Simvastatin 40 mg daily
- Furosemide 20 mg daily
- Esomeprazole 40 mg daily
- Zolpidem 5 mg daily
- Multivitamin daily
- Heparin SQ
Past Medical History cont.

- **Social History:**
  - Lives with wife, has 2 grown children.
  - Previously worked as a manager for an explosives plant.
  - No history of tobacco, etoh use.

- **Family History:**
  - Mother with uterine cancer.
  - No diabetes, liver disease.

- **ROS:**
  - Weight loss
  - Diarrhea since hospitalization
  - Urinary frequency since hospitalization
Physical Exam

- T 96.8, BP 135/61, Pulse 60, Resp 18, SpO2 98% on room air
- Ht 178 cm (5' 10.08"), Wt 81.8 kg (180 lb 5.4 oz), BMI 25.82 kg/m²
- Constitutional: Patient appears well-developed, well-nourished, in no acute distress.
- HEENT: Conjunctivae are not injected. Sclerae anicteric. Pupils are equal, round, and reactive to light. Extraocular movements are intact.
- Neck: Supple. No thyromegaly or nodules palpated.
- Cardiovascular: Regular rhythm and rate. III/VI systolic murmur appreciated. Intact distal pulses.
- Pulmonary/Chest: Normal respiratory effort. No wheezes or crackles.
- Abdomen: Normoactive bowel sounds. Soft, nontender, nondistended.
- Musculoskeletal: 1+ peripheral edema.
- Neurological: Alert and oriented to person, place, and date.
- Skin: Skin is warm and dry. Appears tan.
- Psychiatric: Normal mood and affect.
Laboratory Data

Ca 9.4, Phos 2.1, Mg 1.9
Albumin 3.9
TB 0.6, alk phos 60, AST 46, ALT 53
INR 1.0, PTT 26.8
Assessment and Plan

- Please stop hydrocortisone.
- Obtain critical sample.
- Please check ACTH.
  - If he does have primary adrenal insufficiency, his ACTH should still be elevated despite recent exposure to hydrocortisone.
**Critical Samples**

<table>
<thead>
<tr>
<th>Time</th>
<th>Serum Glucose</th>
<th>Insulin (uIU/mL)</th>
<th>C-peptide (pmol/mL)</th>
<th>Proinsulin (pmol/L)</th>
<th>ß-hydroxybutyrate (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>22:00</td>
<td>59 mg/dL</td>
<td>116 (28.5)</td>
<td>2.89 (0.30-2.35)</td>
<td>4800 (3-20)</td>
<td>&lt;0.10 (&lt;0.30)</td>
</tr>
<tr>
<td>23:00</td>
<td>65</td>
<td>108 (&lt;28.5)</td>
<td>2.09 (0.30-2.35)</td>
<td>3800 (3-20)</td>
<td>&lt;0.10 (&lt;0.30)</td>
</tr>
<tr>
<td>24:00</td>
<td>47</td>
<td>116 (28.5)</td>
<td>2.09 (0.30-2.35)</td>
<td>4800 (3-20)</td>
<td>&lt;0.10 (&lt;0.30)</td>
</tr>
<tr>
<td>1:00</td>
<td>46</td>
<td>108 (&lt;28.5)</td>
<td>2.09 (0.30-2.35)</td>
<td>3800 (3-20)</td>
<td>&lt;0.10 (&lt;0.30)</td>
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Other tests:
- 10/28 7AM ACTH <5.0
- 10/30 4AM ACTH <5.0, cortisol 10.3
Work-up of Hypoglycemia

Serum glucose 59 mg/dL
Insulin 116 uIU/mL (<28.5)
C-peptide 2.89 pmol/mL (0.30-2.35)
Proinsulin 4800 pmol/L (3-20)
β-hydroxybutyrate <0.10 mmol/L

Plan:
Check insulin antibody
Obtain better imaging of pancreas

Insulinoma: 34 patients
Insulin 43.9 +/- 28.7

Imaging

CTA pancreas:
No evidence of insulinoma
Further imaging/testing?

- Retrospective review of 40 patients with insulinomas:
  - CT scan: 62% sensitivity
  - MRI: 82% sensitivity
  - Endoscopic ultrasound: 94% sensitivity

- Retrospective review of 28 patients with insulinomas:

<table>
<thead>
<tr>
<th>Imaging technique</th>
<th>No. performed (%)</th>
<th>No. localised (%)</th>
<th>No. where localisation corresponds to histology (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT</td>
<td>23</td>
<td>10 (43.5%)</td>
<td>10 (100.0%)</td>
</tr>
<tr>
<td>MRI</td>
<td>17</td>
<td>12 (70.6%)</td>
<td>11 (83.3%)</td>
</tr>
<tr>
<td>Endoscopic US</td>
<td>21</td>
<td>18 (85.7%)</td>
<td>16 (88.9%)</td>
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<tr>
<td>Octreotide</td>
<td>15</td>
<td>5 (33%)</td>
<td>4 (80.0%)</td>
</tr>
<tr>
<td>Angiography</td>
<td>30a</td>
<td>29 (96.6%)</td>
<td>29 (100.0%)</td>
</tr>
<tr>
<td>ASVS</td>
<td>30a</td>
<td>28 (93.3%)</td>
<td>28 (100%)</td>
</tr>
</tbody>
</table>

Angiography and arterial stimulation venous sampling

- **Angiography**
  - Insulinomas are seen as well-defined, round vascular blushes.

- **ASVS**
  - Hyperosmotic calcium causes degranulation of cells within the neoplasm.

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Case cont.

- Prior to proceeding with invasive testing, attempt to obtain critical sample when blood glucose <45.
- Blood sugars maintained in the 70-150.
- Refused to stay beyond 11/5 AM.
- Discharged with glucometer, instructed to have outpatient follow up with Endocrinology for 72 hour fast.
- Insulin antibody returned 4.59 nmol/L (0-0.02)
Insulin Autoimmune Syndrome

- Antibody directed against endogenous insulin.
  - Hypoglycemia caused by binding and release of insulin from the antibodies.
  - After meals, usually hyperglycemic initially followed by hypoglycemia a few hours later.
- Associated with inappropriately elevated insulin levels (>100), postprandial (42%) and fasting (31%) hypoglycemia (both 24%).
- Occurs most frequently in men and women between ages 40-80.
- Associated with rheumatological diseases, hematologic diseases, and medications (captopril, imipenem, PTU, hydralazine, procainamide, isoniazid, penicillin G).
- Diagnostic Features:

<table>
<thead>
<tr>
<th>TABLE 1. Baseline Endocrine Characteristics of 2 Patients With Insulin Autoimmune Syndrome, Present Report*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient</td>
</tr>
<tr>
<td>---------</td>
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<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
</tbody>
</table>

Our patient   (59)      116      8.7      4800   +

*Our patient's data includes HbA1c (59), blood glucose (116), insulin (8.7), and anti-insulin antibodies (positive) as indicated.*

Insulin Autoimmune Syndrome

- **Treatment:**
  - Low carbohydrate meals to prevent postprandial hypoglycemia.
  - Prednisone used in 38% of patients.
    - Lowers the titer of insulin antibodies.
  - Variable results with acarbose, somatostatin, and diazoxide.
  - Discontinuation of incriminating drugs.
- **Prognosis:** Improved or resolved in majority of patients within 3-6 months.
Take Home Points

- Chronic renal failure is the number one cause of hypoglycemia in non-diabetic hospitalized patients.
- Invasive studies are better at localizing insulinomas than noninvasive studies.
- Angiography with arterial calcium stimulation is the most sensitive test for localization of insulinomas.
- Checking for insulin antibodies can save an invasive procedure.
- Insulin autoimmune syndrome is rare.
References