



53 year old Female with Hypoglycemia

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HPI

- 53 yo F referred to the endocrine clinic for hypoglycemia x 1 year.
- History of a non-secreting metastatic neuroendocrine tumor diagnosed 12 years ago.
- Admitted 1 year ago to an outside hospital with a documented blood glucose of 30. No further evaluation for hypoglycemia. Given accu-check.
- Blood glucose 50 – 70 in the morning after fasting >8 hrs with symptoms of shakiness and tooth pain, which resolved after eating.

Past Medical History

Neuroendocrine tumor diagnosed 1999:

- GIB: work-up revealed duodenal mass
 - EGD: biopsy of duodenal mass - normal duodenal mucosa
 - X-lap:
 - *Duodenal mass* in wall of 2nd part of duodenum – not bx
 - *Peripancreatic nodule* and *portal lymph node* –
- Pathology: **metastatic poorly differentiated neuroendocrine tumor, +chromogranin, +synaptophysin**
- Duodenal mass bypassed for obstructive symptoms because of metastatic diagnosis (proximal jejunum → stomach)
 - Repeat CT 1999 – 2011 stable
 - No further treatment

Past Medical History

Neuroendocrine tumor
GERD
Iron-deficiency anemia

Medications

Nexium
Creon
Neurontin
Ferrous sulfate
Tylenol prn

NKDA

Family History

F: DM2, HTN
M: DM2
4 healthy children
No pancreatic CA
No neuroendocrine tumors

Social History

Works in housekeeping
No tobacco or illicits
Rare EtOH

Physical Exam

VS: **BP:** 130/70 **HR:** 56 **Ht:** 5'6 **Wt:** 187 lbs **BMI:** 30

Gen: Well-appearing female in NAD

HEENT: anicteric sclera

Neck: thyroid normal size/texture, no nodules

Chest: CTAB

CV: +S1/S2, no LE edema

Abd: midline incision, +BS, soft, nontender, nondistended, no
hepatosplenomegaly, no masses

Skin: no rash, normal temperature/texture

Lymph: no lymphadenopathy

ROS

- Shakiness and tooth pain with fasting
- 10 pound unintentional weight gain over the past year
- Daily hot flashes since menopause at age 42
- No chest pain or palpitations
- No SOB or wheezing
- No abdominal pain/nausea/vomiting/diarrhea
- No history of diabetes mellitus
- No history of steroid use

Labs – Hospitalization 1 year ago

Serum glucose: 74 mg/dL

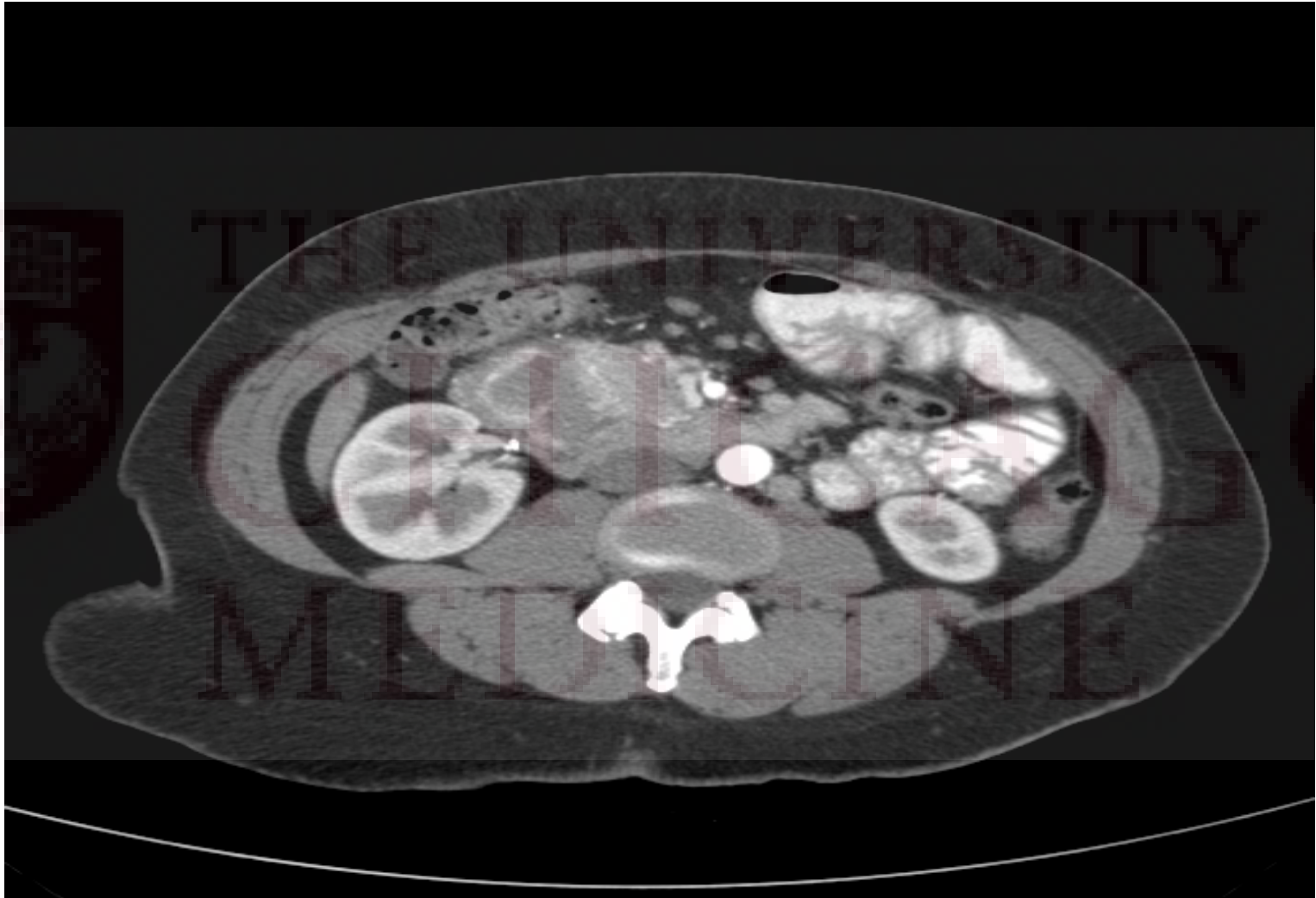
Insulin level: 16.8 uIU/mL (<28.5)

Cortisol: 19 mcg/dL (6am)

Sulfonylurea screen: negative

	1/2002	9/2006	11/2007	4/2010	3/2011
Chromogranin A level	37 ng/mL (6-39)	186 pg/mL (<225)	139 pg/mL (<225)	176 pg/mL (<225)	244 pg/mL (<225)

CT C/A/P



Peripancreatic mass 4.1 x 2.5 cm, slightly smaller compared to previous study.
Normal liver.

Labs

Blood glucose log

	7 am	noon	8pm
4/10/11	68		
4/14/11	54		
4/15/11		77	
4/18/11	52		72
4/23/11	56		
4/27/11	58		

HgbA1c: 5.8

140	109	15	62
4.0	24	0.9	

Ca: 9.0

LFTs normal

TSH: 1.2

	9.3	
6.3		227

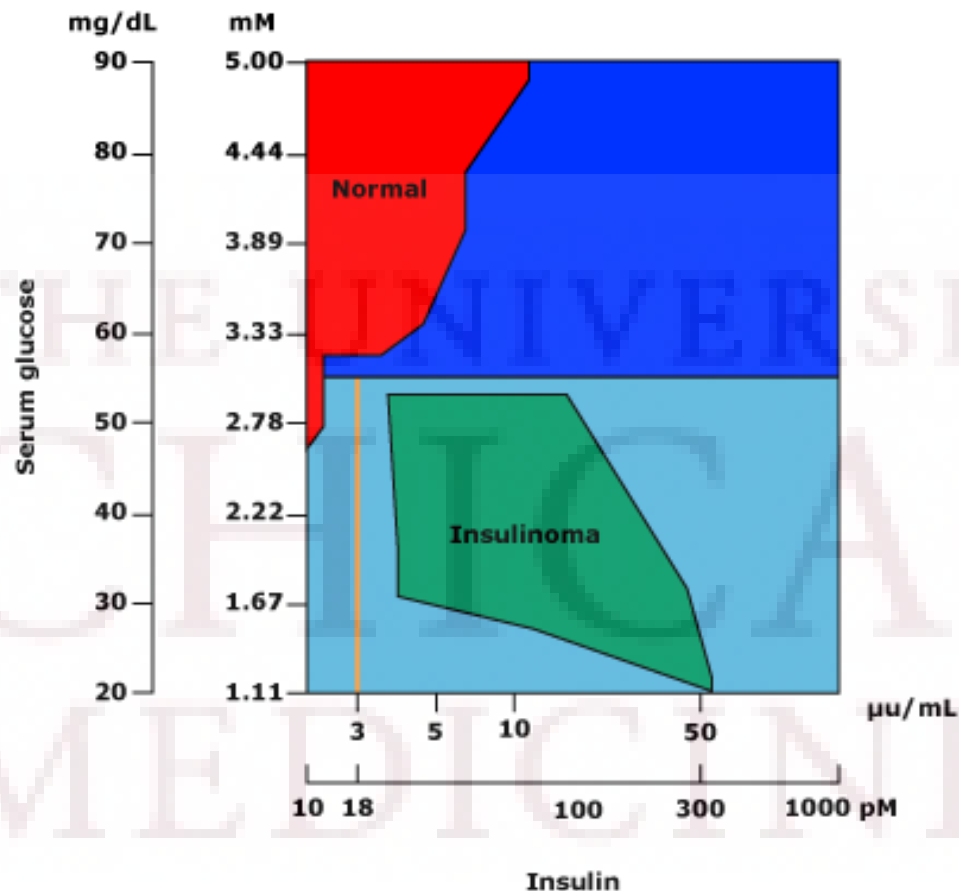
MCV: 72.3

Ferritin: 10

Formal Fast

	10 hours (8am)	14 hours (noon)
Accu-check	52	48 (symptoms)
Serum glucose	62	52
Insulin (<28.5 uIU/mL)	17.3	10.9
Proinsulin (3 – 20 pmol/L)	18	18
C-peptide (0.3 – 2.35 pmol/mL)	0.92	0.95
Cortisol (mcg/dL)	20	18
Beta-hydroxybutyrate (<0.3 mmol/L)	<0.1	0.14

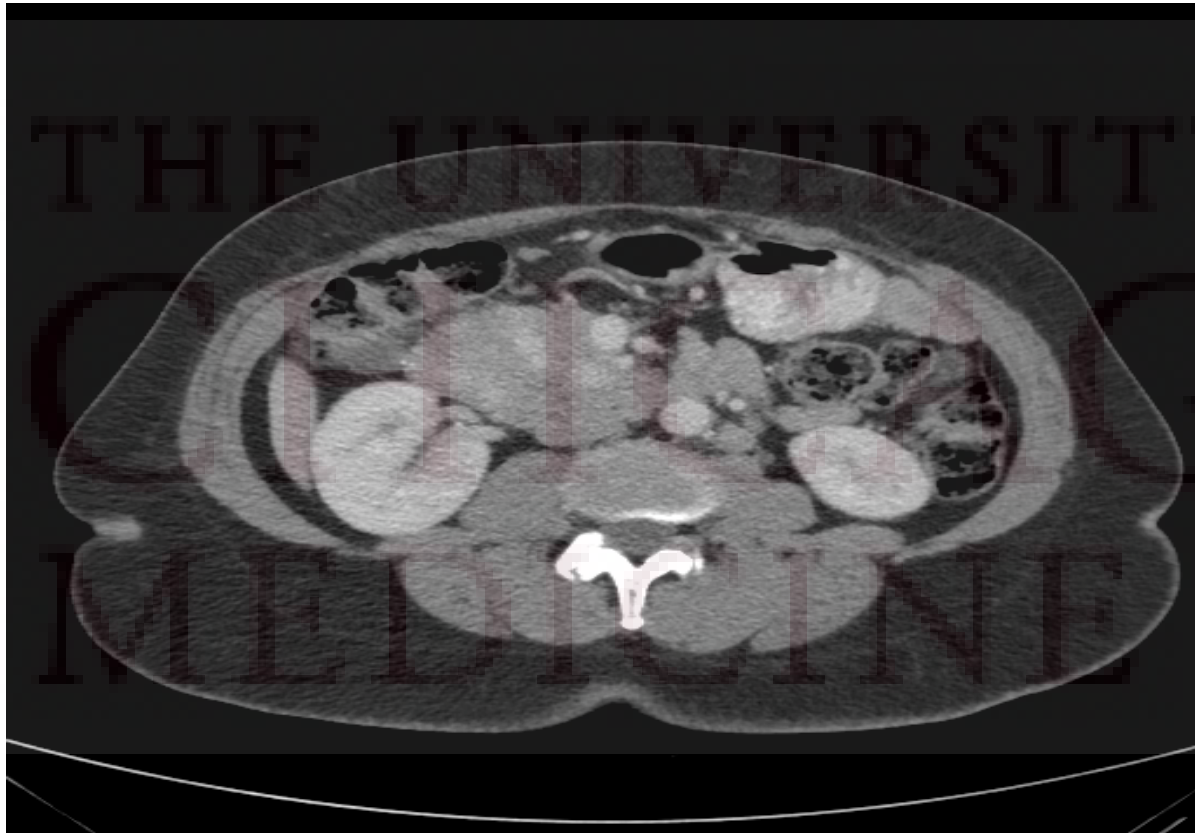
Plasma glucose and insulin concentrations after a prolonged fast



Relation between plasma glucose and insulin concentrations in normal subjects and patients with insulinoma after a prolonged fast.

Data from: Service, FJ. Diagnostic approach to adults with hypoglycemic disorders. *Endocrinol Metab Clin North Am* 1999; 28:519.

Repeat CT



Peripancreatic mass: 4.6 x 2.8 cm, previously 4.2 x 2.6 cm.
Increased retroperitoneal lymphadenopathy, index node 1.4 x 1.2 cm
previously 1.2 x 1.1 cm. Normal liver.

Octreotide Scan



Two adjacent tubular foci of mild radiotracer uptake in the central abdomen that correspond to tumor on CT. Normal physiologic bowel activity vs mildly octreotide avid tumor.

Utility of Octreotide Scan

- 90% of NETs have a high concentration of somatostatin receptors – can use radiolabeled octreotide to image.
- Most effective in visualizing gastrinomas, glucagonomas, nonfunctioning pancreatic tumors.
- Insulinomas and poorly differentiated NETs express low levels of somatostatin receptors.
- Radiolabeled octreotide might be predictive of a clinical response to therapy with somatostatin analogs.

Lamberts SW. NEJM. 1990.

Modlin IM. Gastroenterology. 1997.

Impression/Recommendation

- Increase in tumor growth for the first time in 12 years AND
- Elevated levels of insulin relative to the low blood glucose
- Start octreotide

Neuroendocrine tumors

- Can non-functioning neuroendocrine tumors become functioning?
 - Review of the literature: likely insidious onset
- Functional and non-functional NETs are difficult to separate based on histopathology, immunohistochemistry, somatostatin receptor expression or scintigraphy.
- Only differentiating features are symptoms.

Take Home Points

- True documented hypoglycemia should be evaluated with a formal fast.
- Neuroendocrine tumors are rare, should be monitored closely for function, and consider treatment before functionality is obvious.