63 year-old Man with Hypoglycemia

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Endorama

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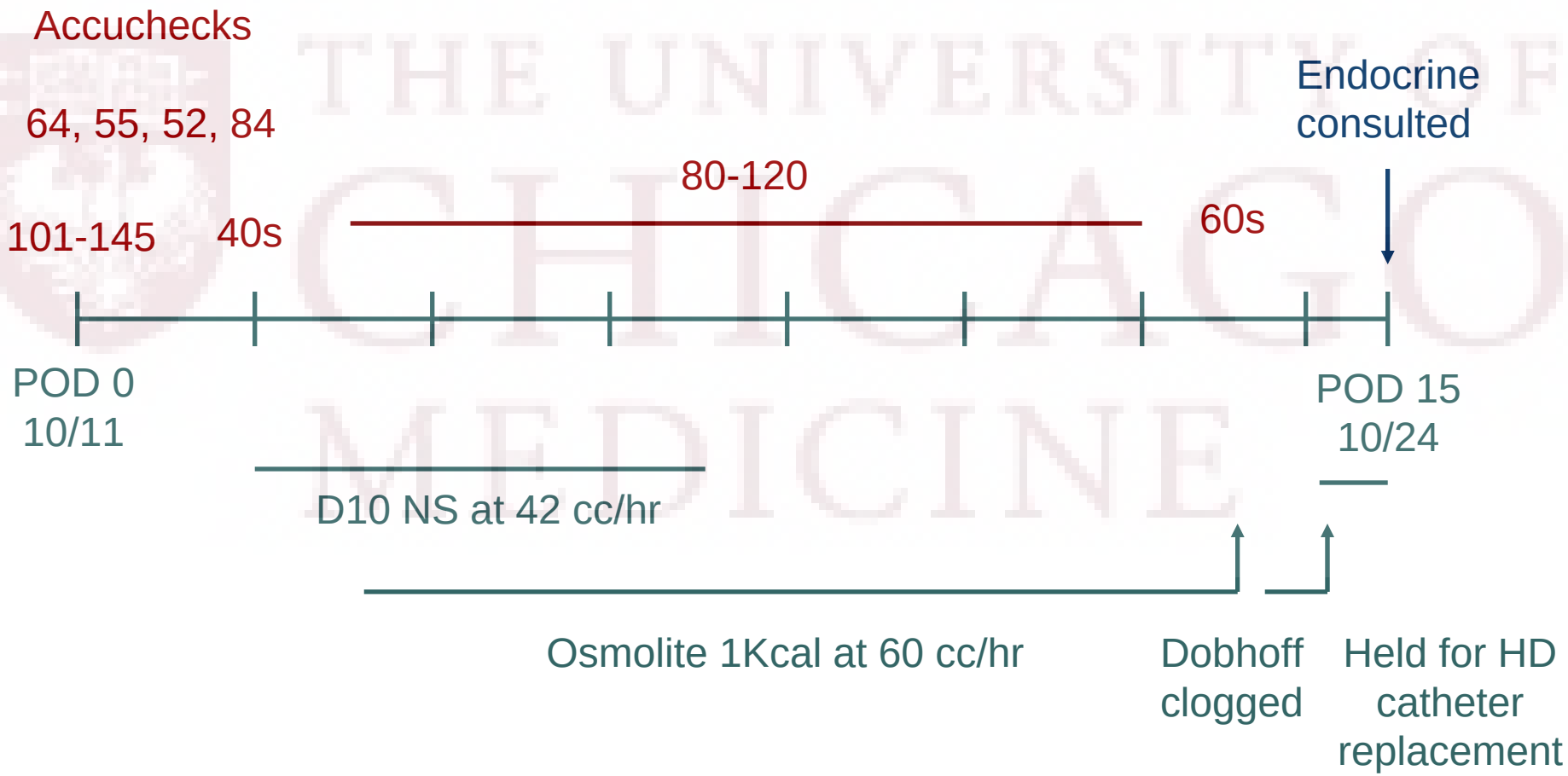
History of Present Illness

- 63-year-old man with past medical history significant for systolic CHF (EF 25%), critical aortic stenosis (valvular area of 0.8 cm^2), CAD, and ESRD on HD who was discharged earlier in the day after hospitalization for decompensated heart failure.
  - Hospitalization: 9/23/11-10/2/11
    - Aortic valvuloplasty
    - Complicated by watershed infarction noted on MRI
  - After leaving the hospital, he went to McDonald's, had a hamburger, and acutely developed shortness of breath and chest pain.
  - Underwent bioprosthetic AVR and CABG.
    - Complicated by sepsis, presumed to be secondary to line infection.
    - Noted to be persistently hypoglycemic POD #1

Glucose Trend

- Hospitalization: 9/23/11-10/2/11
  - Serum glucose: 64-114
  - Accuchecks: 67-120
- Current Hospitalization: 10/2/11-10/11/11
  - Serum glucose: 71-119
  - Accuchecks: 85-161
- Aortic valve replacement and CABG: 10/11/11
- POD #1:
  - Serum glucose: 53
  - Accuchecks: 64, 55, 52, 84

Glucose Trend cont.



Past Medical History

- Past Medical History
  - Systolic congestive heart failure, EF 25%
  - Severe aortic stenosis
  - Coronary artery disease
  - h/o stroke in 2001 with expressive asphasia
  - ESRD on HD for past 3 years
  - Hypertension
  - Hyperlipiemia
- Allergies: NKDA
- Medications:
  - Ampicillin 1 gram q12 hr
  - ASA 81 mg daily
  - Carvediol 6.25 mg BID
  - Lisinopril 5 mg daily
  - Simvastatin 40 mg daily
  - Thiamine 100 mg daily
  - Folic acid 1 mg daily
  - Ipratropium nebulizer 6 hrs
  - Mucomyst nebulizer q6 hrs
  - Sennosides-Docusate
  - Heparin SQ

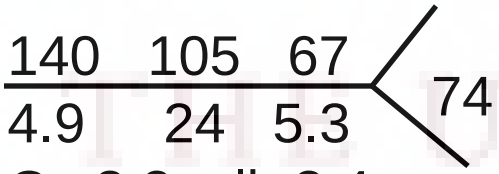
Past Medical History cont.

- Social History:
  - Lives with his wife, has 4 grown children
  - Previously worked in a funeral home.
  - Denies history of tobacco use.
  - Prior heavy ETOH user until 2001: ½ pint per day from 1997-2001
  - Denies history of illicit drugs
- Family History:
  - Sister with DM2.
  - No family history of cancer.
- ROS:
  - Unable to obtain due to delirium.
  - Unintentional weight loss: 187 lbs to 132 lbs over 2 years.
  - Per wife, appetite was good at home and the other hospital.

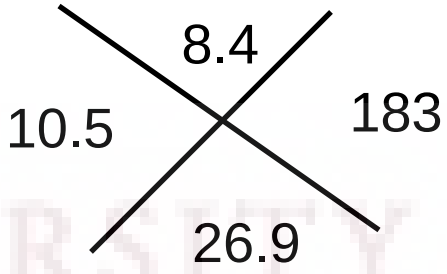
Physical Exam

- T 95.7, BP 107/70, Pulse 91, Resp 35, SpO2 100% on trach collar
- Ht 177.8 cm (5' 10"), Wt 59.9 kg (132 lb 0.9 oz), BMI 18.95 kg/m^2
- Constitutional: Patient appears chronically ill. Follows commands. Does not answer questions. Mildly lethargic.
- HEENT: Conjunctivae are not injected. Sclerae anicteric. Pupils are equal, round, and reactive to light.
- Neck: Trach collar in place.
- Cardiovascular: Regular rhythm and rate. Diminished distal pulses.
- Pulmonary/Chest: Normal respiratory effort. Diffuse rhonchi. Incision c/d/i.
- Abdomen: Normoactive bowel sounds. Soft, nontender, nondistended.
- Musculoskeletal: LUE edematous.
- Neurological: Weak grip strength bilaterally.
- Skin: Skin is warm and dry.
- Psychiatric: Difficult to assess mood and affect.

Laboratory Data



Ca 8.2, alb 3.4



84%N, 7%L, 6% M, 2%E

TB 1.1, DB 0.6, alk phos 57, AST 81, ALT 9
INR 1.3
Prealbumin 3 mg/dL (21-41)

9/28: HgbA1c 5.1%
10/13 12PM Cortisol 23.7
10/17: 2AM Cortisol 13.9
10/23: TSH 3.37

Causes of Hypoglycemia

TABLE 1. Causes of hypoglycemia in adults

- Ill or medicated individual
  - 1. Drugs
    - Insulin or insulin secretagogue
    - Alcohol
    - Others (Table 2)
  - 2. Critical illnesses
    - Hepatic, renal, or cardiac failure
    - Sepsis (including malaria)
    - Inanition
  - 3. Hormone deficiency
    - Cortisol
    - Glucagon and epinephrine (in insulin-deficient diabetes mellitus)
  - 4. Nonislet cell tumor
- Seemingly well individual
  - 5. Endogenous hyperinsulinism
    - Insulinoma
    - Functional β-cell disorders (nesidioblastosis)
      - Noninsulinoma pancreatogenous hypoglycemia
      - Post gastric bypass hypoglycemia
    - Insulin autoimmune hypoglycemia
      - Antibody to insulin
      - Antibody to insulin receptor
    - Insulin secretagogue
    - Other
  - 6. Accidental, surreptitious, or malicious hypoglycemia

TABLE 2. Drugs other than antihyperglycemic agents and alcohol reported to cause hypoglycemia (24)

- Moderate quality of evidence (⊕⊕⊕◯)
  - Cibenzoline
  - Gatifloxacin
  - Pentamidine
  - Quinine
  - Indomethacin
  - Glucagon (during endoscopy)
- Low quality of evidence (⊕⊕◯◯)
  - Chloroquineoxaline sulfonamide
  - Artesunate/artemisin/artemether
  - IGF-I
  - Lithium
  - Propoxyphene/dextropropoxyphene
- Very low quality of evidence (⊕◯◯◯)
  - Drugs with >25 cases of hypoglycemia identified
    - Angiotensin converting enzyme inhibitors
    - Angiotensin receptor antagonists
    - β-Adrenergic receptor antagonists
    - Levofloxacin
    - Mifepristone
    - Disopyramide
    - Trimethoprim-sulfamethoxazole
    - Heparin
    - 6-Mercaptopurine
  - Drugs with <25 cases of hypoglycemia identified (see Ref. 24)

J Clin Endocrinol Metab. 2009 Mar;94(3):709-28.

Common causes of hypoglycemia in hospitalized, non-diabetic patients

- Retrospective review: 88 patients with BS <50.
- Causes found in 72% of patients, 24% with more than one.
- Common causes:
  - Chronic renal failure, 25%
  - Alcohol intoxication, 15%
  - Liver failure, 12%
  - Sepsis, 12%
  - Cancer, 12%
  - Endocrine disorders, 12%
- 16% died.

Endocr Pract. 2005 Mar-Apr;11(2):91-6.

Assessment & Plan

- Assessment:
  - Contributing factors:
    - ESRD
    - Cardiac failure
    - Malnutrition: pre-albumin 3
    - ? liver disease: history of ETOH use, slightly elevated INR
    - Sepsis: line infection
  - Rule out: insulinoma, adrenal insufficiency, malignancy
- Plan:
  - Halve the rate of dextrose infusion for 2 hours then stop.
  - Once blood sugar is <50, please draw C-peptide, insulin, pro-insulin, beta hydroxybutyrate, and cortisol levels.

Critical Sample

Insulin <2.0 uIU/mL (<28.5)
C-peptide 0.81 pmol/mL (0.30-2.35)
Proinsulin 9.5 pmol/L (3-20)
ß-hydroxybutyrate 0.11 mmol/L (<0.30)
Cortisol 13.5 mcg/dL

Work-up of Hypoglycemia

TABLE 3. Patterns of findings during fasting or after a mixed meal in normal individuals with no symptoms or signs despite relatively low plasma glucose concentrations (*i.e.* Whipple's triad not documented) and in individuals with hyperinsulinemic (or IGF-mediated) hypoglycemia or hypoglycemia caused by other mechanisms

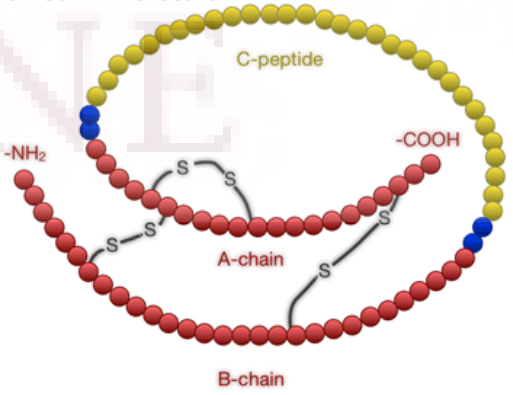
Symptoms, signs, or both	Glucose (mg/dl)	Insulin (μU/ml)	C-peptide (nmol/liter)	Proinsulin (pmol/liter)	β-Hydroxybutyrate (mmol/liter)	Glucose increase after glucagon (mg/dl)	Circulating oral hypoglycemic agent	Antibody to insulin	Diagnostic interpretation
No	<55	<3	<0.2	<5	>2.7	<25	No	No	Normal
Yes	<55	≫3	<0.2	<5	≤2.7	>25	No	Neg (Pos)	Exogenous insulin
Yes	<55	≥3	≥0.2	≥5	≤2.7	>25	No	Neg	Insulinoma, NIPHS, PGBH
Yes	<55	≥3	≥0.2	≥5	≤2.7	>25	Yes	Neg	Oral hypoglycemic agent
Yes	<55	≫3	≫0.2[a]	≫5[a]	≤2.7	>25	No	Pos	Insulin autoimmune
Yes	<55	<3	<0.2	<5	≤2.7	>25	No	Neg	IGF[b]
Yes	<55	<3	<0.2	<5	>2.7	<25	No	Neg	Not insulin (or IGF)-mediated

Neg, Negative; Pos, positive; PGBH, post gastric bypass hypoglycemia.

[a] Free C-peptide and proinsulin concentrations are low.

[b] Increased pro-IGF-II, free IGF-II, IGF-II/IGF-I ratio.

Proinsulin molecule



Accucheck 52 mg/dL
Insulin <2.0 uIU/mL (<28.5)
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ß-hydroxybutyrate 0.11 mmol/L (<0.30)
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More tests

- IGF-1: 77 ng/mL (75-212)
- IGF-II: 546 ng/mL (288-736)
- CT chest:
  - Thrombus at brachiocephalic confluence.

Follow up

- Difficult course include PEA arrest.
- Weaned off D20 gtt on 11/8. Had no further hypoglycemic episodes.
- Started on stress dose steroids for ?adrenal insufficiency.
- Cort stim: 19.3 (ACTH 215) →22.3→21.7
- Discharged to rehab on 11/15.

Risk Factors in our Patient

- ESRD: 1545 admissions of ESRD patients
  - 3.6% admitted with hypoglycemia, 32% were non-diabetic
  - Causes:

Table 1. Etiologies and mortality rate of hypoglycemic events in 56 ESRF patients

Etiology:	No (%)	Non-diabetic	Died (% of all deaths)
Hypoglycemic agents	26 (46%)	0	0 (0%)
Sepsis	22 (39%)	6	12 (66%)
Severe Malnutrition	4 (7%)	2	3 (16.5%)
Liver failure	1 (2%)	1	1 (5.5%)
Alcohol	1 (2%)	1	0
Malignancy	1 (2%)	1	1 (5.5%)
Unknown	1 (2%)	1	1 (5.5%)

  - Mechanisms:
    - Decreased degradation of insulin, sulfonylureas
    - Decreased renal gluconeogenesis
    - Hyperkalemia associated with hyperinsulinemia and hypoglycemia
    - Malnutrition in ESRD
    - Autonomic neuropathy with diminished counter-regulatory hormonal reaction to hypoglycemia

Ren Fail. 2000 Mar;22(2):219-23.

Risk Factors in our Patient

- Starvation
  - Depleted hepatic glycogen reserves and gluconeogenic substrates.
    - Supported by sensitivity to short-term fasts.
  - Depleted fat stores.
    - Supported by undetectable serum ketones.
  - Can lead to low insulin levels that are insensitive to glucose infusion.
  - Delayed insulin response to feeding with postprandial hypoglycemia.
    - Protected by continuous feeds.

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