Refractory Hypoglycemia in a Patient with AIDS

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Case Presentation - HPI

- 62-year-old female with AIDS (CD4 70) not on HAART and hepatitis C presented with diarrhea for 2 months.

- ROS: No F/C/V. Weight loss over several months. Fatigue. Dyspnea on exertion. Mild abdominal discomfort. Diarrhea – nonbloody, 9-10 BM/day.

Case Presentation – Hx

- Past medical hx: HIV not on HAART, HCV – untreated, recent B/L PNA
- Past surgical hx: TAH/RSO
- Home meds: Aspirin 81mg qd, methadone 50mg qd, multivitamin
- Allergies: None
- Family hx: Noncontributory
- Social hx: Lives with son. Former smoker. Former IV heroin user, on methadone. Does not drink.

Case Presentation – EMS arrival at home

Vitals:

- Afebrile
- BP – 126/82
- HR – 98
- RR – 18
- SaO2 – 70%, room air
- Fingerstick blood glucose – 100 mg/dL

Case Presentation – Arrival to MFSH

Vitals:

- Afebrile
- BP – 106/82
- HR – 74
- RR – 18
- SaO2 – 90-92% on 4L/min NC

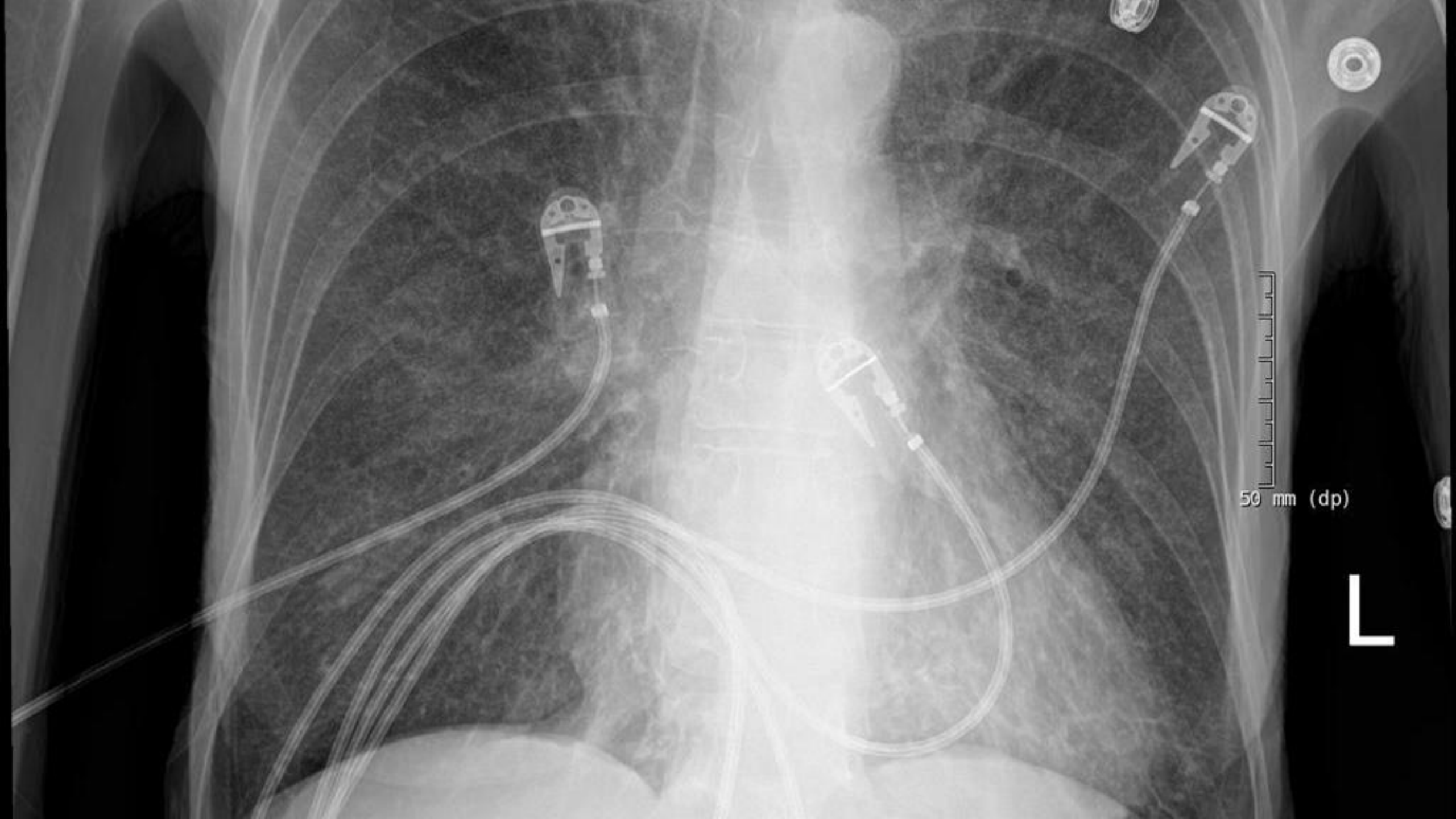
Case Presentation – Physical Examination

- Chronically ill-appearing, frail/elderly
- BMI 15 kg/m^2
- Increased AP chest diameter
- Coarse breath sounds without any wheezing, diminished air movement in the bibasilar areas with rhonchi
- Cyanotic fingernails

Case Presentation – Initial Workup

Admission, day 1:

- K 2.5
- BUN/Cr 24/0.76, GFR>60
- Glucose 58
- LFTS:
  - TP 6.3, globulin 5.1 (H, 1.3-4.7), Total bili 0.6, Bili direct 0.35 (H, 0-0.3), AST 43, ALT 21, Albumin 1.2
- ALP 132
- Lipase 39
- ABG, on 4L/min NC: pH 7.46/pCO2 35/pO2 80/HCO3 25
- CT Abd/Pelvis: Fatty liver. Questionable bowel wall thickening. Intra/extrahepatic biliary tree dilation that extends to ampulla where there is no mass lesion. Pancreas, spleen, adrenal glands, kidneys normal.
- Chest X-ray: Diffuse interstitial process as noted. Edema versus a diffuse pneumonitis are considerations.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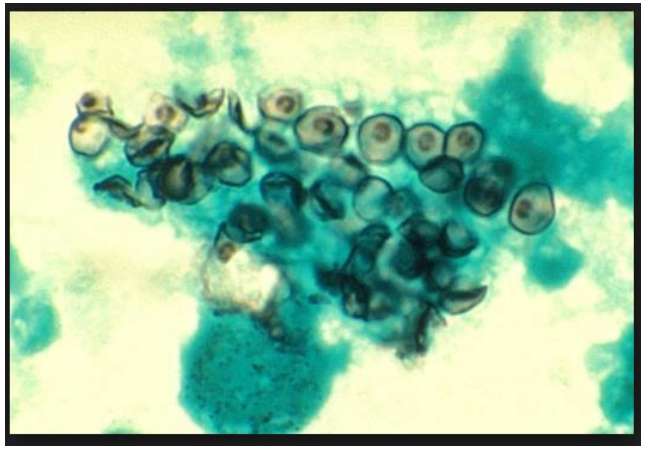
Case Presentation – Initial management

- TMP-SMX double-strength 2 tabs TID
- Prednisone 40 mg BID
- Stool studies sent: Cdiff, O+P, cryptosporidium, isospora, cyclospora, giardia

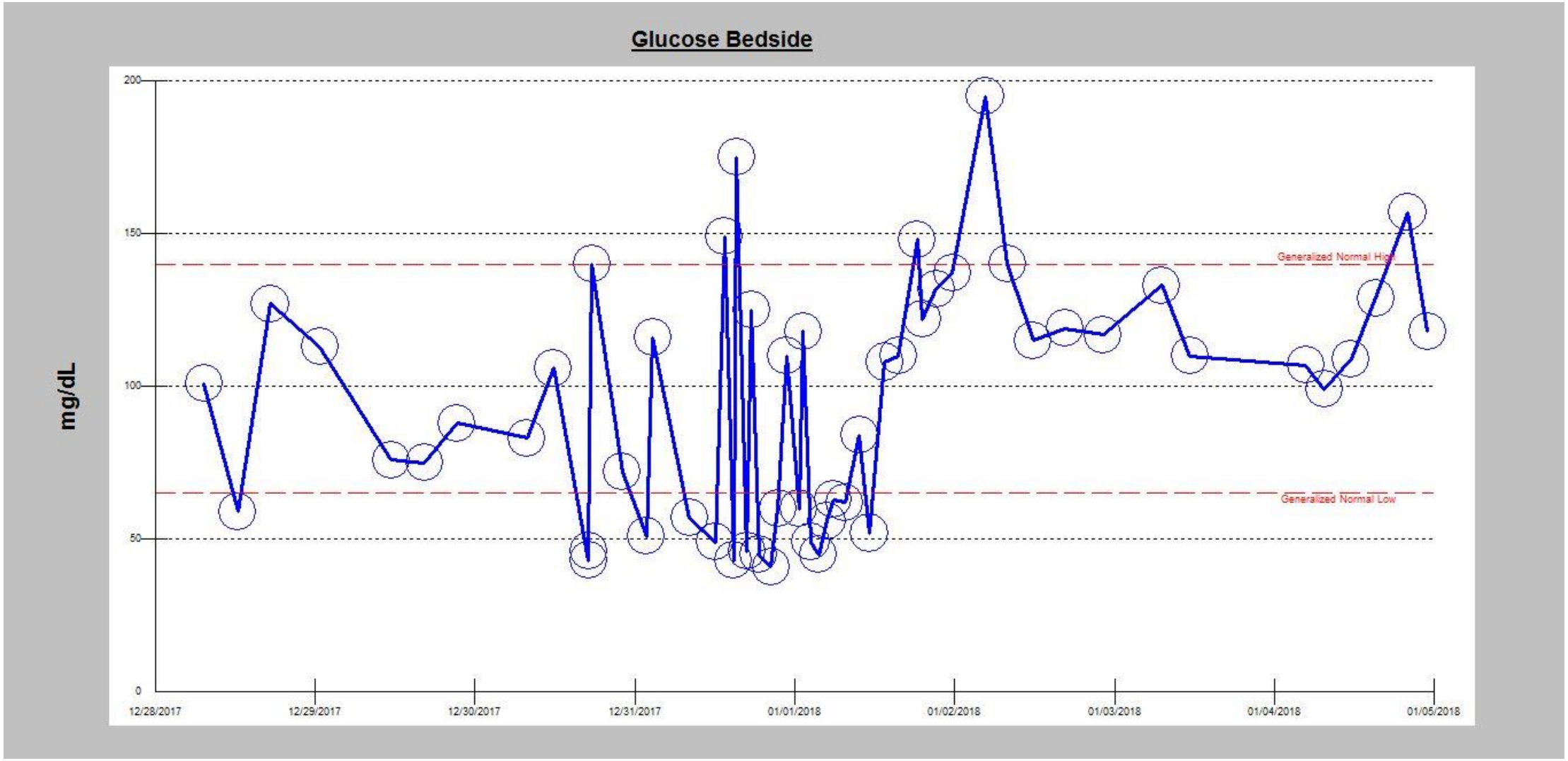
- Azithromycin 1200mg weekly for MAI prophylaxis

Case Presentation – Hospital Course

- Stool testing confirmed cryptosporidiosis. Diarrhea was managed supportively and did not persist beyond day 2 of hospitalization.
  - Crypto infection is predominantly associated with diarrhea and biliary tract disease – ALP, bili
- Day 3: Confirmation of PCP by BAL
- Worsening SaO2
  - ABG, on 6L/min NC: pH 7.47/pCO2 29/pO2 57/HCO3 20/6 (BD -2.2)
  - HFNC FiO2 70% at 35L/min
- Day 4: REFRACTORY HYPOGLYCEMIA

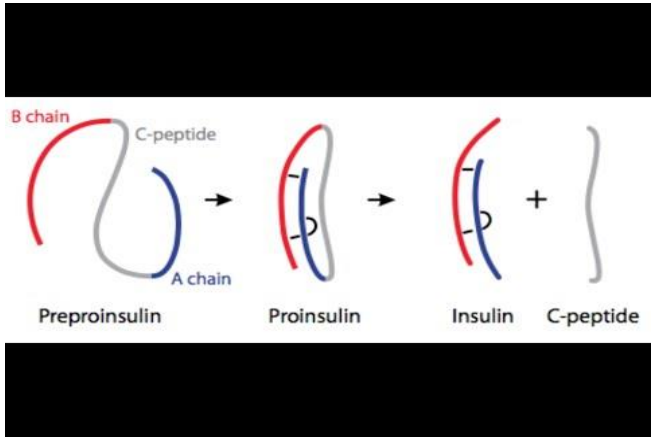


Case Presentation – Refractory Hypoglycemia



Case Presentation - Workup for hypoglycemia

- Drugs: Bactrim (rare)
- Critical illness, malnourishment
- Hormone deficiency: Cortisol nl
- Endogenous or exogenous hyperinsulinism:
  - C-peptide level: 7.78 ng/mL (NL: 0.8-3.1 ng/mL)



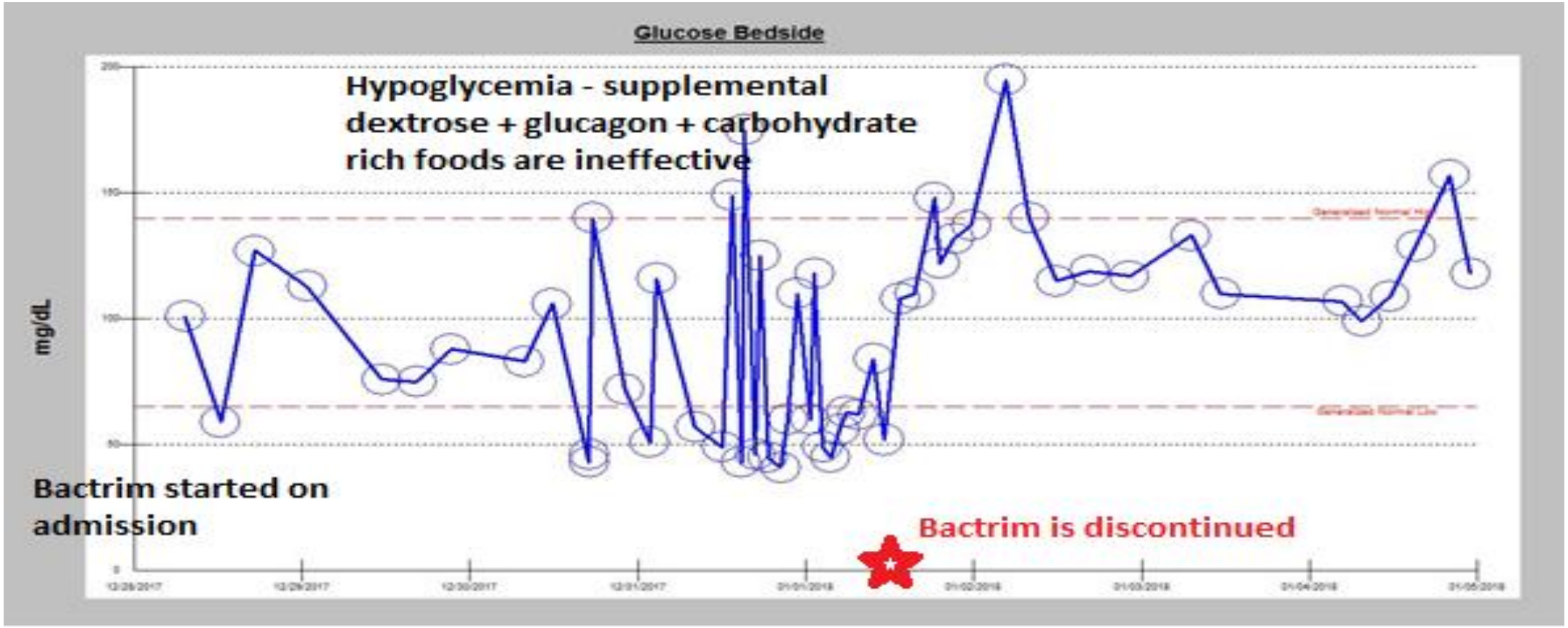
Causes of hypoglycemia in adults
Ill or medicated individual
1. Drugs
Insulin or insulin secretagogue
Alcohol
Others (refer to UpToDate table on drugs that cause hypoglycemia)
2. Critical illnesses
Hepatic, renal, or cardiac failure
Sepsis (including malaria)
Inanition
3. Hormone deficiency
Cortisol
Glucagon and epinephrine (in insulin-deficient diabetes mellitus)
4. Nonislet cell tumor
Seemingly well individual
5. Endogenous hyperinsulinism
Insulinoma
Functional beta 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

Drugs other than antihyperglycemic agents and alcohol reported to cause hypoglycemia

Moderate quality of evidence
Cibenzoline
Gatifloxacin
Pentamidine
Quinine
Indomethacin
Glucagon (during endoscopy)
Low quality of evidence
Chloroquineoxaline sulfonamide
Artesunate/artemisin/artemether
IGF-1
Lithium
Propoxyphene/dextropropoxyphene
Very low quality of evidence
Drugs with >25 cases of hypoglycemia identified
Angiotensin-converting enzyme inhibitors
Angiotensin receptor antagonists
Beta-adrenergic receptor antagonists
Levofloxacin
Mifepristone
Disopyramide
Trimethoprim-sulfamethoxazole
Heparin
6-mercaptopurine

IGF-1: insulin-like growth factor 1.

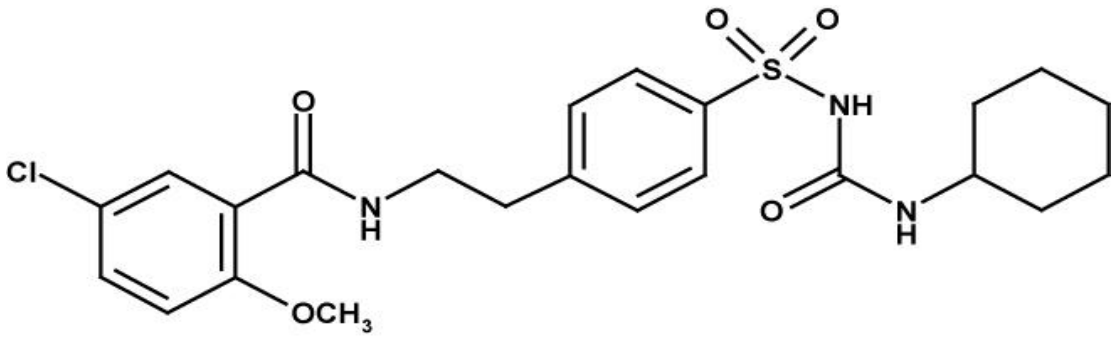
Case Presentation – Refractory Hypoglycemia



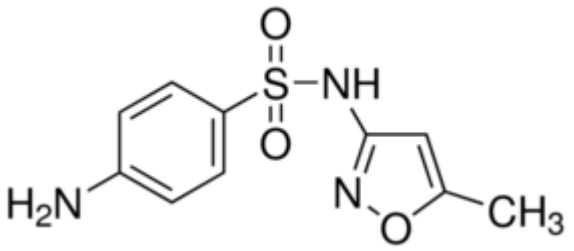
- TMP-SMX -> Clindamycin, primaquine
- Normoglycemia is achieved (w/o any supplemental dextrose) 24 hours following the last administered dose of TMP-SMX. ½ life of SMX is 9-12 hours.

Discussion – [Trimethoprim-sulfamethoxazole}-induced hypoglycemia in a nondiabetic patient with aids & normal renal function

- [TMP-SMX]-induced hypoglycemia reported with concomitant use of sulfonylureas or meglitinides in diabetic patients and/or in patients with renal insufficiency – rare.
- Chemical similarities between SMX and sulfonylureas may cause cross-reactivity, resulting in a sulfonylurea-like effect associated with TMP-SMX.
- Our patient on TMP-SMX -> C-peptide level elevated at 7.78 ng/mL (normal: 0.8-3.1 ng/mL) -> hypoglycemia was due to increased endogenous insulin secretion.



Glyburide



Discussion – [Trimethoprim-sulfamethoxazole}-induced hypoglycemia in a nondiabetic patient with aids & normal renal function

- Case reports of hypoglycemia following TMP-SMX administration in nondiabetic patients or those without renal insufficiency - extremely rare.
- Our patient was not diabetic and had normal renal function but was significantly malnourished and glycogen-deficient in the setting of AIDS.
- Then understandably, stimulants of insulin secretion in such patients can have catastrophic consequences.

Take Home Points…

- Avoid stimulants of insulin secretion in patients who are malnourished

- Monitor patients who are started on TMP-SMX for hypoglycemia if:
  - Diabetic patients on sulfonylureas or meglitinides
  - Patients with renal impairment
  - *Patients with malnutrition*

THANK YOU FOR LISTENING.
QUESTIONS?