3 yo boy with congenital anomalies and hypoglycemia

Endorama
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HPI

• 35 mo Caucasian boy w/ complex medical history, GH def & h/o hypoglycemia presents w/ episodes of hyper- and hypoglycemia
• 30 min. postprandially mom noticed “lethargy” → BG 352 mg/dL
• 1 hr PP → BG 267 mg/dL
• 3.5 hrs PP → BG 40 mg/dL at PMD
• BG 156 in the Comer ED
• Admitted for evaluation and management
ROS

- Dx with SOD and GH def. at age 12 mo following episode of hypoglycemia
- Treatment with Nutropin 0.3mg/kg/week
- Baseline: BG nadir 50-60 mg/dL once q1-2 mo
- Past 2 months:
  - ↑ mid-afternoon episodes (BG 30-50) with 2 episodes of BG > 200
  - ↑ episodes of “lethargy”
  - Multiple URIs w/ O2 requirement, recently weaned
  - Changed from po ad lib diet to strict feeding schedule: Neocate 8 oz TID thickened + po diced/chopped food
- Poor weight gain and poor appetite
- Stable, chronic diarrhea
- Baseline abdom distention slightly increased
PMH

**Problem List**
- Chromosome 17 inversion
- Septo-optic dysplasia
- GH deficiency
- Tricuspid atresia/ASD/VSD
- Portal vein thrombosis w/ extrahepatic portal HTN
- Esophageal varices
- FTT
- h/o dysphagia
- Right eye visual impairment
- Bilateral hearing impairment
- Recurrent otitis media
- Steatorrhea
- Global developmental delay

**PSH**
- 2 mo: B-T shunt
- 4 mo: Glenn procedure
- 12-18 mo: cauterization of varices followed by Sugiura procedure
- ~15 mo: G-tube & Nissen fundoplication
History cont’d

**Birth Hx**
- Full-term c-section
- Postnatal resp distress → CHD
- Dysmorphic features

**Family History**
- Mother: prematurity, Tetralogy of Fallot, obesity
- Father: sleep apnea, obesity
- Healthy 4 yo brother
- No diabetes, other congenital anomalies

**Medications**
- Lasix
-Prevacid
-Nutropin AQ 0.3mg/kg/wk
-Probiotic
-Augmentin for recent AOM
Physical Exam

T 37.4 C  HR 124  RR 40  BP 125/72  O2Sat 85%
Lt: 83.7cm (- 3 SD), wt: 12 kg (5th%), Wt-for-Lt: 60th%, HC 49.6 cm (48th%)
Gen: small, thin
HEENT: prominent forehead, hypoplastic L pinna, low set ears, hypertelorism, small, thin lips, anteverted nose, no thyromegaly
CV: 3/6 SEM, RRR, 2+ pp, sl. cyanosis of lips and nail beds, mid-sternal scar
Lungs: CTAB, no wheezes, + loud upper airway noise
GI: markedly distended with prominent superficial veins, L transverse scar, + G-tube, + splenomegaly
GU: Stretched penile Lt 4.3 cm, testes descended bilat, large bilat inguinal hernias
MSK: no muscle atrophy, + digital clubbing
Neuro: unable to elicit DTRs, normal tone and gait
Skin: pale, nl pigment
Differential Diagnosis?

In a 3 yo w/

- postprandial hyper- and hypoglycemia
- SOD w/ GH def, FTT, chronic diarrhea
- s/p cardiac and GI surgery

- Dumping syndrome
- Impending type 2 DM, insulin autoantibodies (rarely presents this way in children)
- Glycogen synthetase def. (less likely)
**Initial labs**

1 week prior, non-fasting @ 1:10pm
- Serum glucose 145 mg/dL, nl lytes
- Cortisol 6.3 mcg/dL ACTH 11.1 pg/mL
- nl TFTs

Upon admission
- Serum glu 145  C-peptide 3.26 pmol/mL (0.3-2.35)
- HbA1c 5.8%  GAD65/IA2/Insulin ab neg

Planned OGTT
BG > 60 during 12 hr overnight fast
Evaluation

7:51p
Serum BG 250
B-OH butyrate 0.81 mmol/L

8:30p
BG 283
Serum 9:45p
BG 33
BG 122
BG 40
BG 36
BG 97
BG 83

10:15a
Serum
BG 222
BOHb 0.17
Insulin 47.6

9:45a
8oz Neo

4a
Cortisol 19.5

6:20p
8oz Neo + Chicken

BOHb 0.26
Insulin 3.1 mcU/mL
C-peptide 0.75 pmol/mL
Proinsulin 10 pmol/L (3-20)
ACTH 8.1 pg/mL
Cortisol 5.4 mcg/dL

12p
8oz Neocate

3p
Turkey

3p
BG 112
BG 324

10a
BG 84
Diagnosis

- Postprandial hyperglycemia with mild ketosis followed by hypoglycemia with inappropriately elevated insulin level:

**Dumping Syndrome**
- In children, most frequently occurs post-fundoplication, especially with pyloroplasty
  - Sx: refusal to eat, lethargy, nausea, tachycardia, diaphoresis, watery diarrhea
  - Early: within 30-60 min post-prandially
  - Late: within 90-240 min post-prandially\(^1\)
Glucose Pattern

Neo = Neocate, CS = cornstarch, A = Acarbose
Clinical Questions

- Pathogenesis of dumping syndrome following Nissen fundoplication?
- Current treatment strategies for pediatric disease?
- Acarbose: safe and efficacious in children?
**Pathogenesis**

**Early DS**
- Hyperosmolar chyme in duodenum
- ↑ secretion of serotonin, badykinin, CCK, peptide YY, neurotensin, VIP, GIP, GLP-1

**Late DS**
- Impaired counterregulatory hormone secretion
- ↑ absorption of monosaccharides
- ↑ glucose absorption
- Hyperglycemia
- Excessive insulin secretion
- Hypoglycemia

**Impaired relaxation of fundus (Vol vs Vagus N. injury)**
- Rapid delivery of chyme to duodenum
- ↑ intestinal blood flow
  - circulatory bld flow + R-A-A axis

**Vasomotor sx**
- Abdominal pain

Treatment

- Octreotide (adults)
- Impaired relaxation of fundus (Vol vs Vagus N. injury)
- Rapid delivery of chyme to duodenum
- Hyperosmolar chyme in duodenum
  - ↑ secretion of serotonin, Bradykinin, CCK, peptide YY, neurotensin, VIP, GIP, GLP-1
- ↑ intestinal blood flow, circulatory bld flow + R-A-A axis
- ↑ absorption of monosaccharides, ↑ glucose absorption
- Hyperglycemia
  - Excessive insulin secretion
  - Hyperosmolar chyme in duodenum
  - ↑ secretion of serotonin, Bradykinin, CCK, peptide YY, neurotensin, VIP, GIP, GLP-1

- Small, freq feeds
  - Continuous feeds
- Cornstarch
  - Limit mono- & disaccharides
  - ↑ Complex carbs
  - Acarbose
  - Diazoxide

- Vasomotor sx
  - Abdominal pain
- Hypoglycemia

References:
Acarbose treatment in children

• Acarbose
  o α-Glucosidase inhibitor
  o Delays oligosaccharide → monosaccharide conversion

• May be well tolerated and effective, data limited
  o Ng et al: 6 pts s/p Nissen fundoplication and severe, symptomatic hypoglycemia (mean nadir of 33 ± 2 mg/dL) at 120-140 min post-prandially
    • All responded to Acarbose prior to each bolus feed: 12.5 up to 50 mg
    • Adverse effects: flatulence
  o Cunto et al: 8 pts s/p Nissen with confirmed post-prandial hypoglycemia
    • 4/8 received high-dose Acarbose w/ each feed: 30-100mg
    • No adverse effects
    • Surveillance period unknown
Conclusion

• Suspect dumping syndrome in children with insulin dysregulation with a history of gastric surgery

• Dumping syndrome is caused by increased gastric motility resulting in hormonal dysregulation

• Acarbose may be a safe and effective adjunct to dietary modifications and cornstarch, though more long-term studies are needed


