22 Month-Old Boy with Hypoglycemia

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Endorama
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HPI

- 22 mo Caucasian M with no significant PMH presented to an OSH with AMS
- Difficult to arouse at 11am, taken to ED by 1pm
- Fingerstick glucose 63 mg/dL
- Given dextrose→ BG 43 1 hr later, became more responsive
- Given 1 amp D25 then started on D10 0.9NS

HPI

- Glucose 56 Na 139 K 3 Cl 99 HCO3 17 BUN 0.26 AG 23
- VBG: pH 7.353 HCO3 16.8 BE -8
- Urine ketones 15 (small), lactic acid nl, ammonia nl, tox screen + ETOH normal
- EKG: prolonged QTc
- Non-contrast head CT nl
- Transferred to Comer PICU

In the PICU

- Dexi 73 on D10 (GIR 3.7 mg/kg/min)
- BMP: Bicarb 17, nl electrolytes
- Repeat tox screen & salicylate levels nl
- Consulted Poison Control → consistent with sulfonylurea ingestion
- GIR increased to 4.7 due to BG drops despite D10 boluses
- Returned to baseline mental status within 10 hours of presentation
- Endocrine & Genetics consulted

Additional History

- Pt has been healthy and growing well
- Erratic eating and sleeping pattern
  - Often misses breakfast, picky
- 1 day prior
  - Cousins's birthday party: ate 2 plates fruit, 2 bites of cake, hot dog w/out bun, regular and diet soda, last meal ½ cup of spaghetti 9:30pm
  - Paternal aunt with recently diagnosed T2DM
- Paternal grandfather with T2DM previously on pills, now diet-controlled, and HTN taking HCTZ, lives in the home

ROS

- Constitutional: - fever, wt loss, signif wt gain
- HEENT: neg
- CV: neg
- Resp: neg
- GI: - diarrhea, vomiting, constipation
- GU: + decreased UOP x 1 day
- Neuro: + somnolent, - seizures, syncope, tremor
- MSK: neg
- Skin: neg

History Cont'd

- PMH: Not significant last PMD visit age 18 mo
- Meds: none
- Lives at home with mother (8 months pregnant), father, PGF, 2 older brothers

- Fam Hx
  - PGF-HTN & T2DM
  - Paternal aunt T2DM
  - No T1DM, autoimmune d/o, short stature
  - Mother: 62 inches tall
  - Father: 70 inches tall

PE

- Wt:12.2kg (46%) Ht: 84.5cm (20%) Wt-for-Lt: 85%
  BP 80/30
- Gen: Alert, playful
- HEENT: no midline defects
- Neck: no thyromegaly
- CV: RRR, - murmurs, 2+ periph pulses
- Resp: CTAB, nl effort
- GI: soft, NTND, no hepatomegaly
- GU: circumcised, phallus nl, testes descended bilaterally
- Msk: nl ROM and strength
- Neuro: nl tone, CN intact bilaterally
- Skin: unremarkable

Summary

- 22 mo M w/ AMS, hypoglycemia, metabolic acidosis, small ketosis, nl vitals and exam
- Occurred following ~14 hr fast
- No significant PMH
- Inconsistent eating pattern
- Wt-for-Lt 85th%
- ? Access to anti-diabetic medication

Differential Diagnosis

- Ingestion:
  - Hypoglycemic agents sulfonylureas, B-blockers, salicylates, ethanol
  - + Metabolic acidosis
  - Exposure unclear, + ketones, neg tox screen
- Ketotic Hypoglycemia
  - + Age, presence of ketones
  - - Elevated wt-for-lt
- Growth hormone deficiency
  - + Age, clinical presentation

Differential Diagnosis

- Central Adrenal insufficiency
  - o - Normal growth
- Metabolic disorders
  - o Organic acidemia
    - + Metabolic acidosis
    - - Age
  - o Defects in gluconeogenesis or glycogenolysis
    - + Fasting hypoglycemia with mild ketosis
    - - Post-prandial hyperglycemia, lactic acidosis, hepatomegaly
- Recommended further diagnostic testing: 18-hour fast
  - o Parents refused inpatient fast
  - o Obtained screening labs
  - o Advised BG monitoring and frequent feeds

Labs

- 03:59 glucose 94 b-OHbutyrate 0.14 mmol/L (< 3)
- ACTH < 5 pg/mL cortisol 4.9 mcg/dL
- GH 3.3 ng/mL
- IGF-1 31 ng/mL (55-327) IGF-BP3 1.7 mcg/mL(1.2-6.4)
- TSH 3.2 mcU/mL free T4 1.29 ng/dL
- Serum sulfonylurea level (acetohexamide): QNS
- Acylcarnitine profile: nl
- Serum amino acid profile: nl
- Urine organic acids: c/w physiologic ketosis

1 month later…18-Hour Fast

- Modified CHOP fast protocol
- BG 118→ 76 from Time 0 to 16 hours
- Hour 18: BG 52, serum glucose 46
- Critical Sample
  - b-OHbutyrate 2.48 mmol/L
  - C-peptide 0.04 pmol/mL Insulin < 2 uIu/mL
  - ACTH 94.8 pg/mL Cortisol 29.3 mcg/dL
  - GH 0.5 ng/mL IGF-1 43 ng/mL
- Glucagon Challenge: not performed
- Follow-up with Peds Endo at UIC

Clinical Inquiries

- Presentation of sulfonylurea ingestion in children
- Normal GH response during spontaneous hypoglycemia in children
- Sensitivity of GH level during spontaneous hypoglycemia in children

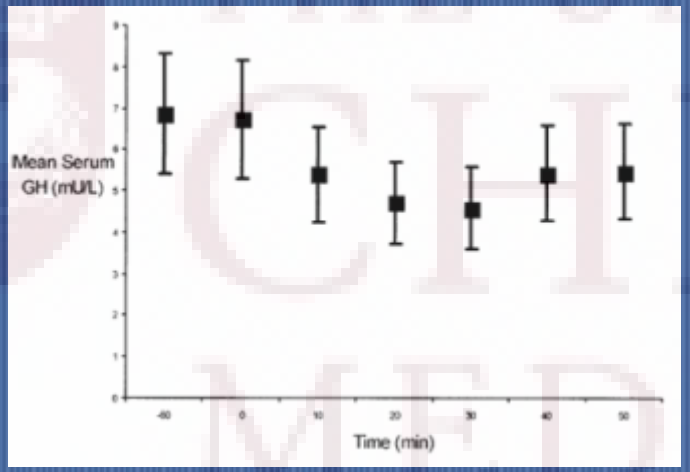
Sulfonylurea Ingestion

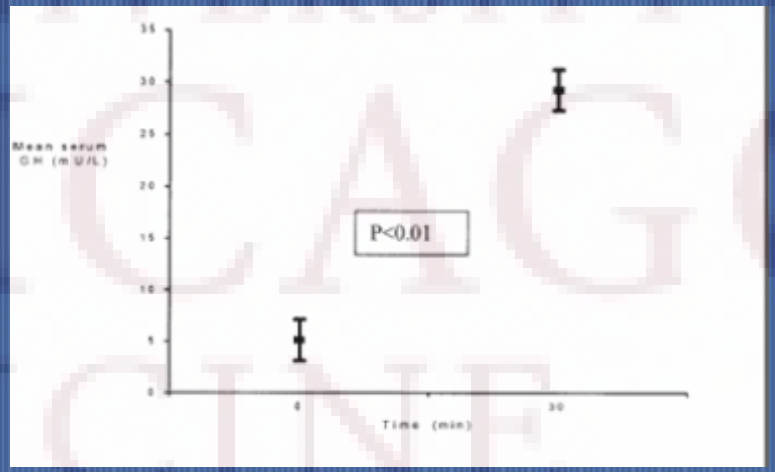
- Incidence of hypoglycemia is unclear-some report 35-45%[1]
- Significant hypoglycemia can occur with glipizide 5 mg, glyburide 2.5 mg, chlorpropamide 250 mg[1]
- Slight increase in severity of hypoglycemia reported with glipizide vs. glyburide[1]
- Most develop hypoglycemia by 8 hrs
- Treatment: dextrose, octreotide 5-20 mcg/kg/day by 6-8 hrs bolus or continuous infusion

[1]Levin et al. Hypoglycemia after accidental sulfonylurea ingestion. *Pediatr Emer Care* 2011: 27; 846-849.
[2]Caletto DP et al. Case Files of the medical toxicology fellowship training program at the Children's Hospital of Philadelphia: a pediatric exploratory sulfonylurea ingestion. *J Med Toxicol* 2006; 2(1): 19-24.

Low GH in Spontaneous Hypoglycemia

- Hussain K. JCEM 2003; 88(8): 3715-3723
- 22/47 children age 1 month-11years developed fasting hypoglycemia
  - Appropriate GH rise in 1/22 at time of hypoglycemia vs 16/16 in insulin tolerance test group

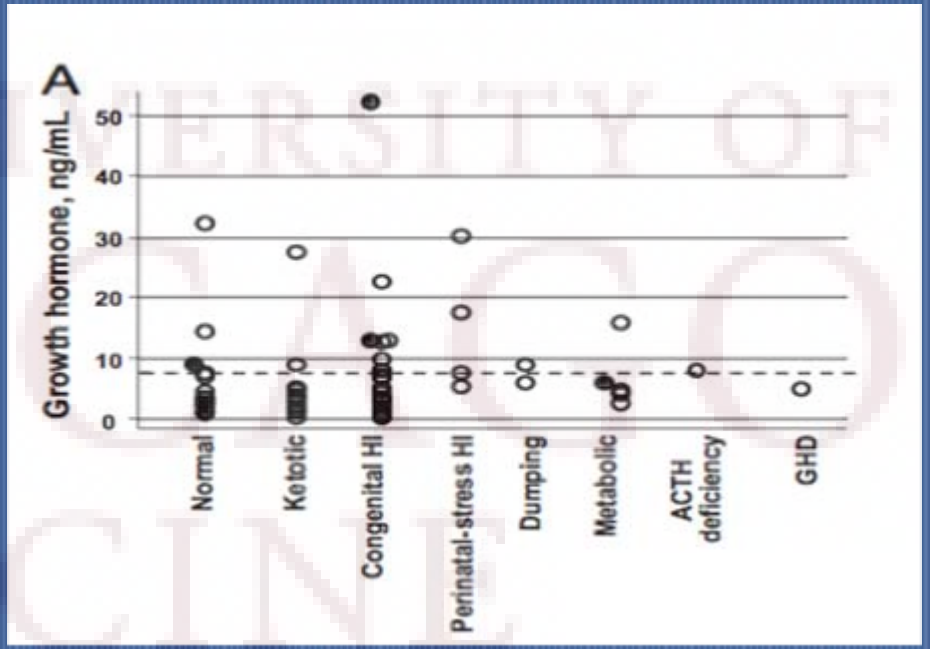




- Explanations
  - Missed peaks due GH pulsatility
  - Rapidity of hypoglycemia
  - ? IV insulin role in modulating GH secretion directly or via decrease in FFA

Poor Specificity of Low GH during fasting hypoglycemia in diagnosis of GHD

- Retrospective review of 68/151 fasts
- age 2d-14y (2y)
- 80% of nl or ketotic hypoglycemic normal had GH < 7.5
  - 1 was diagnosed with GHD (only one with abnl growth)
  - Specificity 30%
- No association btw age, diagnosis, fast duration, rapid glucose decline



Kelly et al. *Pediatrics* 2008; 122:e522-e528