5-year-old female with hypoglycemia

Endorama
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Chief complaint and HPI

- 5-year-old female transferred from OSH to PICU with lethargy, dehydration, and low blood sugar
- USOH until 2 days PTA
- N/V, no po intake except small amounts of water
- To OSH ER day PTA- dx'd w/ UTI, d/c'd home w/ Abx
- DOA cont'd n/v, lethargic→ taken to ED

HPI, continued

- Exam consistent with moderate-severe dehydration
- Cont'd lethargy after total 40 ml/kg IVF bolus
- Labs significant for serum BG of 52
- Rcv'd D10 (2 ml/kg), placed on D5NS at 1500 ml/m^2/d prior to txfer to Comer ICU

OSH labs

8.11	12.1 / 35.8	330
134	93 / 4.4	17
25	0.45	52

- Head CT- negative
- Urine toxicology screen- negative

Hospital Course

- Continued on IVF in PICU w/ improvement
- IVFs d/c'd; transferred to floor HD #2
- Tolerated small po intake x1
- HD#3- emesis of water and lethargy
  - POC BG= 44
  - Serum BG= 45
- IVFs of D5NS resumed, Peds Endo consulted for hypoglycemia

Past Medical History

- FT, NSVD, no complications
- Autism spectrum disorder
- GERD
- UTIs x3
- Pneumonia x2
- Previous episodes of lethargy
  - During illnesses w/ poor po intake
  - 2 years old- after refusal to eat in the care of her GP x ~16 hours
- Medications- None
- Allergies: Azithromycin- delerium

FAMILY HISTORY
- Negative for DM
- Negative for hypoglycemia

SOCIAL HISTORY
- LAHW parents

REVIEW OF SYSTEMS
- Nausea, vomiting- now resolved
- Appetite improved, tolerating po intake
- No concern for ingestions
- No access to hypoglycemic agents

Physical Examination

- Wt: 20 kg (75th); Ht: 102.8 cm (15th)
- Gen: WD, WN; NAD
- HEENT: W/o dysmorphic features; PERRL; MMM; NL thyroid examination; neck supple
- CV: RRR, NL S1, S2, no murmurs
- Pulm: CTA b/l
- Abd: Soft, NT, ND, no masses
- GU: Tanner I
- MSK: NL ROM, No edema, TD, deformity
- Neuro: Nonfocal, 2+ DTRs

DIFFERENTIAL DIAGNOSIS FOR HYPOGLYCEMIA IN A CHILD?

DDx of hypoglycemia in children

Ketones absent
- Hyperinsulinemia
  - Congenital
  - Beta-cell adenoma
  - Reactive hypoglycemia
  - Medication
  - Munchhausen by proxy
- Fatty acid, organic acid oxidation defects

Ketones present
- Idiopathic Ketotic hypoglycemia
- IEMs
- GH deficiency
- Cortisol deficiency
- Ingestions (alcohol, salicylates)

EVALUATION?

OSH labs

134	93	25	52
4.4	17	0.45	

- Anion gap: 24
- Day PTA Urine ketones: 40, glc: neg
- DOA Urine ketones: 150, glc: neg

Laboratory evaluation

139	98	16	45
3.8	15	0.4	

- Beta-hydroxybutyrate: 6.84
- Lactic acid: 1.1 (later that day w/ BG-146, bicarb 20)
- Cortisol: 43.2
- GH: could not be added

- HbA1c: 5.1
- POC BGs: 91-154 throughout the remainder of the hospitalization

Idiopathic ketotic hypoglycemia

- Most common form of hypoglycemia in young children
- Hypoglycemia and ketosis uniformly provoked by a brief fast after hypocaloric high fat, low carbohydrate diet
- Characteristic inability to respond to glucagon after brief fast
- Usually appears between the first and third years of life, and remits spontaneously by age 6-8

Mechanism of IKH-Huidekoper, et al

- Study looked at glucose kinetics during fasting in 12 children with a h/o KH.
- Assessed glucoregulatory hormones, plasma ketones, FFA, alanine
- Assessed rates of endogenous glucose production (EGP), glucose uptake, gluconeogenesis, glycogenolysis
- 5/12 became hypoglycemic
  - Youngest of subjects (2.5-3.9 years)

Mechanism of IKH

- Alanine levels significantly lower at the end of the test in hypoglycemic subjects
- Ketones, FFA levels were WNL during duration of fasting in all subjects

Mechanism of IKH

Hypoglycemic
- EGP: -31.9%
- GGL: -66.2%
- GNG: 6.8%

Normoglycemic
- EGP: -17.9%
- GGL: -50.8%
- GNG: 19.5%

Mechanism of IKH

- IKH is caused by the inability to sustain an adequate EGP during fasting, possibly because of a limitation in the supply of alanine

Mechanism of IKH-Pagliara, et al

- Objective: determine if the primary defect in IKH is a deficiency of gluconeogenic precursors or an abnormality in the hepatic gluconeogenic enzyme system
- 8 children with IKH and 7 age-matched controls

TABLE II

Plasma Glucose and Alanine and Blood β-OHB, Lactate, and Pyruvate Levels in Normal and Hypoglycemic Children before and after Ketotic Premeation

Experimental conditions	Glucose	β-Hydroxy-butyrate	Alanine	Lactate	Pyruvate
	mg/100 ml	mM	μM	mM	mM
Normal hospital diet					
Normal (7)	81 ± 3.0*	0.18 ± 0.08	315 ± 15	1.42 ± 0.26	0.076 ± 0.017
Ketotic hypoglycemia (8)	68 ± 4.0	1.22 ± 0.37	211 ± 10	1.24 ± 0.17	0.080 ± 0.012
P	<0.05	<0.05	<0.01	NS	NS
Hypocaloric low carbohydrate diet					
Normal (7) 32–36 hr‡	68 ± 2.0	2.56 ± 0.44	225 ± 5	1.37 ± 0.13	0.080 ± 0.017
Ketotic hypoglycemia (8) 8–16 hr‡	53 ± 3.0	3.70 ± 0.32	155 ± 17	1.23 ± 0.15	0.090 ± 0.019
P	<0.01	<0.05	<0.02	NS	NS

* All values represent mean ± SEM.
‡ Period beginning with feeding of hypocaloric diet.

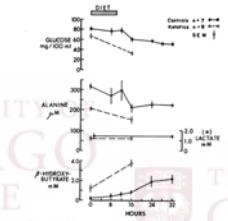
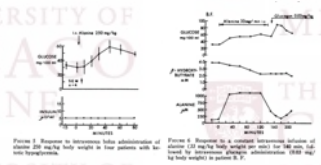


FIGURE 1 Substrate changes after the ketogenic diet in ketotic hypoglycemic and control children.



Conclusion: A deficiency in gluconeogenic precursor (alanine) rather than a defect in the hepatic gluconeogenic enzyme apparatus is the most likely etiology of IKH

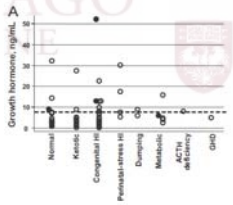
Utility of GH and cortisol values during hypoglycemia

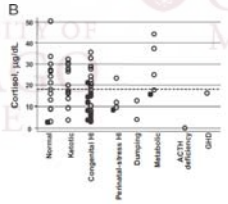
- Study aim: To determine if GH and cortisol obtained during fasting hypoglycemia can identify children with deficiencies
- Retrospective chart review of all diagnostic fasting tests (n=151)
- Hypoglycemia defined as SBG ≤50 mg/dL
- NL GH level defined as ≥7.5 ng/mL
- NL cortisol level defined as ≥18 mcg/dL

- 70% had GH and cortisol levels below "normal" thresholds

TABLE 1 Patient Characteristics ($N = 84$)

Variables	GH Available	Cortisol Available
Total (female), n	68 (37)	76 (39)
Age	2 (2 d to 14.3 y)	1.8 (2 d to 14.3 y)
<1 mo (>26 d), n	4	8
>1 mo, n	64	69
Final diagnosis, n		
Normal	15	15
Ketotic hypoglycemia (n = 16)	16	15
Hyperinsulinism		
Congenital (N = 37)	24	33
Perinatal-stress induced (N = 5)	4	4
Late dumping syndrome (N = 3)	2	2
Glycogen storage disease type 1 (N = 1)	1	1
Fatty acid–oxidation defect (N = 4)	3	4
Isolated GH deficiency (N = 2)	1	1
Isolated corticotropin deficiency (N = 1)	1	1
Blood glucose nadir, median (range), mg/dL	45 (25–50)	
Fasting duration, median (range), h	14.3 (10 min–33)	
Time BG < 60 mg/dL, median (range), h	1 (0–9.5)	





Summary

- Idiopathic ketotic hypoglycemia is the most common form of hypoglycemia in young children
- IKH is caused by the inability to sustain adequate glucose production related to decreased alanine supply
- While GH and cortisol deficiency need to be ruled out, the utility of assessment at the time of hypoglycemia is questionable

References

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