Beyond the Naked Eye: A Case Presentation on a Rare Form of Congenital Hyperinsulinism (HI)

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Patient Demographics

- **Patient:** 3 yo Hispanic girl transferred from the midwest for evaluation of hyperinsulinism following
- **Birth Hx:**
  - 36 weeker, LGA, born via VBAC,
  - no complications at birth and no notable hypoglycemia
- **PMH:**
  - RSV
  - Recurrent UTI, mild/mod enlarged kidneys on u/s-no hydronephrosis, VCUG negative

Patient Demographics

- **FMH:**
  - Paternal GGM: diabetes
  - Mother: anemic
  - Father: reflux
  - Siblings: 2 older brothers healthy

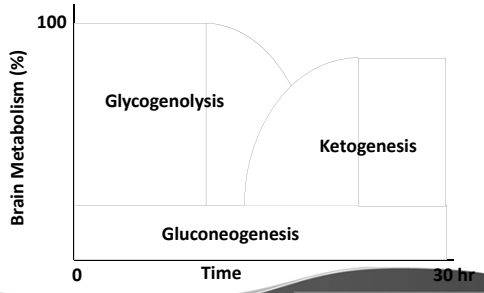
Hypoglycemia Evaluation at OSH

- Additional history
  - At 2 yo seizure after sleeping 11 hours
  - At PCP Fasting BG = 25 mg/dL and insulin = 3.21 uU/mL
  - Fasted 10 hours and BG fell to 42 mg/dL
  - Critical sample:

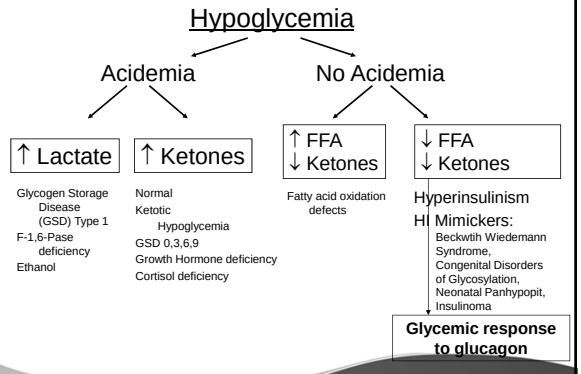
Test	Result	Normal	Comments
BG	42 mg/dL	70-100 mg/dL	
BOHB	0.26 mmol/L	>2 mmol/L	
Insulin	8.1 uU/mL	<2 uU/mL	
C-peptide	0.33 ng/mL	<0.1 ng/mL	
Cortisol	11.5 mcg/mL	>10 mcg/dL	
GH	0.77 ng/mL	>10 ng/mL	Passed
Glucagon Stim	42 to 76 mg/dL		Positive

  - Treated with diazoxide and octreotide

Fasting in Children with Normal Glucose Metabolism



Hypoglycemia



Hypoglycemia Evaluation at CHOP

- **To Confirm HI Diagnosis:**
  - Repeat diagnostic fast

Time	Blood sugar 70-100 mg/dL	BOHB > 2 mmol/L	Comments
2 hours	> 70 mg/dL		Slow dextrose wean
	44	< 0.33	
Glucagon Stim	< 50 to > 80		In 40 minutes

Diagnosis of HI
1. **BG less than 50 mg/dL**
2. **Suppressed BOHB**
3. **Elevated insulin or c-peptide**
4. **Positive response to glucagon**

- **Genetic Testing:** HI genetic testing negative (x6 genes)

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Hypoglycemia Management Plan

- **Management:**
  - Patient failed medical therapy with her primary endocrine team
    - Diazoxide 1st line therapy
    - Octreotide 2nd line therapy
  - Diazoxide d/c'd
  - Managed on IV Dextrose
- **Plan:**
  - PET
  - Surgery

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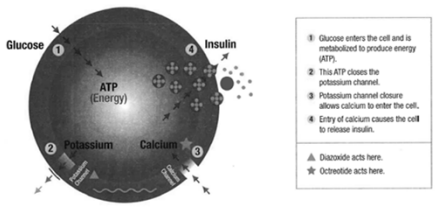
How ßeta cells produce insulin



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Common Surgical Forms of HI

CHOP Congenital HI Center Statistics

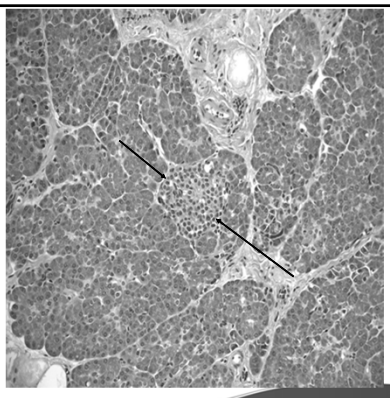
Surgical Patients (N=433):

- Diffuse: 43%
- Focal: 50%
- Atypical: 7%
  - Localized Islet Cell Nuclear Enlargement: 2.5%
  - Beckwith-Wiedemann Syndrome: 3%
  - Turner Syndrome: 1.5%

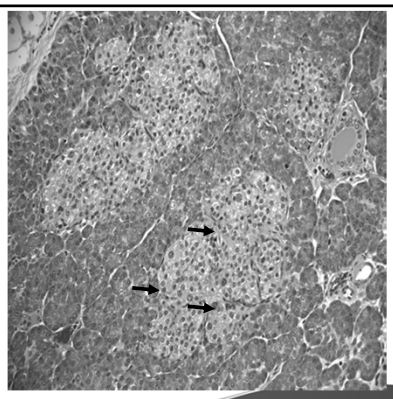
Hypoglycemia Management Plan

- **Imaging:** 18 F-DOPA PET scan negative
  - Special isotope that targets neuroendocrine cells in the pancreas
  - Differentiates between diffuse vs focal HI
  - 85% sensitivity
  - 98% specificity
- **Surgery:** Underwent 40% distal pancreatectomy for localized islet cell nuclear enlargement (L.I.N.E)

Normal islet: seen in head and proximal body

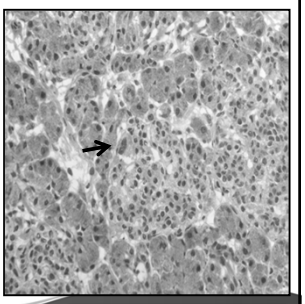


Nucleomegaly: more prominent in sections from tail



Localized islet cell nuclear enlargement (L.I.N.E.)

- Islet cell nucleomegaly similar to diffuse HI but confined to specific region(s) of pancreas
  - Otherwise normal islets elsewhere
- Older infants at age of presentation
- Clinical improvement with partial pancreatectomy



Hypoglycemia Management Plan Post-Op Course

- Full PO feeds within 1 week of surgery
- Cure fast after 5 days of monitoring on full feeds
- She lasted 18 hours, 12 hours >70 mg/dL . BG at the end of the fast was 49 mg/dL with BOHB of 2.1 mmol/L
- Cured!

Criteria for Cure

1. BGs >70 mg/dL for 12 hours.
2. BOHB above 2 mmol/L
3. No response to glucagon

CHOP Data for L.I.N.E. Type HI

- 11 cases
  - None had detectable genetic mutation found in blood sample
  - 9 have undergone NGS sequencing on the pancreatic tissue
  - Genetic mutations found in 5/9
    - 2 GCK
    - 3 ABCC8 (most common genetic form of HI)
    - 2/4 that remain negative no pancreatic tissue available

Conclusions

- HI is a complex disease that requires further research to improve diagnosis and management options
- Genetic testing on blood samples may not be sensitive enough to pick up all mutations
- Genetic mutations may be detected in pancreatic tissue leading to surgical treatment and cure!
- HI patients may require referral to a HI center with expertise in imaging, and medical and surgical management

References:

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