WHAT IS HYPERINSULINISM?

- The leading cause of hypoglycemia in infants and children
- Excess secretion of insulin without regulation by glucose
WHY TEST GENETICS IN CHILDREN WITH HYPERINSULINISM?

- Genetic mutations correlate with clinical pathology
  - Diffuse
  - Focal

- Genetic Syndromes may have a hypoglycemia component
  - Beckwith Wiedemann (Overgrowth)
  - Kabuki Syndrome
  - Soto Syndrome
  - Turner Syndrome

WHAT GENETIC TESTING CAN TELL US?

- The type of hyperinsulinism
- Whether or not certain medications will be effective
- What the treatment course will most likely be
GENETICS

- Each person has 2 copies of each gene
  - 1 from their mother and 1 from their father
  - 46 chromosomes total- 23 pairs

- Heterozygous- inherited from one parent
- Homozygous- inherited from both parents
- De Novo- not previously seen in the family

INHERITANCE

- Autosomal: not sex related
- Sex-linked: on sex chromosome (X or Y)
- Autosomal Dominant: one copy of the gene in each cell is enough to cause the disorder. (carrier parents likely has HI, may not be aware). Each parent 50 %
- Autosomal Recessive: both copies of the gene in each cell have the mutation. Each child 25 %
HOW IS GENETIC TESTING OBTAINED?

• Blood draw or saliva sample
• Ensure insurance approval prior to obtaining
  • Try to send during inpatient admission
• Send parental genetics with child’s

WHERE SHOULD GENETICS BE SENT?

• University of Pennsylvania
• University of Chicago
• Athena Labs
• Prevention Genetics - charge for parental genetics
GENETIC MUTATION INDICATIVE OF FOCAL HYPERINSULINISM

- Gene: ABCC8
- Zygosity: Heterozygous
- Inheritance: paternally inherited
- Recessive
- Loss of maternal allele

MANAGEMENT OF FOCAL HYPERINSULINISM

- PET Scan to locate lesion
- Resection of lesion
- Cure
A CASE OF DIFFUSE HYPERINSULINISM

- Patient: GW
- Gene: ABCC8
- Zygosity: Heterozygous
- Inheritance: De Novo
- Dominant

MANAGEMENT OF DIFFUSE HYPERINSULINISM

- Can medication be used?
  - Review genetics
- Can glucose needs be met with enteral dextrose?
  - Nasogastric tube vs. Gastrostomy tube
  - Glucose infusion rate (GIR) >10 mg/kg/min
  - 98% Pancreatectomy
- Will develop diabetes by adolescence
PHARMACOLOGIC TREATMENT OPTIONS FOR HYPERINSULINISM

• Diazoxide: works at the potassium channel (KATP)
  • Ashkenazi Jewish mutation - known recessive homozygous, potassium channel does not exist so diazoxide will not work
• Enteral Dextrose
• Octreotide: works at the calcium channel
• Lanreotide: works at the calcium channel

DIAZOXIDE (PROGLYCEM)

• How Diazoxide works:
  • Allow the potassium channel of the cell to open
  • The opening of the potassium channel inhibits the secretion of insulin
DIAZOXIDE MONITORING LABS

• CBC with differential
• Uric Acid
• Diazoxide level
• Basic Metabolic Panel (BMP)

DIAZOXIDE: SPECIAL CONSIDERATIONS

• Dosing: Diazoxide up to 15 mg/kg/day
• Cost
  • Made by Teva Pharmaceuticals
  • FDA mandates it be made
• Prior Authorizations
• Co-Pays
• Availability
• Taste
DIAZOXIDE SIDE EFFECTS

- Fluid Retention:
  - Diuril (Chlorothiazide): monitor BMP
- Excess hair growth
- Neutropenia

ENTERAL DEXTROSE

- GW did not respond to Diazoxide
  - Enteral dextrose
    - Gastrostomy tube placement
    - Octreotide injections at 8am and 2pm
    - Feeds via gastrostomy tube
OCTREOTIDE (SANDOSTATIN)

• Method of Action:
  • Works on the calcium channel
  • Inhibits insulin release
  • Also inhibits release of other endocrine hormones:
    • Thyroid hormone
    • Growth hormone

OCTREOTIDE SIDE EFFECTS

• Octreotide suppresses insulin and other hormones that make things grow

• Monitoring:
  • Thyroid labs
  • Growth factors
  • LFTs
  • Abdominal US
OCTREOTIDE: SIDE EFFECT MANAGEMENT

• Hypothyroidism

• Growth concerns

• Gallstones: Ursodiol

OCTREOTIDE ADMINISTRATION

• Dosing: Octreotide up to 15 mcg/kg/day

• Subcutaneous

• Concentration: Octreotide 200 mcg/ml

• Insulin pump

• Insulin syringe
  • conversion
OCTREOTIDE AND NECROTIZING ENTEROCOLITIS (NEC)

• Avoid Octreotide in children < 2 months
• Caution in former preemies

LANREOTIDE (SOMATULINE)

• Long acting form of Octreotide
• Dosing: Lanreotide 60 mg every 28 days
• Side effects and monitoring - same as for Octreotide
• “Deep Sub Cutaneous” injection
• Apply EMLA prior to injection
LANREOTIDE

- Get insurance approval
- Assure someone will give
- Stopping Octreotide
- Admission after 4th dose
- Assess for nodules

RESOURCES

- Children's Hospital of Philadelphia website
  - www.chop.edu
- Congenital Hyperinsulinism International (CHI)
  - https://congenitalhi.org
- Mcknight@email.chop.edu