A rare genetic cause for neonatal hypoglycemia

Sigrún Hallgrímsdóttir¹ and Kolbeinn Guðmundsson²
¹The State Diagnostic and Counselling Centre, ²Children’s Hospital, Landspitali - National University Hospital

Nordic conference on rare diseases
June 1st 2012
Case description

• A baby girl born after a 39 weeks uncomplicated pregnancy with elective cesarian section
• Apgar scores 8 and 9 after 1 and 5 minutes respectively
• Heavy for gestational age, 4475 g
• General appearance normal
Case description cont.

• Mild respiratory difficulties shortly after birth
• No risk factors for infections
• Blood glucose levels 1,1 mmol/L (normal range 4,0-6,4 mmol/L)
• Very slight rise with oral feeding
• Increasingly tachypnoeic
• Admitted to the NICU for iv glucose infusion
Neonatal hypoglycemia

- A drop in blood glucose levels is a normal physiological response to extrauterine life which usually resolves without symptoms or complications
- Can be prolonged or more severe in some instances
- Risk factors include:
  - LGA, SGA, preterm, mothers with DM or GDM, infections, delivery by c/s
- Hypoglycemia occurs in 16% of LGA newborns of nondiabetic mothers [Schaefer-Graf et al 2002]
NICU

- Respiratory difficulties soon resolved
- Persistent hypoglycemia/low normal glucose levels despite full oral feeds and iv glucose infusion
- Weaning off infusion at day 4 failed
- Increasing carbohydrate need – she received up to 11.8 mg/kg/min (normal need 4-6 mg/kg/min)
- Newborn screen normal
- Further diagnostic workup begun
Persistent hypoglycemia - workup

• Physical examination
  – Dysmorphism associated with certain syndromes that include hyperinsulinism
  – Organomegaly

• Diagnostic imaging

• Laboratory workup
  – Glucose regulation
  – Hormone deficiency
  – Inborn errors of metabolism
NICU - workup

- General appearance normal and no organomegalies
- Abdominal ultrasound normal
- Repeated measurements showed inappropriately elevated insulin levels
- Other hormonal measurements normal
- Pro-insulin C-peptide and ammonia levels were also elevated
- => Hyperinsulinism/hyperammonemia syndrome
NICU - treatment

• Started on Diazoxide 15 mg/kg/day
• Glucose infusion could be discontinued within the first day of treatment
• Discharged at 3 weeks of age
HI/HA syndrome

- Congenital hyperinsulinism affects 1 in 40,000-50,000 and is characterized by dysregulated secretion of insulin
- Hyperinsulinism/hyperammonemia is the second most common form of congenital hyperinsulinism
- Symptomatic hypoglycemia and persistent hyperammonemia
- Increased frequency of seizures, developmental delay and behaviour problems
- Severity of symptoms varies significantly
HI/HA syndrome cont.

- Gain of function mutation in the mitochondrial enzyme glutamate dehydrogenase encoded by GLUD1 (chr. 10q23.3)
- Several causative missense mutations have been described
- Majority of cases sporadic
- Our patient has a de novo p.Gly446Ser in exon 12
- Symptom severity potentially linked with different mutations/domain of protein involved
Current condition

• Our patient is now almost three years old
• Cont. Diazoxide ~ 12 mg/kg/day, mild hypertrichosis but no other side affects
• No major drops in blood glucose levels and insulin levels have been normal
• No seizures and EEG have been normal
• Growth and development have been normal
References


