Neonatal Diabetes: The Rewards and Challenges
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AV Presentation
- Presented with diabetes at 42 days of life
- Increased thirst
- Increased urination/ diarrhea
- Weight loss
- Irritability

AV Presentation Labs
- Glucose: > 900 mg/dl
- Bicarb: 11
- Sodium: 138
- Urine Ketones: large
Hospital Course
- Seizures secondary to cerebral edema
- IV insulin for 3 days 0.08-0.1 unit/kg/hour
- Teaching

AV Initial Management
- Diluted NPH insulin
  - 10 units/cc
  - To give 0.1 units draw up 1 unit
  - NPH U-10 2.2 units every 6 hours
- Frequent blood glucose testing
- Structured feeding schedule:
  - 4a, 8a, 12n, 4p, 8p

AV and Diabetes
- Family coping
- Structured lifestyle
- Daycare
AV gets an Insulin Pump

- December of 2004 - age 5 years
- AV started on a Medtronic insulin pump

The Phone Call

- A different type of diabetes
- Hattersly's article on KCNJ11 Neonatal Diabetes
- We Dr. Stanley, myself and Susan Becker called mom with a proposal

Neonatal Diabetes

- Genetic form of diabetes
- Develops within the 1st months of life
- Estimated prevalence 1:100,000-300,000 live births
- Heterozygous / homozygous mutations in KCNJ11 or ABCC8
- Encoding 2 subunits
  - Kir 6.2
  - SUR1
Permanent Neonatal Diabetes
The most common cause of Permanent Neonatal Diabetes (NDM) is a mutation in KCNJ11.
Patients with KCNJ11-related NDM are at increased risk for delays in learning, social-emotional and behavior development, ADHD and sleep difficulties.

Transient Neonatal Diabetes
Mutations less strongly activating
Develops in the first few weeks of life, resolves within a few months of age
May recur in adolescence
Caused by imprinted region of 6q24

Genetics
Athena Genetics
ABCC8: p.L225p
De Novo mutation
Reported as a “gain of function” mutation
Ordering Genetic Testing

University of Chicago

University of Pennsylvania

Athena

What do the genetic mean?

- Loss of function mutation in ABCC8
- Increase activity in the KATP Channels
- Decrease insulin secretion since the membrane does not depolarize normally

Transitioning from Insulin to Glyburide

In December 2006, following the protocol by Hattersley, we transitioned AV from his insulin pump to glyburide.

Initial dosing was Glyburide 7.5 mg/day, we gradually increased to Glyburide 15 mg/day = 0.6 mg/kg/day
Glycemic Control on Glyburide

HbA1C levels were maintained less than 6% until 2012 when adolescence and puberty came into play.

Glyburide Side Effects

- Glyburide is generally used for older adults with Type 2 Diabetes
- Side effects typically seen with Glyburide are also complications seen in the elderly population.

The Importance of Sulfonylurea Therapy

- Neonatal Diabetes is associated with learning and behavior issues. Sulfonylurea therapy is important for learning issues.
Illness and Glyburide

- AV experienced very minimal hyperglycemia
- Family monitored closely during times of illness
- AV has not required any insulin since initiation of glyburide

Growing up on Glyburide

- Without glyburide AV would experience elevated blood sugars
- It's difficult to impress upon a teen that pills are just as crucial as injections

Diabetes Management

- As time went on mom began to realize that we were correct- blood glucose levels did not need to be monitored 6-8 times / day
- As AV got older we were asking for blood sugars to be tested
Food Choices

- Sweetened Beverages
- Junk food
- Eating like a teen

A1C Creeping up

- 6-7 % range
- 7/2015: A1C 7.4 %: intervention needed

Januvia (Sitagliptin)

- DPP-4 Inhibitor. Believed to exert its actions by slowing the inactivation of incretin hormones
- Starting dose: Januvia 25 mg each morning (lowest dose)
Why does Januvia work?

- Januvia inhibits the enzyme that degrades GLP1 (incretine), thus as a result GLP1 has a more prolonged half life and its actions on stimulating insulin secretion is extended.