A Sweet Baby: A Case of Neonatal Diabetes Mellitus

[1]M. Blalock, MD; [1,2]M. Ferm, MD; [1,2]R. Roberts, MD, MPH.

[1]Department of Pediatrics, Baylor College of Medicine/Texas Children's Hospital

[2]Division of Diabetes and Endocrinology, Department of Pediatrics, Baylor College of Medicine/Texas Children's Hospital

2024 ANNUAL CONFERENCE PESTOLA PEDIATRIC ENDOCRINE SOCIETY OF TEXAS, OKLAHOMA, LOUISIANA, AND ARKANSAS
SAVE THE DATE | APRIL 5-7, 2024
SAN ANTONIO, TEXAS

The authors have no financial disclosures or conflicts of interest to report.

Introduction

- Neonatal Diabetes Mellitus (NDM) is rare with an incidence of 1 in 90,000-160,000 live births.[1]
- A single gene defect affecting insulin production or secretion often causes NDM.[2]
- Some of the genetic defects are responsive to sulfonylureas which allows for discontinuation of insulin therapy.[2]

Case Presentation

- An 8-week-old male (history of IUGR, SVD at 40 weeks, consanguineous parents) presented to the ER with respiratory distress, vomiting, and poor feeding.
- On physical exam, he was afebrile, tachycardic, tachypneic with retractions, and severely dehydrated.
- Biochemical evaluation demonstrated severe hyperglycemia and ketoacidosis:
  - pH 6.84
  - Bicarbonate <2 mEq/L
  - Glucose 809 mg/dL
  - βhydroxybutyrate 6.5 mmol/L
  - C-peptide 0.05 ng/ml
- Management per DKA protocol was initiated with the two-bag system.

Hospital Course

HD 1
- Admitted to PICU.
- Sulfonylurea trial discussed but deferred given parental consanguinity and patient acuity.

HD 2-3
- Intubated and sepsis work-up initiated.
- EEG monitoring with abnormal spikes.
- Rapid WES and 6q24 methylation panel sent.

HD 6
- Extubated.
- Maintained on IV insulin with plans to transition to subcutaneous insulin.

HD 10-19
- Positive *KCNJ11* mutation.
- Sulfonylurea therapy started.
- Insulin discontinued.
- Discharged on glyburide monotherapy.

Figure 1: Hospital Course

Discussion

- With parental consanguinity, only ~10% of patients with NDM will respond to sulfonylurea trials, thus they are generally not attempted prior to genetic testing.[1,2]
- Our patient has a maternally-inherited autosomal dominant *KCNJ11* c.602G>A mutation.
- The *KCNJ11* gene encodes for the Kir6.2 subunit of the K_{ATP} channel depicted in Figure 2.[3,4]
- NDM associated *KCNJ11* mutations prevent ATP mediated closure of the K_{ATP} channel, stopping insulin release.[2]
- Sulfonylureas can sometimes overcome these mutations by closing the K_{ATP} channel and inducing endogenous insulin release.

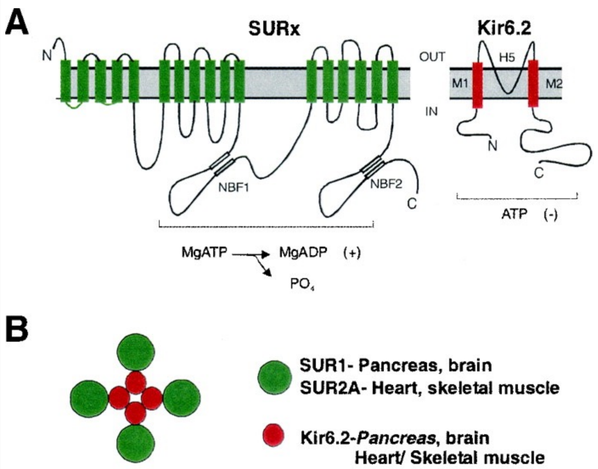

Figure 2: Part A depicts the two subunits of the K_{ATP} channel: the sulfonylurea receptor (SURx) and the inner potassium channel (Kir6.2).[4] Part B shows the octamer configuration of the subunits.[4]

- Mutations in *KCNJ11* are seen in both transient and permanent NDM with or without DEND (Developmental delay, Epilepsy, and Neonatal Diabetes) syndrome.[3,5]
- Our patient's glyburide dosing has been titrated based on glycemic patterns. While on glyburide, he has had improved growth (Figure 3).

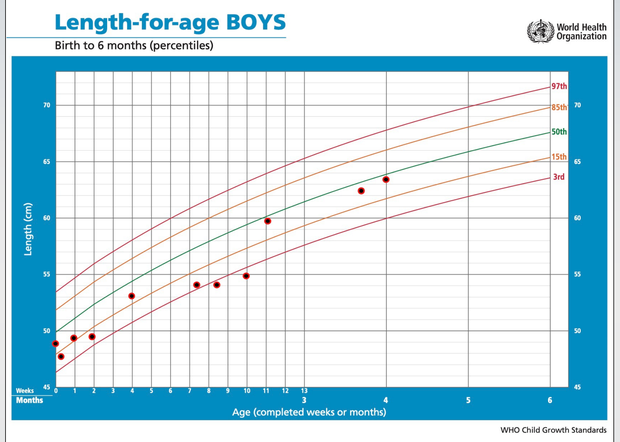

Figure 3: Length for age growth chart of our patient.[6]

Conclusions

This rare case of NDM brings into question whether sulfonylurea trials should be done while awaiting genetic results even in cases of consanguinity.

References

1. Lemelman MB, Letourneau L, Greeley SAW. Neonatal Diabetes Mellitus: An Update on Diagnosis and Management. *Clin Perinatol*. 2018;45(1):41-59.
2. Dahl A, Kumar S. Recent Advances in Neonatal Diabetes. *Diabetes Metab Syndr Obes*. 2020;13:355364.
3. KCNJ11 potassium inwardly rectifying channel subfamily J member 11 [Homo sapiens (human)] Library of Medicine. Updated January 21, 2024.
4. Koster JC, Permutt MA, Nichols CG. Diabetes and Insulin Secretion: The ATP- Sensitive K+ Channel (K_{ATP}) Connection. *Diabetes*. 2005; 54 (11): 3065-3072.
5. Cho JH, Kang E, Lee BH, Kim GH, Choi JH, Yoo HW. DEND Syndrome with Heterozygous KCNJ11 Mutation Successfully Treated with Sulfonylurea. J Korean Med Sci. 2017;32(6):1042-1045.
6. Length/height-age. World Health Organization. Updated 2024.