OBSERVATIONS

The Diagnosis of Neonatal Diabetes in a Mother at 25 Years of Age

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Neonatal diabetes (ND) is defined as persistent hyperglycemia in the first 3 months of life (1). Heterozygous—usually autosomal-dominant—activating mutations in *KCNJ11*, which encode the Kir6.2 subunit of the ATP-potassium (K_{ATP}) channel, cause the majority of cases (2). Sulfonylureas close the K_{ATP} channel by an ATP independent route (2).

A 25-year-old Bangladeshi woman with type 1 diabetes gave birth to a baby girl. The mother had been on insulin for more than 20 years with inadequate glycemic control but never ketoacidosis. The baby was small for gestational age (2.4 kg, <3%). On day 2 of her life, the baby was noted to be increasingly hyperglycemic, reaching 312 mg/dL by day 7. Given the clinical suspicion for ND, a trial of glyburide was initiated at 0.45 mg/kg/day, and the baby responded well. The dose of glyburide was titrated to achieve normal serum glucose (0.02 mg/kg/day).

The genetic test for the *KCNJ11* gene was done, but the results were not expected for months, and the family planned to return to Bangladesh within weeks. The mother was admitted to the hospital for a trial of glyburide. She responded remarkably well and was weaned off insulin in 2 days. GAD 65, islet cell, and anti-insulin antibodies were all negative.

The *KCNJ11* gene mutation was positive for the baby. This G>A mutation at nucleotide 149 results in the substitution of glutamine for arginine at codon 50, which confirms the diagnosis of ND due to the mutation in the K_{ATP} channel.

ND is a form of monogenic diabetes that rarely occurs (1:300,000–500,000 births) (3). ND can be transient (TND) or permanent (PND) (1).

Among children who require insulin in the first year of life, those who develop diabetes at <6 months of age have less prevalent autoimmune markers and more protective HLA, suggesting a mechanism other than autoimmunity (4).

About 50% of the cases of ND constitute TND, some of which recur later in life as type 2 diabetes (1). PND is hyperglycemia early in life without a period of remission (3). *KCNJ11* gene mutations account for 50% of the cases in PND (2).

Glucose metabolism raises ATP levels in the β-cell causing depolarization by the closing of the K_{ATP} channel and eventually leading to insulin release. The mutation in the K_{ATP} channel, which contains the ATP binding site, results in less sensitivity to ATP (2). Our patient had a mutation within the ATP binding site.

Sulfonylureas promote insulin secretion via an ATP-independent route and allow better glycemic control with fewer complications than insulin in PND (2).

The diagnosis of ND responsive to sulfonylurea in the baby raised the suspicion that the mother may have the same condition. Although the mother was unable to get genetic testing, her response to sulfonylurea is consistent with PND.

ND is commonly mistaken for type 1 diabetes. Questioning the diagnosis of type 1 diabetes and obtaining genetic testing is important in specific candidates, such as patients with the onset of diabetes prior to 1 year of age who have a strong family history of early-onset diabetes and a relatively benign course. We suggest that a controlled trial of sulfonylurea be done in these patients if genetic testing is not feasible. This approach may improve glycemic control and quality of life for these patients.

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