TWO NEONATAL DIABETES CASES WITH DIFFERENT MUTATIONS AND TREATMENTS

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BACKGROUND AND AIM
Neonatal diabetes is a monogenic diabetes that can be due to different mutations. Here we report two patients with neonatal diabetes and with two different mutations and treatments.

Case 1
A female infant of consanguineous parents was born at 37 weeks of gestation by normal vaginal delivery with a birth weight of 1900 gr. After birth she was followed in neonatal intensive unit for respiratory distress and hyperglycemia. She didn’t have azidosis nor ketosis. She was treated with subcutaneous kritalized insulin. She had 2 healthy siblings and one sibling on growth hormone treatment due to growth hormone bio- activity. Her family history was insignificant for diabetes.

At the age of 1 month she was referred because of uncontrolled high blood glucose levels. On admission her body weight was 2330 gr, height was 47 cm, head circumference was 35 cm. Her physical examination was normal except hip dysplasia.

Laboratory tests revealed a venous glucose of 354 mg/dl with glycosuria, but no ketonuria or acidosis. Serum C-peptide level was 0.01 ng/ml (normal range: 0.9-4.3 ng/ml), hemoglobin A1c was 7.3% (normal range: 4.8-6%) and tests for diabetes autoantibodies (antiGAD, ICA, IA2) were negative. In the complete blood count Hb level was 9.5 mgr/dl, and mean corpuscular volume MCV was 85.1 fl (normal range: 81-99 fl). The blood film showed no signs of megaloblastic anemia. Serum folic acid, thiamine and vitamin B12 levels were normal. Serum thyroid hormones were with in normal limits (TSH: 1.75 mIU/L, FT4: 1.06 ng/dl). Kidney and liver function tests were all within normal ranges.

DNA sequencing and genetic analysis
A homozygous g.23508363A > G mutation affecting a highly conserved nucleotide within a recently identified distal enhancer PTF1A was identified. Functional analysis showed that this mutation disrupts enhancer activity and is likely to result in decreased PTF1A expression during pancreatic development (Weedon et al. 2014 Nat Gen 46:61-64). Her mother and sister had the same mutation heterozygously. Her brother had no mutation. Unfortunately his fathers genetic analysis couldn’t be done.

CONCLUSION
Although it can be diagnosed clinically genetic analysis is relevant thus regarding to the mutation, treatment and prognosis can be determined.

Case 2
A male infant of nonconsanguineous parents was born at 35 weeks of gestation by spontan vaginal delivery with a birth weight of 3400 gr. His seizures as arm movements had started when he was 1 months old which then progressed as tonic clonic convulsions. He was the first and only child of his family and his family history was insignificant for diabetes.

At the age of 3 months he was referred because of high blood glucose levels and failure to thrive. On admission his body weight was 4460 gr (-3.78), height was 62.5 cm (-0.40), head circumference was 40 cm. His physical examination revealed hypotonia and decreased muscle strength in 4 extremities. He was not following with his eyes.

Laboratory tests revealed a venous glucose of 600 mg/dl with glycosuria, but no ketonuria or acidosis. Serum C-peptide level was 0.72ng/ml (normal range: 0.9-4.3 ng/ml), hemoglobin A1c was 11.4% (normal range: 4.8-6%) and tests for diabetes autoantibodies (antiGAD, ICA, IA2) were negative. In the complete blood count Hb level was 11.4mg/dl, and mean corpuscular volume MCV was 84 fl (normal range: 81-99 fl). The blood film showed no signs of megaloblastic anemia. Serum folic acid, thiamine and vitamin B12 levels were normal. Serum thyroid hormones were with in normal limits (TSH: 1.75 mIU/L, FT4: 1.06 ng/dl). Kidney and liver function tests were all within normal ranges.

DNA sequencing and genetic analysis
He was heterozygous for a previously reported KCN11 missense mutation, p.C166Y. The p.C166Y mutation has been reported previously in patients with developmental delay, epilepsy and neonatal diabetes (DEND) syndrome (littera). This mutation is predicted to be pathogenic and the result confirmed a diagnosis of neonatal diabetes due to a mutation in the Kir6.2 subunit of the KATP channel (Flanagan et al. 2006 Diabetologia 49:1190-1197). Unfortunately his parents genetic analysis couldn’t be done.