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Case Report

Transient Neonatal Diabetes Mellitus in an Extreme Preterm Infant: Successful Switch from Insulin to Sulfonylurea Therapy

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Abstract

Background: Neonatal diabetes mellitus is a rare condition, with prevalence of about 1 in 500,000 live births. Mutation in ABCC8 gene accounts 12% of all cases of neonatal diabetes mellitus. Most patients with ABCC8 gene mutation can successfully transfer on to sulfonylureas. In this case report, we shared our experience with extreme preterm infant with neonatal diabetes mellitus, who successfully treated with oral sulfonylurea.

Case Presentation: we describe extreme preterm infant was born at 24+4 week gestation, birth weight was 600 gram, hyperglycemia was noted at 3rd day of life, genetic analysis revealed a heterozygous missense mutation on ABCC8-gene, the patient was initially treated with insulin infusion, after availability of genetic testing results, the patient was gradually transitioned from insulin to an oral sulfonylurea.

Conclusion: An oral sulfonylurea was an effective and safe therapy for transient neonatal diabetes mellitus in our extreme preterm infant.

Keywords: *Neonatal Diabetes Mellitus (NDM); TNDM; PNDM; Insulin; Sulfonylurea Therapy*

Background

Neonatal diabetes mellitus (NDM) is defined as persistent hyperglycemia that lasts more than two weeks and diagnosed in the first 6 months of life. It is rare condition, with prevalence of about 1 in 500,000 live births [1,2]. NDM might either be transient (TNDM) or permanent (PNDM). TNDM represents about 40 - 60% of all NDM cases [3], most cases are small for gestational age and recover by three to six months of age [1,4], but are predisposed to developing type 2 diabetes in late life, usually around adolescence [5]. NDM is non autoimmune disorder and it is usually caused by genetic defects, leading to abnormal development or absence of the pancreas or islets, or dysfunction of B-Cells, resulting in low insulin secretion. Mutations in the ABCC8 and KCNJ11 genes are a common cause of neonatal diabetes. Molecular analysis of chromosome 6 anomalies and KCNJ11 and ABCC8 genes can provide a method to differentiating transient from permanent neonatal diabetes [6-9]. Oral sulfonylurea therapy is recommended for patients with mutations in ABCC8 and KCNJ11. The use of oral sulfonylurea significantly improved long-term glycemic control, as well as improve the neurological abnormalities in pa-

tients with neonatal onset diabetes due to ABCC8 or KCNJ11 mutations [10]. Transfer from insulin to oral sulfonylurea in patients with neonatal diabetes is well described, but less experience in an extreme preterm infants.

Case Report

A male preterm was born to a 35 years old gravida 2, para 1 at 24+4 week gestation, the mother has diabetes mellitus type 1. The delivery was via emergency caesarean section because of placental abruption, the Apgar scores at 1st, 5th and 10th minutes were 4/6/8. Birth weight was 600 gram (15th percentile), length 31 cm (33rd percentile) and head circumference 24 cm (85th percentile). The infant was immediately intubated and given surfactant, he suffered with complicated course with severe respiratory failure associated with pulmonary hemorrhage, the patient was extubated at 9th day of life. Hyperglycemia was noted at 3rd day of life, the serum glucose was 550 mg/dl, an insulin infusion was started. Blood sugar continued to fluctuate (maximum 600 mg/dl, minimum 16 mg/dl), a further investigation was done, c-peptide was 0,2 ng/ml (0,9 - 7,1 ng/ml), pancreatic elastase in stool was 387 µg/g (> 200 µg/g). Ultrasound Abdomen revealed no structural abnormalities, cranial ultrasound was also normal. Genetic analysis revealed a heterozygous missense mutation on ABCC8-gene (C.184c> T, p.His62 Tyr), genetic test for the father was normal, while genetic test for the mother reveals also a heterozygous mutation on ABCC8 gen. After availability of genetic testing results, the patient was gradually transitioned from insulin to an oral sulfonylurea at 42th day of life. Glibenclamide suspension was started with 0,2 mg/kg/d in two divided doses, then has been increased to 0.3 mg/kg/d, it has been reduced again to 0,2 mg/kg/d because of low blood glucose levels, with this dose the blood glucose was stable und in normal range. After three weeks because of hyperglycemia two attempts to stop glibenclamide were failed, but after 6 weeks (86th day of life) glibenclamide has been completely stopped. The infant was presented 6 months after discharge (at age of 9 months) in our Diabetes OPD, he continued to have normal blood glucose. HbA1c was 5,5%, the weight was 5,9 Kilogram (3. percentile), and length 62,5 cm (3. percentile).

Discussion

Mutation in ABCC8 gene accounts 12% of all cases of neonatal diabetes [11]. The sulfonylurea receptor (SUR1) acts as the regulatory subunit of ATP-sensitive potassium channel in pancreatic beta cells. The activating mutation in the ABCC8 gene, which encodes SUR1, might cause both a permanent and transient NDM [12].

TNDM affects about 50% of all children with neonatal diabetes. Although remission occurs usually in the first six months, relapse in childhood or adolescence occurs in up to 50% of patients [13].

Oral sulfonylurea therapy is safe and effective in the short-term in most patients with diabetes due to ABCC8 mutations, who have been able to stop insulin completely and have better control with less hypoglycemia. About 85% of patients with neonatal diabetes due to ABCC8 gene mutations can be successfully treated with oral sulfonylurea treatment [14].

There were different sulfonylureas such as glipizide, glimepiride and glibenclamide (also known as glyburide). In our patient the treatment with glibenclamide suspension was started on day 42 of life, starting dose was 0,2 mg/kg/d in two divided doses, then increased to 0,3 mg/kg/d, after two days insulin was no more needed. Dose reduction was necessary because of two hypoglycemia episodes, other side effects was not reported.

In a study by Rafiq., *et al*. side effects such as nausea, vomiting, diarrhea and hypoglycemia has been reported. According to the same study four patients could not be successfully transferred from insulin to sulfonylurea, unsuccessful patients were diagnosed as diabetic later, two of the patients had neurological complications [14].

A genetic analysis was done which revealed heterozygous missense mutation (c.184c>T,p.His62 Tyr) in ABCC-gene. This mutation is very rare, the mutation of ABCC8-gene not only associated with neonatal diabetes, but also with hyperinsulinismus and diabetes mellitus. In comparison with Kir6.2 patients, lower doses of both insulin and sulfonylurea were needed in SUR1 patients [14].

Conclusion

An oral sulfonylurea was an effective and safe therapy for transient neonatal diabetes in our extreme preterm infant. We recommend a low starting dose (0,1 - 0,2 mg/kg/d), gradual increase in dose as well as close blood glucose monitoring.

Bibliography

1. Shield JP., *et al*. "Aetiopathology and genetic basis of neonatal diabetes". *Archives of Disease in Childhood Fetal and Neonatal Edition* 76.1 (1997): 39-42.
2. Von Muhlendahl KE and Herkenhoff H. "Long-term course of neonatal diabetes". *The New England Journal of Medicine* 333 (1995): 704-708.
3. Flanagan SE., *et al*. "Mutations in ATP-Sensitive K+ Channel genes Cause Transient Neonatal Diabetes and Permanent Diabetes in Childhood or Adulthood". *Diabetes* 56 (2007): 1930-1937.
4. Gentz JC and Cornblath M. "Transient diabetes of the newborn". *Advances in Pediatrics* 16 (1969): 345-363.
5. Temple I Karen and Schield Julian PH. "6q24 transient neonatal diabetes". *Reviews in Endocrine and Metabolic Disorders* 11.3 (2010): 199-204.
6. Chantal Metz., *et al*. "Neonatal diabetes mellitus: chromosomal analysis in transient and permanent cases". *The Journal of Pediatrics* 141.4 (2002): 483-489.
7. Michel Polak Helene Cave. "Neonatal diabetes mellitus: a disease linked to multiple mechanisms". *Orphanet Journal of Rare Diseases* 2 (2007): 12.
8. Katharina Warnke., *et al*. "Clinical presentation and long-term outcome of patients with KCNJ11/ABCC8 variants: Neonatal diabetes or MODY in the DPV registry from Germany and Austria". *Pediatric Diabetes* (2022): 1-10.
9. De Franco E., *et al*. "The effect of early comprehensive genomic testing on clinical care in neonatal diabetes; an international cohort study". *Lancet* 386 (2015): 957-963.
10. Caroline de Gouveia Buff Passone, Elisa Laurence Vaivre-Douret., *et al*. "Sulfonylurea for improving neurological features in neonatal diabetes: A systemic review and meta-analyses pediatric Diabetes 23.6 (2022): 675-692.
11. Babenko AP., *et al*. "Activating mutations in ABCC8 gene in Neonatal Diabetes mellitus". *The New England Journal of Medicine* 355 (2006): 456-466.
12. Proks P., *et al*. "Aheterozygous activating mutation in sulphonylurea receptor SUR! (ABCC8) causes neonatal diabetes". *Human Molecular Genetics* 15 (2006): 1793-1800.
13. Temple IK., *et al*. "Transient neonatal diabetes: widening the understanding of the etiopathogenesis of diabetes". *Diabetes* 49 (2000): 1359-1366.
14. Rafiq M., *et al*. "Effective treatment with oral sulphonylurea in patients with diabetes due to SUR1 mutation". *Diabetes Care* 31 (2008): 204-209.

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