ORIGINAL RESEARCH PAPER

Neonatology

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TRANSIENT NEONATAL DIABETES -A RARE GENETIC NEONATAL HYPERGLYCEMIA

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ABSTRACT

Neonatal diabetes mellitus is very rare condition that causes hyperglycemia and growth retardation in the first week of life in neonates. Of the two types transient neonatal diabetes presents with clinical features of Small for Gestational Age(SGA),macroglossia,umbilical hernia ,cardiac and neurological developmental defects occasionally.Diagnosis is confirmed through genetic analysis.Transient neonatal diabetes has good prognosis and resolves by 18 months of age on treatment. A case report of transient neonatal diabetes born to primigravida mother due to loss of methylation at the 6q24 locus of PLAGL1 DMR in leucocyte DNA diagnosed at a secondary care centre was presented.

Neonatal hyperglycemia is common problem seen in low birth weight, preterm infants receiving parenteral glucose and also seen in sick newborn. Neonatal diabetes mellitus is very rare, seen in 1 in every 300,000 to 400,000 live births.(peurto rico). Newborns typically present with hyperglycemia and growth retardation in first week of life. Diagnoses is confirmed by genetic analysis. We present a case report of transient neonatal diabetes due to loss of methylation at the 6q24 locus.

Case History-

A primigravida mother delivered full term IUGR female child born of non consanguineous marriage. Birth weight was 1.4kg. Mother was on regular antenatal checkup. Antenatal scan was suggestive of IUGR and no anomalies. Baby was shifted to NICU for low birth weight. On routine screening, hyperglycemia was documented (>250mg/dl) requiring insulin drip. C peptide levels were low (<0.01ng/ml) ruling out insulinoma while HbA1c was 9%.Thyroid profile was normal. There was no ketoacidosis. The mother's blood sugar levels and other endocrine reports were normal.Genetic analysis detected loss of methylation at PLAGL1 DMR in leucocyte DNA that confirmed the diagnosis of transient diabetes due to loss of methylation at the 6q24 locus. Patient responded well to oral sulphonylureas and was discharged on oral hypoglycemic drug.

DISCUSSION-

Neonatal diabetes mellitus is an uncommon metabolic disorder. There are two types of neonatal diabetes, persistent permanent neonatal diabetes and other is remitting and relapsing transient neonatal diabetes. The permanent neonatal diabetes mellitus is caused by the mutation the KCNJ11, ABCC8, INS, GCK, PDX1 etc genes. Transient neonatal diabetes is characterized by hyperglycemia within first 6 weeks of life. Major cause of TNDM is mutation at chromosome 6q24 due to defect in methylation. Three types of defects are identified at the locus-1) paternally inherited duplication. 2) Parental uniparental disomy, 3) Complete loss of methylation of the maternal allele at 6q24 due to epimutation. The clinical features are severe intrauterine growth restriction, hyperglycemia in neonatal period and resolves by 18 months of age, dehydration and no ketoacidosis(Isabel , TND 6q24). There is decreased or negligible C peptide level. Other features associated with 6q24 methylation defects includes macroglossia, umbilical hernia, rarely cardiac and neurological developmental defects. Management includes insulin therapy during the initial phase and long term oral hypoglycemic drugs. Genetic testing of our patient detected loss of methylation at the PLAG1 DMR in leucocyte DNA using methylation specific multiplex ligation dependent probe amplification (MS MLPA) and confirmed the diagnosis of transient neonatal diabetes mellitus due to loss of methylation at the 6q24 locus. Our patient was treated with insulin during the initial phase and was discharged on oral sulphonylureas.

CONCLUSION-

Detailed investigation is needed for neonatal hyperglycemia included genetic analysis. Transient neonatal diabetes is rare disorder with good

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