A Novel SLCA16A1 mutation in An Infant with Hypoglycemia and Severe Metabolic Ketoacidosis

Reem Hasnah, Sara Al-Khawaga, Saras Saraswathi, Basma Haris, Shihab Mundekkadan, Amira Saeed, Sanaa Sharari, Idris Mohammed, Faiyaz Ahmad Khan, Khalid Hussain*

*Department of Pediatric Medicine, Division of Endocrinology, Sidra Medicine, Doha, Qatar.

E-mail: khusain@sidra.org

Disclosure-None of the authors have any potential conflict of interest.

INTRODUCTION

Recurrent episodes of ketoacidosis with or without hypoglycemia have recently been reported with homozygous or heterozygous mutations in the solute carrier family 16 member 1 (SLC16A1) gene. This gene encodes for the monocarboxylate transporter 1 (MCT-1) which plays a key role in lactate, pyruvate and ketone body transport. The Objectives of this study is to describe the youngest patient with a novel SLC16A1 gene who presented with recurrent episodes of acidosis and hypoglycemia.

CASE REPORT

The patient was born following a NVD, with a birth weight of 3.2kg. At 3 days of age she presented with hypothermia and acidosis. At 6 months of age, she presented again with vomiting and was biochemically noticed to have hypoglycemia and metabolic acidosis. Family history was significant for consanguinity (first degree cousin parents) - Figure 2. The patient has repeated episodes of hypoglycemia and seizures of which an MRI of the head displayed bilateral symmetrical abnormal T2/FLAIR hyperintense white matter signal changes - Figure 3.

METHODS

Whole Exome Sequencing (WES) analysis was performed in the patient and her parents using NetGen sequencing on an Illumina system. Sequence and copy number alterations were reported according to the Human Genome Variation Society (HGVS) and International System for human Cytogenetic Nomenclature (ISCN) guideline, respectively.

RESULTS

Exome sequencing showed that the patient was homozygous for the c.218delG pathogenic variant in the SLC16A1 Gene (PGly73ValfsX8 in exon 3 in the SLC16A1 gene). The patient’s mother and father were heterozygous for the mutation- Figure 1. The c.218delG variant has not been reported previously as a pathogenic variant nor as a benign variant. The c.218delG variant causes a frameshift starting with codon Glycine 73, changes this amino acid to Valine residue and creates a premature Stop codon at position 8 of the new reading frame. This identified variant is anticipated to cause loss of normal protein function either through protein truncation or nonsense-mediated mRNA decay. The c.218delG variant is not observed in large population cohorts.

CONCLUSION

We report a novel mutation in the SLC16A1 Gene leading to recurrent metabolic acidosis and hypoglycemia. Our patient is one of the youngest presenting with this disorder. Further research will be required to understand the role of the MCT-1 in key tissues such as the liver and muscle and ketone body metabolism. Disruption of MCT1 in the central nervous system produces axon damage and neuronal loss in mice, yet it remains unclear at this stage whether this is a direct effect of the absence of MCT1 in the brain or caused by episodes of profound ketoacidosis. Nevertheless, neurodevelopmental follow up should be considered in this patient.