He was born from a non-consanguineous marriage. He was the second child in the family. His parents and older sister were well and healthy. There was no known history of neonatal hypoglycaemia nor early-onset diabetes in his family.

At 2 years, the patient still required diazoxide with episodes of hypoglycaemia when feeding was delayed. He was referred to the genetic team. Further investigation revealed compound heterozygous mutations at the ABCC8 gene (likely autosomal recessive type) which were c.2992C>T (path); similar to his mother, and another mutation c.4607C>T (VUS). The father did not have any ABCC8 mutations.

CONCLUSION

Clinical suspicion of CHI should be highly considered in macrosomic babies with persistent hypoglycaemia in the absence of maternal diabetes. Expedited genetic study should be considered to assist clinical management.

EP_P003

EXTREME SPECTRUM OF DYSGLYCAEMIA IN TWO SISTERS WITH CDKN1C MUTATION

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INTRODUCTION/BACKGROUND

CDKN1C mutation is mainly associated with Beckwith-Wiedemann syndrome (BWS), an overgrowth disorder, and IMAGe syndrome, an undergrowth disorder. In both conditions, hypoglycaemia can be part of the presenting features. Defect in this gene has not been directly linked with diabetes; however, evidence supports the hypothesis that loss of CDKN1C function leads to increased beta cell proliferation and causes hypoglycaemia. Some hypotheses also suggest that overactivity of CDKN1C gene results in the opposite phenotype: decreased proliferation of beta cells leading to reduced insulin production and onset of diabetes.

CASE

We report two cases of Malay siblings who presented with dysglycaemia of opposite ends of the spectrum. Both siblings were not dysmorphic with normal BMI. The elder sister, now 21 years, presented at the age of 5 years with hyperglycaemic symptoms and was treated as type 1 diabetes. Her diabetes autoantibodies were negative. She has been on insulin with an average HbA1c of 8%.

The younger sister presented at 16 years with frequent postprandial hypoglycaemia episodes associated with recurrent cramps and muscle weakness. Investigations showed hyperinsulinaemic hypoglycaemia with concurrent hypokalaemia. PET scan and MRI were negative for insulinoma. Oesophagogastroduodenoscopy did not find any suspicious gastrointestinal lesions. Munchausen by proxy was excluded. Her symptoms improved with oral diazoxide but not fully resolved. She is dependent on potassium supplements. Genetic testing on both sisters revealed same mutation at the CDKN1C gene, reported as variant of uncertain significance (VUS).

CONCLUSION

In our patients, CDKN1C mutation manifested with polar opposites of dysglycaemia. The molecular function of the gene in glucose homeostasis is yet to be defined.

EP_P004

UNVEILING THE MYSTERIES: GENETIC PERSPECTIVE ON PRIMARY ADRENAL INSUFFICIENCY

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INTRODUCTION

Primary adrenal insufficiency (PAI) in childhood is rare and potentially life-threatening. The most common cause is congenital adrenal hyperplasia (CAH) resulting from 21-hydroxylase deficiency. Advancements in molecular genetics have revealed more genetic mutations causing PAI, which helps in explaining associated clinical features and prognosis. Clinical data and genetic tests were reviewed for two patients who presented with PAI.

CASE 1

LA presented with hypotonia and global developmental delay at the age of 1 year, with normal brain MRI/MRA and inborn error of metabolism (IEM) workup. She defaulted follow-ups until she presented again with generalized hyperpigmentation to dermatology at 3 years. Workup showed ACTH >278 pmol/L, normal 17-hydroxyprogesterone (17-OHP), and no rise in cortisol (<1.8 nmol/L) on ACTH stimulation test. Adrenal ultrasound was normal. Genetic