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

testing was positive for NGLY-1 gene mutation, which is associated with global developmental delay, movement disorders, seizures, liver disease and alacrimia.

CASE 2

MI presented with being "easily tired" and hyperpigmentation since the age of 6 years. The endocrine team was consulted due to low cortisol. Investigations revealed ACTH >278 pmol/L, normal 17-OHP and flat response following ACTH stimulation test. Adrenal CT was normal. Genetic studies came back positive for ABCD1 mutation, a condition of adrenomyeloneuropathy, associated with progressive lower limb weakness and spasticity in the third or fourth decade of life.

With hydrocortisone replacement and fludrocortisone therapy, LA and MI improved noticeably by decreasing skin hyperpigmentation.

CONCLUSION

Non-specific presentations of PAI and the rising numbers of genetic aetiologies discovered warrant genetic testing in affected individuals. This will facilitate prompt diagnosis based on clinical features and prognostication. It provides opportunities for tailored patient management, family counselling and heightened surveillance of possible co-morbidities.

EP_P005

CO-OCCURRENCE OF OCULAR MYASTHENIA GRAVIS, TYPE 1 DIABETES MELLITUS AND GRAVES' THYROTOXICOSIS IN A YOUNG CHILD

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INTRODUCTION

Ocular myasthenia gravis (OMG), type 1 diabetes mellitus (T1DM) and Graves' thyrotoxicosis (GT) are autoimmune conditions in childhood. However, co-occurrence and sequential onset of these diagnoses is uncommon. It could signify a spectrum of polyglandular autoimmune syndrome type 2 with polygenic inheritance.

CASE

A 6-year-2-month-old female presented with progressive drooping of both eyelids for the past two months. Chest CT showed normal thymus, and the anti-acetylcholine receptor was positive (4.89 nmo/L) [reference value (RV) <0.25 nmol/L]. The diagnosis of ocular myasthenia gravis was ascertained. She responded well to pyridostigmine.

Nonetheless, she presented again at 8 years and 11 months old with polyuria, polydipsia and nocturia for three weeks, and significant weight loss. She had severe DKA requiring intensive care. Biochemical markers were consistent with T1DM: low C-peptide (57 pmol/L), low insulin (4.3 pmol/L), positive anti-ICA (45.61 IU/mL) (RV <28 IU/mL) and anti-GAD (98.18 IU/mL) (RV <17 IU/mL), while anti-IA2 was low (<2.5 IU/mL) (RV <28 IU/mL).

While her initial thyroid function was normal, thyroid auto-antibody screening was positive for anti-TPO (222 IU/mL) (RV <35 IU/mL). Following multiple daily insulin injections, her glycaemic control and weight gradually improved. Ten months later, at 9 years and 10 months old, her HbA1c worsened, and her mother reported a sudden increase in insulin needs with weight loss. She manifested symptoms of hyperthyroidism and was found to have tachycardia, tremors and diffuse goitre. She did not have Graves' ophthalmopathy; bilateral ptosis remained the same. Anti-TSH receptor antibodies were significantly positive (26.30 IU/L) (RV <1.75 IU/L).

CONCLUSION

OMG in young children is rarely associated with T1DM. Screening for diabetes auto-antibodies should be considered. In T1DM children, GT should be taken into account when there is unexplained weight loss or deterioration in glycaemic control.

EP_P006

AN UNUSUAL CASE OF MASSIVE NEONATAL GOITRE

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INTRODUCTION

Congenital hypothyroidism occurs in one out of 3000 live births in Malaysia. Over 95% of the cases have no clinical manifestations at birth. In this peculiar case, we present a patient with massive neonatal goitre with congenital hypothyroidism.

CASE

An 8-month-old male was diagnosed prenatally to have a neck mass on a detailed scan at 37 weeks. It was reported to be highly vascularised with possible goitre. Maternal biochemical markers showed euthyroid status, but neck ultrasound revealed multinodular goitre. There were no suggestive risk factors for iodine deficiency. Because of the possibility of airway compression, caesarean section was recommended and he was delivered via ex-utero