Neurological examination revealed central hypotonia. He had failure to thrive during infancy where he was on orogastric feeding for 1 month, achieved brief normalisation at 1 year old, followed by hyperphagia and rapid weight gain since the age of 2 years old. He is a product of a non-consanguineous marriage. He also has isolated central hypothyroidism with left cerebral hemiatrophy.

Chromosomal study showed 46XY karyotype. A series of imaging including abdominal ultrasound, KUB, pelvis, cranium, echocardiogram and brain MRI - was normal. He was suspected to have Prader Willi Syndrome, but methylation test was normal. Genetics team co-managed and treated him for Temple Syndrome with maternal uniparental disomy 14 with Prader Willi Syndrome like phenotype.

CONCLUSION

Temple syndrome is largely manifested by physical defects necessitating obligatory supportive therapies early in the life of affected individuals. The syndrome has shown that a subset of patients develop obesity. BMIs increased along the reference curves in most patients. Endocrine anomalies are prevalent, with truncal obesity developing as early as 4 to 6 years.

EP_P015

IT'S MODY! NOT TYPE 2 DIABETES

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INTRODUCTION/BACKGROUND

MODY (maturity-onset diabetes of the young) is a rare form of diabetes which represents a clinically heterogeneous group of autosomal-dominant disorders caused by mutation in genes involved in beta cell development and insulin secretion. The classic phenotype of MODY includes nonketotic noninsulin-dependent diabetes with diagnosis before age 25 years and an affected parent. However, there is clinical overlap between MODY, type 1, and type 2 diabetes resulting in frequent misdiagnosis of MODY. Data collection was done by reviewing the electronic medical records of the selected patient and salient points were noted.

CASE

TSE, presented at the age of 9 years old with hyperglycaemia detected on routine monitoring. On presentation, she was asymptomatic and her investigations revealed nonketotic hyperglycaemia (RBS 10.5 mmol/L). Clinically there was no evidence of acanthosis nigricans and her BMI was within normal range. Further investigations revealed HbA1c of 8.6% with an abnormal OGTT (FBS: 8.9 mmol/L, 2 hours post: 20.97 mmol/L). Her pancreatic autoantibodies came back as all negative and had a high c-peptide level of 357.9 pmol/L. She was treated initially with oral metformin. On further history, the mother had early-onset diabetes and there was a strong family history of early-onset diabetes on the maternal side. Genetic testing by whole exome sequencing revealed a heterozygous variant in HNF1B. She was further investigated and renal function, lipid profile and ultrasound of the abdomen and kidneys were normal. She was subsequently transitioned to insulin therapy.

CONCLUSION

HNF1B has a wide phenotypic spectrum, and affected individuals may present with isolated renal disease, isolated diabetes, or both. This case highlights the importance of the precision medicine approach in MODY. Molecular genetic testing can identify the subtypes and has profound implications on diabetes treatment and prediction of future development of co-morbidities, allowing early preventive or supportive treatment.

EP_P016

HYPOPHOSPHATASIA, RARE BONE MINERALISATION DISORDER THAT MIMICS OSTEOGENESIS IMPERFECTA AT BIRTH

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INTRODUCTION/BACKGROUND

Hypophosphatasia is a genetic disorder characterized by impaired mineralization of bones and teeth that results in fractures and deformities. It affects less than 1:100,000 live births with different clinical spectrums. It is caused by loss-of-function mutations of ALPL gene that encodes tissue nonspecific alkaline phosphatase (TNSALP), leading to low activity of this enzyme that usually mediates the breakdown of inorganic pyrophosphate that blocks mineralization. We reported an infant who was initially admitted to NICU at birth.

CASE

Antenatally, the patient was detected with possible osteogenesis imperfecta and unilateral lung hypoplasia by a detailed foetal scan at 32 weeks gestation. His mother had GDM and underwent LSCS at 37 weeks 5 days with a weight of 2.42 kg. He was born with generalized bowing deformities of both upper and lower limbs, a broad

forehead, wide wide-spaced nipple, and no blue sclera. His respiratory assessment was normal. His skeletal survey reported generalised osteopenia with bowed limbs and plastic fracture over the right femur consistent with osteogenesis imperfecta. He had normal serum calcium, persistently low ALP (18-25 IU/L), iPTH: 69.3 pg/ml (14.9-56.9) and 25 (OH) vit D3: 51.70 nmol/L (insufficient). There was no family history of bone diseases and parents were not consanguineous. His genetic results showed heterozygous, autosomal recessive, likely pathogenic, ALPL (NM_000478.6), Exon 2, c.29T>C, p. (Ile10Thr), and ALPL (NM_000478.6), Exon 9, c.991G>A, p. (Val331Met). He continued to improve without treatment and was last reviewed at 5 months old, with appropriate development and no fracture.

CONCLUSION

There are very few cases of hypophosphatasia reported locally. It is important to highlight the differential as compared to osteogenesis imperfecta. Hypophosphatasia could present differently, with our case reflecting the benign perinatal type, whereas others would require enzyme replacement, or asfotase-alfa as the first medical treatment for perinatal, infantile and juvenile onset of the disease.

EP_P017

CONGENITAL HYPOTHYROIDISM WITH DIFFERING PHENOTYPE IN TWO SIBLINGS WITH THE SAME DUOX2 MUTATION

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INTRODUCTION/BACKGROUND

Congenital hypothyroidism (CH) is caused by thyroid gland structural or functional defects. Thyroid dysgenesis is typically sporadic but dyshormogenesis is frequently inherited as autosomal recessive. Dual oxidase 2 (DUOX2) gene mutation causes abnormal iodide organification in thyroid hormone synthesis.

We report 2 siblings with CH sharing the same mutation in DUOX2, however only one had permanent CH.

CASE

A 14-year-old female had CH detected at birth by high cord TSH (>100 m IU/L), and thyroid function test (TFT) on day 3 of life (TSH >100 m IU/L, free T4 8.57 pmol/L). Thyroid replacement was started at a dose of 8 mcg/kg/day. Ultrasound at age 3-year-old showed a hypoplastic thyroid gland. She had permanent CH as TFT was deranged when thyroxine was withheld at age 3. Her younger brother, now aged 9 years, had CH diagnosed at age 1 month when he presented with prolonged jaundice (TSH 56.4 m IU/L, free T4 8.89 pmol/L). His cord TSH was normal (7.18 m IU/L). Thyroxine replacement was started at a dose of 7 mcg/kg/day. Ultrasound at age 3 showed a normal-sized thyroid gland. Thyroxine was stopped at age 3, and subsequent TFT remained normal, indicating transient CH. Both had no goiter, nor comorbidity. No other family members had a thyroid disorder. Parents were non-consanguineous. Whole exome sequencing (3Billion, South Korea) revealed both siblings had the same pathogenic heterozygous DUOX2 mutation (c.3329G>A). It was inconclusive as the second abnormal allele was not detected.

CONCLUSION

The same DUOX2 mutation can have different phenotypes within the same family. Genetic testing has a role in evaluating CH etiology, especially when at least two family members are affected. Newborn siblings of a child with CH need timely monitoring of TFT if cord TSH is normal. Other genetic methods are needed to detect the second variant of DUOX2 in these siblings.

EP_P018

BONE HEALTH SURVEILLANCE AMONG AT-RISK CHILDREN AND ADOLESCENTS IN KUCHING, SARAWAK, MALAYSIA

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INTRODUCTION/BACKGROUND

Chronic health conditions impose poor bone health due to underlying inflammatory conditions, reduced weight-bearing activity and pubertal delay.

METHODS

This prospective study was conducted as the pilot project for bone health surveillance among at-risk children and adolescents followed up by a multidisciplinary team from Paediatrics Department, Sarawak General Hospital from January to February 2024. A bone health screening questionnaire was administered, followed by a physical examination, and biochemical and radiological investigation.

CASE

A total of sixteen subjects (6 males, 10 females) with a mean age of 10.7 ± 2.74 years were recruited. Four subjects had