PE-06

THE JOURNEY OF HYPOPHOSPHATEMIC RICKETS (HR) CHILDREN IN A MALAYSIA PAEDIATRIC ENDOCRINOLOGY CENTRE: A CASE SERIES

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INTRODUCTION
Rickets caused by chronic hypophosphatemia are categorized to those that are FGF23-excess and those from other causes. The most prevalent genetic form of FGF23-related HR is X-linked hypophosphatemic rickets (XLH) secondary to inactivating mutations in the PHEX gene. Treatment options for XLH consist of coventional treatment with phosphate supplement and active vitamin D or Burosumab. Burosumab (currently not available in Malaysia), a FGF23-neutralising antibody has been shown to be clinically superior to conventional therapy.

METHODOLOGY
We describe 7(2 boys) children with HR on conventional treatment under follow-up in our centre.

RESULTS
All presented with bowing of legs between the age of 12-18 months except for a girl who was diagnosed at 6 years old. Diagnosis was made based on clinical, radiological and biochemical findings. At presentation, all had hypophosphatemia, elevated ALP, reduce tubular-reabsoprtion of phosphate and normal levels of vitamin D, calcium, PTH, blood gas and urinary calcium/creatinine. 57% (n=4) have a maternal family history of rickets. FGF23 levels and genetic tests were not done, as it is not available. All children were treated with oral phosphate (mean dose 39 mg/kg/day) divided 4-5x per-day and active vitamin D (calcitriol or alfacalcidol). On follow-up, 3 (42%) had no improvement in genu varus, 4(57%) had persistent elevation of ALP, 5 (70%) poor growth and 5 (70%) mild elevation of PTH (mean-11.44 pmol/L, normal range 1.3-9.3 pmol/L). Two underwent surgical intervention to correct the lower limb deformity. Five (71%) are overweight, which may lead to worsening of their lower limb deformity. Non-compliance to medications is reported in all children, which likely contributed to the poor outcome. None had dental complications, persistent bone pain, hearing impairment, hypercalciuria or nephrocalcinosis.

CONCLUSION
Conventional treatment with phosphate supplements and active vitamin D is unsuccessful in a proportion of patients or/and associated with adverse effects of treatment. Compliance is also a major issue in all our patients.

PE-07

HYPOTHYROIDISM IN INFANTS OF MOTHERS WITH GRAVES' DISEASE: A CASE SERIES

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INTRODUCTION
Maternal hyperthyroidism may cause a wide spectrum of infantile thyroid abnormalities. The maternal thyroid status, presence of antithyroid antibodies and dose of antithyroid drugs(ATD) can affect thyroid alterations of the fetus and neonate. While hyperthyroidism in neonates of maternal Graves' disease (GD) are well-described, hypothyroidism is less commonly reported.

RESULTS
We describe five infants with hypothyroidism born to mothers with GD. In our case series, three mothers were diagnosed with Grave's Disease prior to pregnancy, one during pregnancy and one postnatally. Two mothers had elevated TSH-receptor antibodies (TRAb), the remainder did not have any levels checked. Four were treated with Carbimazole ranging 10-30 mg once daily (OD) and one was treated with Propylthiouracil 50 mg OD. All mothers had poorly controlled hyperthyroidism. Three infants developed central hypothyroidism from Day 9 to 2 months of life. They had low free-thyroxine (FT4) ranging between <3.2 to 7.5 pmol/L with inappropriately low-normal Thyroid Stimulating Hormone(TSH) levels of 0.018 to 3.385 mU/L. One infant had an initial hyperthyroid phase that was treated with Carbimazole prior to converting to hypothyroidism. Two infants developed primary hypothyroidism at Day 4 to 18 of life. Their TSH readings were high between 96.55 to 105 .29 mU/L with fT4 between 6.3 and 18.2 pmol/L. All five patients were started on L —Thyroxine.

CONCLUSION

Maternal gestational hyperthyroidism causes a hyperthyroid fetal environment due to increased thyroxine transfer which leads to suppression of the fetal hypothalamic-pituitary-thyroid axis and central hypothyroidism of the newborn. Primary hypothyroidism could be a result of transplacental passage of antithyroid drugs(ATD) during pregnancy or transplacental passage of maternal blocking antibodies. Early diagnosis and adequate treatment of mothers with GD is imperative to prevent the deleterious consequences of thyroid impairment during the neonatal period. Infants of maternal GD should be monitored for both hyperthyroidism and hypothyroidism.

PE-08

CASE SERIES OF NEONATAL DIABETES WITH KCNJ11 MUTATION_ TRANSFER FROM INSULIN TO SULPHONYLUREA

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INTRODUCTION

Permanent neonatal diabetes, presenting before 6 months old, signifies a monogenic cause. Mostly, it involves mutation of KCNJ11 gene that encodes the Kir6.2 subunit of the ATP-sensitive potassium channel (KATP). The landmark findings by Gloyn et al (NEJM 2004) on oral sulphonylurea (SU) binding to KATP and closing it by a non-ATP dependent route has markedly changed the landscape of management.

METHODOLOGY

Cross-sectional review of medical records.

RESULTS

3 patients (A, B, C) included. (A) presented at day 14, while (B&C) both at 2-month-old. (A) had hyperglycemia without ketosis while (B&C) had severe DKA. (B) also had seizures with delayed motor development (possibly intermediate DEND). All were initiated with subcutaneous insulin at diagnosis. Genetic tests were performed at 8-year-old, 1-year-old, and 5-month-old, respectively. Both (B&C) were similarly heterozygous for a pathogenic KCNJ11 missense variant with p.(Arg201Cys). Transfer to SU was performed based on the published protocol by Prof Andrew Hattersley from the University of Exeter. Time to SU varied with the slowest transfer at 8-year-9-month-old and quickest at 1-year-7-month-old. All transfers were successful with insulin weaned off. Noticeable improvement of HbA1c and C-peptide were demonstrated after 12 weeks. HbA1c decreased from 8% to 5.7%, 8.9% to 6.2%, and 9.6% to 5.8%; C-peptide improved from undetected (<33 pmol/L) to 185 pmol/L, 861 pmol/L, 73 pmol/L, respectively. (B) showed minimal response initially to gliclazide but an excellent response to glibenclamide. Initial glibenclamide dose varied from 0.8 mg/kg/day to 1.6 mg/kg/day. No hypoglycemia or GI complications. (A) needed to restart insulin at 13-year-8-month-old, 5 years after the transfer. (A) was the last to transfer to SU and required a higher initial dose.

CONCLUSION

Neonatal diabetes warrants rapid and focused genetic analysis to identify the genotypes with modifiable outcomes. Early genetic confirmation facilitates the transfer to oral SU for better glycaemic and neurodevelopmental outcomes and potentially improves the durability of the treatment.

PE-09

NEWLY DIAGNOSED T1DM PATIENTS - A DESCRIPTIVE STUDY IN A CHILDREN'S HOSPITAL

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INTRODUCTION

Type-1-diabetes mellitus (T1DM) is the most commonly diagnosed type of DM in children and adolescents. Typically, the presentation of T1DM is either as classic new onset DM, silent DM, or diabetic ketoacidosis (DKA). We aim to describe the epidemiological profile, clinical presentation, and factors related to delayed diagnosis in our patients.

METHODOLOGY

We retrospectively evaluated all newly diagnosed T1DM patients that presented to our centre from January 2015 till May 2021. Diagnosis of T1DM is based on clinical phenotype, with or without antibody confirmation.