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A FAMILY WITH HEREDITARY PARAGANGLIOMA SECONDARY TO SDHD MUTATION

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INTRODUCTION

A third of pheochromocytoma and paraganglioma (PPGL) tumours are part of a hereditary syndrome. Hereditary PPGL shows autosomal dominant inheritance with variable penetrance. Genetic testing is recommended in all patients diagnosed with PPGL regardless of age at presentation and family history. SDHD is the most frequently mutated gene in head and neck PGLs and associated tumours have low malignancy rate. This gene is maternally imprinted with silencing of the maternal allele, thus, the risk of developing paragangliomas is limited to offsprings who inherit the pathogenic variant from their father. Paternally inherited pathogenic variants are highly penetrant by age 50. We describe a family with hereditary paraganglioma due to mutation in the SDHD gene.

RESULTS

The index patient is a 23 year-old female who was diagnosed to have bilateral adrenal pheochromocytoma with carotid and cardiac paragangliomas. Genetic screening revealed that she has SDHD mutation. Further family history revealed that 2 out of 3 paternal aunts have carotid paragangliomas. Her father, youngest of 5 siblings, paternal uncle and grandfather passed away at age 42, 40, 39 years old, respectively, due to severe headache and possible haemorrhagic stroke. Six other family members underwent genetic screening as well. Five family members were positive for SDHD mutation. These include the index patient's elder sister, 3 paternal aunts (2 with carotid paragangliomas) and one male cousin.

CONCLUSION

Genetic testing for family members of patients with hereditary paragangliomas is recommended after thorough genetic counselling. Genetic testing for first- and second-degree relatives is recommended for SDHD-related paraganglioma. Healthy asymptomatic carriers for the gene mutation should undergo clinical assessment, plasma and/or urine metanephrines and normetanephrines and a combination of whole-body MRI (head and neck, abdominal and pelvic) and PET-CT imaging at initial screening. Thereafter, recommendations for long-term surveillance include annual clinical and biochemical evaluation along with whole body MRI repeated every 2-3 years.

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SERUM ADIPONECTIN AND OTHER PREDICTORS OF NEED FOR INSULIN THERAPY IN GESTATIONAL DIABETES MELLITUS: A PILOT STUDY

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INTRODUCTION

The prevalence of gestational diabetes mellitus (GDM) is increasing in Malaysia. Adiponectin is an adipokine that is expressed in adipose tissues and placenta. Plasma adiponectin levels are decreased in several metabolic disorders, including obesity, inflammatory states, insulin resistance, and type 2 diabetes. To our knowledge, there are no published reports on the association between plasma adiponectin levels and need for insulin therapy in GDM. The aim of this study was to assess the association of 1) adiponectin and 2) other predictors such as BMI and HbA1c; with the need for insulin therapy in GDM.

METHODOLOGY

In this prospective pilot study, we recruited women with GDM from combined antenatal clinic. Demographic, anthropometric and clinical data were obtained during the interview. Blood was drawn for insulin, c-peptide, adiponectin and triglyceride at recruitment.

RESULTS

Of the 142 women included in this study, 16.2% required insulin therapy and 83.8% of patients were able to maintain adequate glycaemic control with diet. We did not find adiponectin at GDM diagnosis to be a significant predictor of need for insulin therapy in both univariate and multivariate analyses. The most robust significant correlation of adiponectin in mothers with GDM ($r > 0.5$) was an inverse association with HOMA IR and fasting insulin which is reflective of insulin resistance. Significant associations of insulin requirement in univariate analysis included history of GDM, history of insulin-requiring GDM and glycaemic variables at diagnosis (higher fasting, 2-hour glucose, AUC glucose). Upon multivariate analysis after adjusting for pre-pregnancy BMI and maternal insulin resistance, only Chinese ethnicity (OR= 4.17, CI 1.32-13.16), history of GDM requiring insulin therapy (OR 10.67, CI 1.78-63.90), and AUC glucose (OR=2.14, CI 1.32-3.45) were significantly associated with increased need for insulin therapy.

CONCLUSION
Women with GDM who have an elevated AUC glucose, previous insulin-requiring GDM and are of Chinese ethnicity are at higher risk of requiring insulin therapy.

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OSTEOPOROTIC FRACTURE IN ADRENAL CUSHING'S: IS IT UNCOMMON?

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INTRODUCTION
Osteoporosis is a known complication of Cushing's syndrome (CS). The prevalence of osteoporosis due to endogenous CS has been reported to be 50–59% and about one-third to half of patients with hypercortisolemia-induced osteoporosis experience fragility fracture. We described a case of CS due to Left Adrenal Adenoma complicated with T12 Fracture.

RESULTS
A 25 year- old Malay female presented with 7 months history of amenorrhea. Clinical examination revealed significant hirsutism, acne, purple striae over abdomen and marked proximal myopathy. Her fasting blood sugar was 8.2 mmol/L. She was treated as Polycystic Ovarian Syndrome (PCOS) by gynaecologist and started on oral contraceptive pill (OCP). She was referred to us for further work up of CS, but it was planned after we wash out the OCP.

She was admitted for severe lower back pain with bilateral sciatica. Further history revealed that she had history of fall 3 months earlier but was asymptomatic. Clinical assessment with imaging confirmed T12 fracture with compressive myelopathy involving the nerve roots. Adrenal and spine MRI was done in view of clinical suspicion of CS, which showed that the left adrenal is homogenously enlarged with lobulated margin measuring 2.6 cm x 2.8 cm x 3.0 cm. Her CS was confirmed biochemically with a raised 24-hour Urinary Cortisol at 1345nmol level. Her morning cortisol was 738.2 nmol/L which is elevated while her serum Adrenocorticotrophic hormone was suppressed at <1.10 pmol/L. She proceeded with pedicle screw fixation of her T12 spinal fracture at first and later underwent left adrenalectomy with HPE report of Adrenal Cortical Adenoma with ganglioneuromas.

CONCLUSION
Literature have shown that osteoporosis is more prevalent in adrenal than pituitary CS. A retrospective analysis has shown that age, body mass index, duration of amenorrhea, extent of hypercortisolism do not significantly affect the prevalence of osteoporosis in CS.

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TWO CASES OF IMMUNE CHECKPOINT INHIBITOR INDUCED THYROIDITIS FROM UNIVERSITY MALAYA MEDICAL CENTRE

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INTRODUCTION
Immune checkpoint inhibitor (ICPi) is a known but rare cause of thyroiditis. However, there is a lack of local evidence due to scarce availability of ICPi as a novel treatment for oncology patients. We presented two cases of thyroiditis following treatment with PD-1 checkpoint inhibitors (anti-PD-1) namely pembrolizumab and cemiplimab.

RESULTS
Case A was a 49-year-old female who received pembrolizumab for recurrent metastatic HER2-negative breast cancer after mastectomy, radiotherapy and chemotherapy. Her thyroid function test at baseline was free T4 17.2pmol/L (normal range: 11.5-22.7) and TSH 0.63 mIU/L. After 3 weeks of pembrolizumab, she had biochemical hyperthyroidism (free T4 45.5 pmol/L; TSH <0.01 mIU/L), mildly raised thyroid stimulating immunoglobulins (0.94 IU/L; normal range: <0.55) and a normal thyroid ultrasound. She was treated with tapering dose of carbimazole 20mg daily but developed hypothyroidism (free T4 4.2 pmol/L; TSH 61.55 mIU/L) 5 weeks later while on carbimazole 5mg daily. She remained clinically and biochemically euthyroid with levothyroxine 100 mcg daily. Case B was a 63 year-old male who received cemiplimab for non-small-cell lung cancer with brain metastases after stereotactic brain surgery. He was euthyroid at baseline (free T4 -NA; TSH 0.55 mIU/L). After 3 months of cemiplimab, he had deranged thyroid function test (free T4 23.9 pmol/L; TSH 0.03 mIU/L), which progressed to biochemical hypothyroidism (free T4 7.5 pmol/L; TSH 49.61 mIU/L) 10 months later. He was treated with levothyroxine 25 mcg daily with latest free T4 15.4pmol/L and TSH 18.12 mIU/L

CONCLUSION
Thyroid function test screening is required for all patients undergoing treatment with ICPi. Clinicians need to have a high index of suspicion for ICPi-associated thyroid dysfunction which can be appropriately treated with medical therapy.