very important. Early diagnosis is crucial for appropriate management and genetic counselling.

EP_P016

WHEN GENITAL AMBIGUITY LEADS TO GENETIC DISCOVERY: A CASE OF NR5A1-RELATED DISORDERS OF SEXUAL DEVELOPMENT

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INTRODUCTION

Disorders of sexual development (DSD) encompass a broad, heterogeneous groups of congenital conditions characterized by atypical development of genetic, gonadal, or phenotypic sex accompanied by abnormal development of internal and/or external genitalia. Early diagnosis is crucial to preserve fertility, ensure normal sexual function and support appropriate sex assignment, which significantly impact psychosocial well-being.

CASE

A child assigned female at birth was referred to a Paediatric Endocrinologist at 6 weeks old for evaluation of ambiguous genitalia. Clinical examination revealed penoscrotal hypospadias, rugated labioscrotal folds, palpable gonads with phallus size of 2 cm. The child is the youngest of 2 siblings, with no family history of consanguinity. Notably, the father had hypospadias, which was surgically corrected in childhood. Pelvic ultrasound revealed bilateral oval echogenic structure within labial fold, suggestive of testes, with no visible uterine structure. Hormonal investigations revealed a high testosterone level (13.1 nmol/L) and an antimullerian hormone level of 103 pmol/L, indicating normal Sertoli cell function. Karyotyping confirmed 46,XY genotypes. Further genetic testing identified a heterozygous variant of uncertain significance in the NR5A1 gene. The child was treated with monthly intramuscular testosterone for three months, resulting in phallus growth to 3 cm.

Thorough genital examination during newborn assessment is essential to prevent missed diagnoses of DSD. This patient was diagnosed with an undervirilized male phenotype associated with an NR5A1 mutation – a principal genetic alteration implicated in DSD. The NR5A1 gene plays a crucial role in early gonadal development, testis determination and steroidogenesis.

CONCLUSION

This case highlights the importance of early recognition and management of DSD. Genetic testing for NR5A1 mutation should be considered in cases of 46,XY DSD with ambiguous genitalia, particularly when accompanied by a family history of hypospadias.

EP_P017

LATE DIAGNOSIS OF OVO-TESTICULAR DISORDER

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INTRODUCTION

Ovo-testicular disorder of sex development (OT-DSD), formerly known as true hermaphroditism is a rare condition characterized by the presence of both ovarian and testicular tissue in an individual.

CASE

A 16-year-old Malay, female, was initially referred at the age of 9 years for further evaluation of ambiguous genitalia. She was born with ambiguous genitalia and was raised as a female. However, the family defaulted follow-up due to logistic issues. She had no history to suggest adrenal crises or progressive skin hyperpigmentation. Clinically, she was short and underweight for age (<3rd percentile), not dysmorphic, with normal hydration. Detailed genital examination revealed penoscrotal hypospadias with no palpable gonads. Biochemically, 17-OHP was normal, testosterone was elevated with evidence of germ cell failure having elevated LH and FSH. Her chromosomal analysis revealed 2 populations of cells: 46,XX (27) -77% and 46,XY (8)-23%. PCR-based molecular analysis for the SRY gene confirmed the absence of SRY gene. Genitogram at 10 years old showed no demonstrable urogenital fistula. She underwent diagnostic laparoscopy and HPE. The right gonads showed features consistent with ovotestis (true hermaphrodites) and left gonad features compatible with streak gonads. Her serial hormonal workups showed primary gonadal failure with elevated FSH (51.44) and LH(14.86) with low testosterone (<0.087) and estradiol (<18.35). She was started on estradiol valerate while waiting for her vaginal construction operation.

OT-DSD is rare and most reported cases occurred in individuals with 46,XX karyotype. However, 46,XY and mosaic karyotypes(46,XX/46 XY) have also been observed.

CONCLUSION

Early and accurate diagnosis is essential for optimal management requiring a multidisciplinary approach including endocrinologists and surgeons.

EP_P018

ATYPICAL PRESENTATION OF SEVERE PROGNATHISM IN PATIENT WITH CONGENITAL ADRENAL HYPERPLASIA

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INTRODUCTION

Congenital adrenal hyperplasia (CAH) is a group of autosomal recessive disorders due to mutation in the genes that regulate adrenal steroidogenesis. The commonest form is due to 21-OH enzyme deficiency in which the classic form is divided into salt-losing or simple virilizing types.

CASE

A 20-year-old Malay male has been under our follow-up since his early infancy. He was diagnosed to have a salt-losing form of CAH in the neonatal period as he had adrenal crises associated with skin hyperpigmentation. The boy was treated with oral hydrocortisone 10-15 mg/m^2/day and oral fludrocortisone 150 mcg to 200 mcg per day. However, starting from the age of five, he experienced medication adherence issues due to inadequate supervision and logistical challenges.. At the age of 15 years, he was diagnosed to have testicular adrenal rest tumour. He later complained of progressive difficulty chewing his food due to the development of mandibular hyperplasia or prognathism. He was treated with high dose glucocorticoid and ketoconazole to control his hyperandrogenism and referred to the maxillofacial team for further management.

CONCLUSION

Despite being detected early and managed promptly, the outcome of treatment relies strongly on the compliance of the patient. Non-adherence to medication may lead to unforeseen detrimental complications which could worsen the long-term prognosis.

EP_P019

AN ADOLESCENT WITH UNEXPLAINED DIABETES MELLITUS AND ASSOCIATED CONGENITAL GENITOURINARY ANOMALIES: A CASE REPORT

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INTRODUCTION

Maturity-onset diabetes of the young (MODY) is a rare form of diabetes found in Malaysia and worldwide, with at least 14 recognized types linked to different genetic mutations. MODY Type 5 (MODY 5) is caused by mutations in the HNF1 gene, which encodes hepatocyte nuclear factor 1 beta. This condition is characterised by diabetes and various extra-pancreatic features, including abnormalities in the kidneys and urogenital system.

CASE

We present a young female patient who initially presented with diabetes mellitus, later diagnosed with congenital renal anomalies, including a right single kidney and Müllerian anomalies. Her strong family history of diabetes and renal issues underscores the importance of recognising this diagnosis. A diagnosis of a monogenic form of diabetes was suspected since she had an onset of diabetes at the age of 13 years, absent acanthosis nigricans, positive family history with onset less than 30 years old and renal/Mullerian duct abnormalities. A targeted gene panel, whole exome sequencing panel, was performed to test for MODY. The panel indicated a positive result for the HNF1B gene mutation c.766C>T (p. Pro256Ser), resulting in an amino acid change at codon 256 from proline to serine (p. Pro256Ser).

CONCLUSION

This case highlights the importance of recognising the potential overlap between diabetes, renal disorders and Müllerian anomalies, particularly in young patients without a clear family history. Genetic testing is the gold standard for diagnosing MODY, but access and affordability can be challenging for patients in Malaysia.