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.

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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.