complicated by thyroid storm during the current pregnancy. Her TRAb levels prior to conception were over 23-fold above normal. The infant was born with suppressed cord TSH and markedly elevated TRAb level which is 13-fold above normal. She developed symptoms of neonatal hyperthyroidism in the second week of life and was started on carbimazole and propranolol, which were weaned off by the third week. Subsequent TFTs showed a phase of subclinical hyperthyroidism followed by hypothyroidism by two months of age requiring thyroxine replacement.

CONCLUSION

These cases highlight the diverse presentation of neonatal thyroid dysfunction associated with maternal GD, ranging from transient hypothyroidism to biphasic thyroid disturbances following neonatal hyperthyroidism. High maternal TRAb levels, as seen in Case 2, may serve as a predictor of a more severe case of evolving neonatal thyroid disease. Continuous postnatal monitoring is essential, as thyroid dysfunction may not be evident at birth and can evolve over time. Timely diagnosis and appropriate management are key to prevent complications and supporting optimal neurodevelopmental outcomes.

EP_P026

FAMILIAL DYSALBUMINEMIC HYPERTHYROXINEMIA: A RARE CAUSE OF EUTHYROID HYPERTHYROXINEMIA

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INTRODUCTION

Euthyroid hyperthyroxinemia is a common clinical conundrum. It requires careful assessment to establish an accurate diagnosis. Differential diagnosis of euthyroid hyperthyroxinemia include assay interference, thyroid hormone resistance syndrome, familial dysalbuminemic hyperthyroxinemia (FDH) and TSH-oma.

CASE

A 7-month-old male was referred for incidental finding of persistent euthyroid hyperthyroxinemia. His birth history was unremarkable. Antenatally, his mother did not have any thyroid disorder. His paternal grandmother has been undergoing treatment for hyperthyroidism. Thyroid stimulating hormone (TSH) was elevated at 16.89 mIU/L. Routine prolonged jaundice investigations revealed free thyroxine (FT4) of 33.7 pmol/L and TSH of 7.4 mIU/L. Other investigations were normal. Clinically, he was euthyroid, not dysmorphic, no goitre and thriving well with normal developmental milestones. Repeated thyroid function test (TFT) via standard immunoassay at 2, 3 and 5 months of age showed similar results of high FT4 with unsuppressed TSH. FT3 was not available. TFT using a different assay was not done. Thyroid antibody screening was normal. He was initially suspected of having thyroid hormone resistance syndrome.

Family screening showed similar TFT pattern for his father and sister who were clinically euthyroid. His mother's TFT was normal. His family was referred for confirmatory genetic testing. Whole exome sequencing (WES) for his father identified a pathogenic missense mutation in albumin gene, resulting in the replacement of an arginine with a histidine (p.Arg242His) that is associated with FDH. No genetic testing was done for the children.

CONCLUSION

FDH is a rare cause of euthyroid hyperthyroxinemia. It is an autosomal dominant disorder characterized by an abnormally increased affinity of a mutant albumin molecule to serum thyroxine causing elevated total thyroxine (T4) and elevated or normal FT4 with normal TSH level. Genetic analysis is important to establish diagnosis, to avoid further unnecessary laboratory testing and even inappropriate treatment in FDH.

EP_P027

ATYPICAL GENITALIA IN SILVER-RUSSELL SYNDROME

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INTRODUCTION

Silver-Russell Syndrome (SRS) is a clinically heterogeneous disorder which is often associated with growth restriction.

Genital abnormalities can be present but are not part of the diagnostic criteria. We describe one case of Silver-Russell Syndrome with atypical genitalia.

CASE

A 4-month-old male was referred to our clinic for atypical genitalia. He was born premature at 36 weeks 1 day, small for gestational age (SGA) with birth weight of 1.34 kg (<3rd centile), length of 41 cm (<3rd centile) and relative macrocephaly with head circumference of 32 cm (50th centile).

On further examination, he had dysmorphic features with prominent forehead, frontal bossing and triangular facies. His limbs were asymmetrical with hemihypertrophy of the left upper and lower limbs and bilateral 5th finger clinodactyly.

Examination of the genitalia revealed underdeveloped scrotum with no scrotal fusion, micropenis with stretched penile-length 0.5 cm (<10th percentile), penoscrotal hypospadias and non-palpable gonads. The EMS score was 0, in support of undervirilization.

Investigations revealed intact mini puberty with LH, FSH and testosterone of 1.6 U/L, 14.4 U/L and 2.95 nmol/L, respectively. Other anterior pituitary hormones were normal and 17-OHP was not elevated. Karyotype was normal with 46,XY. Short beta-hCG stimulation test revealed good testosterone level, with normal testosterone to androstenedione (T:A) ratio and testosterone to dihydrotestosterone (T:DHT) ratio, excluding both 17-hydroxysteroid deficiency and 5-alpha reductase deficiency respectively.

He was assessed by the genetic team and was noted to fulfill all the six NH-CSS criteria for clinical diagnosis of Silver-Russell syndrome. SRS methylation testing was sent to determine the molecular mechanism for future recurrence risk counselling.

CONCLUSION

Although SRS is primarily a growth disorder, it may present with atypical genitalia along with growth failure and dysmorphic features. Hence, it should be considered in the differential diagnosis of a newborn with dysmorphic features, SGA and atypical genitalia.

EP_P028

UNRAVELING THE MANIFESTATION OF VITAMIN D-DEPENDENT RICKETS TYPE 1 IN PREMATURE INFANT

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INTRODUCTION

Vitamin D-dependent rickets type 1 (VDDR1) is one of the genetic causes of calciopenic rickets. This rare autosomal recessive disorder is due to the defective 1-α hydroxylase which results in deficient active vitamin D or 1,25-dihydroxyvitamin D. It manifests as stunted growth, skeletal deformities and bone pain in young children. Diagnosing this uncommon disease requires a high index of clinical suspicion and is confirmed through genetic testing.

CASE

A seven-month-old female was born prematurely at 24 weeks of gestation with birth weight of 600 grams. Both parents were non-consanguineous. She had a stormy neonatal period with prolonged ventilation due to severe respiratory distress syndrome. In early neonatal phase, she had hypocalcaemia and hypophosphataemia, with subsequent gradual increment of alkaline phosphatase (ALP) – the overall picture initially pointing towards osteopaenia of prematurity. With time, she developed severe skeletal deformities which were bowing of the limbs, palpable widening of distal radius and double malleoli, Harrison's groove and long bones fracture. Apart from low calcium (1.88 mmol/L) and phosphate (1.32 mmol/L), other bone profiles showed: 25-hydroxyvitamin D levels were insufficient (47 nmol/L), both parathyroid hormone (PTH, 47.9 pmol/L) and serial ALP (1008 U/L) were elevated. A 1,25-dihydroxyvitamin D level was not investigated in view of financial limitations. Radiological imaging revealed rickets changes over the metaphyseal plate, including Looser's zone at the humerus and tibia. Considering the severe clinical manifestations of rickets, but inconsistent with insufficient level of stored 25-hydroxyvitamin D, this indicates deficient active vitamin D level that is consistent with clinical VDDR1. The whole exome sequencing was negative, but further workup for more expensive genetic study such as whole genome sequencing will incur additional costs.