CONCLUSION

This case highlights the challenge of initiation of GH therapy, in a patient with a background history of recurrent craniopharyngioma and residual disease. Proper counselling with the patient and family is crucial to explain the clinical indications, risks and benefits of the GH therapy. A multidisciplinary approach of the management involving the paediatric endocrinologists, oncologists, neurosurgeons, radiologists, rehab physicians and dietitians together with close surveillance of primary disease are extremely important.

PA-P-10

MIXED GONADAL DYSGENESIS WITH ISODICENTRIC Y CHROMOSOMES: A CASE SERIES

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INTRODUCTION

Isodicentric Y chromosomes are formed by intrachromosomal recombination or fusion of sister chromatids following Y chromosome breakage.

CASES

CASE 1

A four-month-old male with ambiguous genitalia had a stretched penile length (SPL) of 2.4 cm, glandular hypospadias, palpable right gonad and empty left scrotum. External genitalia score (EGS) was 7 and external masculinization score (EMS) was 6.5. Investigation showed normal 17-OHP [33.04 nmol/L, reference value (RV) 12-36], ACTH (2.1 pmol/L, RV 1.6-13.9) and s erum cortisol (239.15 nmol/L, RV 145-619); and elevated renin (>550 mU/L, RV 4-89). He was in mini-puberty at three months, with LH 1.7 mU/mL, FSH 5.4 mU/mL, testosterone 3.14 nmol/L and anti-Müllerian hormone (AMH) 350.3 pmol/L (RV 235.5-1125.9). Ultrasonography showed a right testis with empty left scrotal sac and no Müllerian structures. Karyotype revealed 73% (45,X) and 27% (46,X idic{Y}) p11.2 with isodicentric chromosome Yq.

CASE 2

A four -month-old male presented with ambiguous genitalia, SPL 2.5 cm, perineal hypospadias, palpable right testis at the inguinal region, impalpable left testis, EGS 5.5 and EMS 5.5. Work-up showed normal 17-OHP (19.9 nmol/L) and serum cortisol (255 nmol/L); and elevated aldosterone (>3656 pmol/L) and renin (128.9 mU/L). Investigations post-delivery revealed mini-puberty with LH 6.59 IU/L, FSH 4.84 IU/L, testosterone 5.86 nmol/L and estradiol 43 pmol/L. AMH at 4 months was 435.8 pmol/L. Abdominal ultrasonography showed embedded penis with bilateral inguinal testes and no Müllerian structures. FISH with SRY gene probe revealed the first cell line (74.5%) of isodicentric chromosome Y and the second cell line (25.5%) of 45,X.

CONCLUSION

Patients with isodicentric Y chromosomes have various presentations necessitating follow-up to monitor growth, puberty, fertility, gonadal dysgenesis and short stature.

PA-P-11

CLINICAL FEATURES AND SHORT-TERM OUTCOMES OF CHILDREN WITH TURNER SYNDROME IN A CHILDREN'S HOSPITAL

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INTRODUCTION

Turner syndrome (TS) is the most common sex chromosome abnormality in females. This syndrome is usually diagnosed in females with characteristic features and a partial or complete absence of one X chromosome. We aimed to describe the clinical features and short-term outcomes of the children with TS being seen at our hospital.

METHODOLOGY

This is a descriptive study. Children with TS who attended the endocrine clinic in Sabah Women and Children's Hospital were enrolled. We obtained their pertinent data through a review of their case folders. Diagnosis of TS was confirmed via chromosomal study postnatally. Their clinical features and short-term outcomes were described.

RESULTS

Four females with TS were included in our study. The mean age at diagnosis was 6.3 ± 4.8 years old. All had previous medical encounters before diagnosis. All four females had 45, X mosaicism by chromosomal analyses. All of them had the classical features of short stature, webbed neck, broad chest, and deep-seated nails. Two had thyroid antibodies detected but only one had thyroid dysfunction. None had hearing loss, cardiac or renal problems. Two received growth hormone treatment, however only one completed the treatment with a modest response in height gain. Three received pubertal induction at a mean age of 11.4 ± 0.3 years with pubertal progression.

CONCLUSION

A high index of suspicion is needed to diagnose females with TS despite this being a relatively common syndrome. Early diagnosis may confer a better outcome in this group of children.

BASIC SCIENCE

PA-BS-01

STEROID HORMONE ESTROGEN INDUCES METASTATIC PROCESS IN BREAST CANCER THROUGH REGULATION OF GENE SPLICING EVENT IN VITRO

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INTRODUCTION

The misregulation of alternative pre-mRNA splicing (AS) has important roles in tumor progression and metastasis. The connection between AS and cancer cells metastasis was first established when specific CD44 splice variants were detected in metastatic pancreatic cancer cells that were not present in the primary tumor. Notably, estrogen signaling has been reported to involve abnormal gene splicing which leads to metastatic phenotype change in breast cancer cells. This study aimed to investigate the mechanism by which estrogen affects gene-splicing that promotes progression of estrogen receptor positive (ER+) breast cancer cells in vitro.

METHODOLOGY

For all experiments, ER+ breast cancer cell line MCF7 was cultured and stimulated with 10 nM estrogen (17-beta estradiol, E2) for 24 hours. Protein samples were run for proteomic analysis using LC-MS/MS, as well as for protein and gene expression by western blot and RT-PCR, respectively. For monitoring the abnormality in gene splicing, CD44 gene was used as a splicing reporter. The change in cellular behavior was monitored for 24 hours using xCELLigence® real-time cell monitoring system.

RESULTS

Proteomic analysis showed that serine-arginine protein kinase 1 (SRPK1), one of the key kinases in regulating alternative splicing mechanisms, was among the ER-signaling targets and was upregulated seven-fold in the stimulated cells. Both SRPK1 protein and gene expression were also upregulated. The level of CD44 splice isoform, CD44s, was found increased by 50%. No significant change was detected in CD44v6 level, suggesting positive correlation between increased SRPK1 and CD44s expression. Finally, cell monitoring assay showed a slight increase in proliferation after 24 hours of estrogen treatment.

CONCLUSION

This study demonstrated that estrogen can induce overexpression of SRPK1 and trigger abnormal splicing of CD44 gene which eventually accelerates breast cancer progression by increased proliferation ability.