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.