PSEUDO-PRECOCIOUS PUBERTY IN ANDROGEN INSENSITIVITY SYNDROME SECONDARY TO A PREPUBERTAL ESTROGEN PRODUCING SERTOLI CELL TUMOR

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INTRODUCTION

Complete androgen insensitivity syndrome (AIS) is an X-linked hereditary disease secondary to loss-of-function mutations in the androgen receptor (*AR*) gene, in 46, XY patients. Subjects undergo poor development of secondary sex characteristics, except for breast development induced at puberty by testicular sex hormones. AIS patients are prone to develop germ cell cancer, even though with lower incidence than in dysgenetic gonads secondary to defects in organogenesis.

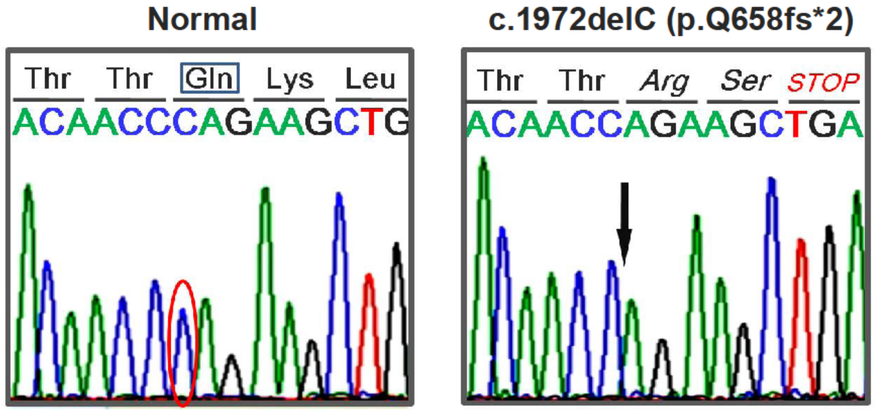
CASE REPORT

We described a 3-year(y)-old girl referred because growth acceleration and progressive breast development. She had fully developed female phenotype without sexual ambiguity. Pelvic ultrasound (PU) revealed Mullerian structures and two gonads resembling ovaries.
Physical examination revealed: Height (H): 116.3cm (HSDS: +3.8), Bone age (BA): 7y, Breast development (Tanner IV) and scarce pubic hair.
Endocrine studies revealed serum basal pubertal estradiol (39pg/ml) but pre-pubertal testosterone (0.2ng/ml), LH and FSH levels failing to respond to acute GnRH stimulation. Diagnosis of pseudo precocious puberty (PPPUB) secondary to excessive steroid production was made.
The source of the abnormal sex steroids was undetermined.
At 8.2y she was readmitted to the Hospital. H: 148.1cm (HSDS: +4), BA:16y.
Hormonal studies:
LH.RH test LH (mUI/ml): 4.9 /17.82 /19.2 FSH (mUI/ml): 1.64 /0.76 /0.75
The diagnosis of central precocious puberty was made.
However; the etiology of her prepubertal sexual development remained undetermined.
Patient was lost to follow-up until 20y of age. H:150 cm (HSDS:-1.75), referred because of primary amenorrhea. Serum testosterone levels: 5.9ng/ml
CAIS diagnosis was suspected

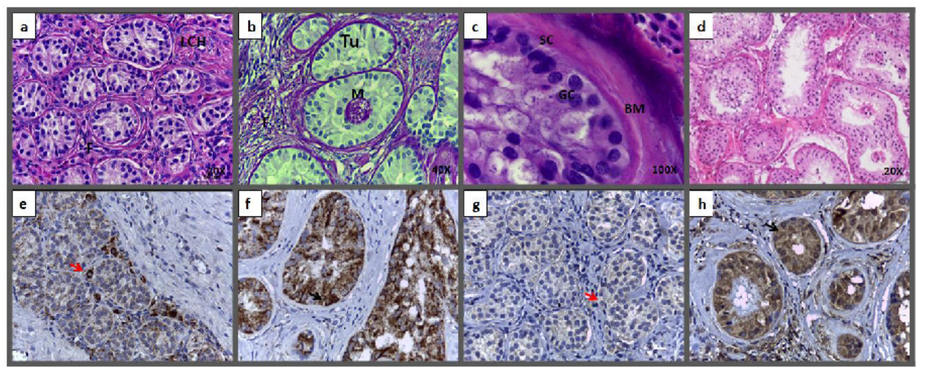
RESULTS

PU discarded the presence of Mullerian structures. Karyotype was 46, XY. Molecular studies revealed a loss-of-function mutation in the androgen receptor gene, c.1972delC (p.Q658fs*2). Bilateral gonadectomy was performed. Histologic study of both gonads showed abundant signs of testicular dysgenesis and in one, a tubular structure with cylindrical epithelium, characteristic of a Sertoli cell tumor (SCT), was observed.
Positive inmunoexpression of CYP11A1 and CYP19 (aromatase) proteins was found only in the SCT.

MOLECULAR STUDIES



HISTOLOGY



a) Testis: Immature seminiferous cords, with scarce germ cells (GC); fibrous interstitium (F) with Leydig cell hyperplasia (LCH).
b) SCT intratubular microlithiasis, F
c) Acidophilic Sertoli cell (SC), thickening of basal membrane (BM).
d) Normal pubertal testis, with spermatogenesis figures.
e) Aromatase immunoexpresion in LC (red arrow).
f) Aromatase immunoexpresion in SCT (black arrow)
g) Positive CYP11A1 (P450scc) immuno-expresion in LC (red arrow)
h) Positive CYP11A1 (P450scc) immuno-expresion in SCT (black arrow).

CONCLUSSION

We are reporting for the first time Pseudo-Precocious Puberty in an AIS patient.
Prepubertal sex development can be secondary to estrogen synthesis by a Sertoli Cell Tumor in a dysgenetic gonad.

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