EARLY EMBRYONIC TESTICULAR REGRESSION SYNDROME PRESENTING WITH FEMALE EXTERNAL GENITALIA

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Introduction

- Testicular regression syndrome (TRS) is a rare disease characterized by testicular dysfunction that causes varying degrees of virilization defect according to the emergence period in fetal life.
- The majority of cases present with normal male external genitalia. However, ambigious genitalia or, more rarely, female external genitalia can be found depending on the extent and timing of the intrauterine accident.
- Here, we present a case of TRS with normal female external genitalia, mullerian remnants and streak gonad.

A 15-year-old ♀

➢ She was admitted to our outpatient clinic due to primary amenorrhea and absence of breast development. .

➢ **Medical history;** she was born after uneventful pregnancy with birthweight of 2250 gram at 38 gestational weeks.

✓ There was no remarkable family history and she has two healthy brothers. The parents were relatives (first-degree cousins)

✓ **The physical examination;** weight was 53.3 kg (-0.28 SDS), height 160.9 cm (-0.12 SDS), blood pressure 100/60 mmHg, and the rest of systemic examination was unremarkable.

✓ According to Tanner stage, pubic hair was stage 3-4 and breast development was stage 1.

✓ She has normal female external genitalia with separate vaginal and urethral openings.

✓ There was no cliteromegaly or palpable gonad.

➢ **Laboratory** examination revealed normal kidney-liver-thyroid function tests, ions, morning cortisol / ACTH, and DHEA-S. In addition, LH and FSH were markedly high; estrogen, anti-mullerian hormone, and inhibin B levels were low.

Hormonal follow-up (Table 1)

Parameters	Value	Normal
Glucose (mg/dL)	93	60-100
Sodium (mmol/L)	139	138-145
Potassium (mmol/L)	5.4	3.5-5.5
FSH (mIU/mL)	83.0	1.6-17
LH (mIU/mL)	39.4	2.4-6.6
Estradiol (pg/mL)	<20	21-251
Prolactin (ng/mL)	12.84	5.8-26.5
Total Testosterone (ng(dL)	36,2	<85
DHEA-S	240.3	73-350
Cortisol (mcg/dL)	9.2	3.9-16.4
ACTH (pg/mL)	29.1	<46
17- hydroxyprogesterone (ng/mL)	0.47	<2
Androstenedione (ng/mL)	0.81	0.3-3.3
Beta-hCG	<1.2	<5.0
Anti-mullerian hormone (ng/mL)	<0.01	1.52-9.95
Inhibin B (pg/mL)	<5	45-290

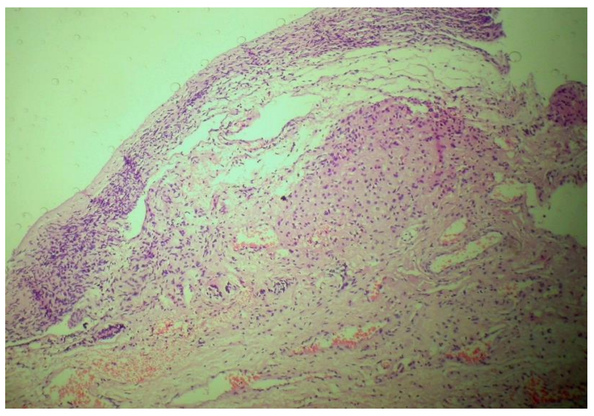

Figure 1: Streak gonad structure with thin stromal tissue and Leydig cells (H&E X100)

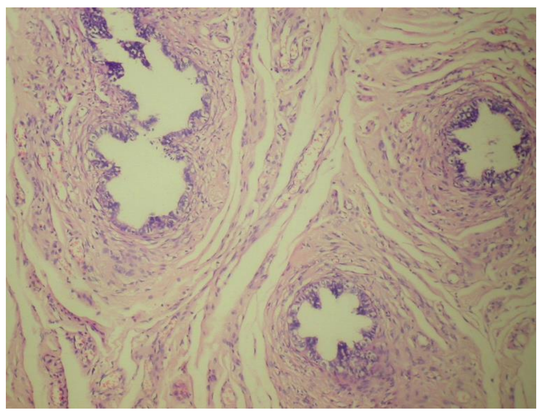

Figure 2: Spermatic cord with ductus deferens sections (H&E X100)

Further investigations

➢ Pelvic ultrasonography and MRI showed no uterus or gonads. The lumbar region bone mineral density was decreased (L1-4 0.554 g / cm2; -4.46 SDS).

➢ Laparoscopic evaluation showed mullerian structures (rudimentary uterus and fallopian tubes) and streak gonads.

Genetic analysis and follow-up

➢ Karyotype was 46, XY and SRY (+).

➢ Genetic analysis of genes involved in the development of gonad revealed no mutation.

➢ Bilateral gonadectomy was performed.

➢ The pathological examination revealed spermatic cord, immature seminiferous tubules, and leydig cell groups in the stoma (Figure 1 and 2).

➢ There was no evidence of neoplasia. Estradiol treatment for pubertal progression was started.

Discussion and Conclusion

✓ Antenatal or perinatal vascular thrombosis or torsion are thought to be the causes of TRS; however, the precise etiology has yet been identified.

✓ Patients with TRS present with different phenotype depending on the occurrence period of testicular dysfunction. However, female external genitalia are rarely reported. TRS should be kept in mind in cases with female external genitalia but male karyotype with 46,XY, elevated gonadotropins, and mullerian remnants