A NOVEL COMPOUND HETEROZYGOUS MUTATION IN *CYP19A1* RESULTING IN AROMATASE DEFICIENCY WITH NORMAL GONADOTROPIN LEVELS AND OVARIAN TISSUE

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Introduction

- Aromatase deficiency leading to virilization in mother and female fetuses during pregnancy is a rare disease.
- It is characterized by impaired estrogen production, increased gonadotropins, and ovarian cysts.
- Herein, we report a clinical phenotype of a virilized female due to a novel compound heterozygous mutation in *CYP19A1*.

A 4-month-old ♀

➢ She was referred due to cliteromegaly.

➢ **Medical history;**

✓ She was born with a birthweight of 2710 gr at 35th week of gestation.

✓ Her clitoris size had regressed after birth.

✓ The parents were no relatives.

✓ Her mother had developed acne, hair loss, voice change, and hirsutism during pregnancy.

➢ **The physical examination;**

✓ Her weight was 6.8 kg (0.36 SDS),

✓ Height was 64 cm (0.48 SDS),

✓ Clitoral length was 1 cm, and labia minora was posteriorly fused.

➢ **Laboratory;**

✓ Gonadotropin levels were normal at the time of admission but increased by the age of 6 months (Table 1).

✓ Initial evaluations excluded congenital adrenal hyperplasia.

✓ Ultrasonography revealed a normal uterus and but no ovarian tissue.

Further investigations

➢ Karyotype was identified as 46,XX and *SRY* was negative.

➢ Laparoscopic evaluation showed normal uterus and ovaries.

➢ The biopsy specimens from both gonads were histologically consistent with ovarian tissue and the karyotype analysis of this specimens revealed 46,XX.

Genetic analysis and follow-up

➢ The diagnosis of aromatase deficiency was considered and a previously unidentified compound heterozygote mutation in *CYP19A1* [IVS10 + 1 G> A; p.R115Q (c.344 G> A)] was found.

➢ The parents were carriers: the mother and the father have heterozygous mutations p.R115Q (c.344 G>A), IVS10+1 G>A, respectively.

➢ *In silico* analyzes categorized the variant to be pathogenic.

➢ During the follow-up, the fusion at the posterior of the labium minus was surgically corrected and no ovarian cyst was observed with pelvic ultrasonography until now.

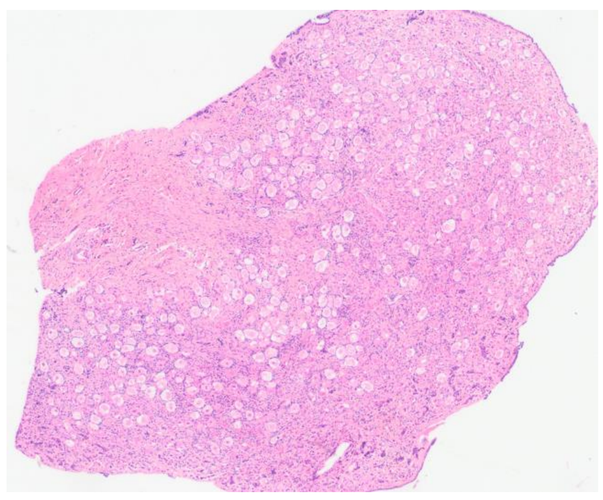

Figure: Normal ovarian tissue histology of our patient

Hormonal follow-up (Table 1)

	16th day	4th month	6th Month	8th month	11th month	17th month
FSH (mIU/mL)	6,4	7,02	36,3	18,7	27,9	75,1
LH (mIU/mL)	0,53	0,97	4,36	1,27	0,77	15,64
Estradiol(pg/mL)	5,0	<20	<20	<20	<20	<20
T. testosterone (ng/dL)	78	<10	<10	-	-	-

Conclusion

✓ Aromatase deficiency should also be considered even if the initial FSH and LH levels are normal and ovarian cysts are lacking.