Case Presentation

DSD

Dr Hossein Zaeri
Pediatric Endocrinologist
Sari, 2025

Chief Complaint

- A Two month old girl who was referred by Pediatric surgeon for evaluation for Testicular Feminization
- **Patient Name; Sevin**

During surgery, Testis like structure was seen in the sac of Inguinal Hernia in both sides.then, A Biosy was taken.

History

Prenatal and Prinatal history

- First Child (Second Pregnancy)
- First Pregnancy; Abortion with unknown Ethiology
- No History of any Medical problems during Pregnancy
- Drug –
- **Family History**
- Parents were normal and
- Parents are Consanguine
- No history of same problem in Family

First Visit

Physical Exam

- **General; NL**
- **Genitalia;** Comlete Normal Female Genitalia
- **Ingunial;** Right: - Left: Testis was Palable

Plan;

- *Laboratory Evaluation*
- *Pelvic Sonogeraphy*
- *Karyotype*
- *Pathology*

Results

Lab; *Basal 8AM*

	Results	Nl values
LH	0.22 mIU/ml	
FSH	3.26 mIU/ml	
Estradiol	< 9 Pg/ml	
Testosterone	0.06 ng/ml	
17OHP	7 ng/ml	
DHEAS	2 µg/dl	
Androstenedion	20 ng/dl	
DHT	30 ng/dl	
Na , K	normal	

Results

Pelvic Sonography; *x2*

Uterus; _

Ovaries; _

Hypoplastic Vagina

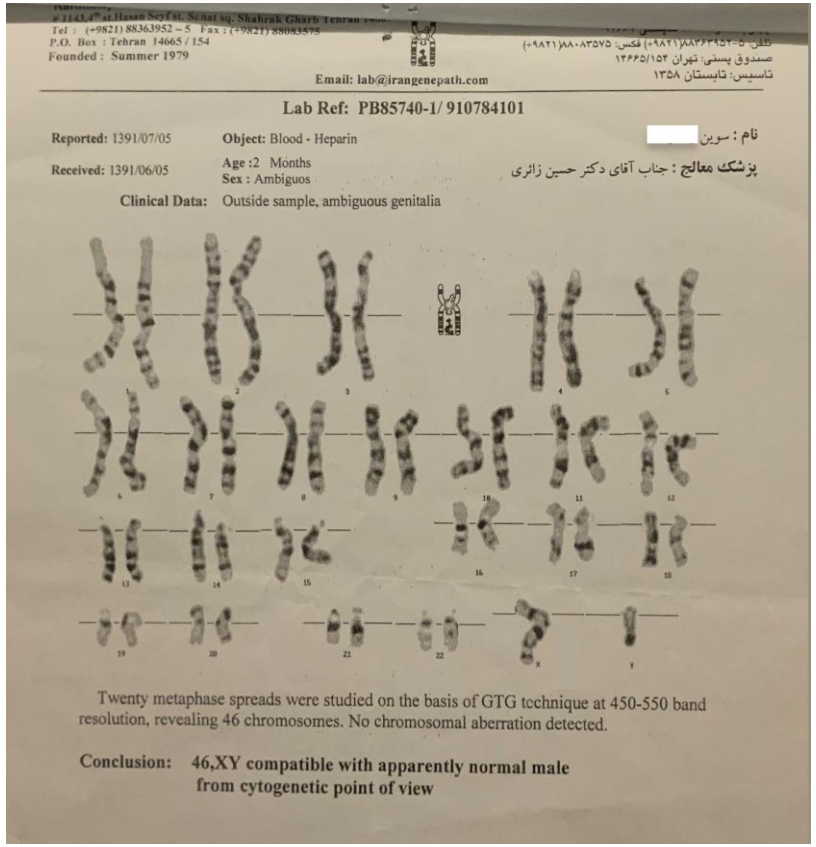
Left testis; +

Inguinal size=10x5.5 mm

Right Testis; _

Results

Karyotype; 46XY Normal Male



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تلفن: ۵-۸۸۳۶۳۹۵۱ (۰۹۸۲۱+) فکس: ۸۸۰۸۳۵۷۵ (۰۹۸۲۱+)
صندوق پستی: تهران ۱۴۶۶۵/۱۵۴
تاسیس: تابستان ۱۳۵۸

Lab Ref: PB85740-1/ 910784101

Reported: 1391/07/05
Received: 1391/06/05
Object: Blood - Heparin
Age :2 Months
Sex : Ambiguos
Clinical Data: Outside sample, ambiguous genitalia

نام : سوین
پزشک معالج : جناب آقای دکتر حسین زائری

Twenty metaphase spreads were studied on the basis of GTG technique at 450-550 band resolution, revealing 46 chromosomes. No chromosomal aberration detected.

Conclusion: **46,XY compatible with apparently normal male from cytogenetic point of view**

Results

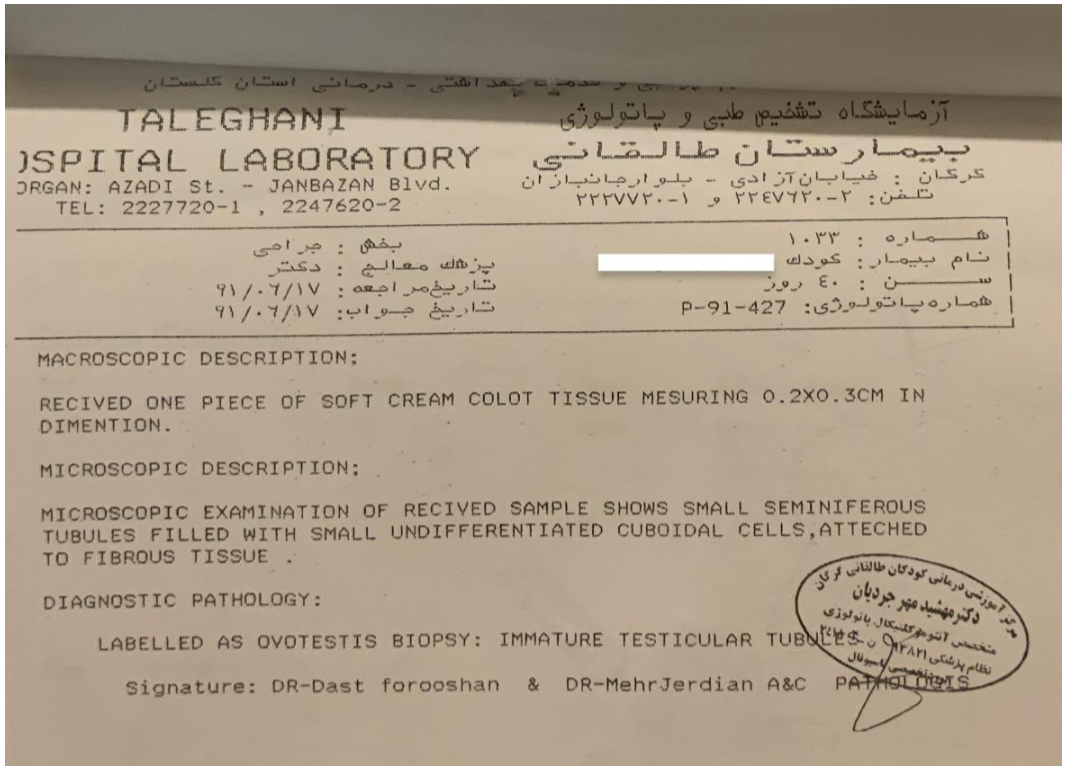
Pathology;

Small siminiferous Tubules filled

with small undifferentiated cuboidal

Cells attached to fibrous tissue

Dx; *Immature testicular Tubules*



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آزمایشگاه تشخیص طبی و پاتولوژی
بیمارستان طالقانی
گرگان : خیابان آزادی - بلوار جانبازان
تلفن: ۲-۲۲۴۷۶۲۰ و ۱-۲۲۲۷۷۲۰

هماره : ۱۰۳۳
نام بیمار: کودک
سن : ۴۰ روز
هماره پاتولوژی: P-91-427

بخش : جراحی
پزشک معالج : دکتر
تاریخ مراجعه : ۹۱/۰۶/۱۷
تاریخ جواب: ۹۱/۰۶/۱۷

MACROSCOPIC DESCRIPTION:

RECIVED ONE PIECE OF SOFT CREAM COLOT TISSUE MESURING 0.2X0.3CM IN DIMENTION.

MICROSCOPIC DESCRIPTION:

MICROSCOPIC EXAMINATION OF RECIVED SAMPLE SHOWS SMALL SEMINIFEROUS TUBULES FILLED WITH SMALL UNDIFFERENTIATED CUBOIDAL CELLS,ATTECHED TO FIBROUS TISSUE .

DIAGNOSTIC PATHOLOGY:

LABELLED AS OVOTESTIS BIOPSY: IMMATURE TESTICULAR TUBULES

Signature: DR-Dast forooshan & DR-MehrJerdian A&C PATHOLOGISTS

دکتر مهشید مهرجردیان
متخصص آناتومیک کلینیکال پاتولوژی

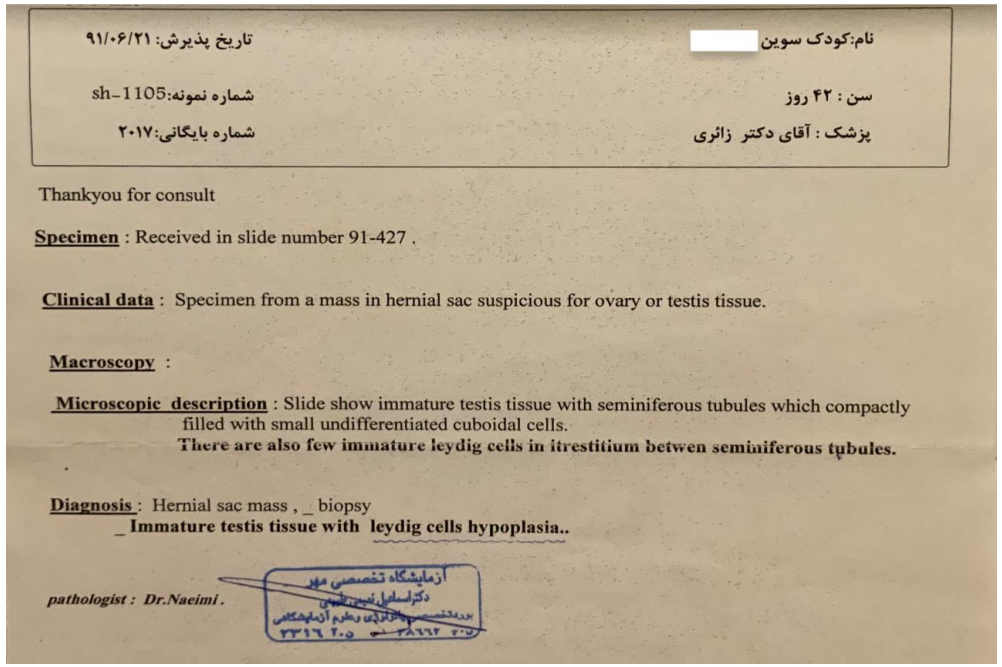
Next Plan

hCG Stimulation Test.

First day	4th day
Testosterone; 0.03 ng/ml	Testosterone ; 0.06 ng/ml
DHT; 162 ng/dl	DHT; 58 ngdl

+ Report Biopsy by Second Pathologist

Immature Testis tissue with **Leydig Cells Hypoplasia**



تاریخ پذیرش: ۹۱/۰۶/۲۱ — نام:کودک سوین

شماره نمونه:sh-1105 — سن : ۴۲ روز

شماره بایگانی:۲۰۱۷ — پزشک : آقای دکتر زائری

Thankyou for consult

Specimen : Received in slide number 91-427 .

Clinical data : Specimen from a mass in hernial sac suspicious for ovary or testis tissue.

Macroscopy :

Microscopic description : Slide show immature testis tissue with seminiferous tubules which compactly filled with small undifferentiated cuboidal cells.
There are also few immature leydig cells in itrestitium betwen seminiferous tubules.

Diagnosis : Hernial sac mass , _ biopsy
_ **Immature testis tissue with leydig cells hypoplasia..**

pathologist : Dr.Naeimi .

آزمایشگاه تخصصی مهر

Final Decision/Plan

At the age of 5 mo

Diagnosis; 46XYDSD, ***Leydig Cell Hypoplasia***

Plan;

Gender Assignment; ***Female***

Follow Up and

+ Mutation Study; LHCGR

Gonadectomy after age one (1-3 years old)

HRT at appropriate age

Vaginoplasty at 14 to 16 y

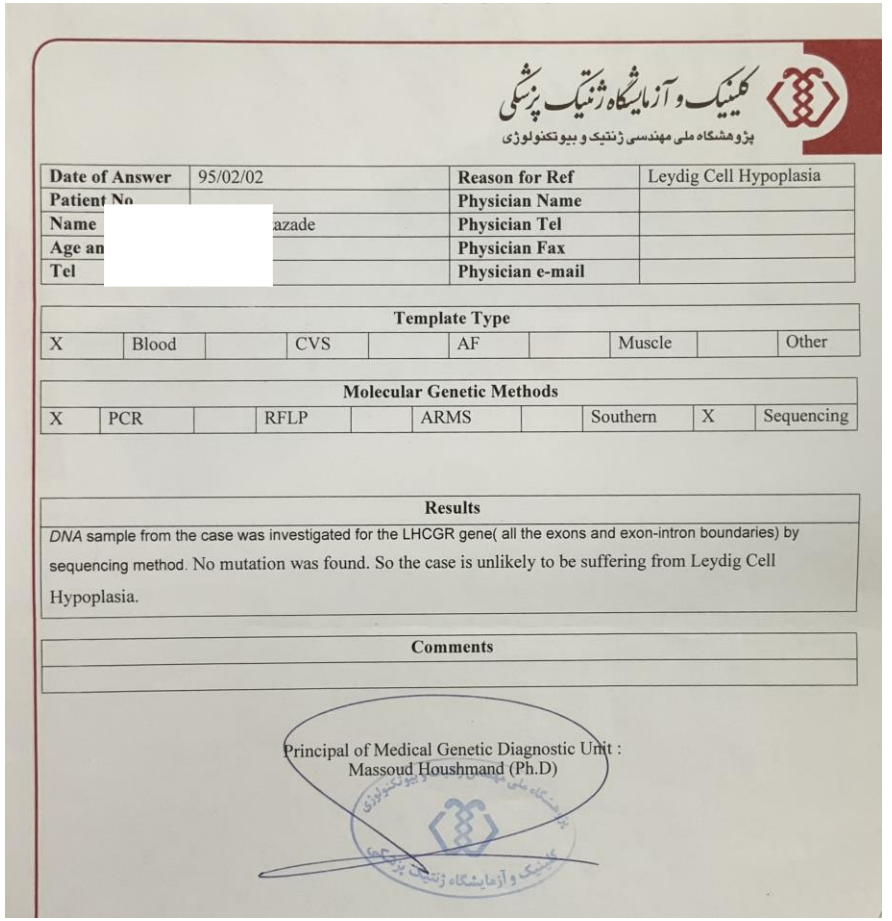
Follow Up

- Growth monitoring
- ***Gonadectomy*** at the age 3
- ***LHCGR mutation;*** Negative (age; 4)

Genetic Study

LHCGR ; no mutation was found

At the age of 4



کلینیک و آزمایشگاه ژنتیک پزشکی
پژوهشگاه ملی مهندسی ژنتیک و بیوتکنولوژی

Date of Answer	95/02/02	**Reason for Ref**	Leydig Cell Hypoplasia
Patient No		**Physician Name**	
Name	azade	**Physician Tel**	
Age an		**Physician Fax**	
Tel		**Physician e-mail**	

Template Type									
X	Blood		CVS		AF		Muscle		Other

Molecular Genetic Methods									
X	PCR		RFLP		ARMS		Southern	X	Sequencing

Results

DNA sample from the case was investigated for the LHCGR gene(all the exons and exon-intron boundaries) by sequencing method. No mutation was found. So the case is unlikely to be suffering from Leydig Cell Hypoplasia.

Comments

Principal of Medical Genetic Diagnostic Unit :
Massoud Houshmand (Ph.D)

Genetic Study

Whole Exome Sequencing ; ☞ *c.104_108delCCCTG Variant in CYP17A1, p.Pro35fs)*

At the age of 9

WES was erformed

Test Information

Molecular test: Molecular Analysis for the c.104_108delCCCTG variant in *CYP17A1* gene
Methods: DNA extraction; Polymerase Chain Reaction (PCR); Direct Sequencing

Family Segregation

	Affection Status	Zygosity	Genotype	Gene	Variant Coordinate
Sevin [redacted] (Proband)	Affected	Hom	del/del	*CYP17A1*	Chr10(GRCh37): 104597011_104597015del CAGGG NM_000102.3 c.104_108delCCCTG (p.Pro35fs)
Ali [redacted] (Father)	Healthy	Het	N/del		
Maryam [redacted] (Mother)	Healthy	Het	N/del		

Interpretation

Based on this molecular study, **Ali [redacted]** and **Maryam [redacted]** are both Heterozygote for the c.104_108delCCCTG variant in *CYP17A1* gene. Therefore, the c.104_108delCCCTG variant in *CYP17A1* gene **can be** the cause of disease in **Sevin [redacted]**. **Genetic counseling is highly recommended.**

Remarks

These results should be communicated by a human geneticist or a genetic counselor. If you have any further question please do not hesitate to contact us again.

Variant in CYP17A1;

- **A rare mutation;** ***c.104_108delCCCTG Variant in CYP17A1, p.Pro35fs)***

The CYP17A1 variant, c.104_108delCCCTG (p.Pro35fs)is described as a Pathogenic variant according to American college of Medical Genetics(ACMG)The Phenotype is caused by mutation in the gene encoding Steroid 17-monooxygenase(CYP17A1; OMIM : 609300)

This Mutation affect only 17,20 lyase activity not 17 alpha Hydroxylase Activity

c.104_108delCCCTG Variant in CYP17A1, p.Pro35fs)

- ***Geller et al.(1997) reported 2 patients with 46,XY karyotyes with isolated 17,20-layse deficiency caused by different homozygous mutations in the CYP17A1 gene.***
- ***The first patient*** *showed genital ambiguity at birth and assigned female gender. When seen at 13 months of age, the patient showed a 2.2-cm phallus, Perineal hypospadias, Bilatrtal gonads palpable in a bifid scrotum, and a blind vaginal pouch seen on urethrocystograms.the parents were first cousins. Serum cortisol and electrolytes and blood pressure were normal. Gonadotropins were at normal prepubertal level in this patient. Testicular stimulation with hCG elicited grossly subnormal response of Testosterone, DHEA and Anderostenedione. Basal and hCG-Stimulated progesterone was normal.*

c.104_108delCCCTG Variant in CYP17A1, p.Pro35fs)

- ***Geller et al.(1997) reported 2 patients with 46,XY karyotyes with isolated 17,20-layse deficiency caused by different homozygous mutations in the CYP17A1 gene.***
- ***The second patient** also showed genital ambiguity at birth and assigned Male gender. Gynecomastia developed at 14 years of age. And at 16 years the Breasts were Tanner Stage V; Pubic Hair was Tanner Stage IV, but there was minimal body hair. The Genitalia were Characterized by 4.5 cm phallus, Perineal Hypospadias, Bifid Scrotum, small descended Testis on the right and left inguinal canal, and a blind vaginal pouch. The Parents Denied Consanguity[PMID: 9326943]*

Current Condition of the Patient

- Age; 12 6/12
- On HRT; estrogen Conjugated 0.625 daily from age 11
- Height; 155
- Tanner Stage; T4
- BA; 11
- Follow UP; to be Continued . . . . … …. .

سپاس از توجه شما

پایان