Genetic Analysis Reveals Complete Androgen Insensitivity Syndrome (CAIS) in Female Children Surgically Treated for Inguinal Hernia

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INTRODUCTION

ANDROGEN INSENSITIVITY SYNDROME (AIS)

An X-linked genetic condition (*AR* gene mutation) causing inability of the cell to respond to androgens.

Genetically male (46, XY), present with a range of characteristics:

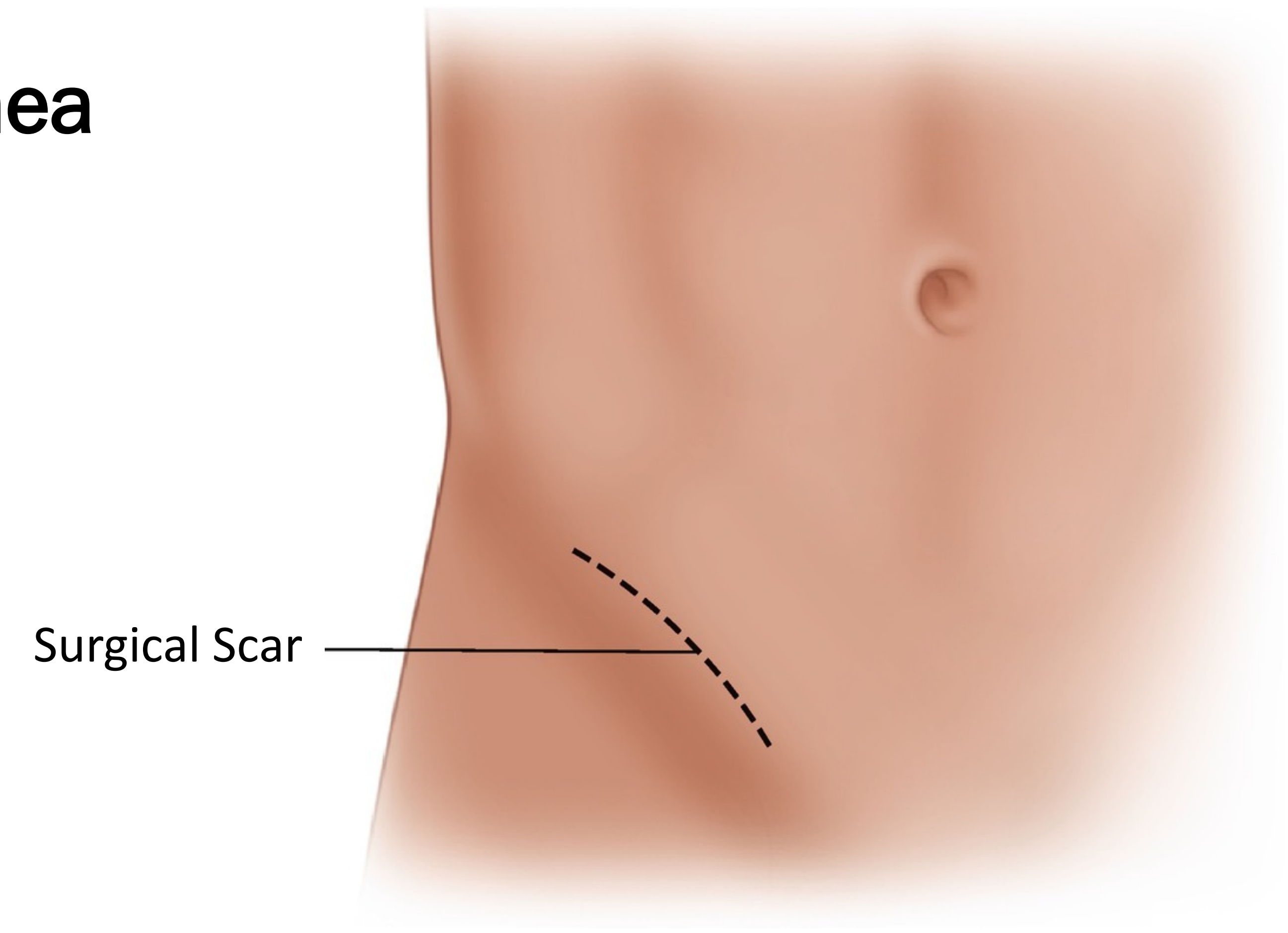
Classification	Phenotypes	Prevalence
Complete AIS	Present at puberty with primary amenorrhea; or Inguinal swelling in infants	2 to 5 in 100,000
Partial AIS	Severe hypospadias, Ambiguous genitalia	Least as common as CAIS
Mild AIS	Gynecomastia, Infertility	Unknown

Hughes IA. Androgen Insensitivity Syndrome. *The Lancet. 2012*

COMPLETE ANDROGEN INSENSITIVITY SYNDROME

CASE PRESENTATION

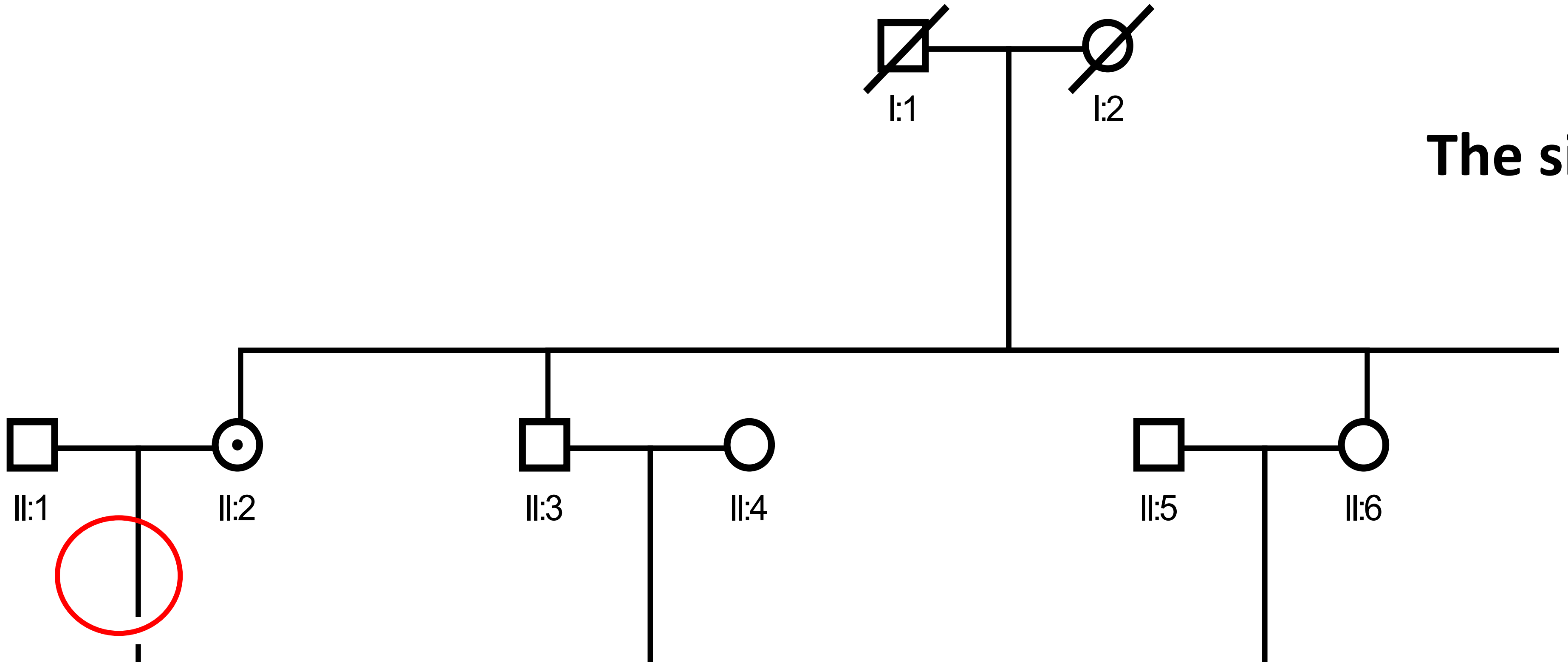
- A 20 years old girl with chief complaint of **primary amenorrhea**
- She has **surgical scar** in the inguinal region
- Past medical history: **inguinal hernia surgery** at the age of 5 years in a rural hospital; however, **no follow-up had been performed.**



CASE PRESENTATION

In our interview, she mentioned that she has younger sister who **experienced the same surgery** when she was 2 years old.

But her mother did not take her to our clinic for a medical consultation.



The sister has the same condition

↓

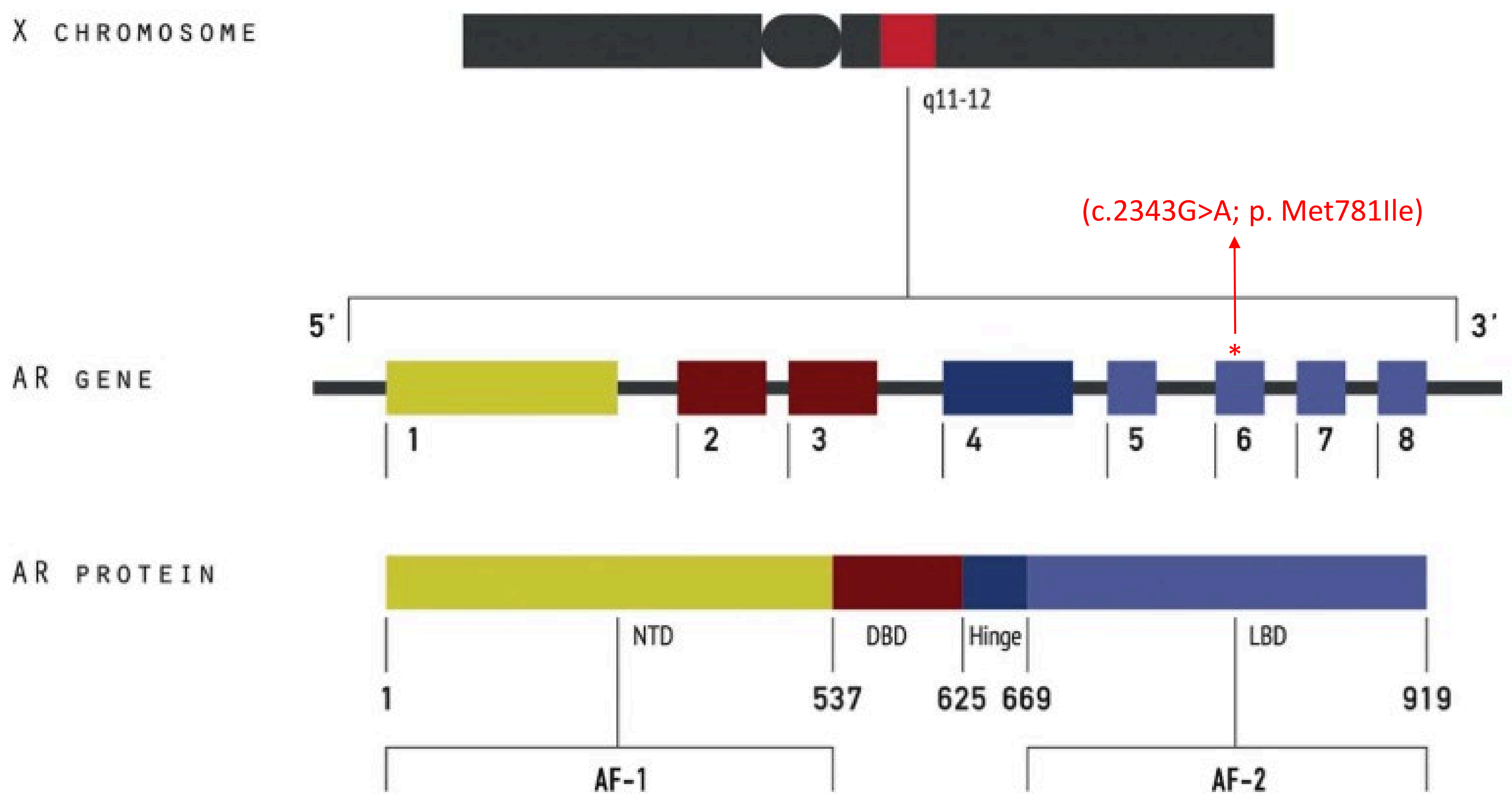
Inherited ?

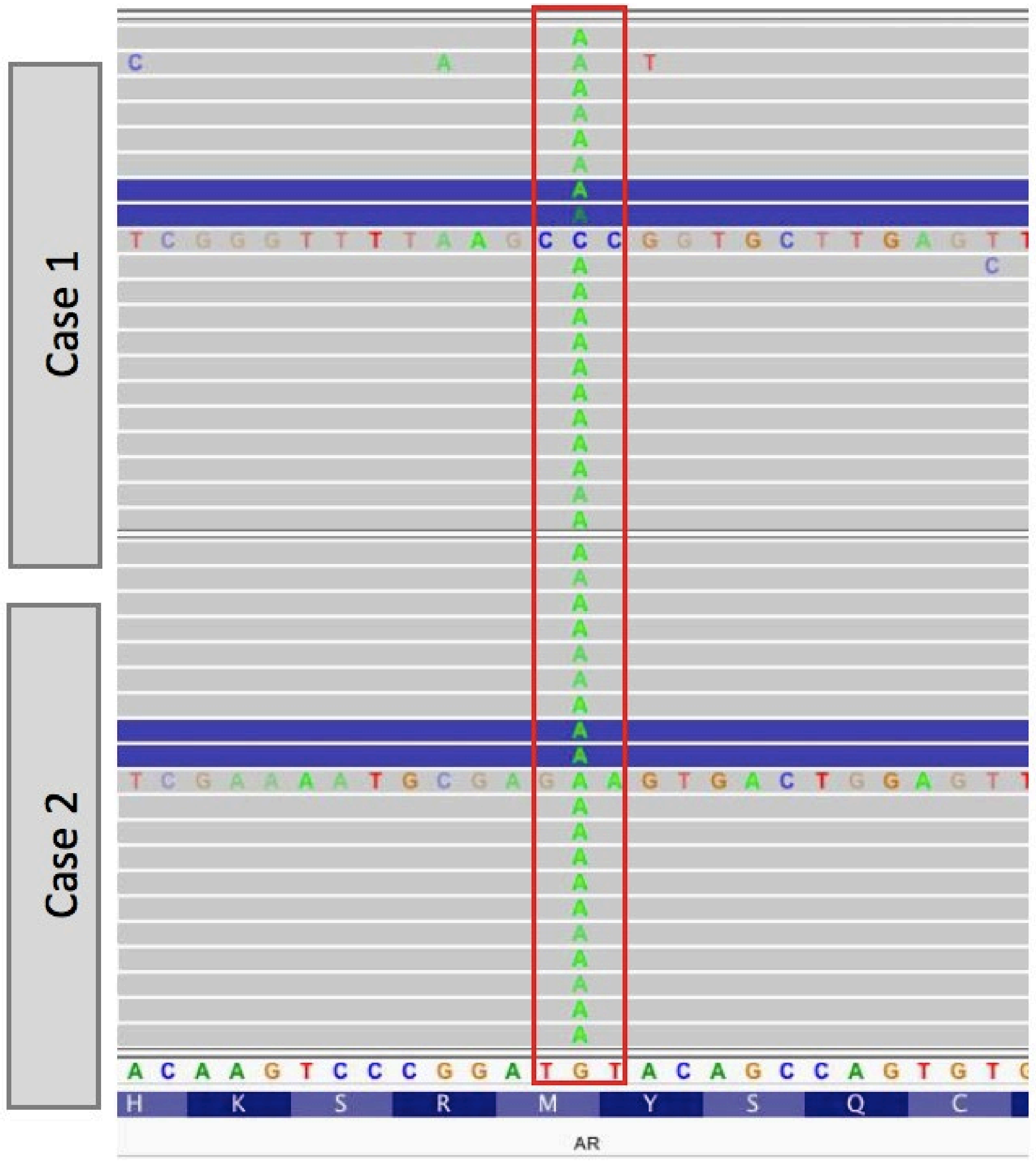
EVALUATIONS

Secondary sex sign	$A_1M_3P_2$
External Genitalia	Labia majora (+)/(+) Normal Clitoris Labia minora (+/+) Introitus vagina (+) Bilateral inguinal solid palpable masses resembling gonads
Hormonal Assay	Testosterone ↑ FSH ↑ LH ↑
Sonography	Absence of a uterus and ovaries, and the presence of isoechoic oval structure in both inguinal regions consistent with testicles.
Chromosomal analysis	**46, XY**

Presumptive Diagnosis: Complete Androgen Insensitivity Syndrome (CAIS)

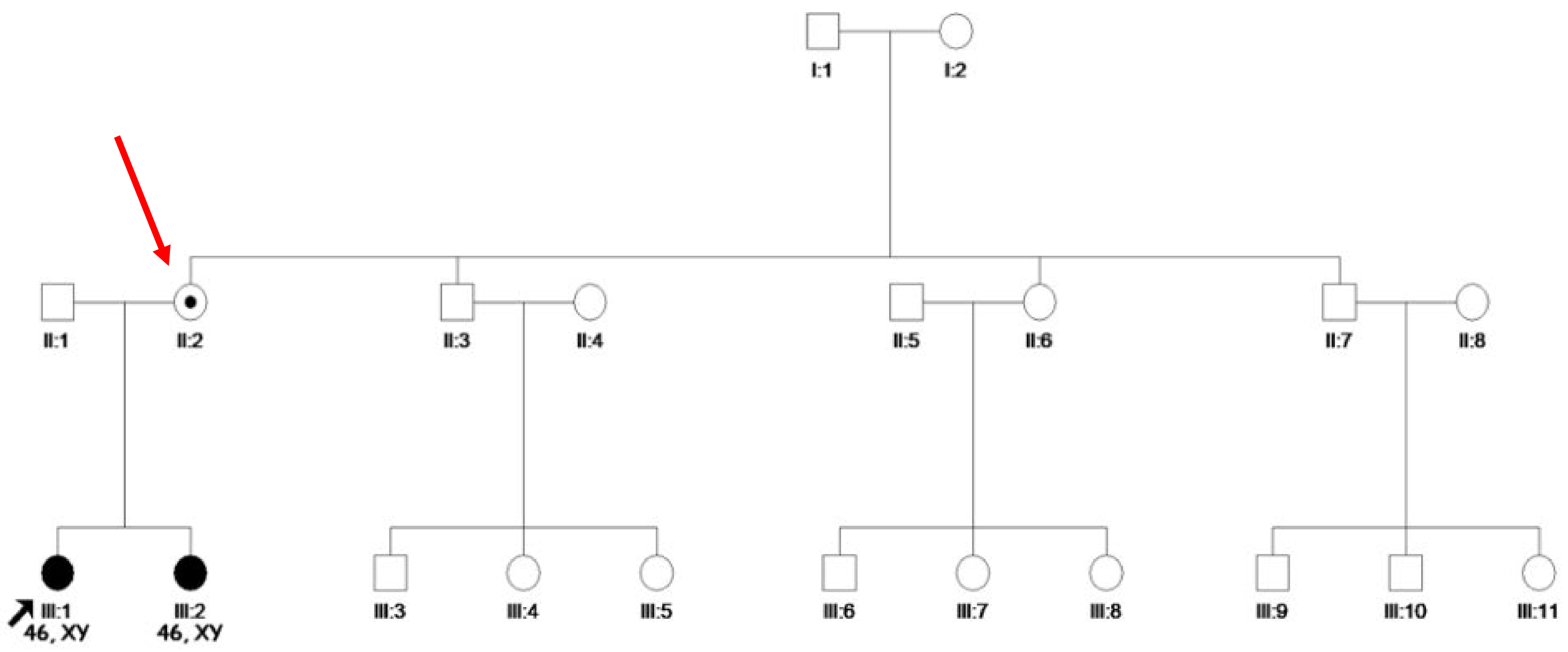
MOLECULAR GENETIC TESTING

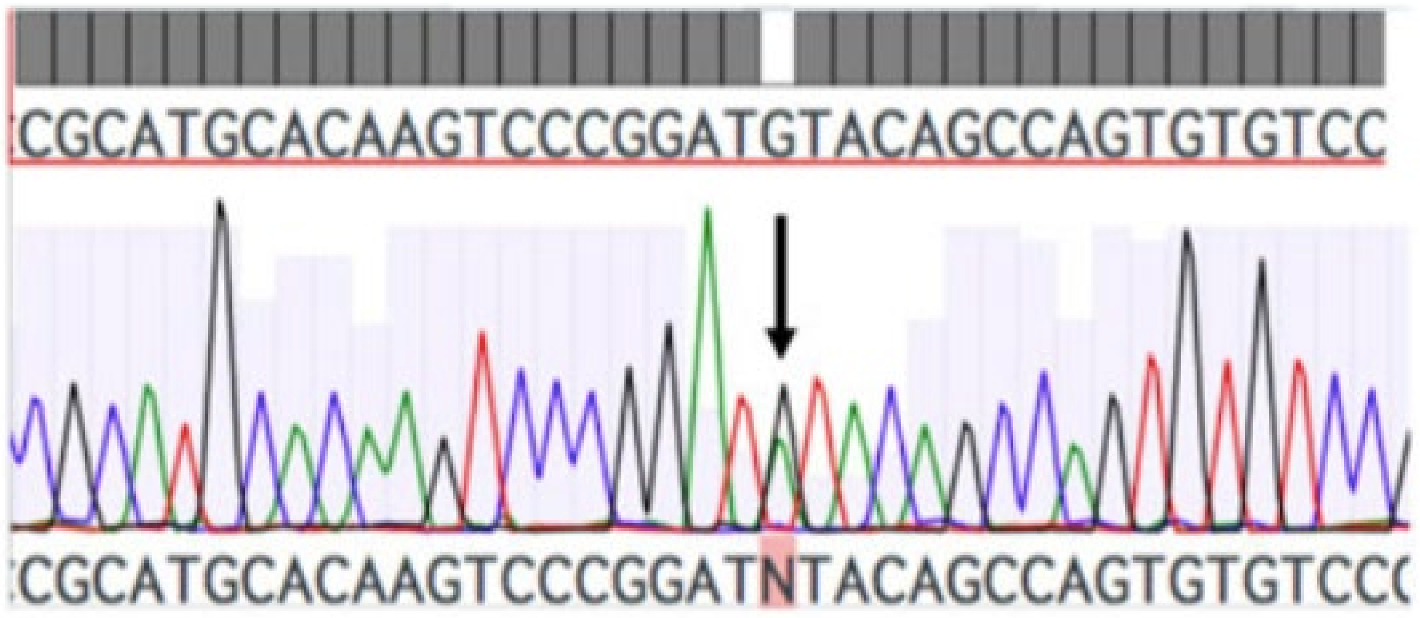




c.2343G>A; p. Met781Ile

AR GENE ANALYSIS OF THE MOTHER





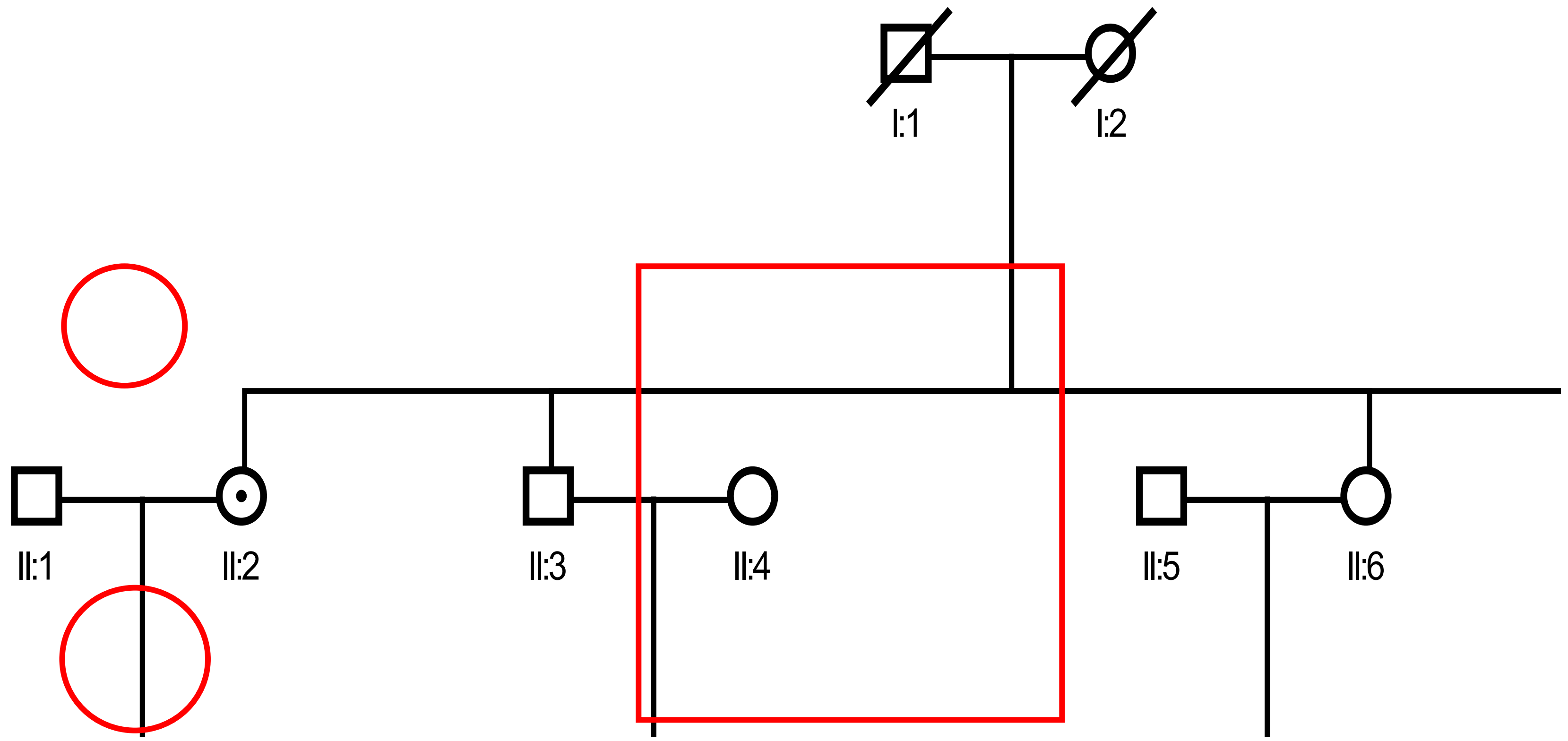
Partial sequence of the AR gene confirmed the presence of the variant in the mother; indicating the mother was **hemizygous** for the G to A change at nucleotide 2343

The mother is carrier for this condition

GENETIC COUNSELING

1. The risk of having the *AR* gene mutation in family members:

- Mother is a carrier
- Sibling is affected
- Other family members



GENETIC COUNSELING

2. Gender Identity:

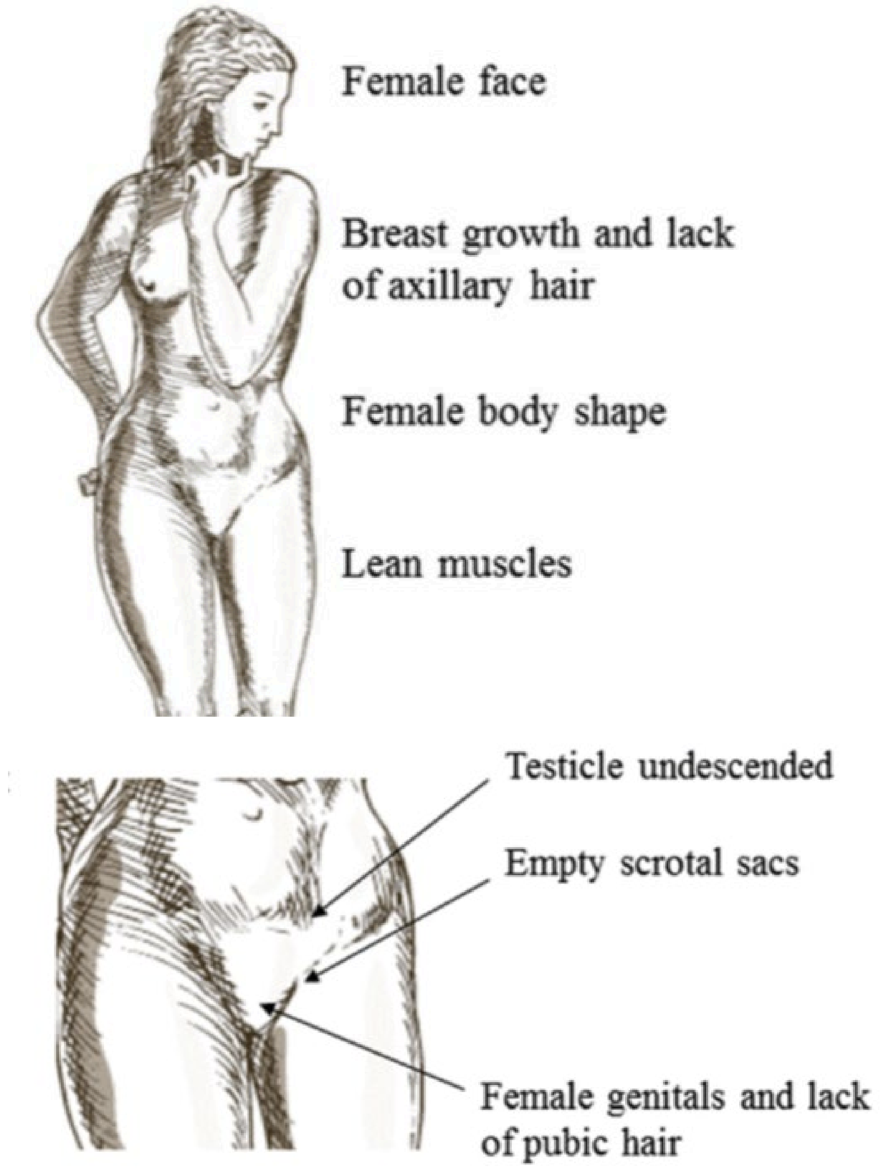
- CAIS : She is genetically male, with female external genitalia
- Patient wanted to keep her female gender

3. Reproductive Function:

- Infertility; she has external sex characteristics of females, but no uterus → No menstrual cycle and are unable to conceive a child
- Inguinal testis → gonad removal to avoid the risk of malignancy

4. Management and Intervention:

- Consented for testes removal
- Hormonal replacement therapy



CAIS phenotype

N. Mendoza et al. / J Pediatr Adolesc Gynecol (2016)

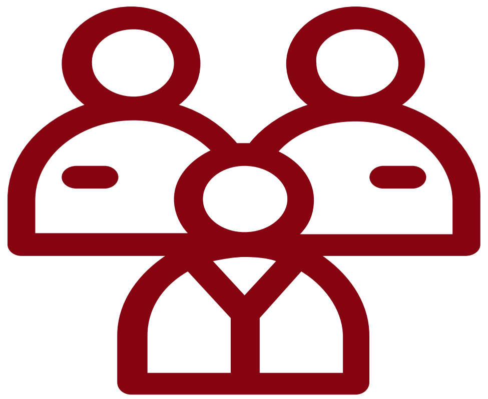
DISCUSSION

- A **comprehensive patient care** of girls presenting with primary amenorrhea with history of inguinal hernia.
- A comprehensive evaluation, including **history taking** and **pedigree construction**, may result in subsequent testing within family → **carriership status.**
- A **lack of awareness** of inguinal hernia in girls leads to a late identification of CAIS.
- Bilateral hernias containing gonads and a family history of CAIS should prompt clinicians to consider the diagnosis of CAIS.
- A **genetic diagnosis** should be done as soon as possible to avoid malignancy and gender dysphoria for the at-risk family members after genetic counseling.

CONCLUSION

The Diagnosis of genetic disease

Genetic Counseling



A comprehensive evaluation by Multidisciplinary Team in DSD

The optimal managements

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