

# A Turkish family with 46,XY disorder of sex development due to 17 $\beta$ -Hydroxysteroid dehydrogenase type 3 deficiency

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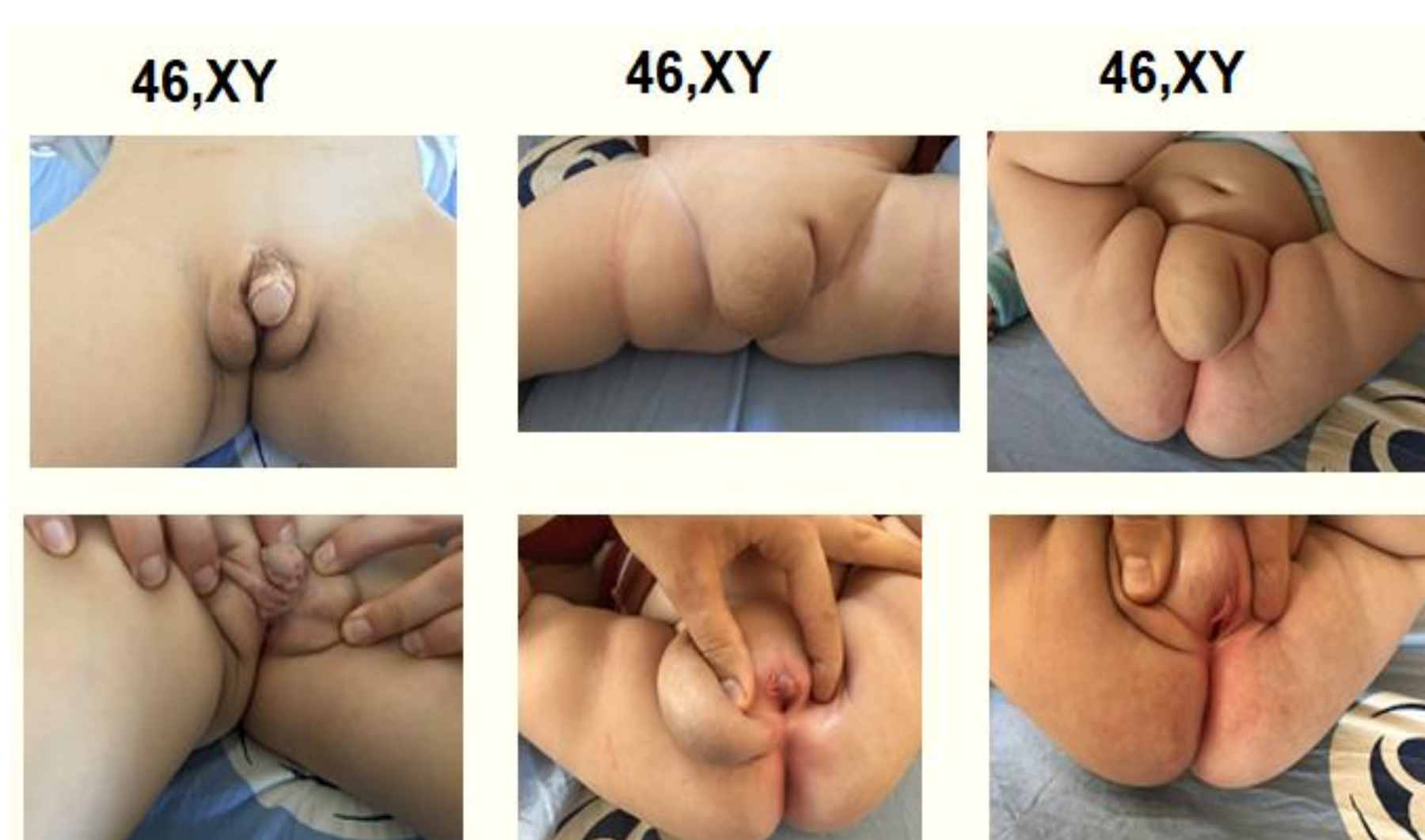
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## Introduction

17  $\beta$ -Hydroxysteroid dehydrogenase type 3 (17 $\beta$ -HSD3) is expressed mostly in the testes and converts the inactive  $\Delta$ 4-androstenedione (A) to testosterone (T). 17 $\beta$ -HSD3 deficiency is a rare autosomal recessive disorder and the most common testosterone biosynthesis defect leading to 46,XY Disorders of Sex Development (DSD). To date, more than 40 mutations of HSD17B3 have been reported. 46,XY patients with 17 $\beta$ -HSD3 deficiency would present with wide variable external genitalia (Sinnecker Type 5  $\rightarrow$  Tip 2, but mostly Sinnecker Type 4,5).

## Case

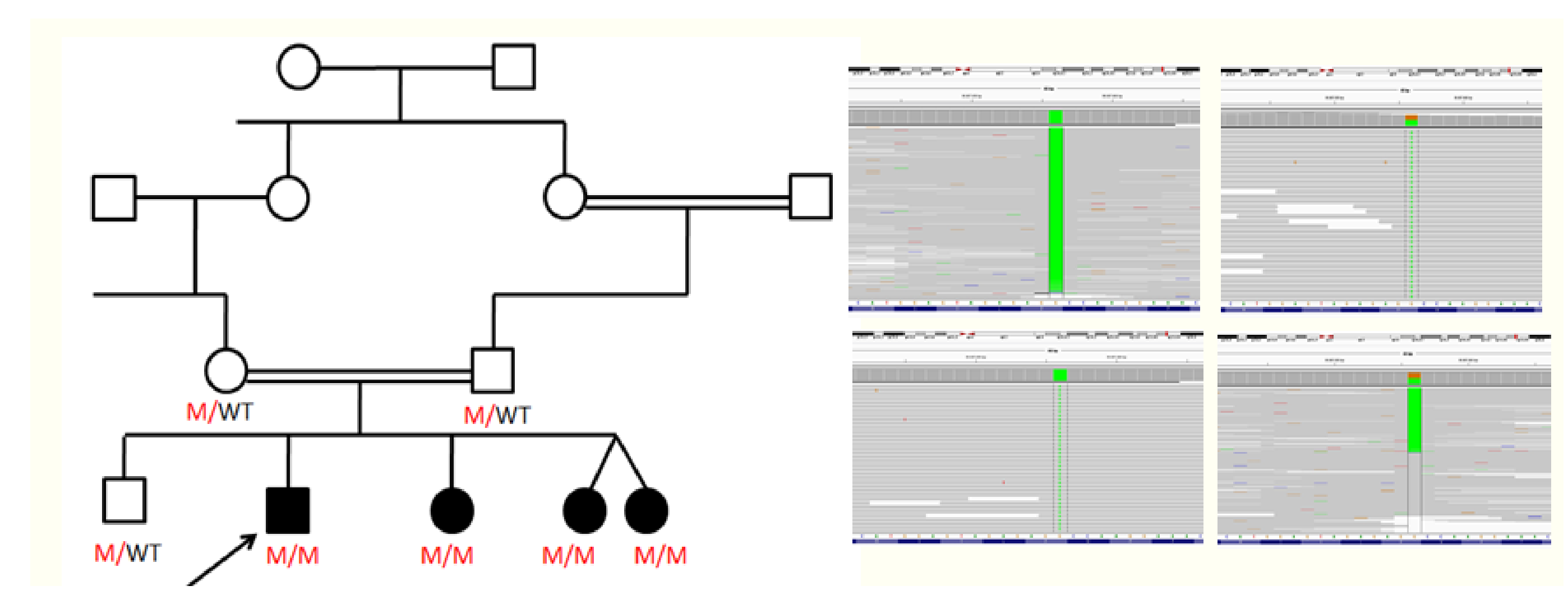
The patient was referred to our practice at the age of one year due to atypical external genitalia. Patients' parents were first-degree cousins. On physical examination displayed nearly complete female external genitalia and bilateral mass in her groin (Prader stage 2 & Sinnecker Type 4). Chromosomal analysis revealed a 46,XY karyotype, therefore patient diagnosed 46, XY DSD. In laboratory, T/A ratio was less than 0.8. When the patient was seven years old, his newborn twin sisters referred to us due to the same clinical condition; external genitalia and laboratory parameters. Their chromosomal analysis revealed a 46,XY karyotype too.



**Image 1.** External genital appearance of patients

	Older Brother	Case 1		Sister	Case 2	Case 3
Age	10 years	1 year	7 year, 8 month	3 years	Infant	Infant
chromosome	-	46,XY		46,XX	46,XY	46,XY
Prader stage	5	2	4	2	2	2
Fallus	5.6 cm	1.5 cm	3.5 cm	Female	1.2 cm	1.2 cm
Gonads	Scrotum	Inguinal	Scrotum (after orchiopexy)	-	Inguinal	Inguinal
Hipospadias	-	Perineal	Repair	-	-	-
chordee	-	+	Repair	-	-	-
Inguinal hernia	-	-	-	-	+	+
Mullerian structures	-	-	-	Uterus, Overler +	-	-
Laboratory	-	3 years FSH: 1.5 LH: 0.24 T: <0.1 A: $\approx$ 0.3	7 year, 8 month FSH: 0.95 LH: 0.05 T: 0 A: 691	3 year, 2 month FSH: 3.67 LH: 0.2 T: 0 A: 102	10 month FSH: 1.12 LH: 0.78 T: 0 A: 59	10 month FSH: 0.8 LH: 0.88 T: 0 A: 103
T/A rate	-	0.33	0	0	0	0

**Table 1.** Clinical and Laboratory Findings of the Cases



**Image 2.** Patient's mutation analysis and pedigree

## Results

We detected a de novo homozygous c.577C>T (p.P193S) mutation in HSD17B3 gene in three siblings. Parents and one brother were heterozygous for this mutation. Furthermore, same homozygous mutation was detected in a sister with 46, XX chromosomes without any complaint. In silico variant analysis, DANN Score was 0.9989 (Disease causing).

## Conclusion

We reported 3 siblings patients with 17 $\beta$ -HSD3 deficiency. Ambiguous genital phenotype, 46,XY male karyotype and the ratio of testosterone versus androstenedione less than 0.8 could suggest the diagnosis.