

# DSD 46,XY and serum steroid profile ambiguity due to combined 17-beta hydroxysteroid dehydrogenase/ 21-hydroxylase deficiencies

P2-324

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**Objective and hypotheses.** To describe and to characterize a case of DSD 46,XY presented with unusual serum steroid profile.

**An 18-years-old professional female athlete is presented with primary amenorrhea.**

**Physical examination** showed increased muscle mass, no breast development, male pattern of hair distribution, clitoris enlargement and blind-ending pseudo-vagina.

**Ultrasound examination** revealed bilateral inguinal gonads and no uterus.

**Karyotype** analysis showed 46,XY.

**Hormonal examination** revealed unusual serum steroid profile:

17-OHP 27,8 nmol/l (1,5-7,2);

DHEA-S 16,4 mkmol/l (0,9-11,7);

Testosterone 13,4 nmol/l (12-33);

Androstenedione 29,4 nmol/l (1,4-7,9).

**LC-MS/MS was performed to clarify the diagnosis.**

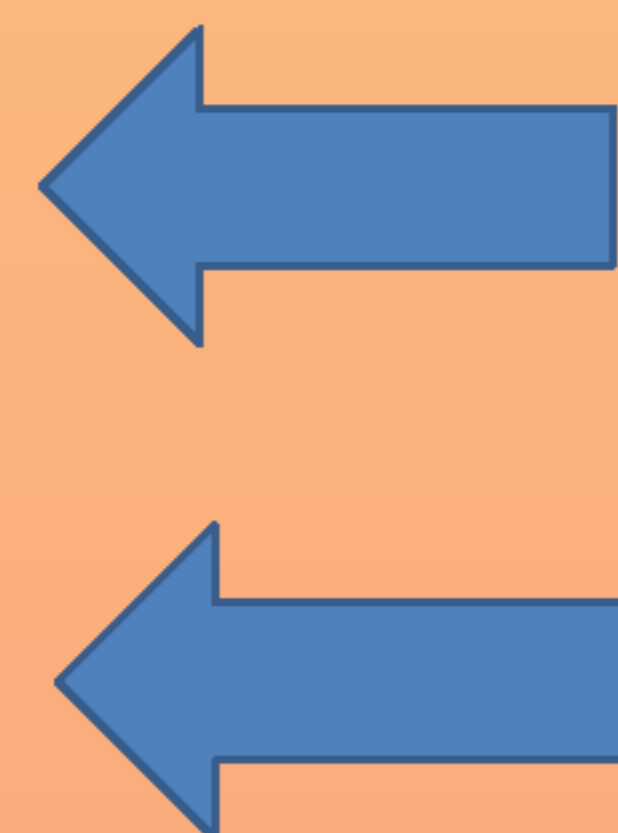
## Steroid profile assayed by LC-MS/MS

Hormone	Result	Normal range (male references)
17-OHP	35.6 nmol/l	1,5–7,2 nmol/l
Cortisol	353 nmol/l	150-650 nmol/l
Androstenedion (A)	29.5 nmol/l	1,4–7,9 nmol/l
Testosterone (T)	12.9 nmol/l	12-33 nmol/l
Testosterone/ Androstenedione	0.44	>0.8

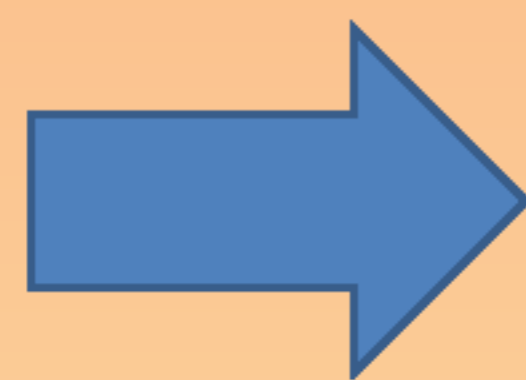
Nonclassical CYP21A2 deficiency



HSD17B3 deficiency



Combination of HSD17B3 and CYP21A2 deficiencies was suspected



## Genetic examination (Sanger sequencing)

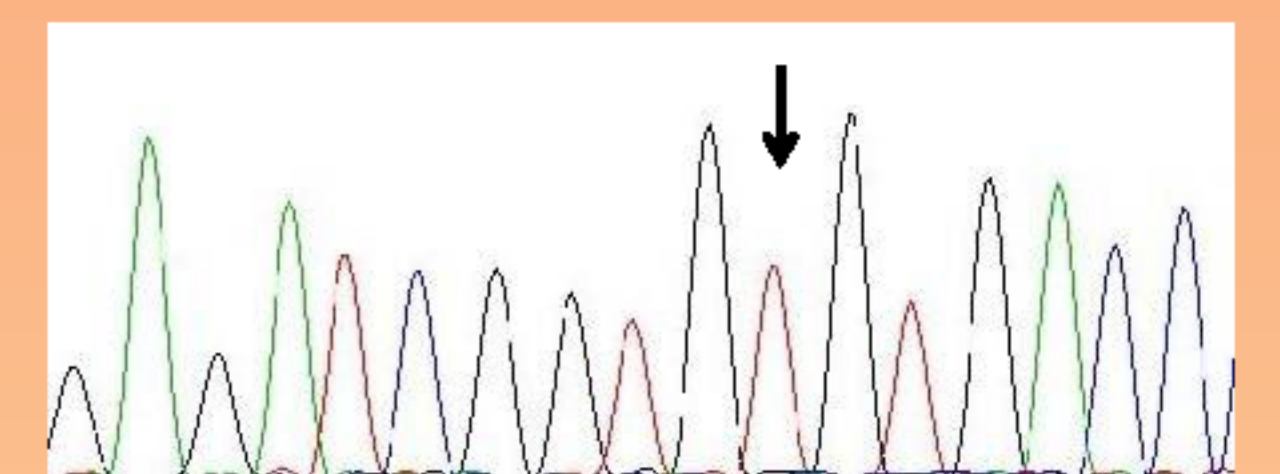
Sequencing of **HSD17B3** gene showed a known pathogenic homozygous splicing mutation c.277+4A>T

Analysis of **CYP21A2** gene revealed a homozygous p.V281L mutation, a frequent finding in non-classical congenital adrenal hyperplasia (NC CAH)

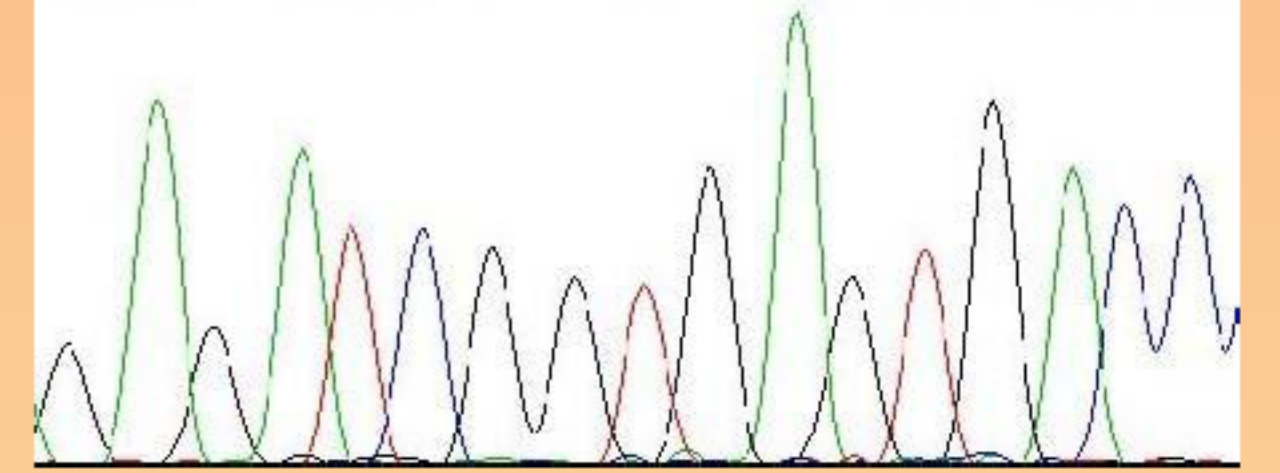


### HSD17B3

G A G A T C G G T G T / A G T G A C C

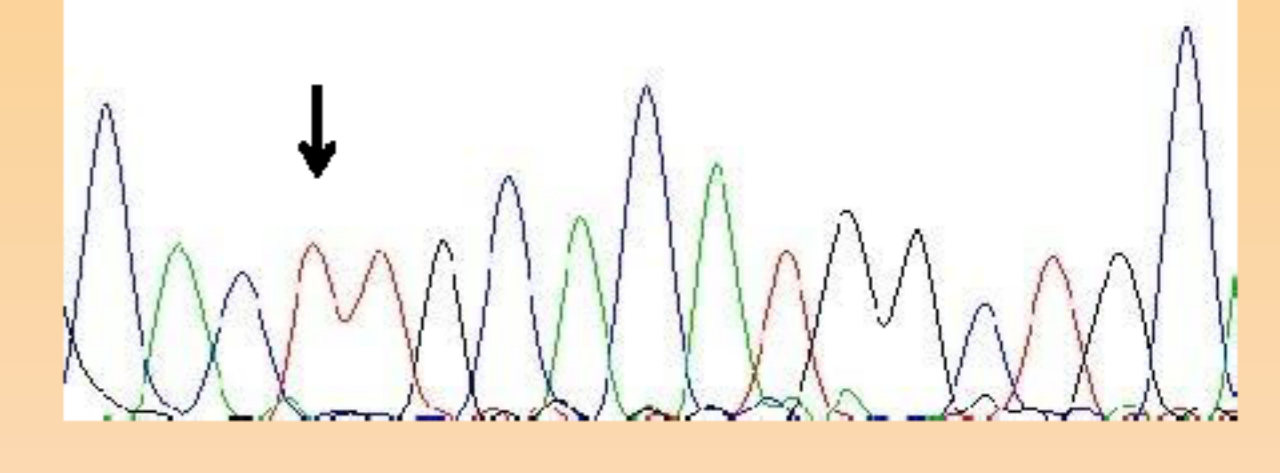


G A G A T C G G T G A G T G A C C

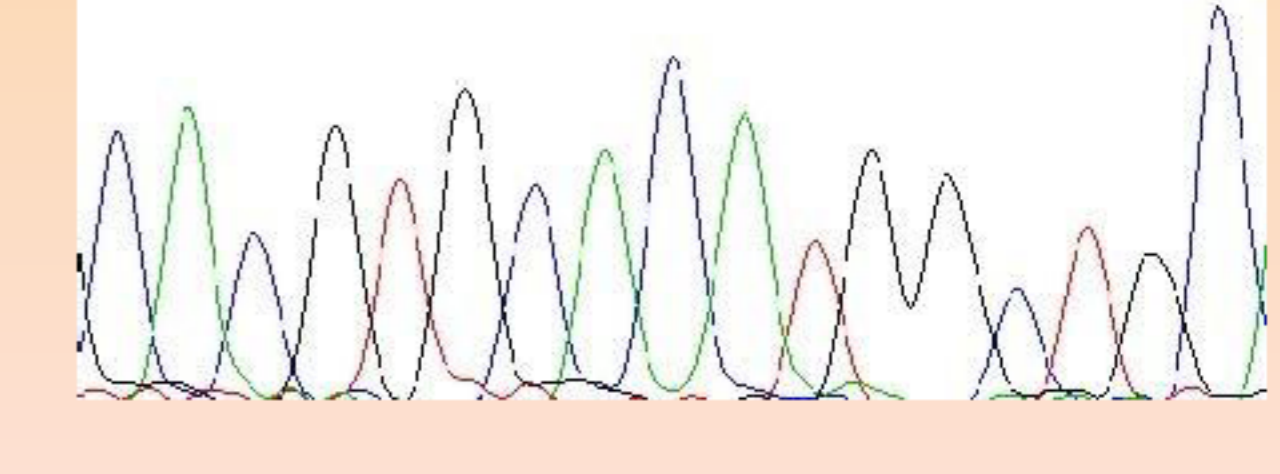


### CYP21A2

C A C T / G T G C A C A T G G C T G C



C A C G T G C A C A T G G C T G C



An accurate and comprehensive assessment of steroid hormones is pivotal for differential diagnosis of disorders of sex development (DSD) 46,XY, a part of which may be due to defects of testosterone biosynthesis.

**Conclusion:** To our knowledge, this is the first description of combined HSD17B3 and CYP21A2 deficiencies. Owing to the fact that NC CAH is frequent in certain populations, its contribution to observed peculiarities of phenotype and/or steroid profiles may be considered.

