

A New Mutation on the *SFR1 (NR5A1)* Gene in a 46 XY Sexual Development Disorder Case without the Adrenal Deficiency

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46,XY patients who have steroidogenic factor-1 (*SFR1/NR5A1*) mutation may have normal female external genitals as well as hypospadias, undescended testis, and ambiguous genitalia (mostly).

The first patient described in the literature had adrenal deficiency, but a lot of others, which were defined later, did not have any adrenal deficiency.

A 20-day-old baby was brought by his parents because of ambiguous genitalia. There was no history of consanguineous marriage. He was born at terms as 3000 grams. On physical examination, phallus was 2x1 cm, he had bifid scrotum, and hypospadias. Both gonads were palpable in the inguinal canal. Adrenal androgens were in normal range. Luteinizing hormone (LH) was 3.33 mIU/mL, follicle-stimulating hormone (FSH) 7.5 mIU/mL, and total testosterone was 72 ng/dL. Pelvic ultrasonography did not show any uterus, and his karyotype analysis was as 46,XY. Regarding the clinical and laboratory findings, partial androgen insensitivity syndrome or 5- α reductase

deficiency were thought as preliminary diagnosis. He was decided to be raised as a boy, so orchiopexy and hypospadias reparation were performed. The case did not show up to his later follow-ups until he was 11 and at that time he had pubic hair growth at stage 3, axillary hair growth as ++ and bilateral testes in scrotum (6 mL). LH: 7.1 IU/L, FSH: 23.1 IU/L, total testosterone: 164 ng/dL, testosterone/dihydrotestosterone ratio: 22. After human chorionic gonadotropin stimulation, his total testosterone was 368 ng/dL (Δ testosterone: 204 ng/dL). Androgen receptor and 5- α -reductase gene's molecular analysis did not show any mutations. New generation sequence analysis on the *NR5A1* gene demonstrated a new undefined heterozygous T272P (c.814A>C) mutation. On analysis of the mother and father, the father had a T272P mutation mosaic as 17%. A study on his buccal smear was performed in order to confirm the mosaicism and it showed same level of mosaicism. Standard dose of adrenocorticotrophic hormone stimulation test was performed due to the *NR5A1* mutation and the peak cortisol value was found to be 27.8 μ g /dL, so the adrenal deficiency was excluded.

Even though there is not any adrenal deficiency, there can still be a *NR5A1* mutation in cases of 46 XY sexual development disorder. Here, we presented a patient with a new mutation on the *NR5A1* gene. Also, new generation sequence analysis method could detect the low levels of mosaicism in parents by its high discriminative powers.

Key words: 46,XY, sexual development disorder, steroidogenic factor-1, adrenal, hypergonadotropic hypogonadism