

A Novel Mutation in Steroidogenic Factor (SF1) Gene in a Patient with 46, XY DSD without Adrenal Insufficiency

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Introduction: Steroidogenic factor-1 (*SF1/NR5A1*) is a nuclear receptor, which regulates genes that have functions in the development of adrenal glands and gonads, reproduction, and other metabolic functions. In humans, *SF1* mutations were first described in patients with 46,XY disorders of sex development (DSD), and primary adrenal failure .

Case Report: A 20-day-old infant was admitted due to ambiguous genitalia. Physical examination revealed a 2x1 cm phallus, bifid scrotum, and hypospadias. Both gonads were palpable in the inguinal canal. Serum levels of adrenal androgens (17-OH progesterone, DHEAS, androstenedione) and gonadotropins were within normal limits. Uterus could not be visualized on pelvic ultrasonography. In peripheral blood chromosome analysis 46, XY karyotype was detected. Initially, partial androgen insensitivity and 5 α -reductase deficiency were suspected. The patient was reared as male according to the decision of *Gender Assignment Council*. After decision, he underwent orchiopexy and surgical repair for hypospadias. At the age of 11 years, his pubertal development was normal with pubic hair Tanner stage III and both testes palpable as 6 mL. Hormonal evaluation revealed: LH: 7.1 IU/L, FSH: 23.1 IU/L, total testosterone: 164 ng/dL, and testosterone/dihydrotestosterone ratio was 22. After hCG stimulation test (3000 IU/day, three days), total testosterone level was measured as 368 ng/dL (Δ testosteron = 204 ng/dl). Next generation sequencing of *SF1* gene revealed a novel heterozygote mutation at T272P (c.814A>C). Analyses of the parents detected 17% mosaicism in the father's leukocyte DNA. Buccal smear sample to confirm mosaicism status of the father also detected the same level of mosaicism. Adrenal insufficiency was excluded with a standard dose ACTH stimulation test, which revealed a peak cortisol level of 27.8 μ g/dl.

Conclusion: We report a novel mutation in SF1 gene in a patient with 46, XY DSD without adrenal insufficiency. Our findings show that testis may be more sensitive to partial loss of SF1 function than the adrenal gland in humans . Also, we detected a low-level paternal mosaicism with next generation sequencing.

