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INTRODUCTION:
Steroidogenic factor-1 (SF-1), encoded by the NR5A1 gene, regulates several genes involved in male sexual determination, such as SOX9 and AMH, cholesterol mobilization and synthesis of a number of steroidogenic enzymes, like 3βHSD, and androgen biosynthesis, like INSL3. Mutations in NR5A1 have been associated to a broad phenotypic spectrum in 46, XY subjects, including pure gonadal dysgenesis, infertility, anorchia or hypospadias, often in conjunction with normal adrenal function.

PATIENTS AND METHODS:
Male patient.
At birth: Scrotal Hypospadias, micropenis, undescended teste and bifid scrotum.
Study:
1. karyotype 46 XY
2. Biochemical analysis (one month old): LH: 2.5 mU/ml, FSH: 3.7 mU/ml, Testosterone: 67.5 ng/ml, DHT: 1.7 ng/ml, DHEA-S: 400 ng/ml, Cortisol: 10.4 mcg/dl.
3. Abdominal ultrasound: normal
4. Good response of the penis to treatment with testosterone.
Familial background: maternal uncle presented with scrotal hypospadias at birth.
Genomic DNA was isolated from peripheral blood leukocytes and genetic characterization was performed using a targeted gene panel by NGS. PCR and Sanger sequencing was used for variant confirmation and the test parentes and affected family members to establish the mode of inheritance.

RESULTS:
HETEROZYGOUS NR5A1 C.250C>T; p. Arg84Cys mutation.
Functional studies demonstrated that this mutation:
- diminishes DNA binding site affinity
- diminished transcriptional activity.

CONCLUSIONS:
Our results agree with previous studies in which the complex penetrance, expressivity and inheritances of the alterations found in the NR5A1 gene, give rise depending on the mutation to phenotypes in 46 XY patients that encompass from pure gonadal dysgenesis to completely asymptomatic carriers, whereas in 46 XX patients lead to mild fotmos such as primary ovarian failure.