Two patients presenting the extremes of the phenotypic spectrum of 5-alpha reductase deficiency; one with at new mutation.

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Introduction

The large phenotypic spectrum of Disorders of Sex Development are caused by mutations in many different genes, but a large phenotypic spectrum of sexual disturbances may also be seen with different mutations in the same gene.

Objectives

To report on one new mutation in the 5-alpha reductase (SRD5A2) gene, and describe the extremes of the phenotypic spectrum of 5-alpha reductase deficiency presented in two patients.

Methods

Patient one was admitted four days old due to a micropenis. Parents were non-consanguineous healthy Somalians. Birthweight was 3820 g and birth length was 54 cm at term.
Patient two was admitted for suspicion of clitoromegali six months old. Parents were non-consanguineous healthy Danes. Birthweight was 1322 g, birth length was 42 cm at gestational age of 33 weeks.
The children had hormonal, chromosomal and genetic analyses. The second child also had an abdominal ultrasound.

Results

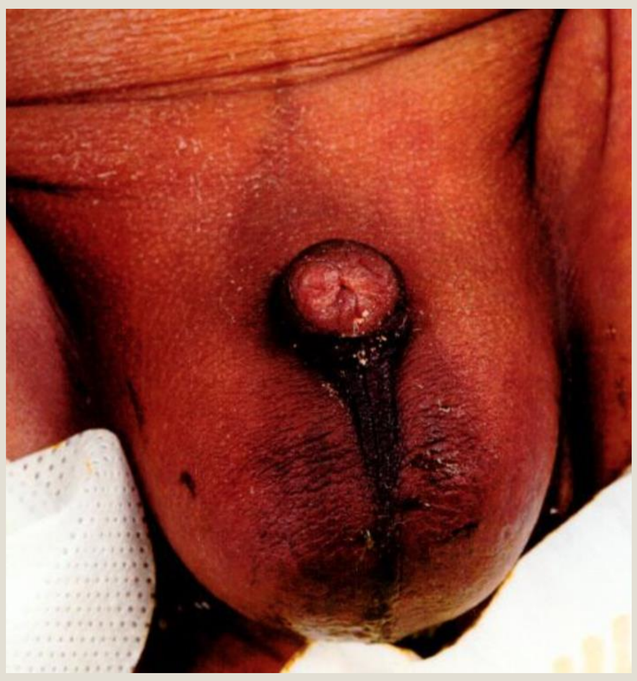
Patient one had a penis length of 2.1 cm with urethral orifice at the top of glans penis and retention of testes at the left side, normal testes at the right side and normal scrotum.
The second child had a clitoris length of 1.5 cm with an urethral orifice in the normal female position, bilateral gonads in labia majora but a female like vaginal opening.
Both children had the male karyotype 46,XY and normal hormonal axes. Testosterone / dihydrotestosterone ratio was 75 (HCG stimulated) in patient one and 15 (unstimulated) in patient two. Abdominal ultrasound of patient two was without Müllerian structures.
Genetic analysis of the SRD5A2 gene: Patient one was homozygous for a novel mutation c.682G>A (p.Ala228Thr), patient two was homozygous for c.692A>G (p.His231Arg).

Conclusions

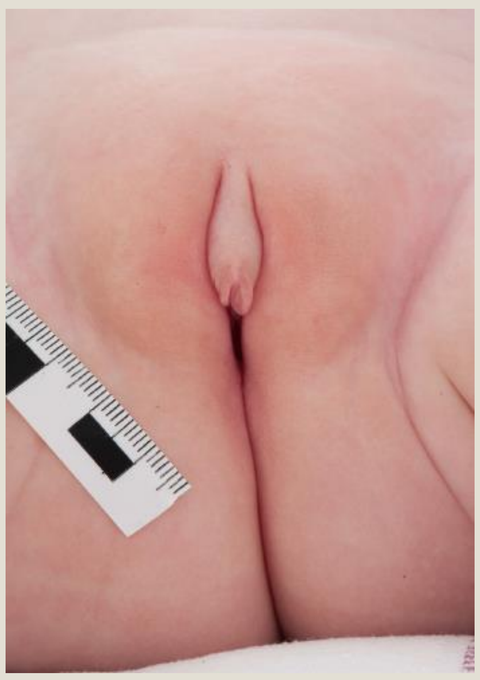
We report a new disease-causing mutation in the SRD5A2 gene, c.682G>A, and underline the very heterogeneous phenotype in patients with 5-alpha reductase deficiency, exemplified by two patients.

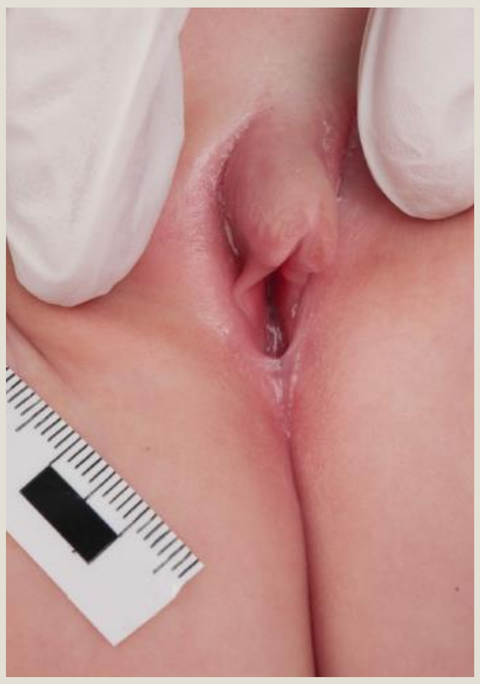
There are no conflicts of interest.

Patient one



Patient two





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