A rare case of sex reversal during puberty

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Background:
Disorders of sexual development (DSD) are rare and, in particular in developed countries, they are predominantly diagnosed during early childhood. DSD show a wide variety of phenotypes and can be difficult to classify.

Clinical Case:
A 34-year-old refugee from Somalia was referred because of a suspected DSD. Due to ambiguous, but predominantly female external genitalia at birth he was classified and raised as a girl in Somalia, whereas his subjective gender identity has always been male. Puberty led to a significant virilization of the body but only to a very limited virilization of the external genitalia. The patient presented himself with an undoubtedly male-type body composition, a deep voice, an adequate androgenic hair distribution, ongoing androgenetic alopecia and no gynecomastia. External genitalia were ambiguous, but now predominantly male with micropenis and hypospadias glands [fig1]. Small testes could be palpated in both labia, between which a small perineal orifice appeared.

Fig 1: Prader’s classification of grades of genital ambiguity (4); patient’s finding marked by circle

Diagnostic laparoscopy did not show any female internal genitalia. Sex hormones lay within normal male ranges: LH 8.4 mE/ml (n 1.7-8.6), FSH 7.1 mE/ml (n 1.5-12.4), testosterone (T) 704 ng/dl (n 249-836), dihydrotestosterone (DHT) 13.3 ng/dl (n 10-60), DHEAS 214.8 μg/dl (n 160-449), androstenedione 3 ng/ml (n 1.23-3.75), Estradiol 54 ng/ml (n 27.1–52.2), whereas Mullerian inhibiting hormone was remarkably increased (35.48 ng/ml, n 1.5-4.3) [table 1]. Chromosome analysis showed a regular male karyotype 46,XY,i(11)(p11.3)(SRY+) [fig2]. Highly increased T/DHT-ratio of 54 (n 8-16) [fig 3] in combination with the masculinization defect strictly limited to external genitalia without gynecomastia led to the clinical diagnosis of steroid 5 alpha-reductase 2 deficiency (SRD).

Conclusions:
This case of a rare DSD elucidates impressively how an enzyme deficiency affects the mechanisms of androgen action in the process of sexual differentiation.

References:
(3) The Human Gene Mutation Database at the Institute of Medical Genetics in Cardiff.