Undervirilization in a premature male infant: an unusual case

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Abstract: The birth of a newborn with abnormal genitalia (atypical sex) constitutes a major social emergency, and presents a difficult diagnostic challenge for the Neonatologist providing care, who should involve, an experienced multi-disciplinary team in the management [1-4].

INTRODUCTION
The birth of a newborn with abnormal genitalia (atypical sex) constitutes a major social emergency and presents a difficult diagnostic challenge for the pediatrician providing care, who should involve, an experienced multi-disciplinary team in the management [1-4].

The causes of ambiguous genitalia include genetic variations, hormonal imbalances and malformation of the fetal tissues that are supposed to evolve into genitalia [5-7]. We report here on a premature male infant who presented with undervirilized genitalia.

CASE REPORT
A preterm infant was born at 24 weeks of gestation to a 31-year-old Saudi G3, P2, A0 mother. The infant’s mother was healthy and received routine antenatal care. She was not on any medication nor exposed to radiation. He received surfactant and ventilated for 3 weeks. At one month of the infant was seen by pediatric endocrinologist for assessment of possible ambiguous external genitalia. The infant was noted to have fused labioscrotal folds (shallow scrotum) with no palpable gonads, but there was fullness in mid-right inguinal region, and a phallus-like structure measuring 1.5 cm with an opening at the tip of the phallus. The baby did not exhibit any dysmorphic features. Chromosomal study revealed 46XY karyotype and an ultrasound of the pelvis showed no internal female organs. Serum electrolytes and glucose were normal as well as serum LH, and FSH. Serum testosterone (ST) of 2.8 nmol/L (normal 0.1-0.5). Normal thyroid function with free thyroxine (FT4) of 15.7 Pmol/L (normal; 10-25) and thyroid stimulating hormone (TSH) of 1.7 IU/L (normal; <5 IU/L). Random growth hormone 14.3 ng/ml (normal; >10). Serum cortisol 880 nmol/L (normal; >600) and adrenocorticotropic hormone (ACTH) of 8 Pmol/L (normal; 5-15). 5α-reductase was ruled out by doing testosterone, dihydro testosterone ratio after 3 days injections of human chorionic gonadotro pin (HCG) stimulation test.

The baby was given 25 mg testosterone intramuscular. One month later the size of the phallus increased to 1.9 cm in length. At 4 months of age the right testicle was felt in the scrotum and the left one was palpable in the mid-inguinal region. The phallus size was 2-3 cm and the scrotum was still shallow.

DISCUSSION
Disorders of sex development (DSD) are defined as atypical sex. The differential diagnosis is so extensive. The appropriate sex of rearing of a very undervirilized male requires as much information as possible, as well as through multidisciplinary discussions involving the parents, urologist or pediatric surgeon, endocrinologist, geneticist and a clinical psychologist [4-7].

Male sexual differentiation is initiated by SRY gene on the short area of the Y chromosome. Under its influence the undifferential gonads forms a testis, which produces the hormonal milieu that results in male sexual differentiation. Testosterone stimulates the Wolffian structure (epididymis vas deferens, and seminal vesicles) and anti-Mullerian hormone suppresses the development of the Mullerian structure.
fallopian tube, uterus, and upper vagina). The conversion of testosterone to dihydro testosterone occurs in the skin of the external genitalia and masculinized the external structures. Most of this male differentiation takes place by about 12 weeks, after which the penis grows and the testes descent into the scrotum. In the absence of SRY, female sexual differentiation occurs. An error in genital morphogenetic may occur at any step in this developmental pathway [1, 3, 4]. The hormonal results and clinical progress ruled out hypothalamic-pituitary-gonadal axis, 5-α-reductase and androgen insensitivity as a cause.

Ens et al. [8] had reported on a premature infant who presented with undervirilized genitalia, however, they attributed this to intra-uterine growth retardation (IUGR). Placental factors and the possibility of a role for endocrine disruptor chemical have been postulated [9-10].

Advanced in perinatal and neonatal care over the last 30-years have contributed in the survival of many premature babies [11, 12]. In approximately one-half of undervirilized males there was no specific diagnosis. It is tempting to say that immaturity in the growth like what happening with the descent of the testicles. Almost 5% of the full-term babies had undescended testicles, while the ratio can reach 30% in preterm babies [13]. Further follow-up of this baby with genetic studies are needed.

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