A Teenage Girl with Unexpected Pubertal Changes

Nilika Wijeratne,[1,2,3]* Alan R. McNeil,[1] James C.G. Doery,[2,3] Elizabeth McLeod,[4] Philip B. Bergman,[5,6] and Joseph Montalto[1]

1 Department of Biochemistry, Dorevitch Pathology, Heidelberg, Victoria, Australia; 2 Monash Pathology, 3 Department of Medicine, Monash University, 4 Department of Pediatric Surgery, Monash Children's, and 5 Department of Pediatric Endocrinology and Diabetes, Monash Children's, Monash Health, Clayton, Victoria, Australia, 6 Department of Pediatrics, Monash University.

* Address correspondence to this author at: Dorevitch Pathology, 18 Banksia street, Heidelberg, Victoria 3084, Australia. E-mail nilika.wijeratne@monash.edu

CASE DESCRIPTION

A 9-year-old girl presented with persistent labial fusion for pediatric surgical evaluation. On examination, she was noted to have bilateral undescended gonads. A pelvic ultrasound was performed, which confirmed the testicular appearance of gonads and no visible uterus or Müllerian structures. She was referred to pediatric endocrinology.

She was born at term and was the second child of the family. She had no other significant medical problems. Her family history was unremarkable apart from her sister, who had mild, transient labial fusion. Her parents were not related.

The initial investigations revealed a 46, XY karyotype. The serum hormone results are shown in Table 1. After stimulation with 5000 U human chorionic gonadotropin (hCG),[7] the testosterone concentration was 170 ng/dl (5.9 nmol/L), but the dihydrotestosterone (DHT) result was unavailable due to an analytical issue. A urine steroid profile (USP) was inconclusive with individual analyte results within reference intervals (RIs). At this stage, the provisional diagnosis of complete androgen insensitivity syndrome (CAIS) was made and the endocrinologists opted to monitor the patient.

At 13 years of age, she went into puberty with pubic hair development, which led to further laboratory investigations (Table 1). USP revealed an increased etiocholanolone of 1.31 mg/day (4.5 μmol/day) [RI, <0.35 (<1.2)] and a low androsterone of 0.09 mg/day (0.3 μmol/day) [RI, <0.44 (<1.5)], resulting in extremely low 5α- to 5β-reduced steroid metabolites ratio of 0.06 (RI, 0.5–1.9). Pregnanediol, pregnanetriol, and cortisol metabolites concentrations were within reference ranges. The testosterone/DHT ratio was 12.6 (RI, <10) after hCG stimulation.

QUESTIONS TO CONSIDER
• How would you explain the differential diagnosis of an undervirilized genetic male?
• What tests could be used to investigate disorders of sex development?
• What is the most probable diagnosis in this patient?

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Table 1. Patient's serum hormone results.

Analyte	Concentration at the age of 9 years	Concentration at the age of 13 years	Reference interval (prepubertal, male)
Testosterone, ng/dL (nmol/L)	<8.7 (<0.3)	412 (14.3)	<14 (<0.5)
FSH, mIU/mL (IU/L)	1 (1)	4 (4)	<3 (<3)
LH, mIU/mL (IU/L)	0.3(0.3)	7 (7)	<1 (<1)
DHT (using RIA), ng/dL (nmol/L)	<12 (<0.4)	14.5 (0.5)	14.5–55 (0.5–1.9)
Androstenedione, ng/dL (nmol/L)	40 (1.4)	172 (6)	14–85 (0.5–3)
DHEAS, ug/dL (umol/L)	–	173 (4.7)	18–122 (0.5–3.3)
Estradiol, pg/mL (pmol/L)	–	8 (29)	<5.5 (<20)

FSH, follicle stimulating hormone; LH, luteinizing hormone; RIA, radioimmuno assay; DHEAS, dehydroepiandrosterone sulphate.

Final Publication and Comments

The final published version with discussion and comments from the experts will appear in the June 2018 issue of *Clinical Chemistry*. To view the case and comments online, go to http://www.clinchem.org/content/vol64/issue6 and follow the link to the Clinical Case Study and Commentaries.

Educational Centers

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