

Pediatrics

Virilization of a female infant genitalia caused by a maternal androgen-producing adrenocortical tumor: A case report

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ABSTRACT

A 4-month-old girl presented us with genital ambiguity. The patient had a persistent urogenital sinus, posterior labial fusion with clitoromegaly. MRI reveals ovary-like mass in left inguinal region and right abdominal cavity. Uterus and vagina was also identified. Her mother was diagnosed with a right androgen-producing adrenocortical tumor 14 months after the birth of a virilized infant.

Introduction

Masculinization of the external genitalia in human is dependent on formation of 5 α -dihydrotestosterone. The vast majority of patients with urogenital sinus (UGS), abnormalities is most commonly secondary to congenital adrenal hyperplasia. We report a rare case of a 46XX female infant with virilization of the external genitalia due to excess androgen exposure by maternal androgen-producing adrenocortical tumor.

A case report

A 4-month-old girl, born after freeze embryo transfer, presented us with genital ambiguity. The patient had a persistent UGS, posterior labial fusion with clitoromegaly (Fig. 1-a,b). A gonad-like mass was palpable in left inguinal region. MRI reveals ovary-like mass in left inguinal region and right abdominal cavity. Uterus and vagina was also identified. Any abnormality was not observed in upper urinary tract. Chromosomal analysis showed a 46XX genotype and SRY was negative. Adrenal steroid hormone levels, including 17-hydroxyprogesterone and 11-deoxycortisol were normal. On the 7th month, bilateral herniorrhaphy for gonadal herniation were performed. Any testis-like tissue was not detected in both gonads and biopsy specimen from left gonad revealed normal ovarian tissue.

Her mother was evaluated after the infant was found to have a normal 46XX genotype with a normal 17-hydroxyprogesterone level. Her mother had been experiencing virilism with a worsening hirsutism and acne before the pregnancy and those symptoms had continued

during the pregnancy. The virilism symptoms were improved after delivery. Her mother was diagnosed with a right androgen-producing adrenocortical tumor 14 months after delivery. Her serum testosterone level was 85 ng/dl (normal, less than 67), and dehydroepiandrosterone-sulfate 571 μ g/dl (normal, 58–327). The serum cortisol was slightly increased and failed to suppress with high dose dexamethasone. She underwent right adrenalectomy 16 months after the birth of a virilized infant.

On the 32 month, feminizing genitoplasty was performed.¹ A parallel incisions were made along either side of the urethral plate to the glans. A vertical median incision was made from the meatus to perineal body. An inverted U-shaped perineal flap was drawn. The UGS was dissected from the corporal bodies (Fig. 1-c). Partial urogenital mobilization was performed.² The erectile tissue was exposed and excised with care not injure the neurovascular bundle. The vagina was opened widely posteriorly into the normal-caliber vagina. The perineal flap was sutured in place to complete the flap vasinoplasty. Finally, labial reconstruction was performed. Post-operative finding, four months after surgery are shown (Fig. 1-d).

Discussion

The most common cause of occult virilization in the newborn is congenital adrenal hyperplasia. Two very rare causes are maternal administration of exogenous androgens or progestational agents and virilizing ovarian or adrenal tumors in the mother. Aromatase deficiency represents an even rarer cause of transplacental transport of excess

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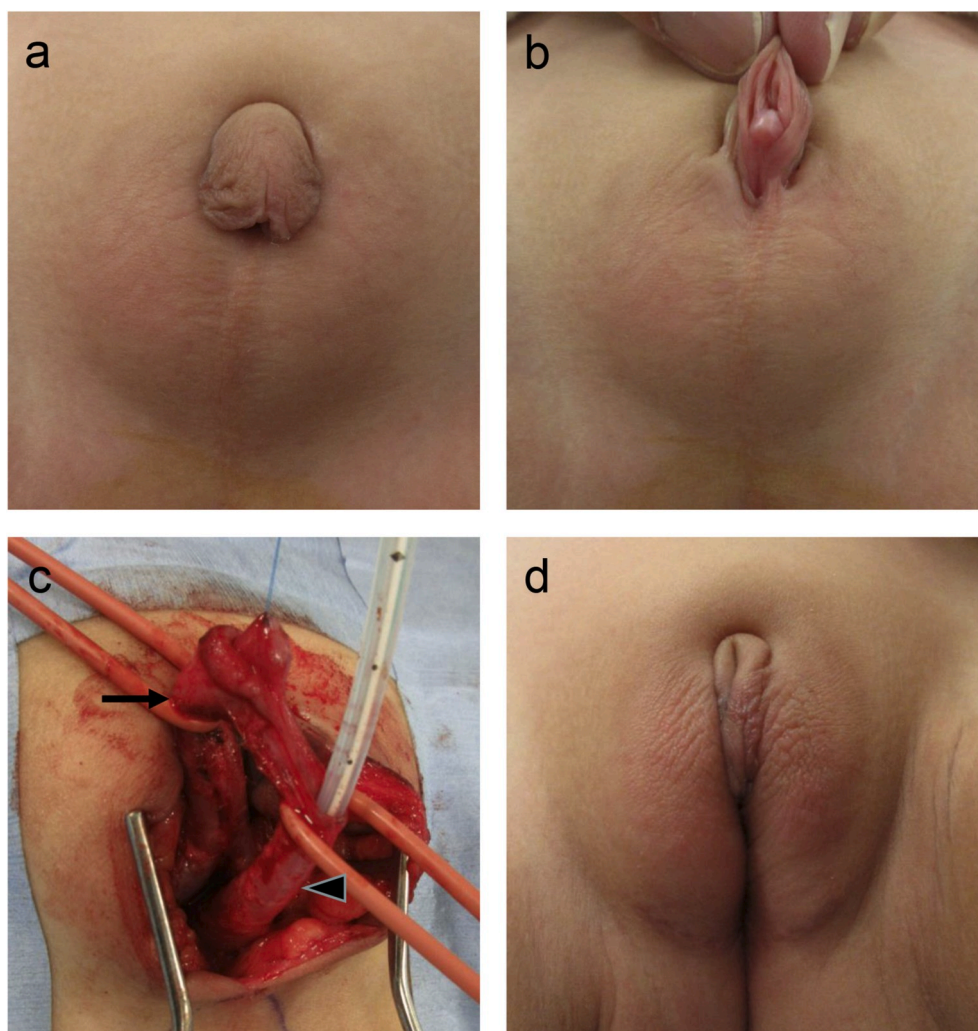


Figure 1. Appearance of the external genitalia. The patient had a persistent urogenital sinus, posterior labial fusion with clitoromegaly (a,b). The urogenital sinus (arrow head) was dissected from the corporal bodies (arrow) (c). Postoperative appearance, four months after genitoplasty (d).

androgens to the fetus.³

The degree of virilization is related to the gestational age at the time of androgen exposure of a female fetus. The critical period of gonadal differentiation is between the 8th and 12th weeks of fetal life.⁴ In this period, excess androgen exposure to a female fetus may cause labial fusion and induce the formation of a UGS, but after 12th weeks, androgen excess may produce only clitoral and labial hypertrophy.⁴ However, Bertalan et al. reported a female infant that hyperandrogenism detected as early as the 7th week of pregnancy and persisting until delivery did not cause virilization.⁵ They described that placental aromatase activity likely played a role in preventing androgen exposure of the fetus. The degree of virilization is also affected the level of androgens in the umbilical cord. In our cases, the mother with relatively mild virilization giving birth to a virilized infant, suggested that a peak of the human chorionic gonadotropin secretion that happened at 9th weeks of gestation might influence the increase of androgen, leading to the fetus virilization.

Conclusion

We encountered a rare case of a 46XX female infant with virilization

of the external genitalia caused by excess androgen exposure by maternal androgen-producing adrenocortical tumor.

Declaration of competing interest

None.

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