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Congenital adrenal hyperplasia: Results of medical therapy on appearance of external genitalia

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Abstract *Objective:* Girls with congenital adrenal hyperplasia show a variable degree of genital masculinization at birth. Antenatal dexamethazone treatment for the mother is known to reduce the severity of this condition. There are however few data on the effect of postnatal steroid therapy on the cosmetic appearance of the external genitalia.
Patients and method: We report the appearance of the external genitalia of three girls with classical congenital adrenal hyperplasia followed up by steroid therapy alone.
Results: Growth of the labia majora and a relative reduction in clitoral size improved the appearance of the external genitalia in these three girls.
Conclusion: There seems to be improvement in the external appearance of genitalia with postnatal steroid therapy. This could allay parental concerns and help in the planning of corrective surgery peripubertally with the informed consent of the child.

Introduction

Girls with congenital adrenal hyperplasia (CAH) are born with a varying degree of masculinization of the external genitalia. The current consensus statement stresses the use of surgery in CAH patients during early infancy [1]. Parental concern over the need for cosmetically normal looking genitalia to enable a normal social life for the child is the major factor guiding early surgery. The surgical management of classical CAH has evolved over the past five decades [2—4]. The need for cosmetically normal looking genitalia, an adequate vaginal introitus allowing normal sexual function and minimization of urinary incontinence have led to the progressive refinement of surgical techniques. However, final outcomes related to sexual function and patient satisfaction continue to be suboptimal [3—6].

David and Forest first showed a reduction in the severity of genital masculinization following antenatal dexamethazone therapy in girls with CAH [7]. Several subsequent studies have confirmed this beneficial effect [8—10]. There is little in the published literature on the effect of postnatal steroid therapy on subsequent growth and development of female external genitalia, but in the absence of steroid therapy there is evidence of progressive virilization [11,12]. Here we report the effect of steroid therapy during infancy and early childhood on the appearance of the external genitalia of girls with CAH.

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Methods

Children diagnosed with CAH who attend our outpatient clinic (a tertiary care hospital) are initiated on steroid treatment. Their parents are educated regarding the medical problem, medications and emergency care. They are also informed of the need for surgery to correct the genital malformation and the benefits of early versus late surgery. Those who opt to have surgery later are followed up with medication and surgery is performed peripubertally. Case reports (including photographs of external genitalia) of three girls with CAH on treatment are given below, and Table 1 summarizes the details. The consent of the parents has been obtained for the photographs. The study protocol was approved by the institutional ethics committee.

Case reports

Patient K

Patient K, product of a non-consanguineous marriage, was presented at age 2 months with complaints of poor oral intake and recurrent vomiting. The parents were also concerned about the genital ambiguity, which was noticed at birth. Family history revealed that their 4-year-old son had features of sexual precocity and another daughter had died at 1 month of age from dehydration. Physical examination revealed a sick child (weight 2.5 kg, pulse 104/min, blood pressure 90/6 mmHg) showing features of mild dehydration. Genital examination revealed clitoromegaly, scrotalized labia, posterior labial fusion and a single urogenital opening (Prader 3). Serum sodium was 138 meq/L and serum potassium was 6 meq/L. 17-Hydroxyprogesterone (17OHP) was more than 12.5 ng/mL, testosterone was 130 ng/dL and serum cortisol 13 mcg/dl. Karyotype revealed an XX pattern. Ultrasound of the abdomen revealed bilaterally enlarged adrenals and presence of the uterus. Hydrocortisone therapy was initiated at 15 mg/day. Vomiting subsided, feeding improved and serum potassium normalized with hydrocortisone therapy. Fig. 1 shows a photograph taken at 4 months of age. The enlarged clitoris is visible and coarse rugosity is shown over the labia. The photograph taken at 2 years of age shows there is still some rugosity of the skin at the posterior/distal part of the labia. Growth of labia majora in the absence of further growth of the clitoris has helped to improve the external appearance.

Patient N

This patient was presented at 2 years 10 months with complaints of fever and vomiting for 2 days. There had been no prior episode of dehydration/hospitalization. Although genital ambiguity was noted at birth, she was diagnosed to have CAH and initiated on steroids at 9 months of age. Compliance to therapy was poor. Examination revealed a febrile child with mild dehydration, pulse 120/min and blood pressure 90/60 mmHg. Examination of the genitalia revealed an enlarged clitoris with posterior labial fusion and a single perineal opening (Prader 3). Serum biochemistry and hematology were normal except for neutrophilic leukocytosis. Chest radiograph revealed a patch of pneumonitis in the left lower zone. Ultrasound of the abdomen showed the presence of crossed fused renal ectopia. Serum testosterone was 185 ng/mL and 17OHP was more than 12 ng/mL. Karyotype revealed an XX pattern. The patient was reinitiated on tablet prednisolone 2.5 mg. Fludocortisone (50 mcg) was added. Antibiotics were given for the chest infection. Genitogram revealed the presence of a common urogenital sinus. Fig. 2 shows photographs taken at 3.2 and 4 years. The genital appearance at 4 years was almost normal.

Patient A

This patient was presented at the age of 2.5 years with complaints of genital ambiguity and failure to thrive. There was a history of poor oral intake. She was the youngest of four affected siblings, of non-consanguineous parentage. The two elder sisters aged 15 and 5 years and one brother aged 11 years were also diagnosed with classical virilizing CAH. She appeared malnourished with a weight of 5 kg (less than third percentile) and height of 78 cm. Genital examination revealed clitoromegaly with posterior labial fusion and scrotalized labia majora. 17OHP was more than 12 ng/mL and serum testosterone was 1.5 ng/mL. Steroids were initiated. There was no further increase in size of the clitoris after starting steroid therapy. The appearance of the labia majora at initial evaluation and a year later is shown in Fig. 3. Clitoral enlargement became less obvious with the development of the labia majora.

Discussion

Current management protocols for infant girls with CAH advocate genital reconstruction surgery during infancy [1]. This decision is mainly guided by parental desire for cosmetically acceptable genitalia. Current surgical techniques are quite different from those of 15—20 years ago [2—4]. Clitoral surgery has advanced from clitorectomy to genital sensation-preserving procedures, i.e. clitoral recession and clitoroplasty. The Fortunoff perineal flap for vaginoplasty was replaced with the use of preputial

Table 1 Clinical and hormonal details of the three patients.

	Age at steroid initiation	Clitoral enlargement	Posterior labial fusion	Urogenital sinus	Testosterone (ng/ml)	17OHP (ng/ml)	Imaging
K	2 months	Present	Present	Present	1.3	>12.5	Adrenals enlarged (USG)
N	9 months	Present	Present	Present	1.85	>12.5	Crossed fused renal ectopia
A	2.5 years	Present	Present	Absent	1.5	>12.5	Adrenals enlarged (USG)