'Who am I …?'

K S H de Silva[1], **Malik Samarasinghe**[2]

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Introduction

Commonest cause of virilization in a girl is congenital adrenal hyperplasia (CAH). 90-95% of CAH is due to 21 – hydroxylase deficiency about 75% of which are of the salt losing type[1,2]. 11□-hydroxylase deficiency is rare and accounts for about 5-8% of CAH. This condition in a girl results in ambiguous genitalia and is therefore detected at birth but if complete virilization occurs baby can be mistakenly identified as a boy resulting in male gender assignment[2,3,4]. Revelation of the true identity will then result in immense psychological trauma to child and parents.

Case report

This is the story of a child whose problems are just beginning. V was transferred from a hospital in the Eastern Province at the age of 6 years and 2 months for further investigation. Child was the first live born of consanguineous parents. First pregnancy had ended in an abortion and the youngest is a boy of 1 year and 4 months.

Patient had been born at 35 weeks of gestation and weighed 1.8 kg. There was a history of stay in premature baby unit (PBU) of one month but details of this period are not available. His development was normal and he had been otherwise healthy with no hospital admissions. There was no history suggestive of dehydration or salt loss and no salt craving. He had always been dark in complexion. Pubic hair was noted at 3 years followed by appearance of facial acne. Phallic enlargement was noted around 5 years and they also noticed that his voice was hoarse. Physical features had markedly increased over the 6 months prior to admission prompting the parents to seek medical advice. Child was not aggressive and there was no history of headache, vomiting, visual disturbances or abdominal pain. He was in the first year at a mixed school and the tallest in class. His friends were mostly boys.

[1]*Senior Lecturer, Department of Paediatrics, Faculty of Medicine, Colombo,* [2]*Lecturer, Department of Surgery, Faculty of Medicine, Colombo.*

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On presentation at Lady Ridgeway Hospital he was 135.5 cm tall (well above 97th centile) (Figure 1) and weighed 29.2 kg (> 97th centile). He was dark with pigmented palms and buccal mucosa. Acne was present but no facial or axillary hair. Examination of the systems was normal with a blood pressure (BP) of 110/75. Subsequent recordings showed an increased BP and he needed anti-hypertensive therapy. He had Tanner Stage III pubic hair, an empty, hyperpigmented, underdeveloped scrotum and a phallus of 8.2cm (Figure 2). Differential diagnoses at this stage were: a girl with complete virilization due to undiagnosed CAH, a boy with precocious puberty or malignancy in undescended testes.

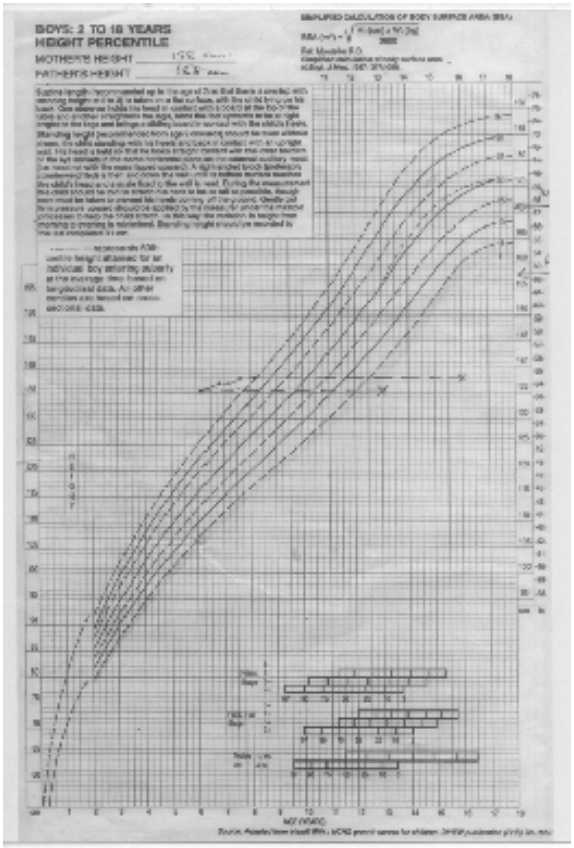

Figure 1. Growth chart showing height percentile.

Figure 2. *Patient at 6 years and 2 months*

To determine sex of child, as an initial investigation buccal smear was examined for Barr bodies. This was suggestive of a XX genotype and female sex was subsequently confirmed by a chromosome analysis showing a 46,XX karyotype. Mutation analysis could not be done. Commonest cause of complete vrilization in a girl is CAH[1]. This was confirmed by a markedly elevated 17 – hydroxyprogesterone level (17-OHP) of 100.8 nmol/l (normal <6 nmol/l). Further evidence of increased adrenal androgen production was demonstrated by a dehydro epiandrosterone sulphate (DHEAS) level of 2.4 µg/ml (normal 0.25-1.0 µg/ml) and total testosterone of 9.0 ng/ml (normal <0.03- 0.1 ng/ml). Serum electrolytes were normal with a sodium of 133.8 mmol/l and a potassium of 3.2 mmol/l. Utrasound scan showed enlarged suprarenal glands with no evidence of a tumour. It also showed a rudimentary uterus but gonadal tissue could not be identified. Bone age was 13 years which was markedly advanced from the chronological age of 6 years and 2 months. LH was 2.0 mIU/ml (normal <1-5 mIU/ml) and FSH <1.0 mIU/ml (normal 1-3 mIU/ml). Plasma renin activity (PRA), 24 hour urinary steroid profile and serum deoxycorticosterone acetate (which is raised in 11□-hydroxylase deficiency) could not be done. Diagnosis of CAH was confirmed by dexamethasone treatment for 4 days which completely suppressed the 17-OHP and testosterone. A micturating cystourethrogram (MCUG) demonstrated a long, male type urethra and with no evidence of reflux. There was no demonstrable vagina.

Discussion

Hypertension is seen in CAH due to 11□-hydro-xylase deficiency but markedly elevated 17-OHP is more suggestive of 21-hydroxylase deficiency2 and with no history of salt losing crises, the final diagnosis was assumed to be non salt losing 21-hydroxylase deficiency CAH3. Definitive diagnosis was not possible due to limited investigative facilities. Child has been brought up as a boy for 6 years and therefore presents several problems in further management.

Gender reassignment

CAH in a girl is usually suspected at birth due to ambiguous genitalia. Male phenotype due to complete virilization[3,4] in this patient resulted in child being brought up as a boy for 6 years. A reassignment of gender at this stage would undoubtedly give rise to immense psychological, emotional and social repercussions although it is only as a girl that this child will have the possibility to retain fertility[4]. Continuing as a boy will result in breast development at puberty with 'menstruation' manifesting as bleeding per urethra4, which will be psychologically very damaging to the child. Therefore to prevent this to some extent, he will need surgery in the form of oophorectomy and hysterectomy.

Precocious puberty

Secondary central precocious puberty is a complication associated with delayed diagnosis and inadequately controlled adrenal androgen production[2,4,5,6]. There is premature activation of the hypothalamo-pituitary-gonadal axis associated with the advanced skeletal maturation which can lead to onset of puberty appropriate for skeletal age but early for chronological age[2,5]. Treatment at this stage with hydrocortisone will almost invariably precipitate central precocious puberty[5,6]. This will result in breast development and cyclical bleeding. Suppression of puberty with a gonadotrophin releasing hormone (GnRH) analogue[4,5,6] would not be practical due to financial and transport constraints. Treatment with hydrocortisone by suppressing androgen production will also result in the innate

female characteristics surfacing which will be very traumatic if the child were to continue as a boy.

Short stature

Although he is the tallest in class now the already markedly advanced bone age will compromise final height resulting in him being a short adult[2,4,7]. If precocious puberty was to occur this would further reduce final height.

Surgical intervention

A decision to continue as a boy will need oophorectomy and hysterectomy to prevent feminization at puberty[4]. If gender reassignment is considered, surgery is needed to reconstruct the external genitalia. After a detailed discussion with the parents regarding implications of both options, they made an informed decision to continue raising V as a boy and wished for early surgery.

Surgery was done at 8 years and 2 months of age. At laparotomy two normal looking ovaries, fallopian tubes and a uterus were identified. Vagina appeared to join the urethra just below bladder neck (urogenital sinus) which was divided at this point and the ovaries, fallopian tubes, uterus and vagina were removed. Post-operative period was uneventful and he was passing urine normally with good bladder control once the bladder catheter was removed.

At present he is a well adjusted boy with a male gender identity. The family is coping reasonably well with the situation. His problems, though, are still not over. His bone age now is 16 years and he is 138 cm tall (Figure 1). This will very likely be his approximate adult height[7]and will be a reason for concern later in life. He will need testicular prostheses around the time of puberty and treatment with testosterone may have to be considered. Child and family will need continued counselling and support to help them cope with the many challenges they will be facing in the future.

References

1. Warne G L, Hughes I A. The clinical management of ambiguous genitalia. In: Brook CGD, editor. Clinical Paediatric Endocrinology. London: Blackwell Science Ltd, 1995; 53-65.

2. Huma Z, Crawford C, New M I. Congenital adrenal hyperplasia. In: Brook CGD, editor. Clinical Paediatric Endocrinology. London: Blackwell Science Ltd, 1995; 536-57.

3. Wyatt DT, Chasalow F I, Granoff A B, Blethen S L. Complete masculinization of the external genitalia in a genetic female with non salt losing 21 hydroxylase deficiency. *Journal of Pediatric Endocrinology* 1987; **2**: 35-8.

4. Woelfle J, Hoepffner W, Sippell W G, Bramswig J H, Heidemann P, et al. Complete virilization in congenital adrenal hyperplasia: clinical course, medical management and disease-related complications. *Clinical Endocrinology* 2002; **56(2)**: 231-9.

5. Pescovitz O H, Comite F, Cassorla, Dwyer A J, Poth M A, et al. True precocious puberty complicating congenital adrenal hyperplasia: treatment with a luteinizing hormone-releasing hormone analogue. *Journal of Clinical Endocrinology and Metabolism* 1984; **58**: 857-61.

6. Soliman A T, Al Lamki S, Al Salmi I, Asfour M. Congenital adrenal hyperplasia complicated by central precocious puberty: Linear growth during puberty and treatment with gonadotropin-releasing hormone analogue. *Metabolism* 1997; **46**: 513-7.

7. Bayley N, Pinneau S. Tables for predicting adult height from skeletal age: revised for the use of Greulich-Pyle standards. *Journal of Pediatrics* 1952; **40**: 423-41.