Original Article

Male genitoplasty for 46 XX congenital adrenal hyperplasia patients presenting late and reared as males

Shilpa Sharma, Devendra K. Gupta

Department of Pediatric Surgery, All India Institute of Medical Sciences, New Delhi, India

ABSTRACT

Aim: To evaluate the clinical profile and management of 46 XX Congenital Adrenal Hyperplasia (CAH) patients presenting with severe virilization and assigned a male gender. **Materials and Methods:** Of 173 children diagnosed with CAH at the Pediatric Intersex Clinic since 1980, seven children with CAH presented late with severe virilization and were reared as males. All of them were assigned the male sex with removal of the female adnexa. Six were treated with male genitoplasty. Appropriate hormonal supplementation was offered after puberty. **Results:** The mean age at presentation was 14.2 years (7 – 21). Six patients had presented after puberty, only one at seven years of age. Staged male genitoplasty comprising of chordee correction, male urethroplasty, and bilateral testicular prosthesis was performed. The female adnexa (uterus, ovaries, most of the upper vagina, and the fallopian tubes) were removed. The mental makeup was masculine in six and bigender in one. Bilateral mastectomy was performed at puberty in all. Hormonal treatment comprised of glucocorticoids and testosterone. Six patients were comfortable with the outcome of the masculinizing genitoplasty. One had a short-sized phallus. One had repeated attacks of urinary tract infection arising from the retained lower vaginal pouch. Social adjustments were good in all, except in one who had a bigender mental makeup. **Conclusion:** CAH patients with severe virilization presenting late and reared as males are extremely rare. However, the assigned gender can be retained adequately as males, meeting the socioeconomic compulsions of the society. The results are satisfactory following appropriate surgical procedures and hormonal supplementation.

Key words: 46XX male, congenital adrenal hyperplasia, masculinizing genitoplasty

Introduction

The usual gender assigned to patients with 46 XX Congenital Adrenal Hyperplasia patients is female as these cases are diagnosed at a very early age universally, worldwide. However, in the developing world with social and cultural taboos, the parents of these children may seek medical advice only after puberty when they want their child to be fit for marriage.

Access this article online	
Quick Response Code:	Website: www.ijem.in
	DOI: 10.4103/2230-8210.102994

Aim

To evaluate the clinical profile and management of patients of 46 XX Congenital Adrenal Hyperplasia assigned a male gender.

Materials and Methods

Of 173 children diagnosed as Congenital Adrenal Hyperplasia (CAH) at the Pediatric Intersex Clinic, seven children who had been reared as males and presented around puberty, were retained with the male gender assignment due to socioeconomic compulsions and the general male behavior of the patients. The clinical profile and the management of these cases were evaluated with a long-term follow-up.

Correspondence Author: Prof. Devendra K. Gupta, Department of Pediatric Surgery, All India Institute of Medical Sciences, Ansari Nagar, New Delhi, India. E-mail: profdkgupta@gmail.com

Results

The mean age at presentation was 14.2 years (7 – 21) [Table 1]. Six patients had presented after puberty, only one at seven years of age. The presenting symptoms were severe hypospadias with chordee, a well-developed phallus, a large urinary meatus opening in the perineum, and bilateral undescended testes in six patients. One patient had a complete male urethra with the meatus reaching at the tip of the phallus. The presenting feature in this patient was gynecomasia and cryptorchidism. The youngest seven-year-old boy presented with severe hypospadias, but without breast enlargement. Breast development was present in all six patients presenting after puberty, at presentation. The seven-year-old boy also had breast development when he reached puberty. Acne and hyperpigmented genitalia were present in one. There was cyclic hematuria in one case that presented post puberty. Pubic hair was of the female pattern in six. The parents of all seven patients knew the genital abnormalities in the children. However, no expert medical help had been sought so far except in one. In six of the seven children, neither the parents nor the children knew of the diagnosis of CAH and its implications so far. The sex of male rearing had been assigned by the parents and the children also behaved as boys in day-to-day life. One patient had been treated with female genitoplasty for CAH at the age of three at this institution and was also advised steroid therapy, but he did not comply with the treatment prescribed. The clitoris started increasing and the parents thought him to be a boy and continued to rear him as a boy till the age of 17, when they visited again for male sex assignment and removal of breast enlargement. Also, he was the only bread earning member in the family. The mental makeup was masculine in six and bigender in one who presented at the age of 14 years. All had 21-hydroxylase deficiency.

Staged male genitoplasty comprising of chordee correction and male urethroplasty was done in six [Figure 1]. The female adnexa (uterus, ovaries, upper two-third of the vagina, and fallopian tubes) were removed in all seven patients [Table 2, Figure 2]. Artificial testicular prostheses were inserted in the labioscrotal sacs. Bilateral mastectomy was performed for the six cases presenting after puberty and also for the seven-year-old boy, when he reached puberty. The mean number of surgeries performed was 4.9 (3 – 7). Hormonal treatment included daily glucocorticoids. Testosterone as monthly injections were also prescribed, post male genitoplasty, to all the seven patients. The follow-up period varied from 4.3 – 16.1 years (mean 9.2 years). Six patients are comfortable with the outcome of the surgery performed in stages, including the masculinizing genitoplasty. All of them are on steroids and testosterone injections. With parental and social support, six of the

Table 1: Age at presentation and follow-up of seven patients of congenital adrenal hyperplasia subjected to male genitoplasty

Age at presentation	Prader stage	Number of surgeries	Follow-up
13	4	6	16.1
15	4	7	11.3
13	4	4	10.5
21	5	3	9
7	4	5	7.2
14	4	5	6.0
14.5	4	4	4.3

Table 2: Surgical steps for male genitoplasty for female chromosome congenital adrenal hyperplasia

Chordee correction and laparotomy for the removal of female adnexae
Male urethroplasty
Testicular prosthesis
Bilateral mastectomy

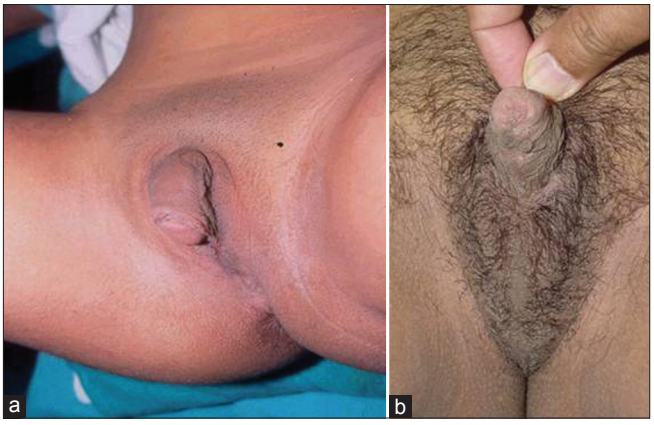

Figure 1: (a) External genitalia in a 46XX congenital adrenal hyperplasia reared and assigned as male (b) Completed male genitoplasty

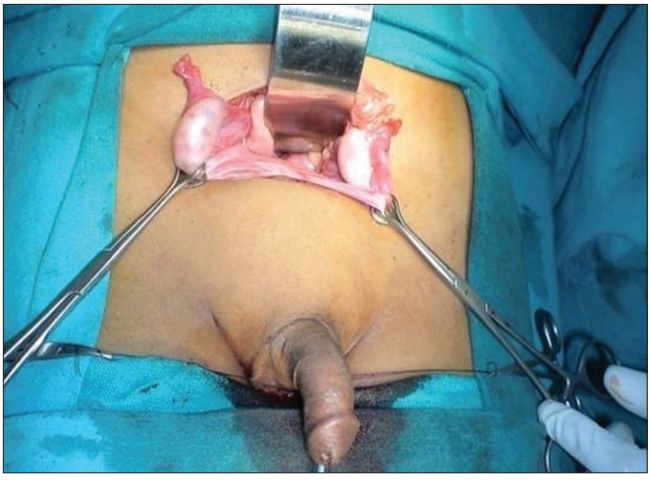

Figure 2: Uterus and adnexa being removed in a 46XX congenital adrenal hyperplasia reared and assigned as male

seven are well-adjusted in the family, pursuing their studies, or occupied well in suitable jobs, serving as bread earners to the family. The one who had earlier undergone clitoroplasty at the age of three years has a moderate sized phallus. One has recurrent urinary tract infections, with foul smell of urine mixed with mucus discharge from the retained lower vaginal pouch. Social adjustment is poor in this patient due to a bigender mental makeup.

Discussion

Even as patients with 46XY Congenital Adrenal Hyperplasia (CAH) have completely normal male looking genitalia and present with electrolyte imbalance, patients with a virilizing type of 46XX Congenital Adrenal Hyperplasia present with ambiguous genitalia. The external genitalia of 46XX CAH may present with a spectrum of virilization varying from nearly female-looking genitalia to completely male-looking ones, with bilateral absent scrotal gonads. (Prader stages 2 – 5).

If the diagnosis of CAH is made early in infancy, the recommended sex of rearing, even in those with fully virilized external genitalia, has been categorically female, worldwide. This has also been the policy of the authors. These female patients with CAH with 46 XX, have normal functioning ovaries, a uterus, and a normal-sized functional vagina. Following female genitoplasty and hormonal control, fertility is expected and thus justifies the female gender assignment in CAH patients, although the long-term outcome has been reported to be disappointing in some cases that were treated for marked virilization at birth.[1] Maybe earlier, the surgical techniques were not so well-defined and the surgical expertise was limited. It has also been found that even as the fertility rate in 46,XX CAH patients is cumulatively only slightly impaired, the fertility rate of severely virilized CAH patients is strikingly low.[2,3] About 95% of the 46,XX CAH infants develop a female gender identity as adults, and only a few have gender dysphoria.[4]

The incidence of CAH infants who are actually reared as male versus female is unknown.[5] Lee *et al.* reported four 46,XX infants, whose parents chose a male sex assignment (after full disclosure) even after the diagnosis of CAH was made in the neonatal period.[6]

All the patients in the series had a male gender identity at presentation. Fully virilized 46XX CAH individuals developed a clear male gender identity during infancy, at the age when gender identity was expected to occur.[7] This was possibly due to the prenatal exposure of the brain to the androgens and also the social and cultural support provided by the parents.[8] The phallic growth in the absence of steroid therapy for the CAH was satisfactory in six patients and moderate in one patient. One case in this series had formation of the urethra till the tip of the glans penis making the diagnosis difficult. In another series of male sex assigned for CAH, only two out of six were completely virilized.[9] A fully virilized 46,XX CAH patient retained sufficient male sexual function.[5]

Six patients had presented after puberty, only one at seven years of age. The parents of all seven patients knew that the genitalia were abnormal. The reason for delayed presentation was a dire need for a male child in the family after the birth of five daughters, fear of losing their child to the Hijra community (nomads who live on earnings by singing and dancing in religious functions) in four, and ignorance that early treatment is needed and available in two. The oldest patient in this series had presented to us at 21 years, while the oldest patient reported in literature was at an age of 69 years.[6]

In this series, the diagnoses were made after the child had firmly established a male gender identity. The earlier reports of such cases often involved patients who died in infancy or childhood due to adrenal insufficiency.[10] It was recommended earlier that 46XX CAH patients reared as males should be reassigned as females when a diagnosis was made during childhood, as the benefit of preserving fertility outweighed a small risk of future gender dysphoria. More recently, however, it has been recognized that gender identity appears to be established in the first few years of life and gender reassignment may be harmful.[7] Even as gender change from female to male during follow-up has been documented in 46,XX CAH patients, the reversal gender change from male to female is unknown.[11]

It has been reported that adult cases of 46,XX CAH living as males retain a male gender identity with a sexual orientation toward females and have even got married to females or have had long-term female partners.[5] Most cases in this series were satisfied with their gender identity, with the surgical outcome being socially and culturally accepted in the society. Other series assigning a male gender to such patients have also reported similar results, advocating that the quality of life for the virilized 46,XX CAH patient proceeds from the initial gender assignment, providing the basis for a secure gender identity.[9,12]

Although the authors would not propagate a male gender assignment for cases of severely virilized 46XX babies presenting in infancy, there are others who feel that these babies manifest worse outcomes if they are assigned as females, propagating a male sex of rearing in the markedly

virilized 46,XX CAH patient, even when diagnosed in the neonate.[12] Authors have the experience to convert completely virilized 46XX CAH males seen at birth, to phenotypical and functional successful females now, with over 12 follow-ups and a completely female mental makeup.

It is the opinion of the authors, that if the CAH virilized cases are presenting late, after five years of age, when the society has already accepted them as males and they have remained well-adjusted as boys at home and in school, it would be wise not to think of changing and reassigning the gender. They should be offered male genitoplasty to raise their self-esteem and improve their social status. Apart from the fact that they would remain infertile, they would function as normal males capable of marriage. They would be able to contribute to the family and the society in all aspects with the best quality of life in the long run.

References

1. Johannsen TH, Ripa CP, Mortensen EL, Main KM. Quality of life in 70 women with disorders of sex development. Eur J Endocrinol 2006;155:877-85.
2. Mulaikal RM, Migeon CJ, Rock JA. Fertility rates in female patients with congenital adrenal hyperplasia due to 21-hydroxylase deficiency. N Engl J Med 1987;316:178-82.
3. Meyer-Bahlburg HF. What causes low rates of child-bearing in congenital adrenal hyperplasia? J Clin Endocrinol Metab 1999;84:1844-7.
4. Dittmann RW, Kappes ME, Kappes MH. Sexual behavior in adolescent and adult females with congenital adrenal hyperplasia. Psychoneuroendocrinology 1992;17:153-70.
5. Lee PA, Houk CP. Review of outcome information in 46,XX patients with congenital adrenal hyperplasia assigned/reared male: What does it say about gender assignment? Int J Pediatr Endocrinol 2010;2010:982025.
6. Lee PA, Houk CP, Husmann DA. Should male gender assignment be considered in the markedly virilized patient with 46,XX and congenital adrenal hyperplasia? J Urol 2010;184:1786-91.
7. Ruble DN, Martin CL. Gender development. In: Damon W, Eisenberg N, editors. Handbook of Child Psychology. 5th ed., vol. 3. New York, NY, USA: John Wiley & Sons; 1998. p. 933-1016.
8. Sharma S, Gupta DK, Amini AC. Follow-up after male genitoplasty for patients with CAH Proceedings of 1st world congress on Hypospadias and Intersex disorders. ISHID, Istanbul; 2005. p. 96.
9. Sripathi V, Ahmed S, Sakati N, Al-Ashwal A. Gender reversal in 46XX congenital virilizing adrenal hyperplasia. Br J Urol 1997;79:785-9.
10. Gillenwater JY, Wyker AW, Birdsong M, Thornton WN. Adrenogenital syndrome producing female pseudohermaphroditism with a phallic urethra. J Urol 1970;103:500-4.
11. Meyer-Bahlburg HF, Gruen RS, New MI, Bell JJ, Morishima A, Shimshi M, *et al.* Gender change from female to male in classical congenital adrenal hyperplasia. Horm Behav 1996;30:319-32.
12. Houk CP, Lee PA. Approach to assigning gender in 46,XX congenital adrenal hyperplasia with male external genitalia: Replacing dogmatism with pragmatism. J Clin Endocrinol Metab 2010;95:4501-8.

Cite this article as: Sharma S, Gupta DK. Male genitoplasty for 46 XX congenital adrenal hyperplasia patients presenting late and reared as males. Indian J Endocr Metab 2012;16:935-8.

Source of Support: Nil, **Conflict of Interest:** None declared.