Original Article

Management of children with disorders of sexual development (DSD): A retrospective analysis

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ABSTRACT

Objective: We retrospectively reviewed data of children who were managed for Disorders of Sexual Development (DSD) presenting after one year of age with a view to understand gender assignment issues in these children.

Methodology: Patients were managed at NICH Karachi, NIRM and Shifa International Hospital Islamabad. All patients were investigated on standard lines to make a proper diagnosis. Karyotyping was performed in all patients. Hormonal essays included, serum testosterone levels, 17-OH progesterone levels, FSH, LH etc. Ultrasonography, urogenital endoscopy and laparoscopy were also performed in selected cases. The aim was to assign the genetic sex to the patient when possible. Male gender was advised to all male DSD responding to exogenous hormonal therapy. Patients with complete androgen insensitivity syndrome were advised female gender. Children having Gonadal dysgenesis (GD) responding to androgen therapy were also advised male gender. Female gender was advised to all children with congenital adrenal hyperplasia (CAH). Gender assignment was performed after a detail consultation with the family and children if they were old enough to comprehend the issue. Male gender was assigned to CAH patients reared as male if child/family insisted to keep the gender of rearing.

Results: Of the 61 patients, 23 were undervirilized male (UVM), 29 had congenital adrenal hyperplasia (CAH), 4 had clitoromegaly, four gonadal dysgenesis and one aphalia. The mean age of presentation of UVM was 8.4 years and CAH was 7.06 years. Clitoromegaly without CAH mean age was 5.6 years. It was not possible to definitely establish the true nature of male DSD in few patients due to limitation of available investigations. Twenty two male DSD patients responded to exogenous testosterone therapy and had male gender assignment. One had female conversion as non-responder. Of the 29 cases of CAH, 27 decided for female assignment and had feminizing genitoplasty. Two children aged 13 and 16 years refused for a female gender assignment and were assigned male gender and reconstructions performed accordingly. Clitoral recession was performed in all the four patients with clitoromegaly. Four patient having MGD was assigned male gender. Single aphallia patient was assigned male gender however adequate phallus reconstruction is still awaited. Older UVM children reared as female accepted male gender happily but CAH children more than 10 years of age reared as male were not happy for a female conversion. Genital reconstruction was most satisfactory in CAH patients. Patients with male gender assignment had multiple procedures and patient's satisfaction response was variable according to the size of the phallus and severity of androgen deficiency. Most patients were however happy for the masculine appearance after chordee correction. Long-term results need to be evaluated.

Conclusion: Older female children reared as male find it extremely difficult for female conversion whereas male children reared as female accept male conversion well. Gender re-assigment in younger children is well accepted by the family.

KEY WORDS: Ambiguous Genitalia, Gender Assignment, Social issues, CAH, UVM, DSD.

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INTRODUCTION

In the developing countries children with genital ambiguity may present late even at puberty.[1] The causes may be multi-factorial and include; lack of awareness, poverty, tendency of hiding sexual issues and above all cultural taboos considering genital ambiguity as a social stigma.[2] The consequences are often serious. Many children when faced with the decision of changing gender after many years of living one life style find it difficult even if they are assigned most appropriate gender.[3,4] This is especially true for genetically female children who are reared as male and at puberty it becomes a difficult decision for them to be converted in to female.[5] If the same decision is made in the neonatal life the child will have minimal psychological trauma. This also partially answers the issue of not assigning gender at birth as proposed by some authors.[6] We conducted the study to understand gender assignment issues in these children.

METHODOLOGY

The patients in this study were managed at National Institute of Child Health (NICH) Karachi, National Institute of Rehabilitation Medicine (NIRM) and Shifa International Hospital, Islamabad. We followed all patients who presented after one year of age with genital ambiguity from January 2003 to Dec. 2010. We were able to get record of Sixty-one children who were included in the study. Karyotyping and ultrasonography was performed in all children. Other investigations included 17-OH progesterone levels, testosterone levels; pre and post HCG stimulation, FSH and LH levels depending upon the nature of DSD. Diagnosis of CAH was made when child had 46XX genetic makeup with high levels of 17-OH progesterone and normal female internal organs. UVM were further classified according to the level of the defect. Children with low level of testosterone were given a challenge of BHCG and response was evaluated by increase in the levels of testosterone and also increases in the size of the phallus.

UVM children were given a challenge of testosterone depot 25-50 mg intramuscular injection at two weekly intervals for maximum of three doses. Change in the size of phallus was documented after 8 weeks and used as a tool for labelling the responders. Those showing good or partial response were classified as responders. Diagnosis of gonadal dysgenesis was made by the presence of asymmetrical gonads, mosaicism on chromosome analysis, no response to HCG stimulation or dysgenetic gonads on histology. Clitoromegaly was labelled when child had significantly prominent clitoris with out any evidence of CAH.

The families and children were explained in detail about the gender issues. Aim was to assign genetic sex to the patient when possible. Patients having CAH were advised female gender and single stage genitoplasty was performed. Two patients refused for female conversion and were assigned male gender. They had removal of all female internal organs with staged repair of hypospadias. Patients having good or partial response to high doses of testosterone had staged repair of hypospadias. One child with completed androgen insensitivity syndrome and having a very small phallus with well-developed vagina had female conversion. Four children with Gonadal dysgenesis were advised male gender after testosterone trail. All patients received replacements and hormonal therapy after surgical corrections as per individual requirement.

RESULTS

We were able to followup 61 patients. Of these, 23 were undervirilized male (UVM), 29 had congenital adrenal hyperplasia (CAH), 4 had clitoromegaly, 4 gonadal dysgenesis and one aphalia. The mean age of presentation of UVM was 8.4 years and CAH was 7.06 years. Clitoromegaly without CAH mean age was 5.6 years. It was not possible to establish the true nature of male DSD in all patients. All the responders to exogenous androgens therapy were advised male gender. One 7 years UVM had female conversion as non-responder and the family accepted the decision as child was reared as a female. Of the 29 cases of CAH, all were advised female gender assignment, 27 decided for female assignment and had feminizing genitoplasty. Two children aged 13 and 16 years refused for a female gender assignment under any circumstances (Fig.1). They were reassigned male gender and reconstructions performed accordingly. Clitoral recession was performed in all the four patients with clitoromegaly. Patient having

Fig-1: 13 years old CAH Patient showing severe virilization and had male gender assignment.

Fig-2: Aphallia. Patient showing complete absence of phallus.

MGD were assigned male gender with gonadectomy and accepted it well. Single patient with aphalia was initially advised female gender but the family refused for a female gender assignment He was reared as a male. Multiple procedures were performed.

Now at the age of 15 years he still has rudimentary phallus but the family seems to be happy with this arrangement (Fig.2). Older UVM children reared as female, accepted male gender happily but CAH children more than ten years of age reared as male were not happy for a female conversion. The 16 years old CAH patient used tight garments to conceal the developing breast resulting in pressure sores and ulcers in the region (Fig.3). In one UVM child reared as female the parents initially wanted a female gender assignment as there were 4 more male children in the family. He had partial response to androgens and also had a good phallus. Ultimately family decided for keeping the male gender in this child.

DISCUSSION

The aim of management in children with DSD is to assign appropriate gender, which shall provide optimal sexual, psychological and reproductive functions. The decision of gender assignment has to be done with full participation of the child and family.

Fig-4: Appearance after gender reassignment in a male DSD.

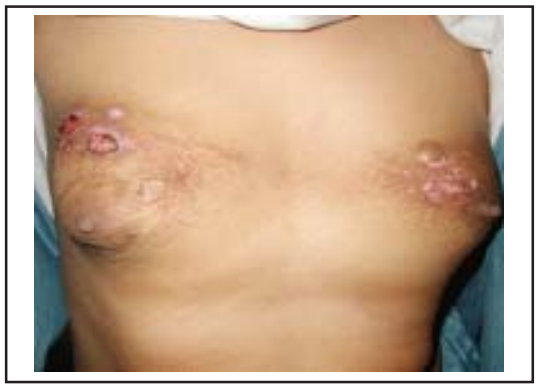

Fig-3: A 15 years old CAH patient reared as male-used tight undergarments to hide the developing breasts resulting in pressure sores and ulcers

Young children may not be able to fully understand gender assignment issues therefore families make the decision on their behalf. In the developing countries children with genital ambiguity often present late.[1] The causes may be multi factorial and include ignorance, poverty, tendency of hiding sexual issues and above all cultural taboos considering genital ambiguity a social stigma. In this region there is a large population living with the stigma of having third sex also called Hijras. These are dejected class of the society. In some areas if a baby is born with genital ambiguity, the leaders of the Hijras community (Guru) may forcibly take away the baby from the family. Most hijras however are normal male and adopt the change for earning their livings.

In a study Anila Mithani showed that nearly 70% of hijras are normal male and only 30 % may have some genital problems and they are forced to live an unwanted life as eunuchs.[7] When a baby is born with genital ambiguity these issue make the family very stressful and they tend to hide the anomaly for the fear of defamation and insult. The child is thus reared as male or female according to the appearance. It is brought to the attention of the clinicians late, some time at puberty. The consequences are often serious

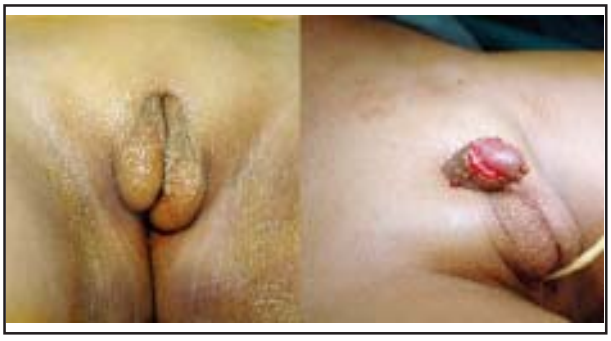

Fig-5: Pre & Post operative appearance in a male DSD patient after stage-I Procedure.

leading to many psychological problems.[2] Many families and children when faced with the decision of changing gender after many years of living one life style find it difficult to change even if they are assigned most appropriate gender. This is especially true for genetically female children with CAH who are reared as male and at puberty it becomes a difficult decision for them to be converted in to female. They have normal internal female organs and shall have normal fertility after surgery.

Therefore there are strong recommendations to assign them female gender.[8,9] Some families however may refuse female conversion in CAH patients who present late. In a case report Dasgupta R et al highlighted the difficulties encountered in gender reassignment in a child of Pakistani origin.[5] This was their first case in 30 years experience and child had staged masculinizing genitoplasty with good results. In our study we had similar problem in two genetically female children with CAH who were reared as male. Both of them were referred near puberty and refused for female conversion even after near one year of counseling. One child was so obsessed with his feminine appearance that he used to wear tight garments to hide the developing breast resulting in pressure sores and ulcers in that area. The decision was also influenced by the family in favour of male conversion. It highlights the importance of family ties in our setup that is different from most developed countries where the decision of the patient is often independent.

It is important to note that families accepted female conversion of their child well if they were diagnosed before puberty. This was also highlighted in one of the undervirilized 7 years, male patient with a very small phallus, developed vagina and complete androgen insensitivity syndrome. When the family was informed that this child couldn't have a male gender assignment due to target organ failure, they accepted female conversion after they were convinced of the problem. Therefore it is easy for the family to accept female gender assignment in early childhood but much more difficult at puberty. Both our CAH patients belonged to the tribal areas of the country, which strongly believe in self-esteem and tribal respects. These are male dominated societies and female are not allowed to go out for work and thus for the family even a incomplete male may still be better than a female as he can earn his living and is not dependent upon others.

Under-virilised males patients who are reared as female accept the change well (Fig.4). In our experience, the decision for male conversion was quick and unanimous by the child and the family. It is important to note that in UVM multiple procedures are required and ultimate outcome is dependent upon the initial size of the phallus, response to androgenic hormones and success of the reconstructive procedures.[10,11] Fortunately in our setup the families accept this reality and are happy with whatever reconstruction has been achieved (Fig.5). Long-term psychological assessment will however be required to ensure the success of these procedures.

There may be a debate whether to keep the enlarged clitoris as clitoral recession may decrease the sensations in children with clitoromegaly.[12] This is not at all a concern in our setup. Parents of these children were briefed about the loss of sensations but they did not consider this to be an important issue and all wanted clitoral recession to give a feminine external appearance.

Our nightmare was a single case of aphallia who presented to us in early childhood. The family was offered a female conversion of the child but disagreed. The child also had a solitary kidney and persistent UTI. He had multiple procedures for penile reconstruction but failed. The plastic surgeon now feels that a forearm free flap may help in reconstruction of his phallus but the family is not sure and have not decided yet for surgery. Male conversion in aphallia may be difficult and female conversion is often advised in these patients.[13] Recently successful male genital reconstruction has been achieved in patients with aphallia.[14] This however will depend upon the expertise available and aphallia may be one anomaly where deferring surgery till puberty may be justified and improvement in the surgical techniques may offer them better results.

Decision regarding gender assignment is a gigantic task for the treating surgeon. Usually a team approach is required however in the developing countries the primary surgeon shoulders all the responsibility of gender assignment and later reconstruction. The decision at times may be very difficult especially when it is not possible to assign the genetic sex. In CAH patients who wish to have male conversion, serious religious, ethical and social issues may arise to convert a near perfect female who can have children to a non-reproductive male with unpredictable outcome? The answer to this question is not only difficult but may never get a consensus due to various social and religious believes.[15] In the developed countries people are now considered as individuals and may have a right for choosing a gender. Many surgeons in the developed countries believe that any genital reconstruction shall be delayed till puberty

when the child is mature enough to understand the various gender related issues and may have the right to choose a gender. Marriages among individuals of same gender are acceptable. Our religion and society has strong feeling on this issue. As genital ambiguity is considered a stigma therefore the families wish to get the answers and genital reconstruction as quickly as possible. The concern of the family is genuine and needs sympathetic consideration.

Technically reconstructive surgery for CAH patients gives the best results usually as a single stage procedure. This was seen in most of our patients that once a proper female genital appearance was reconstructed the family was very pleased. On the contrary in male patients with severe chordee, variable size of the phallus and multiple procedures, the satisfaction of the family is variable.[16] Those having good size phallus have better correction and family is often very happy. In children with small phallus, chances of breakdown and fistulae formation are higher. The main concern in most families is that even after successful repair will these patients be able to spend a normal sexual life and will have children? The answer to these questions are often difficult however several studies have now shown that even small penile size may not be a hindrance in normal sexual life.[17] In a studies by Reilly JM et al and Van Seters et al, children who had micropenis at birth and were reared as male had satisfactory relationship and also produced children.[18,19] Therefore it is now recommended that patients with microphallus shall be reared as male as many of them will grow to a reasonable size at puberty with satisfactory heterosexual relationship.

In summary late presentation of children with DSD is a common problem in our setup. Many patients are referred late and some never get its treatment and are reared as hijras. Patients presenting late will prefer to keep a male gender but in younger children the family will accept male or female gender according to genetic makeup of the child. Early referral and gender assignment may save the child and the family from major psychological trauma.

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