SEX REASSIGNMENT: A CHALLENGING PROBLEM — CURRENT MEDICAL AND ISLAMIC GUIDELINES

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Sexual ambiguity is a complex and often confusing medical problem. In addition to the life-threatening adrenal crises which may accompany some forms, ambiguity of the genitalia may lead to incorrect sex assignment by parents and/or health personnel. Children who present to medical attention beyond the neonatal period constitute a challenging problem due to the grave consequences of this condition. Thirty cases in whom sex reassignment was indicated were seen at King Khalid University Hospital, Riyadh, over a 10-year period. Of these, 27 (90%) were genetic females (20 were 21- and seven were 11-hydroxylase deficient) and three (10%) were genetic males (two partial androgen insensitive and one 5α-reductase deficient). All genetic males who were incorrectly assigned as females accepted reassignment. But 9 out of 27 (33%) of the genetic females who were incorrectly assigned as males refused reassignment. Preference for male sex assignment, delayed diagnosis and sociocultural circumstances seem to be the contributing factors for refusal. A national consensus about this important issue strengthened by the existing religious recommendations is demanded. *Ann Saudi Med 1996;16(1):12-15.*

Ambiguous genitalia are a social and medical emergency.[1,2] Sex assignment of the newborn is usually based on the external genitalia. If this is abnormal, it may be difficult to correctly assign the sex. An incorrect decision can lead to a major dilemma for the child, parents and other members of the family, friends and health personnel, who find themselves confused and in a difficult and unimaginable situation.[3] In a community where this condition is not uncommon,[1,4-7] health personnel will continue to face improperly sex-assigned children and young adults at different ages and circumstances. In this study, we retrospectively reviewed 30 cases in which sex reassignment was indicated. We also discuss the present Islamic guidelines regarding this matter and call for an urgent and unified national consensus, based on the basic scientific knowledge available and supported and approved by the existing Islamic recommendations.

Material and Methods

The medical records of 30 cases in whom sex reassignment was indicated, seen at King Khalid University Hospital (KKUH), Riyadh, over a 10 year period starting in September 1984, were analyzed. Genetic sex was based on chromosomal studies done on lymphocytes. Additional tests included genitogram and pelvic ultrasonography. Definitive etiological diagnosis was based on elevated 17α-hydroxy progesterone in 21-hydroxylase (P450C21) deficiency, elevated 11-deoxycortisone (compound S) in 11β-hydroxylase (P450C11) deficiency, elevated baseline and human chorionic gonadotropin (HCG) stimulated testosterone (T) to dihydrotestosterone (DHT) ratio in 5α-reductase deficiency and satisfactory penile length response to HCG and T in the presence of normal T/DHT ratio in partial androgen insensitivity (Figure 1). In view of the medical recommendation and the available Islamic guidelines, a final decision for the final diagnosis, outcome and recommendations with regard to sex reassignment was made and presented to parents.[8] A period of time for reflection was given. If the parents were in agreement, an appropriate name and a legal certificate signed by at least two physicians were issued to present to civil services, in order to make the proper changes in the child's records. If no agreement was reached, discussion was continued on an outpatient basis.

Results

Thirty children, ages one day to eight years, who were improperly sex-assigned were included in the study. Twenty-seven (90%) were genetic females (46, XX female karyotype) raised as males and three (10%) were genetic

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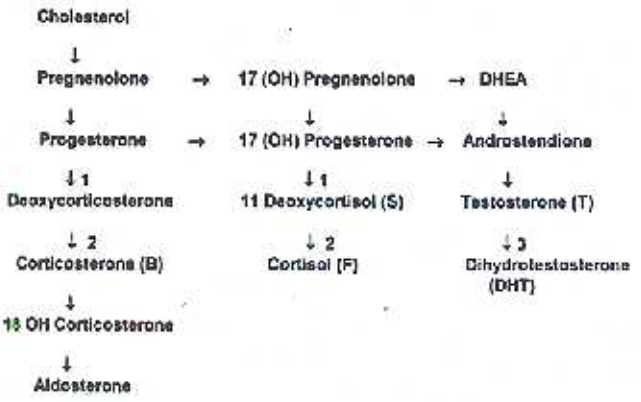

FIGURE 1. Steroid biosynthesis pathway. 1: 21-hydroxylase (P450C21) enzyme; 2: 11-hydroxylase (P450C11) enzyme; 3: 5α-reductase enzyme.

males (46, XY karyotype) raised as females. Twenty (74%) of the genetic females were proven to have 21-hydroxylase (P450C21) deficiency based on elevated 17α-hydroxyprogesterone and seven (26%) were proven to have hydroxylase (P450C11) deficiency based on elevated 11-deoxycortisol (compound S). One of the three genetic males had 5α reductase deficiency and two were androgen-insensitive (Reifenstein's syndrome). All responded favorably to HCG and testosterone. All three genetic males accepted their properly reassigned sex with no hesitation. On the other hand, nine out of the 27 (33%) genetic females refused reassignment. All nine of these children were beyond two years of age (range 2 to 12 years, mean 4.6 years).

Discussion

External genitalia, if well differentiated, are the leading evidence of the sex of the child, which is usually announced even before the baby takes its first breath. When there is a defect (0% to 10% of all newborns),[1,9] however, the healthcare givers (midwife, nurse, physician, etc.) are put under pressure to declare the baby's sex. This may lead to a guessed decision. Instead of taking the chance of assigning the incorrect sex, and affecting the parents' interaction with their child through an improper classification which may need to be changed later on, the announcement of the baby's sex should be deferred until further supportive data are available. This, despite its difficult implications, is always encouraged to prevent a more traumatic time when sex reassignment is suggested at a later age.[3]

The effect of hormones (mainly androgens) on the fetal neuron system[10,11] is most likely a prerequisite to a specific gender. It may even be prior to the male gonadal differentiation influenced by the testicular-determining factor (TDF).[12] This, however, needs powerful reinforcement by parents and other surrounding people, especially later on with regard to the child's self-recognition as a male or a female. It is, therefore, a continuing stimulus to the child, who needs to be interrupted at the proper time in cases of ambiguity, preferably shortly after gestation, when androgen exposure can be minimized through the well-established role of maternal steroids given to mothers with infants who have congenital adrenal hyperplasia due to 21-hydroxylase deficiency[13] or immediately at birth with the proper psychomedical decision and orientation.

Reassigning sex is always a major psychological trauma, not only to the parents but to other members of the family (extended families in particular). Friends and members of the medical team themselves are not immune to this trauma. It also has a huge impact on the child if sex reassignment is done beyond the age of 18 months, the age at which the child has begun to use language and has established a self-concept which is gender differentiated.[3,14] This has been well observed in our series, as all nine cases who refused reassignment have presented beyond this age. Children who presented prior to this age, on the other hand, have all accepted reassignment. Genetic reassignment in a genetic female (46, XX karyotype) raised as a male should not be debated in the presence of the medical facts, psychological and/or psychiatric support, strengthened by the clear-cut religious guidelines (see next page). A multidisciplinary team made up of a pediatric endocrinologist, pediatric surgeon, radiologist, psychologist and psychiatrist, working together on this medical and psychological matter, is a necessity. We feel strongly that genetic female children (46, XX karyotype) should be raised as females, not only due to the ease of reconstruction of female genitalia,[15] but also because of the strong evidence explained earlier.

The majority of our cases (90%) needed reassignment from an incorrectly assigned male sex. The cases in this group were due to congenital adrenal hyperplasia because of 21-hydroxylase deficiency in 20 (74%) and 11β-hydroxylase deficiency in seven (26%), the two conditions characterized by elevated 17α-hydroxyprogesterone and 11-deoxycortisol respectively.[16] This high occurrence is a reflection of the not uncommon autosomal recessive disorder, namely congenital adrenal hyperplasia, seen in this community,[1,4-7] which is most likely due to the high rate of consanguinity.[17] As indicated above, there should be no debate on reassigning the sex of these children to the correct female gender. These children, in addition to the fact that they are genetically female, have normal female internal organs (fallopian tubes, uterus and vagina), and external genitalia where surgery is feasible to do the proper clitoral recession and vaginoplasty.[15,18,19] Furthermore, normal sexuality, fertility and childbearing as adults is well

established.[20-22] The religious recommendations are additional facts which all agree with common sense. The difficulties inherent in this matter are faced by many communities[23] and we feel that our community can be the model for the appropriate outcome of these cases.

The case of a genetic male (46, XY karyotype) raised as a female is rather more difficult. In addition to the suggested steps and guidelines mentioned for the genetic female counterparts, proof is required that the various functions—whether biological, anatomical or, in particular, sexual—are in working order.[24] Male preference in our community, if this exists, puts more pressure on the diagnostic team and should not influence the overall decision, which is based on the diagnosis, the findings, the response to androgens (namely testosterone diagnostic therapy) and the religious guidelines set out on the following page. 5α-reductase deficiency, a condition first described in 1974 and characterized by ambiguity of the genitalia in a genetic male and elevated T to DHT ratio[25] is also not uncommon in our community.[7] This has been reported to cause improper sex assignment in at least one local case, with no details of the outcome, if ever made, of the sex reassignment of the young male who was raised as a female.[26] Of equal importance is androgen insensitivity, which we also feel to be frequent in this community (unpublished data). This is characterized by normal T to DHT ratio in a genetically male child with ambiguity. Diagnosis is further confirmed in the presence of favorable penile response to androgens and the exclusion of other causes of under-muscularization. A definitive diagnosis is also based on tissue receptor studies,[27,28] though this was not feasible in our center.

The current Islamic recommendations put forward by the Senior Ulama Council in Saudi Arabia, statement No. 176, dated 17.3.1413H[18] gives very useful general statements which fulfill the scientific facts and indications. These recommendations are translated as follows: 1) A sex-change operation, i.e., converting a completely developed gender to the opposite sex, is totally prohibited. It is considered criminal. This is clearly supported by the Holy Koran and the Prophet's sayings. 2) Those who have both male and female organs need to be investigated and if the evidence is more male, it is then permissible to treat him medically (by hormones or surgery), to eliminate his ambiguity, and raise him as a male; if the evidence is more female, it is permissible to treat her medically (by hormones or surgery) to eliminate her ambiguity, and raise her as a female. 3) Physicians must explain the results of medical investigations to the child's guardian (be it a male or a female) so they may be well informed.

If this lack of awareness about the importance of having solid evidence to support sex assignment continues, there will be more mistakes made, making sex reassignment in children and sometimes even young adults necessary. Newborn screening for congenital adrenal hyperplasia due to 21-hydroxylase deficiency is becoming feasible in some centers.[29] This obviously will increase early recognition and proper sex assignment. It is especially important in genetic males who, at birth, lack the clinical evidence of this condition. Examining the genitalia for ambiguity and activating a series of investigations and proper counseling to reach a diagnosis and proper sex assignment is easier and more realistic. This practice should continue before and after implementing such a screening program.

We strongly believe there is an urgent need for establishing a central body in Saudi Arabia where cases which need sex assignment or reassignment may be quickly referred so that a proper decision based on medical and Islamic guidelines is made.

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