International Journal Of

Recent Scientific Research

ISSN: 0976-3031

Volume: 7(11) November -2015

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THE OFFICIAL PUBLICATION OF
INTERNATIONAL JOURNAL OF RECENT SCIENTIFIC RESEARCH (IJRSR)
http://www.recentscientific.com/ recentscientific@gmail.com

ISSN: 0976-3031

Available Online at http://www.recentscientific.com

International Journal of Recent Scientific Research
Vol. 6, Issue, 11, pp. 7312-7314, November, 2015

International Journal of Recent Scientific Research

RESEARCH ARTICLE

DISORDERS OF SEX DEVELOPMENT AMBIGUOUS GENITALIA SEX RE-ASSIGNMENT IS A CHALLENGING PROBLEM

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ARTICLE INFO

Article History:

Received 05th August, 2015
Received in revised form 08th September, 2015
Accepted 10th October, 2015
Published online 28st November, 2015

Key words

Ambiguous, sex, genitalia, re-assignment, problem.

ABSTRACT

Background: Disorders of sex development (DSD), formerly known as ambiguous genitalia, is a birth defect where the outer genitalia do not have the typical appearance of either a boy or a girl. The issue is so sensitive and poses a major psychological impact in the family.

Design and setting: A retrospective hospital based study was conducted at King Khalid University Hospital (KKUH) Riyadh, Saudi Arabia during the period January 1989 and December 2014, to define the magnitude of the problem and identify the various aetiological.

Methods*:* Medical records of children with the diagnosis of disorders of sex development were retrospectively reviewed. Data includes age, clinical presentation, given sex, chromosomal sex, family and psychological history and results of relevant laboratory and radiological investigations.

Results: During the period under review, a total of 119 patients were diagnosed with variable aetiologies of ambiguous genitalia. Three patients who were diagnosed with 5-alpha reductase deficiency and initially wrongly assigned a female sex accepted sex re-assignment, while three of the 25 patients with the diagnosis of congenital adrenal hyperplasia, who were initially wrongly assigned a male sex refused sex assignments. Psycho-social factors, mainly influence of grandparents, the superior role of the male sex in the community and inappropriate counselling were among the comment.

Conclusion: The sex-reassignment is not that uncommon. A multidisciplinary team approach guided by the Islamic guidelines should be implemented.

INTRODUCTION

Disorders of sex development (DSD), formerly known as ambiguous genitalia is a birth defect where the outer genitalia do not have the typical appearance of either a boy or a girl. The issue of sex assignment and reassignment is so sensitive and poses a major psychological impact on the family and involves a specialized and experienced multi-disciplinary team to work with the family. Severely virilised or under-virilised patients may initially wrongly assigned. Once such assignment has occurred; it may be difficult to reverse. Prenatal androgen exposure, post-natal hormonal influence, degree of external genitalia visualization, general appearance, and social factors are all important factors which influence gender identity development. The ability to diagnose these disorders has advanced rapidly in the recent years. (1-10)

This article aims to define the magnitude of the issue of sex assignment and reassignment and identify factors associated with it in a major referral hospital, King Khalid University Hospital (KKUH), Riyadh, Saudi Arabia over more than 25 years (January 1989 to December 2014).

MATERIAL AND METHODS

The study population consisted of all patients presented or born at King Khalid University Hospital (KKUH), Riyadh, Saudi Arabia over a 25 year period (January 1989 to December 2014). KKUH is the main teaching hospital of King Saud University, and considered as one of the major referral hospitals in the central province of Saudi Arabia. The hospital provides primary health care services for the local population and also received patients referred from all over the country. Ambiguous genitalia was considered when there was difficulty in determining the sex of patient on initial examination or when the external genitalia showed significant structural deviation from normal appearance of male or female. The karyotyping and appropriate diagnostic radiological (11) and hormonal tests (3-12-13) were performed for all patients in the study where indicated.

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A medical record of patients was retrospectively reviewed and includes age at presentation, chromosomal sex, given sex, clinical presentation, family history and appropriate diagnostic (radiological and hormonal) tests. Detailed psychological history was obtained, in case, sex re-assignment needed.

RESULTS

During the period under review, January 1989 to December 2014, a total of 119 patients were seen and evaluated at the endocrine service of King Khalid University Hospital (KKUH), Riyadh, Saudi Arabia. This includes chromosomal karyotyping, hormonal investigation and various radiological investigations. The aetiological causes were shown in the table 1. Congenital adrenal hyperplasia was the commonest (97%) in 46 XX DSD, while a diversity of causes were seen in 46 XY DSD group. Their ages ranged between newborns to 13 years.

Table 1 Aetiology of Ambigous Genitalia in 119 Patients

Karyotyping	Diagnosis	Number of Patients	%
46 XX DSD	Congenital adrenal hyperplasia		61 (51.3%)
	21-hydroxylase deficiency	51 (48 SW)	
	11-β- hydroxylase deficiency	9	
	3- β-hydroxysteroid Dehydrogenase deficiency	1(1 SW)	
	Isolated clitoromegally		2 (1.7%)
	Androgen insensitivity complete		16 (13.4%)
	partial	11	
	5-α-reductase deficiency	5	
	Congenital malformation (dysmorphism)		9 (7.6%)
	Local anorectal		14(11.8%)
	Generalized		
	Extreme prematurity	4	
	Congenital adrenal hyperplasia (due to 3- β-hydroxysteroid dehydrogenase deficiency)	10	1(0.8%) 5(4.20%)
46 XY DSD	Hypogonadotrophin deficiency Ovotesticular		4(3.4%)
	46, XY, DSD		1(0.8%)
	Hypospadius		3(2.5%)
	Persistence of mullerian duct		1(0.8%)
	Abnormalities of gonadal development		2(1.7%)
	Swyer syndrome	1	
	Denys-Drash Syndrome	1	

SW-salt wasting DSD-disorders of sex development

Twenty-five (39.7%) of the genetic female patients were wrongly assigned as male sex due to severe virilisation. In three patients presented in the neonatal period parents refused sex reassignment as influnced by the grandparents which contributes a major socio cultural pressure despite of their high educational level, as they were afraid from the draw-back of the social trauma. Two patients who were diagnosed in the neonatal period as having congenital adrenal hyperplasia due to 21-hydroxylase deficiency, and refused sex reassignment were referred at 6 and 8 years of age recpectivly for second opinion upon their request. They claimed lack of appropriate information. Sex reassignment was accepted after the appropriate counselling and psycho-social preparation and indicates the importance of team approach of such condition. All patients who were wrongly assigned a female sex accepted sec reassignment. They were dignosed as 5-alpha reductase deficeincy.

DISCUSSION

Disorders of sex development, DSD, formerly known as ambiguous genitalia, are congenital conditions in which the development of chromosomal gonads or anatomic sex is atypical and can be classifies into four different types; female pseudo hermaphrodite (46 XX DSD), male pseudo hermaphrodite (46 XY DSD), true hermaphrodite (ovotesticular DSD), and pure gonadal dysgenesis. A chromosomal karyotype should be done to guide classification. Congenital adrenal hyperplasia is common in genital ambiguity. (1-4)

Reassigning a sex is always a major psycho-social trauma, not only to the parents but to the other members of the family and medical team. Furthermore, a high impact on the child him or herself if the issue of sex reassignment is delayed beyond the age of 18 months. This has been observed in our series. A multidisciplinary team constituted of a pediatric endocrinology, pediatric surgeon or urologist, pediatric radiologist, psychologist, psychiatrist and geneticist working together on the medical and psychological issue is a necessity. (5,8-10,14)Genetic females (46 XX) with normal ovaries and internal female organs (uterus, fallopian tubes, and upper vagina) with variable degrees of virilisation of the external genitalia usually have congenital adrenal hyperplasia and should be raised as females, not only due to the ease of reconstruction of the external genitalia but also because of the high fertility rate and child bearing as adults.(15-17) The surgery generally should be performed early before the child develops gender awareness.(18) However, in contrast, a child with a sexual ambiguity and an XY chromosome creates a rather more difficult and challenging problem. It is more difficult to reconstruct a penis rather than to create a vagina. Moreover, the dominating role of the male gender in the community should not over rule the Islamic Laws which should not be ignored and given a prime consideration.(19) The psycho-social stigma strengthened by pressure from the grandparents should not be overlooked.(20)

Finally, an experienced multidisciplinary team to work with parents and discuss the issue openly and clearly.(5) The current Islamic recommendations put forward by the Senior Ulama Council in Saudi Arabia as well as the accumulative experience of paediatricians and people working within the field should not yield a set of very useful general guidelines.(19,21) These recommendations are translated as follow:

1. A sex change operation (i.e. converting someone with a completely developed gender to the opposite sex) is totally prohibited and it is even considered criminal in

accordance with the Holy Quran and the Prophet's Sayings.

2. Physicians must explain the results of the medical investigations to the child guardians and whether the evidence indicates that the child is male or female so that the guardians are well informed.
3. Those who have both male and female organs require further investigations and if the evidence is more suggestive of a male gender then it is permissible to treat the individual medically (by hormone) or surgery to eliminate his ambiguity as to raise him as a male. If the evidence is suggestive of a female gender then it is permissible to treat her medically (by hormone) or surgery to eliminate her ambiguity and to raise her as a female.
4. Therefore, genetically female children (46 XX, karyotype) with normal ovaries and internal female organs, but with some variable degrees of virilisation of the external genitalia should be raised as female. This discussion is not only due to the ease of reconstructions of the female genitalia, but also due to the ability of these females to have a high fertility rate and to bear children.

Acknowledgement

The author would like to thank Mrs Joeylyn A Zarsuelo for her secretarial assistance and extends his thanks and appreciation to Miss Hadeel Al-Jurayyan for her help in preparing this manuscript.

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How to cite this article:
Nasir A. M. Al Jurayyan, MD., Disorders of Sex Development Ambiguous Genitalia Sex Re-Assignment Is A Challenging Problem. *International Journal of Recent Scientific Research Vol. 6, Issue, 11, pp. 7312-7314, November, 2015*

ISSN 0976-3031