ISSN: 0976-3031

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

International Journal of Recent Scientific Research
Vol. 7, Issue, 11, pp. 14219-14221, November, 2016

International Journal of Recent Scientific Research

Research Article

THE AETIOLOGY OF DISORDERS IN SEX DEVELOPMENT (DSD): REVIEW OF 127 PATIENTS FROM A MAJOR TEACHING HOSPITAL, RIYADH, SAUDI ARABIA

AbeerM.Anteet and Nasir A.M. Al-Jurayyan

Department of Pediatrics, College of Medicine and King KHALID university Hospital (KKUH), King Saud University, Riyadh, Saudi Arabia

ARTICLE INFO

Article History:

Received 16th August, 2016
Received in revised form 25th September, 2016
Accepted 23rd October, 2016
Published online 28th November, 2016

Key Words:

Aetiology, Children, Chromosome Disorder, Sex development, Saudi Arabia

ABSTRACT

Background: Disorders of sex development (DSD), formerly termed ambiguous genitalia, constitute a complex major social and medical emergency.

Design and settings: A retrospective hospital-based study was conducted at King Khalid university hospital (KKUH), Riyadh, Saudi Arabia, during the period from January 1990 to June 2016.

Materials and methods: All the 127 patients evaluated for disorders of sex development (DSD) constituted the subjects of the study. Medical records wereretrospectively reviewed for age, sex, relevant family and social history, pregnancy, clinical manifestations and results of all radiological, laboratory and ancillary investigations.

Results: One hundred and twenty seven children, aged zero to thirteen years of age were evaluated for disorders of sex development (DSD). During the period under review, sixty- nine (54.3%) were female genetic sex (46 XX). The majority (97.3%) were proven to have variable forms of congenital adrenal hyperplasia (CAH). Fifty-eight (45.7%)Patients were male genetic sex (46 XY). A diversity of causes were noted, with androgen insensitivity syndrome, and ano-rectal anomalies, 5-α-reductase deficiency, congenital adrenal hyperplasia, due to 3-β-hydroxysteroid dehydrogenase deficiency, were among the commonest.

Conclusion: Disorders in sex development (DSD) are not rare in our community. A multidisciplinary team approach is mandatory for successful management.

INTRODUCTION

Ambiguous genitalia, currently defined as disorders of sex development (DSD), constitute a complex, major social and medical emergency. Several forms of congenital adrenal hyperplasia can lead to significant salt loss, which, if unrecognised and not appropriately treated, may lead to shock. To ensure that the affected individual has a high quality of life (a successful outcome), medical practitioners must quickly and correctly assign the individual's gender and effectively assuage the family's concerns and anxieties. When approaching the treatment of any child diagnosed with sexual ambiguity, it is important to first review and understand the embryology and physiology of sexual differentiation.(figure1) Although the basic developmental events have long been known, the genetic, biochemical, endocrine, and molecular mechanisms are complex and have only been partially elucidated. (1-7)

Traditionally, the appearance of the external genitalia indicates the appropriate gender assignment. Male development depends on adequate testosterone secretion, peripheral metabolism of testosterone to dihydrotestosterone (DHT), and peripheral tissue response to androgens. Male external genitalia differentiate in response to DHT, which is formed in genital skin and other sensitive structures by the metabolism of testosterone by the 5-α-reductase enzyme. The presence of DHT induces the elongation of the genital tubercle, fusion of the genital folds to form the penis, fusion of the labioscrotal folds to from the scrotum, and the formation of the prostate. The response of these structures to DHT requires the presence of a normal intracellular androgen receptor. The formation of the male external genitalia is complete by the end of the 1st trimester. After the 1st trimester, further development consists only of growth of the penis and the descent of the testes into the scrotum. Both of these developments depend on the levels of foetal pituitary gonadotrophin. In the normal female, the external genitalia do not differentiate into male-specific anatomy; the genital tubercle remains small and becomes the clitoris, and the genital and labioscrotal folds remain unfused to form the labia minora and labia majora, respectively (1-7). In this communication, we highlight our experience with 127 patients with disorders of sex development (DSD), at King Khalid university hospital (KKUH), Riyadh, Saudi Arabia, over the period from January 1989 to June 2016.

**Corresponding author: AbeerM.Anteet*
Department of Pediatrics, College of Medicine and King KHALID university Hospital (KKUH), King Saud University, Riyadh, Saudi Arabia

MATERIALS AND METHODS

The study group consisted of all patients who were born or referred to endocrine service at King Khalid university hospital (KKUH), Riyadh, Saudi Arabia, and evaluated by the author (NJ)for disorders of sex development (DSD), during the period from January 1990 and June 2016. KKUH is the main teaching hospital of the King Saud Universityand considered as one of the major referral hospitals in the central region. The hospital provides primary, secondary and tertiary health care services for the local population.

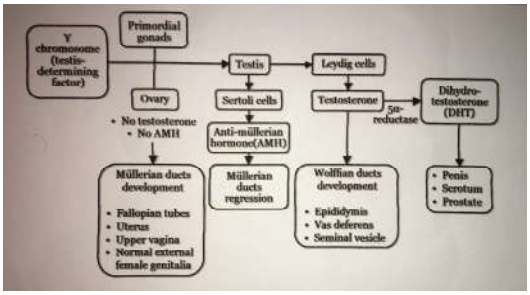

Figure 1. Simplified model for sexual differentiation and the development of internal and external genitalia.

A total of 127 patients with disorders of sex development (DSD), ambiguous genitalia were reviewed. The data collected included age, sex, relevant family and social history, pregnancy, clinical manifestations and results of all radiological, laboratory and ancillary investigations. Genetic sex was based on chromosomal studies. Additional radiological investigations included pelvic ultrasonography, genitography and magnetic resonance imaging (MRI) when indicated. Definitive etiological diagnosis was based on detailed and specified hormonal investigations (Figure 2), (8-12). Ethical approval for this study was obtained from the Institutional Review Board (IRB) at King Khalid University Hospital.

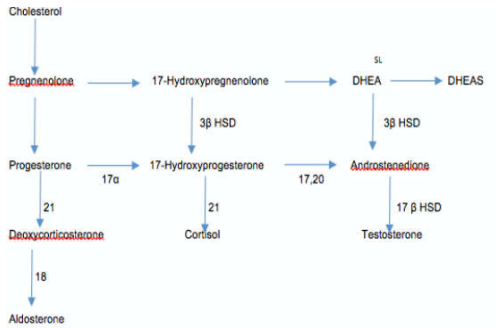

Figure2 Schematic structure for biosynthesis of adrenal cortex hormone (glucocorticoids, mineralocorticoids and sex steroid hormone).

RESULTS

During the period under review, 127 patients aged between newborn to 13 years were evaluated for disorders of sex development (DSD) by theauthor(NJ) at the pediatric endocrine service, King Khalid university hospital (KKUH), Riyadh, Saudi Arabia. Sixty- nine (54.3%) were genetic females (46 XX) whose detailed clinical data is shown in table 1.

The majority (97.1%) were proven to have congenital adrenal hyperplasia (CAH), (figure 3).

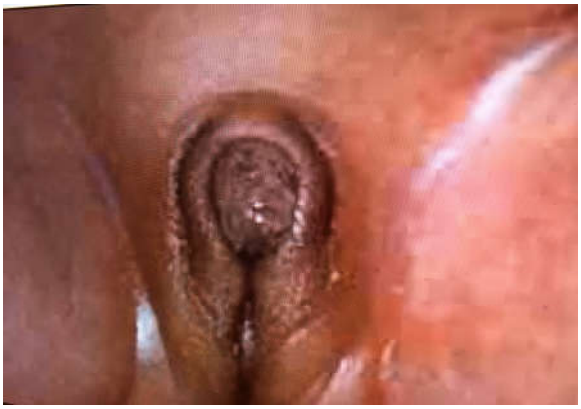

Figure 3 A newborn baby girl (46XX) with congenital adrenal hyperplasia due to 21 hydroxylasedeficiency. Note; the fused labioscrotal folds and hypertrophy of clitoris.

Family history of a similar disorders, hyperpigmentation, and variable degrees of salt wasting suggested the diagnosis. Only two (2.9%) patients were due to exogenous virilization of undetermined etiology.

Figure 4.A newborn baby boy (46XY) with congenital adrenal hyperplasia due to3-β-hydroxysteroid dehydrogenase deficiency.Note; the central urogenital slit.

Fifty-eight (45.7%) patients were genetic males (45 XY) table 2, with an associated generalized multiple congenital and local ano-rectal anomalies in 14 (24.1%) patients.

Table 1 clinical data of 69 patients with 46 XY genetic sex.

			Salt wasting	hyperpigmentation	Family history
Congenital adrenal hyperplasia (CAH) 67(97.1%)	21-α-OH asedeficiency	56 (83.6%)	+ 54	+49	+45
	11-β-OH ase deficiency	10 (14.9%)	_	+ 10	+ 8
	3-β-HSD deficiency	1 (1.5%)	+ 1	_	+ 1
Isolated clitoromegaly 2 (2.9%)		_	_	_	_

Legend to table:
21-α-OH asedeficiency - 21-α-hydroxylase deficiency
11-β-OH ase deficiency - 11-β-hydroxylase deficiency
3-β-HSD deficiency- 3-β-hydroxysteroid dehydrogenase deficiency

A diversity of other causes, androgen insensitivity in 16 (27.6%) patients, 5-α-reductase deficiency in 10 (17.2%) patients, and congenital adrenal hyperplasia (CAH) due to 3-β-hydroxysteroid dehydrogenase deficiency (figure 4) in 6 (10.3%) patients. Testosterone defect due to 17- β-hydroxysteroid dehydrogenase deficiency was present in one (1.7%) patient, while gonadotrophin deficiency in 4 (6.9%) patients.

Table 2 Clinical data of 58 patients with 46 XY genetic sex.

	No.
Androgen insensitivity (16):	
Couple	11 (19.0%)
partial	5 (8.6%)
5-α-reductase deficiency	10 (17.2%)
Congenital malformation (14):	
Local	4 (6.9%)
generalized	10 (17.2%)
Congenital adrenal hyperplasia 3-β-hydroxysteroid dehydrogenase deficiency	6 (10.3%)
Gonadotrophin deficiency	4 (6.9%)
Ovotesticular 46 XY DSD	2 (3.4%)
Hypospadias	2 (3.4%)
Extreme prematurity	1 (1.7%)
Persistent Mullerian duct	1 (1.7%)
Abnormalities of gonadal development (2):	
Swyer syndrome	1 (1.7%)
Denys-Drash syndrome	1 (1.7%)
Total	58 (100%)

DISCUSSION

Disorders of sex development (DSD) formerly termed intersex condition, atypical genitalia, or ambiguous genitalia, constitutes a complex major social and medical emergency. The evaluation of a newborn who has DSD can present a diagnostic challenge to the pediatrician. An efficient and accurate evaluation is needed to provide appropriate management. A multidisciplinary team, consisting of pediatrician, pediatric endocrinologist, geneticist, pediatric surgeon or urologist, psychologist, and a social worker, should supervise and provide the psychological support throughout the process.

Genital ambiguity usually is due to virilization of genetic females or undervirilization of genetic males. Less common are disorders of sexual differentiation that involve gonadal dysgenesis. More than half of our patients (54.3%) had a genetic female sex (46 XX). The majority (97.1%) of which were due to various virilization forms of congenital adrenal hyperplasia (CAH).Also, Al Jurayyan and Osman showed that a high rate of consanguinity and multiple siblings involvement in our community (13).

In males, it is often challenging and difficult; defects in testosterone production, metabolism or peripheral action can lead to ambiguous genitalia. Inadequate testosterone production may occur from Leydig cell deficiency, or inadequate production due to inborn error in androgen biosynthesis.

It is important to differentiate undervirilization in the newborn male from an isolated urogenital defect or syndrome of multiple congenital anomalies. The diagnosis of true hermaphroditism is by chromosomal studies, radiological imaging and hormonal studies which usually precede laproscopic examination (1-12).

In conclusion, a disorder of sex development (DSD) is not that rare in our community. A multidisciplinary team approach is mandatory for successful management.

Acknowledgment

The authors would like to thank Miss Hadeel N. Al-Jurayyan for her assistance in preparing the manuscript.

References

1. Saenger P. Abnormal sex differentiation. *J pediatrics* 1984, 104 (1): 11-17
2. Al Jurayyan NAM. Disorders of sex development: diagnostic approaches and management options-an islamic perspective. Malays J Med Sci. 2011; 18(3):4-12.
3. Gönül Ö.Current Concepts in Disorders of Sexual Development. *J Clin Res Pediatr Endocrinol*. 2011; 3: 22–31.
4. Chi C, Lee H C, Neely EK. Ambiguous Genitalia in the Newborn. Neo Reviews 2008, 9 (2); e 78-e 84.
5. Hughes IA. Disorders of sex development: a new definition and classification. Best PractRes Clin Endocrinol Metab. 2008; 22:119-134.
6. Frimberger D, Gearhart J. Ambiguous genitalia and intersex. Urol Int. 2005; 75: 291-297.
7. Al-Jurayyan NAM. Ambiguous genitalia: two decades of experience. Ann Saudi Med. 2011; 31(3):284-288.
8. AlJurayyan NAM. Imaging of disorder of sex development. Ann Saudi Med. 2013; 33(4):363-367.
9. Mongan NP, Tadokoro-Cuccaro R, Bunch T, Hughes IA. Androgen insensitivity syndrome.Best Pract Res Clin Endocrinol Metab. 2015; 29 (4): 569-580.
10. Prehn C[1], Möller G, Adamski J. Recent advances in 17beta-hydroxysteroid dehydrogenases. *J Steroid Biochem Mol Biol*. 2009; 114(1-2):72-77.
11. Ogilvy-Stuart AL, Brain CE. Early assessment of ambiguous genitalia. Arch Dis Child.2004; 89: 401–407.
12. Cheon CK. Practical approach to steroid 5alpha-reductase type 2 deficiency. *Eur J Pediatr*. 2011; 170:18.
13. AlJurayyan NAM, Osman H. the increased prevalence of congenital adrenal hyperplasia in Saudi Arabia: the role of consanguinity and multiple siblings involvement. *Eur J Res Med Sci* 2015; 3 (11): 31-34.

****

How to cite this article:

AbeerM.Anteet and Nasir A.M. Al-Jurayyan.2016, the Aetiology of Disorders In Sex Development (DSD): Review of 127 Patients From a Major Teaching Hospital, Riyadh, Saudi Arabia. *Int J Recent Sci Res.* 7(11), pp. 14219-14221.