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Research Article

Disorders of Sex Development (DSD): A more than three Decades of Experience at a Major Teaching Hospital

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Abstract

A retrospective hospital-based study was conducted at the Pediatric Endocrine Division, King Khalid University Hospital (KKUH), King Saud University, Riyadh, Saudi Arabia, during the period July 1983 and June 2017.

Methods: Medical records of patients who were diagnosed with DSD were retrospectively reviewed. Data included the etiological diagnosis, clinical history, physical examination, results of laboratory and radiological investigations, medical and surgical options offered, and results of follow-up. Laparoscopy or laparotomy with gonadal biopsies was done when appropriate.

Results: During the period under review, a total of 203 patients with Disorders of Sex Development (DSDs) were evaluated. Their ages ranged between one day and 13 years. Hundred- thirty-nine (68.5%) patients were genetic females (46 XX). Congenital Adrenal Hyperplasia (CAH) is the most common, in 137(98.5%) patients.

Conclusion: Disorders of sex development are a group of heterogeneous conditions with variable aetiologias. Many patients with DSD have a good quality of life and lead a near-normal life, though some have not. The severity of the disorder, initial evaluation and follow-up by a specialized multidisciplinary team, good psychological support, and proper education were important. Finally, sex assignments should be made early after a thorough investigation.

Introduction

Disorders of Sex Development (DSD) are a group of congenital conditions in which the development of chromosomal, gonadal, or anatomic sex is atypical. The definition includes both infants born with ambiguous genitalia and chromosomal syndromes, such as Turner and Klinefelter syndromes. The term DSD was suggested by a group of international experts from the Lawson Wilkin Pediatric Endocrine Society and the European Society for Pediatric Endocrinology in their meeting at the Chicago Consensus Conference 2005. [1-10] DSD is a rare disorder, with an estimated prevalence of 0.01-0.02 percent worldwide [11-16]. This is even higher in a community with increased consanguineous mating [17-19]. DSD, also, constitutes a major complex social and medical emergency as it is associated with salt loss in some patients with adrenal disorders. The management of patients with DSD requires thoughtful contemplative healthcare providers i.e. a multidisciplinary team of experts. [6-10,20-22]. Great advances have been made over recent years in the diagnosis and management of DSD most notably in the field of molecular genetic technologies which have advanced our understanding of the disorder. Furthermore, DSD surgery which is more challenging has been entirely advanced [23-27].

This article primarily focuses on the difficulties encountered during the management of various patients with DSD at King Khalid University Hospital (KKUH), King Saud University, Riyadh, Saudi Arabia during the period July 1983 to June 2017, and shares our experience with other health care providers in the area.

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Materials and methods

During the period under review, July 1983 to June 2017, all patients who were diagnosed to have Disorders of Sex Development (DSD) at King Khalid University Hospital, (KKUH), Riyadh, Saudi Arabia, were retrospectively reviewed.

An etiological diagnosis, detailed clinical history, physical examination, laboratory, and radiological investigations were obtained. The data were collected in a special form. The surgical and or the medical management provided were also reviewed. Laparoscopy or laparotomy with gonadal biopsies was done when appropriate.

Results

During the period under review, a total of 203 patients with disorders of sex development (DSDs) were evaluated (Table 1). Their ages ranged between one day and 13 years. Hundred-thirty-nine (68.5%) patients were genetic females (46 XX). Congenital Adrenal Hyperplasia (CAH) was most common, in 137(98.5%) patients while only two (1.5%) patients with isolated clitoromegaly. Variable degrees of virilization, hyperpigmentation, and clinical evidence of salt wasting were among the clinical features. On the other hand, only 64 (31.5%) patients were genetic males (46 XY), with a diversity of causes. Androgen sensitivity in 20 (31.3%), 5 alpha reductase deficiency in 9 (14 .1%), mixed gonadal dysgenesis in 5 (12.5%), hypogonadotrophin deficiency in 4 (7.8%), multiple congenital anomalies in 9(14.1%), hypospadias in 8 (12.5%), congenital adrenal hyperplasia due to 3 - beta-hydroxylase deficiency in 3 (4.8%), Delayed diagnosis is common.

Thirty -Six (17.7%) patients, with ages varying between one day to 13 years were improperly sex-assigned. Twenty -nine (80.5%) of them were raised as males due to variable virilization secondary to CAH in genetic females (46,XX), while seven (19.4%) were raised as females in genetic males (46,XY). All the genetic males (46,XY) among them accepted sex reassignments while nine of the genetic females (46,XX) refused sex reassignment and preferred to continue to be assigned as males.

Table 1: Aetiological diagnosis in 203 patients.

Diagnosis	Number of patients and (%)
Genetic females (46XX)	139 (68.5%)
Congenital adrenal hyperplasia (CAH)	137 (98.5%)
Isolated clitoromegaly	2 (1.5%)
Genetic males (46 XY)	64 (31.5%)
Androgen sensitivity	20 (31.3%)
5 alpha reductase deficiency	9 (14.1%)
Mixed gonadal dysgenesis	5 (12.5%)
Hypogonadotrophin deficiency	4 (7.8%)
Multiple congenital anomalies	9 (14.1%)
Hypospadias	8 (12.5%)
congenital adrenal hyperplasia due to (3-BHSD)	3 (4.8%)

Discussion

Disorders of Sex Development (DSDs) represent a complex clinical challenge. It is a group of heterogenous congenital conditions in which the chromosomal, gonadal, or anatomic sex is atypical. The definition includes both infants born with ambiguous genitalia and chromosomal syndromes, such as Turner and Klinefelter. The estimated prevalence of the disorder is approximately 0.018% (i.e. one in 5555 persons) worldwide [11-16]. This is even higher in a community with an increased rate of consanguineous mating [17-19].

Management of patients with DSD requires an experienced multidisciplinary team. The team should include specialists in pediatric endocrinology, surgery and/or urology and plastic surgery, clinical genetics, social work, clinical psychology or psychiatry, gynecology, radiology, nursing, and neonatology. This team has the role of providing patients and parents with psychological support and information regarding the diagnosis, sex assignment, and treatment options [6-10,20-22]. Great advances have been made over recent years in the diagnosis and management of DSD most notably in the field of molecular genetic technologies which have advanced our understanding of the disorder. Furthermore, DSD surgery which is more challenging has been entirely advanced [23-27].

In our series of patients, Congenital Adrenal Hyperplasia (CAH) was the most common of XX DSD, while, androgen insensitivity syndromes were the commonest, among XY DSD with a diversity of other aetiologias. This is in accordance with other studies [28-35].

Sex assignment, in patients with Disorders of Sex Development (DSD), is a complex clinical challenge. A systematic clinical investigation to reveal the state of hormonal production and which anatomical structures are present. A sex chromosome (karyotype) analysis should be performed early [36-39].

The decision about gender assignment should be made after the initial medical investigations and in consensus by the multidisciplinary team. Delayed diagnosis and lack of knowledge of sexual development may lead to improper sex assignment. Also, it is important to consider other factors that have an influence on sex assignment, such as psychological, cultural, and religious factors. Parents be informed during the investigation and be involved in the decision-making process [38,40-42].

Many patients have a good quality of life and lead productive lives. Psychological adjustment is variable and depends on the severity of the disorder [43-49]. Our study had many limitations. This was a retrospective study and the long-term follow-up of patients was not always available. Furthermore, molecular studies for specific disorders were not performed. This is the first study from our society.

Conclusion

In conclusion, disorders of sex development are a group of heterogeneous conditions with variable aetiologies. Many

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patients with DSD have a good quality of life and lead a near-normal life, though some have not. The severity of the disorder, initial evaluation and follow-up by a specialized multidisciplinary team, good psychological support, and proper education were important. Finally, sex assignments should be made early in the neonatal period after a thorough investigation. Much can be gained from sharing experiences of other centers from Saudi Arabia. Also, it is essential to study the various biological factors influencing the management of DSD.

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