

Research Article**Radiologic Imaging in Patients with 46 XY, Disorders of Sex Development (DSD): A 25 Years' Experience from a Major Teaching Hospital****Nasir A. M. Al-Jurayyan^{1*}, Rushaid N. A. Al Jurayyan², Ali A.N. Al Haboob³, Sultan R. S. Al Harbi⁴, Meteb A. Al Kubayyer⁵, Fahad B.M. Al Bader⁶, Ahmed A. Al Boukai⁷**¹Professor of Paediatrics and Pediatric Endocrinologist, Department of Pediatrics, College of Medicine & King Khalid University Hospital, King Saud University, Riyadh, Saudi Arabia^{2,4}Lecturer and Senior Registrar in Radiology, Radiology and Medical Imaging, College of Medicine & King Khalid University Hospital, King Saud University, Riyadh, Saudi Arabia³Assistant Professor and Consultant Intensivist, Department of Pediatrics, College of Medicine & King Khalid University Hospital, King Saud University, Riyadh, Saudi Arabia⁵Consultant Radiologist, College of Medicine & King Khalid University Hospital, King Saud University, Riyadh, Saudi Arabia^{6,7}Assistant Professor and Consultant Radiologist, College of Medicine & King Khalid University Hospital, King Saud University, Riyadh, Saudi Arabia***Corresponding author**

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Abstract: Disorders of sex development (DSD), is a group of conditions where the external genitalia appear abnormal. It represents a true medical and social emergency which need a multi-disciplinary team approach for elucidation. The pediatric radiologist plays an important role in defining the genital anatomy which remains one of the most important factors in sex determination, in addition to chromosomal analysis. It was a retrospective hospital-based study, conducted over 25 years between January 1989 and December 2014. Imaging studies (ultrasound, and/or magnetic resonance imaging) were retrospectively reviewed in various patients with 46XY, DSD confirmed by chromosomal analysis and appropriate hormonal investigations. Fifty-six patients were diagnosed to have 46 XY, disorders of sex development (DSD), with variable etiological causes with androgen insensitivity and 5- α -reductase deficiency were among the commonest. In addition to radiological, hormonal and chromosomal studies, laparoscopy studies were needed in four patients. Ultrasound was the primary modality for screening, as it is so sensitive and specific for eliciting the presence or absence of internal organs, but it is less sensitive in identifying the testes, only 6 out of 18 (33.3%) patients and operator dependent. However, Magnetic Resonance (MRI) was more sensitive for testicular tissue identification reaching up to 100%, and can detail various internal structures. At the time of diagnosis of 46 XY, DSD, imaging to characterize the pelvic structures should be ordered. Ultrasound continues to remain the first choice for initial evaluation, as it is cheap, easily accessible and has a high sensitivity and specificity for eliciting the presence or absence of female internal organ; however, it is less sensitive in identifying the tests and is operator dependent. Magnetic resonance (MRI) has been used as a helpful modality for difficult cases as it is more sensitive for testicular tissue identification, and can detailed internal structure.**Keywords:** Imaging, Ultrasound, Magnetic resonance, Disorders of sex development (DSD), 46 XY.

INTRODUCTION

Disorders of sex development (DSD) conditions result from congenital abnormalities in development of the reproductive organs. It constitutes a major complex, medical and social emergency requiring a multidisciplinary team approach. Not only might there be an immediate physiological problem such as shock, hypoglycemia, or subsequent salt loss, but there is also a need to assign a sex, if wrongly assigned, can lead to a major social consequences. Variety of genetic and

environmental factors may influence the disorder. The spectrum of 46 XY DSD is so broad (Table 1) which characterized by incomplete intrauterine masculinization of the external genitalia. Data on incidence and prevalence of the conditions are limited [1-7].

The pathophysiology of the disorder begins with XY genotype. The SRY gene of the Y chromosome directs the gonad to testicle, and produces the Sertoli and

Leyding cells. The Sertoli cells then Societe Anti-Mullerian ducts that would have formed into the uterus, fallopian tubes, and upper which result from congenital abnormalities in development of the reproductive organs. The Leyding cells secrete testosterone which would hormonally stabilize the Wolffian ducts and came masculinization of the external genitalia.

The correct diagnosis and proper characterization of the pelvic anatomy are of paramount importance. Different imaging modalities have been used in the evaluation, from ultrasound (US) to magnetic resonance imaging (MRI) [8-12].

This study was conducted to present our experience in comparing the various modalities (ultrasound and magnetic resonance imaging (MRI) in the assessment of children with 46 XY, disorders of sex development (DSD) at the King Khalid University Hospital (KKUH), King Saud University, Riyadh, Saudi Arabia over more than 25 years.

MATERIALS AND METHODS

Patients with 46 XY, DSD who attended a pediatric endocrine clinic at King Khalid University Hospital (KKUH), King Saud University, Riyadh, Saudi Arabia over a period of 25 years between January 1989 and December 2014, were included in this study. A detailed history and clinical examination were performed in all patients followed by chromosomal analysis and appropriate hormonal assays [2]. This research was approved by the Institutional Review Board (IRB) at King Saud University. Pelvic anatomy was characterized by imaging. Ultrasonography was the primary modality for demonstrating internal organs, while magnetic resonance imaging (MRI) was used as an adjunct modality to detail the anatomy, if necessary. No computed tomography (CT) was performed as it is accessible and more costly than ultrasound.

Furthermore, CT scan does not characterize soft tissues as MRI [9-11].

Ultrasound examinations were performed using real time sector scanners with either 5 or 7.5 MHz transducers. MRI was performed on 1.5 tesla machine in 15 patients.

RESULTS

Fifty-six patients were diagnosed to have 46 XY, DSD in the period under review. Their age ranged from one day to 12 years. Table 2, is showing the variable etiological diagnosis, with androgen in-severity and 5- α -reductase deficiency were the commonest 44.7%. In four patients, laparoscopy, was needed to identify the internal structures.

Ultrasound is the most inexpensive imaging modality and widely available used in all patients. Although, it is so sensitive and specific (up to 96%) in elucidating the absence of female internal organs, however, testes were unable to be localized in 6 of the 18 patients (33.3%) who needed it. MRI was utilized in 15 patients, and showed that it was sensitive (up to 100%) in delineating the gonads and detecting the internal structures.

DISCUSSION

The term disorder of sex development (DSD) includes congenital condition in which development of chromosomal gonadal or anatomical sex is atypical. The spectrum of causes of 46 XY DSD is so broad, Table 1. To elucidate the cause can be a time consuming and sometimes difficult. In addition, to radiological studies, specific diagnostic tests including genetic and hormonal studies, as well therapeutic trials should be performed [2]. In our series, a variety of different causes, Table 2, were noted. The management of patients requires an appropriately trained multidisciplinary team [1-7]. Early diagnosis is important for a better outcome.

Table 1: Known causes of 46 XY disorders of sex development (DSD)

46 XY, DSD, due to abnormalities of gonadal development
<ul style="list-style-type: none"> ○ gonadal agenesis ○ complete gonadal dysgenesis (Swyer syndrome) ○ partial gonadal dysgenesis (Dennys-Drash syndrome, Frasier syndrome) ○ testicular regression syndrome (vanishing testes syndrome) ○ Ovotesticular DSD ○ 46 XY DSD associated with cholesterol synthesis defects such as Smith-Lenil-Optiz syndrome ○ Leyding cell aplasia / hyperplasia, due to, hCG I LH receptor abnormalities
Gonadotrophin deficiency

- Testosterone biosynthesis deficiency**
- STR deficiency
 - P 450 SCC deficiency
 - 3-beta-hydroxysteroid dehydrogenase deficiency
 - 17- α -hydroxylase and 17.20 lyase deficiency
 - Isolated 17, 20 lyase deficiency
 - P450 oxidoreductase POR gene defect
 - 17-beta-hydroxysteroid dehydrogenase III deficiency
 - Persistent Mullerian duct syndromes (AMH or AMH-receptor gene abnormalities)
 - POR gene abnormalities
 - 5- α -reductase type 2 deficiency
 - Complete and partial androgen insensitivity syndromes

Table 2: Aetiological diagnosis of 46 XY, DSD, seen at a major teaching hospital (King Khalid University Hospital)

Diagnosis	No.	%
▪ Androgen insensitivity	16	28.6%
- complete	11	
- partial	5	
▪ 5- α -reductase deficiency	9	16.1
▪ Congenital malformation (dysmorphism)	14	25
- local anorectal	4	
- generalized	10	
▪ Extreme prematurity	1	1.8
▪ Congenital adrenal hypoplasia due to 3- β -hydroxysteroid dehydrogenase deficiency	5	8.9
▪ Hypogonadotrophin deficiency	4	7.1
▪ Ovotesticular – 46 XY, DSD	1	1.8
▪ Isolated hypospadias	3	5.4
▪ Persistent Mullerian ductus syndrome	1	1.8
▪ 46 XY DSD due to abnormalities of gonadal development	2	3.6
- Swyer syndrome	1	
- Denys – Drash syndrome	1	

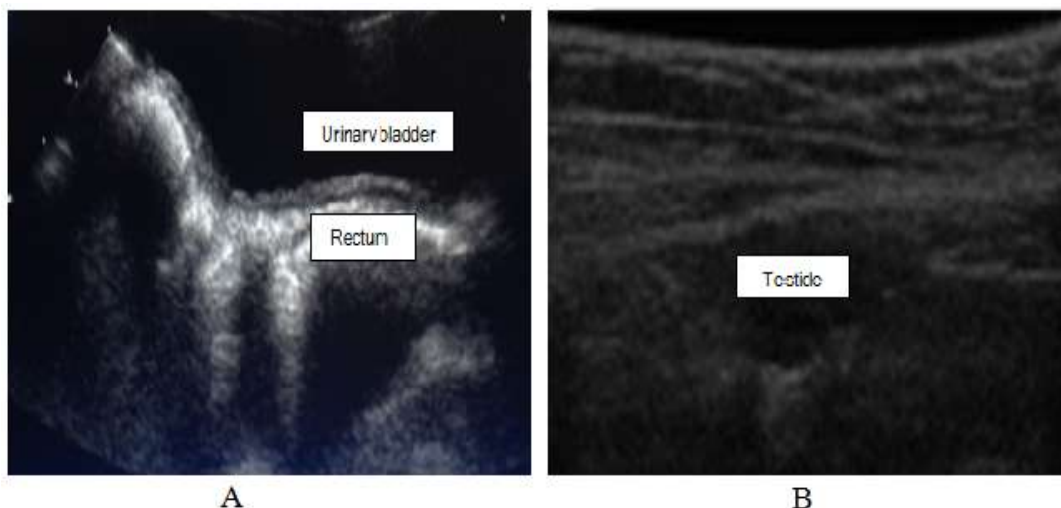


Fig. 1: An ultrasound image of the pelvis, showing no uterus (A), and right testicular tissue (B) within the inguinal canal in a patient with complete androgen insensitivity syndrome (CAIS)

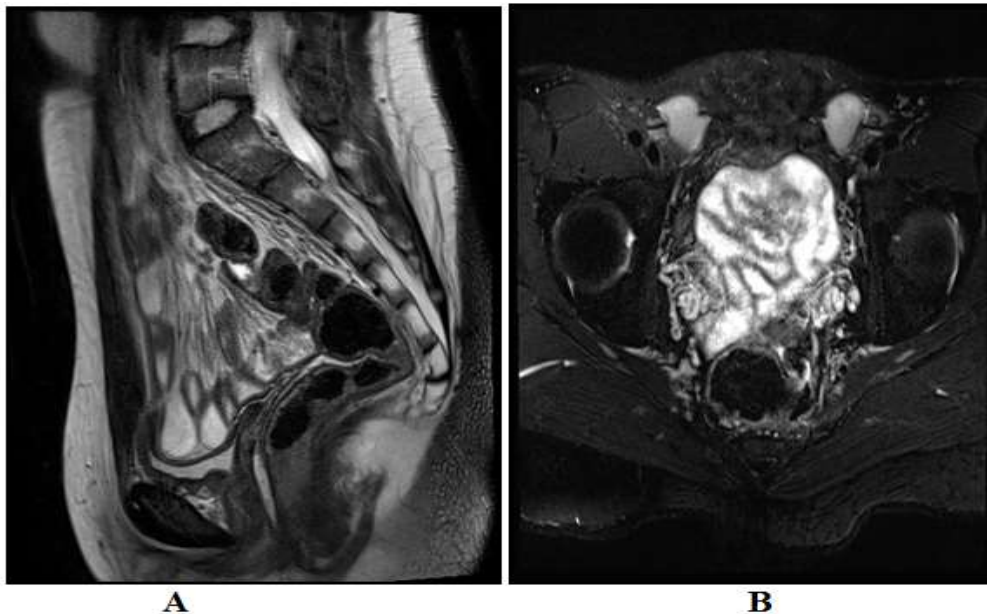


Fig. 2: A T₂-weighted magnetic resonance image (MRI) of the pelvis, showing no uterus and (B) testicles within the inguinal canals (arrows) in a patient with complete androgen insensitivity (CAI)

At the time of diagnosis imaging should be performed to evaluate the internal organs and to locate the testes. Ultrasound continues to remain the best choice for initial evaluation as it is inexpensive, easily accessible and has a high sensitivity and specificity in elucidating the presence or absence of internal organs, however, it is less sensitive and specific for location of gonads (figure 1) and is operator dependent [13-14]. Magnetic Resonance Imaging (MRI) has the ability to image in multiple plans and better contrast resolution without exposure to ionizing radiation [2, 10, 15-16]. In this study, MRI was found useful in the evaluation of 46 XY, DSD patients and found to be very sensitive and specific (Fig. 2) in up to 100%. Computed tomography (CT) was not used in this study. It has the drawback of exposure to high ionizing radiation and does not have the same soft tissue characterization as MRI.

In conclusion, ultrasonography continues to remain the first choice for initial radiological evaluation. MR imaging can serve as a problem-solving modality that can clearly elucidate the internal structures with a better gonadal resolution.

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