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Does MRI add to ultrasound in the assessment of disorders of sex development?

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ABSTRACT

Objective: The objective of the study was to evaluate the need of magnetic resonance imaging and using different approaches (transabdominal, endoluminal and transperineal) in the proper assessment of disorders of sex development regarding gonadal detection and gender differentiation.
Subjects and methods: Twenty five patients with abnormalities of sex disorders were included. They were classified into two groups according to the time of clinical presentation: *Group 1* (*early onset*) included eight cases. Their age ranged from one month to 12 years (mean age = 3.0). They presented with overt genital ambiguity of clitoral hypertrophy in a phenotypic female, non palpable testes or micropenis in a phenotypic male. *Group 2* (*late onset*) included 17 cases. Their age ranged from 16 to 33 years (mean age 18.1). This group presented by distressing puberty symptoms of primary amenorrhea in a female phenotype or undescended testis and behaving as a male. Cases were subjected to Ultrasound and MR imaging examinations. Imaging results were correlated results of chromosomal and hormonal assays as well as laparoscopy findings.
Results: The study included: 10/25 cases (40%) of female pseudo-hermaphroditism, 13/25 cases (52%) of male pseudo-hermaphroditism, one case (4%) of true hermaphroditism and one case (4%) of pure gonadal dysgenesis. The accuracy of multi approach ultrasound was 89.8% compared to 85.7% in MR imaging.
Conclusion: Ultrasound should be considered the initial screening modality in the assessment of developmental sex disorders. MRI examination could be reserved for gonad identification when ultrasound examination fails to do so and for corrective surgery guidance.

1. Introduction

Human sex development is a highly complex process under the control of multiple genes and hormones. Both male and female sexual differentiation follows a timetable of events with predictable development of the gonads, internal genital ducts, and the external genitalia. Completion of sexual maturation occurs during the pubertal years. Abnormalities of sexual differentiation may occur at any step along the way [1].

Disorders of sex development (DSD) defined as a condition in which chromosomal sex is inconsistent with phenotypic sex, or in which the phenotype is not classifiable as either male or female [2].

Abnormalities may result in abnormal differentiation of the gonads, the internal genital ducts, or the external genitalia. The end result of these abnormalities produces predictable clinical syndromes. While many of these defects of sexual differentiation are evident at birth, others will not be identified until puberty at which time the patient may manifest aberrant external maturation or may remain sexually infantile [3].

DSD can be classified on a pathophysiologic basis as disorders of chromosomal, gonadal, or phenotypic sex origin. On the basis of gonadal histologic features, these disorders were originally classified into four broad groups: female pseudohermaphroditism, male pseudohermaphroditism, true hermaphroditism, and gonadal dysgenesis [4].

Not all disorders of sexual differentiation result in ambiguous external genitalia; some disorders can have normal external genitalia (e.g., Turner syndrome (45, XO) with female phenotype, Klinefelter syndrome (47, XXY) with male phenotype) [5].

The purpose of the study was to evaluate the need of magnetic resonance imaging (MRI) in addition to ultrasound (US) using different approaches (transabdominal, endoluminal and transperineal), in the proper assessment of disorders of sex development regarding gonadal detection and gender differentiation.

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2. Subjects and methods

2.1. Subjects

Twenty five patients presenting with abnormalities of sex disorders were included in the study. They were classified into two groups according to the time of clinical presentation: *Group 1* (*early onset*; *prepubertal age group*) had included eight cases. Their age ranged from one month to 12 years (mean age 3.0). They presented with overt genital ambiguity of clitoral hypertrophy with fused labia in a phenotypic female, non palpable testes or micropenis in a phenotypic male.

Group 2 (*late onset: pubertal; adolescents and adults)* had included 17 cases. Their age ranged from 16 to 33 years (mean age 18.1). This group presented with distressing puberty symptoms of primary amenorrhea in a phenotype female or undescended testis with clitromegaly and sometimes gynaecomastia in a phenotype male.

Cases with primary amenorrhea had showed deniable sector of married individuals (*five cases of male pseudo hermaphrodite and one case of true hermaphrodite*), that did not admit such clinical presentation, they showed up for examination to check: (1) primary infertility, (2) difficult intercourse due to small/atretic vagina, those were having well developed breasts and female hair distribution.

Another five cases showed harsh voice and lack of breast development in addition to the co-existing primary amenorrhea.

Patients were referred to the Women's Imaging Unit in the Radiology department from the Obstetric and Gynecology Department, Cairo University Hospital and the Department of Clinical Genetics, Division of Human Genetics and Genome Research, National Research Center to assess the proper gender.

2.2. Methods

All patients were subjected to full clinical and anthropometric assessment especially in children. In patients presenting by ambiguous genitalia, the external genitalia were classified according to Prader [7] staging (stage I–V) which describes increasing virilization from phenotypic female with mild clitromegaly (stage I) up to a phenotypic male with hypospadius (stage V). Karyotyping and hormonal investigations were also performed.

2.2.1. Ultrasound examination

Ultrasound Examination was done using LOGIQ 7 PRO, GE (General electric medial system) through different approaches:

(1) Transabdominal scan using a 3.5–5 MHz sector transducer in adults and linear 7–8 MHz transducer in newly born and infants (adequately filled urinary bladder is mandatory) to check uterus, ovaries or intra abdominal undescended testicles.
(2) Endoluminal; transvaginal (TVS) (in married individuals, $n = 6$) or transrectal (TRUS) approach was performed using 7–8 MHz endoluminal transducer.
(3) Transperineal approach using 7–8 MHz linear transducer for assessment of external genitalia and lower vagina.

In post pubertal unmarried cases with phenotype female the endoluminal probe was used for superficial scanning i.e. translabial approach.

2.2.2. Magnetic resonance imaging

Pelvic MRI was performed for all cases using a 1.5-T magnet (Gyroscan Entra, Philips medical systems). All the patients were imaged in the supine position using pelvic phased-array coil. Full scanning of the inguinal region was considered. Cases were examined by T2-weighted pulse sequences FSE (TR/TE 1600/100 ms) in the axial, sagittal and coronal planes, and matrix 256×192. Axial T1-weighted sequence SE (TR/TE 500/40 ms). Slice thickness 4 mm with 1 mm gap in cases >11 years and 3 mm with no gap in cases <11 years. Scanning time was 2:20 min for each sequence.

2.3. Image analysis

Ultrasound through different pelvic approaches and MR images were reviewed to find diagnostic features of the ovaries, testes and evaluated for the presence or absence of uterus and prostate.

2.3.1. Ultrasound image analysis

- *Gonads* identified as a hypoechoic soft tissue at the adnexal, iliac and sometime inguinal regions; presence of follicles favors an ovary while pure solid appearance with abundant vascularity favors testis.
- *Vagina* was best assessed by superficial scanning using endoluminal probe as it provided better manipulation: in the longitudinal view, the vaginal walls can be easily demonstrated between the urethral walls (hypoechoic linear bands) and the echogenic gases in the rectum. The rectal mucosa and musclosa also are easily demonstrable.
- *Corpora cavernosa* and *corpus spongiosum* (Fig. 4) manifest as homogeneous cylindric structures. The tunica albuginea and the Buck fascia are stuck together and appear as a thin echogenic line surrounding the three corpora compared to homogenous hyperechoic appearance of hypertrophied clitoris.
- *Suprarenal gland* was checked whenever congenital adrenal hyperplasia was suspected regarding; (1) size of the limbs, (2) echogenecity of the gland and (3) surface contour.

MRI anatomy analytic data was based on Secaf et al. [8] and Lierse [9] respectively.

2.3.2. MR imaging analysis

- The presence of the *uterus, cervix and vagina* was assessed best in the T2 sagittal plane.
- *Ovaries:* An oblong shaped tissue of medium to low signal intensity (SI) on the T1-weighted image (WI) and high SI on the T2-WI was checked for along the path of suspected ovarian/testis descent; in the region of the inguinal canal and scrotum [8].
- *Testes* were traced along the following locations: intrascrotal, high scrotal, intracanalicular, or outside the internal inguinal canal [8].
- *Prostate* diagnosed when the zonal anatomy of the prostate was recognized on the T2-WI or suggested when the tissue around the urethra was larger than expected for the urethral muscle.
- *Clitoris:* High SI tissue seen adjacent to the ischium in the anatomical location of the crura of the corpora cavernosa on the T2 WI. Clitoral hypertrophy is diagnosed when the full length of the clitoris extended for >1 cm anterior to the pubic ramus in the sagittal T2WI [9].
- *Penis*: Present when both crura of the corpora cavernosa were detected, together with the corpus spongiosum with its tunica albuginea and the bulbospongiosus muscle.

Imaging results were correlated with results of chromosomal and hormonal assays as well as laparoscopy findings.

3. Results

The study included 25 cases of DSD categorized into two groups listed in Table 1.