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Perineal ultrasound offers useful information in girls with congenital adrenal hyperplasia

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Summary
A variable spectrum of urogenital malformations exists in girls with congenital adrenal hyperplasia (CAH). The vagina may enter the urethra at a variable level, and relations to the sphincter complex vary accordingly. Furthermore, an enlarged clitoris and variations in the bladder sphincter anatomy can be found. Endoscopy, genitography or magnetic resonance imaging (MRI) are commonly used for the assessment of these anomalies, and to provide information for counselling and treatment. When surgery is planned, introitoplasty cosmetical reduction of the clitoris and labioplasty are discussed with the families; introitoplasty is the most demanding aspect.

In order to plan the most appropriate surgical approach, the entrance level of the vagina into the urethra and its relation to the bladder sphincter must be known. Thus, imaging has an important role in CAH. The imaging techniques mentioned above require sedation, anaesthesia or involve ionizing radiation of the gonads and, thus, are relatively invasive. It would therefore be highly desirable to have a minimally invasive and accurate technique that provides images of the individual anatomic situation.

The present paper describes experience with perineal ultrasound in the initial imaging evaluation of girls with CAH. Ultrasound findings were compared to the results of endoscopy that was performed before surgery. From 2006 to 2012, 11 girls had perineal ultrasound and endoscopy. Measurements of clinical relevance for introitoplasty were: the length of the urogenital sinus, the distance to the vaginal opening into the urogenital sinus, and the length of the bladder neck.

This retrospective analysis showed that the entrance point of the vagina into the urogenital sinus could be identified in 10 of 11 girls. In some cases, the correlation of endoscopic and ultrasound data showed a correlation between endoscopic and sonographic findings. The length of the bladder neck and the length of the urogenital sinus could be measured by ultrasound in 10 of 11 girls, and were subsequently confirmed by endoscopy.

This showed, for the first time, that perineal ultrasound could provide the information required for surgical correction of the urogenital sinus anomaly in CAH. Advantages of these techniques are the minimal invasiveness and wide availability. Because long-term problems are not uncommon, perineal ultrasound may also be of value during follow-up. Widespread use of this technique has the potential to reduce costs and morbidity associated with endoscopy and genitography.

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Introduction

Congenital adrenal hyperplasia (CAH) is the most common cause of virilisation of the genitalia in female infants; it occurs with an incidence of 1 in 20,000 female deliveries. The disorder also occurs in boys, but mostly without any genital abnormality.

Congenital adrenal hyperplasia is a genetic, autosomal-recessive disorder caused by mutations that involve the biosynthesis of steroid hormones. The most frequent form of CAH is 21-hydroxylase deficiency. Clinically, the impaired or absent synthesis of glucorticoid and mineralocorticoids are the salient features that may lead to a life-threatening metabolic disarrangement [1,2]. In girls, accumulation of androgenic metabolites causes *in utero* virilisation and the characteristic phenotype. The clitoris is enlarged and the vagina may enter the urethra at a variable level, ranging from a normal perineal to a high subvesical position; several classifications have been proposed to characterise these anomalies. The development of the uterus and the ovaries is typically unaffected. The more severe the enzyme defect, the earlier the onset of clinical symptoms. In Germany, screening for classic CAH is part of routine neonatal screening [3].

The early management of CAH is based on complete diagnosis and hormone substitution. Timing and surgical technique are controversial. When surgery is chosen at an appropriate age, the individual anatomy of the patient's urogenital sinus must be diagnosed; genitography is the established approach to obtain this information. It requires catheterization of the urogenital sinus, injection of contrast under pressure, and radioscopy.

Cystoscopy/genitoscopy provides the same information, but is more invasive and requires general anaesthesia [4]. More frequently, endoscopy is performed immediately before surgery to confirm the information of a precedent imaging procedure, and to safely place catheters into the bladder and vagina to guide the dissection.

Magnetic resonance imaging (MRI) may provide excellent images of the urogenital anatomy in CAH, and thus facilitate the pre-operative planning. However, the technique is very sensitive to motion artefacts and suboptimal images limit its use, especially in small infants. In general, MRI quality is much better in cooperative children and teenagers [2].

Perineal ultrasound has been successfully applied to the diagnosis of urethral valves, urinary incontinence and anal atresia. Perineal application of the ultrasound probe provides images of the bulbospongiosus muscle, the urethra, vagina and rectum [5]. All patients with CAH seen at the present interdisciplinary disorders of sex development (DSD) clinic receive an abdominal ultrasound examination. After the transabdominal scan of the bladder, the ultrasound transducer is applied to the perineum of the CAH patients. It has been surprising to find individual anatomy of the bladder, urethra and vagina easily recognizable in many patients.

To define the value of this technique, ultrasound and endoscopic findings were compared in a group of patients that underwent surgery at the institution. This investigation is the first systematic study of this topic, and it focused on the following questions:

a) What does perineal ultrasound add to the clinical examination of girls with CAH?
b) How do ultrasound findings of urogenital anatomy relate to findings at cystoscopy/genitoscopy?

Materials and methods

The interdisciplinary DSD team assessed all participants. Ultrasound examination was a routine part of the initial clinical evaluation. While surgery was not the primary concern in this setting, it was helpful to understand the individual anatomy of the patient within the spectrum of the disorder.

A retrospective analysis was performed of the data from the female patients' with CAH who had both ultrasound and endoscopy examination between 2006 and 2012. Data were pseudonymised for comparison and no formal ethical approval was sought.

In the period between 2006 and 2012, 35 girls attended the present interdisciplinary DSD clinic. Ten out of 11 girls had salt-wasting CAH. The external phenotype of the genitalia was Prader 2 and 3 in nine, and Prader 4 in two girls. The median age at examination was 19 months, with a range from 6 month to 17 years. The ultrasound findings were compared with endoscopy in every case, and with genitography and MRI when available.

For 11 girls, detailed ultrasound images and reports, as well as endoscopy reports, images and videos were available for analysis, and these data were included. Five patients without ultrasound examination were excluded.

LW carried out all ultrasound examinations and endoscopies after clinical examination. Before the examination, the technique was explained in appropriate terms to the girls and their parents. A General Electric Q/LOGIQ 7 ultrasound machine (GE Healthcare, Chalfont St. Giles) with a 5—8 MHz curved (for intraabdominal)- and a 7—10 MHz linear (for the perineal examination) transducer was used. The patient was placed in a supine position, and the examination involved imaging of the kidneys, adrenal glands, bladder, retrovesical space and perineum. For perineal ultrasound, the image was converted upside-down to obtain a cranio-caudal orientation of the images.

Sagittal sections in the midline were obtained. On the frozen image, several measurements were taken. The distance from the perineal opening to the entrance point of the vagina was measured, and referred to as urogenital sinus length. Furthermore, the distance from the superior end of the bladder neck to the vaginal entrance was measured, and referred to as urethral lengths. The duration of the examination was approximately 20 min.

For endoscopy, patients were examined under general anaesthesia and put in a lithotomy position. In most patients, the examination preceded surgery and included the placement of a vaginal catheter and bladder catheter. A structured examination checklist, which has been recently published [4], was used. For the measurements of the various segments of the urogenital sinus, the recommendations of Rink et al. [7] were followed. Data reported in Table 1 were derived from the operative reports.