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Anatomical measurements of the urogenital sinus in virilized female children due to congenital adrenal hyperplasia

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Summary

Background
Virilized females due to congenital adrenal hyperplasia represent the most common form of female disorders of sexual development. The anomaly therein is an external virilization to resemble male genitalia and a persistent urogenital sinus.

Objectives
To study the anatomical details of the virilized female cases operated upon between 2011 and 2015. This anatomical description is presented to support the current surgical strategy of partial urogenital mobilization to correct this anomaly.

Methods
Thirty cases (presenting to a single tertiary center) were prospectively studied by genitography, cystourethroscopy, and operated upon via a single-stage feminizing genitoplasty. A single surgical team operated upon all cases. External virilization was assessed by the Prader classification. The internal anatomy was studied by measuring the length of the urethra proximal to the confluence, and the vertical depth of the vaginal-urethral confluence from the perineum. The correlation coefficients between the external virilization and the internal anatomical measurements were derived.

Results
The median age at surgery was 19 months (range 6–42 months). External virilization did not obviously correlate with the length of the proximal (prejunctional) urethra ($r = -0.03$, $P = 0.5$), or strongly with the depth of the vaginal-urethral confluence ($r = 0.2$, $P = 0.2$). The mean length of the proximal urethra was 22 mm (range 10–32 mm), and the mean vertical depth of the vaginal-urethral confluence from the perineum was 16 mm (range 8–31 mm).

Discussion
Due to limitations of the radiological and endoscopic evaluation, the accurate anatomical assessment of this condition may be challenging. In order to assess or compare the anatomy of these cases, there are two important points to address: (1) the length of the urethra proximal to the urogenital sinus, as this will impact the urinary outcome; and (2) the depth (level) of vaginal entry into the urogenital sinus, as this will affect the mobilization required to exteriorize the vagina.

Conclusion
The degree of external virilization does not totally correlate with the internal anatomy. The depth of the vaginal-urethral confluence from the perineum is an indicator of the required mobilization for the current perineal approach. In 90% of cases in this age group (1–3 years old), this depth is ≤20 mm. This supports the current understanding that partial urogenital mobilization could be suitable for most cases Figure (Summary).

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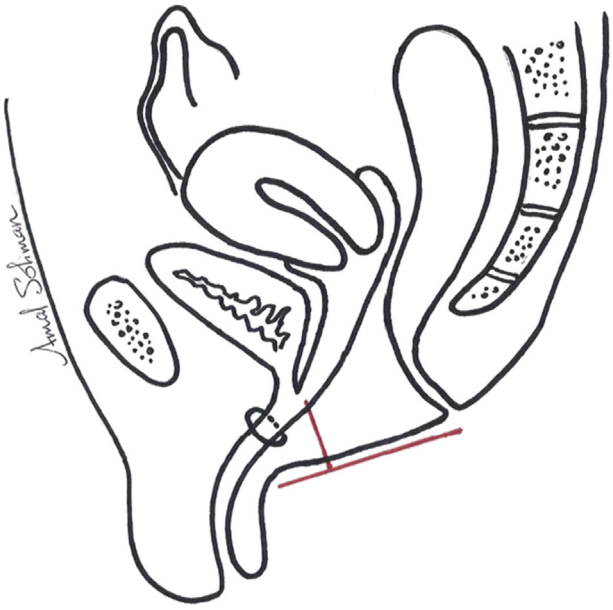

Figure (Summary) Diagram illustrating the vaginal depth from the perineal level (red lines).

Introduction

The traditional theory to explain the severity of the urogenital sinus anomaly in virilized females due to congenital adrenal hyperplasia is that the level of the vaginal entry into the urogenital sinus is determined by the degree of *in utero* exposure to adrenal androgens. Higher exposure is thought to lead to a more proximal entry of the vagina into the urogenital sinus, causing a higher confluence [1]. In a reliable mouse model, it was concluded that prenatal exposure to increasing levels of androgen causes a dose-dependent change in the anatomy, in the form of a distal elongation of the common urogenital sinus and a proximal migration of the bladder neck [2].

Other researchers have postulated that negligible variability in the proximal (prejunctional) urinary tract anatomy, with regard to the urethral length and the level of vaginal entry, occurs with increasing virilization [3].

It appears that both theories differ on the development of the proximal urethra and the level of vaginal entry into the urogenital sinus.

The aim of the present study was to add to these two views by describing the actual anatomical measurements of the urogenital sinus anomaly in virilized congenital adrenal hyperplasia around the age of 1—3 years.

In order to assess or compare the anatomy of these cases, there are two important points to address: (1) the length of the urethra proximal to the urogenital sinus, as this will impact the outcome of urinary function and continence; and (2) the depth (level) of vaginal entry into the urogenital sinus, as this will affect the mobilization required to exteriorize the vagina and dictate the likelihood of vaginal stenosis.

Recent studies have proven that the upper urethra is the most innervated structure of the pelvis, with completely circumferential innervations [4]. Sphincteric nerves cover the lateral and anterior aspects of the upper urethra and vagina [5]. Although these are descriptions of the innervation in normal individuals rather than virilized females, there are recommendations against routinely disrupting this high periurethral area. Dissection of the pubo-uretheral ligament performed during total urogenital mobilization could endanger postoperative continence; consequently, exceptional care is needed when approaching the retro-pubic space [6,7].

The inaccurate classification of the persistent urogenital sinus anomaly into either high or low has led surgical teams to elect a flap vaginoplasty for cases designated as low urogenital sinus, and a pull-through vaginoplasty for cases designated as high urogenital sinus [8,9]. However, it is believed that this does not reflect the true situation, and that most cases lie between being low and high, and need a degree of urogenital mobilization, ranging from partial to total. Hence, to support the current surgical approach, the present study describes the measurements encountered in this group of patients.

Methods

This single-center study was prospectively approved and conducted under the guidance of the research ethics committee of Cairo University, Faculty of Medicine. All the included cases were diagnosed and managed by the Disorders of Sexual Development (DSD) team, based at the Diabetes, Endocrinology and Metabolism Pediatric Unit (DEMPU) of Cairo University Specialized Pediatric Hospitals (CUSPH). All of the cases referred to the DSD clinic that were diagnosed as 46 XX DSD due to congenital adrenal hyperplasia (CAH), with persistent urogenital sinus and external virilization were prospectively included. No cases with this diagnosis were excluded, nor was surgery deferred to a later age. All parents voluntarily provided informed consent for the planned procedure and possible risks, as well as for participation in this study.