CASE REPORT

Idiopathic female pseudohermaphroditism with urethral duplication and female hypospadias

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SUMMARY

Female hypospadias is a rare anomaly of the female urethra where it opens on the anterior vaginal wall anywhere between the introitus and the fornix. It is often associated with other genitourinary anomalies such as Cloacal malformation, female pseudohermaphroditism, nonneurogenic neurogenic bladder and urethral duplication. Idiopathic female pseudohermaphroditism is extremely rare, and most cases occur secondary to adrenogenital syndrome or maternal androgen exposure. We report a unique case of a 1-year and 4-month-old girl who presented with ambiguous genitalia and renal failure secondary to a non-neurogenic neurogenic bladder. On further evaluation, she was found to have urethral duplication with a hypospadiac female urethra. She initially underwent a vesicostomy and was further planned to undergo an appendicular Mitrofanoff at an older age. The mainstay of treatment in these cases includes relief of bladder outlet obstruction and recovery of renal function by adequate urinary drainage. Clitoral reduction, if cosmetically warranted, may be planned at puberty.

BACKGROUND

Female hypospadias is an anomaly of the female urethra where it opens on the anterior vaginal wall anywhere between the introitus and the fornix. It is often associated with other genitourinary anomalies such as malformation, female pseudohermaphroditism, non-neurogenic neurogenic bladder and urethral duplication. Most cases of female pseudohermaphroditism occur secondary to adrenogenital syndrome or exposure to maternal androgens. Female pseudohermaphroditism without any apparent cause is extremely rare. We report a case of idiopathic female pseudohermaphroditism with a hypospadiac vaginal urethra, bladder dysfunction and an accessory phallic urethra. Only seven such cases have been reported in literature to date. Though diagnosis is challenging, the treatment is more straightforward and outcomes are encouraging.

CASE PRESENTATION

A 1-year and 4-month-old child, raised as a female, presented with straining while voiding and ambiguous genitalia. She was a term child, born by vaginal delivery, with no antenatal history of maternal exposure to androgens or any virilisation. Clinically, she appeared dehydrated and malnourished. However, there was no history of any salt wasting symptoms such as vomiting, loose stools or hyperpigmentation. Examination of the external

genitalia revealed a hypertrophied 2 cm clitoris with a pinpoint orifice at the tip ([figure 1](#)), a normal vaginal introitus with a non-visualised urethra and well developed labia, and no palpable gonads and no inguinal hernia. Systemic examination revealed normal movement of all four limbs, a normal spine and normal anal tone, and no evidence of hypertension.

INVESTIGATIONS

Investigations revealed haemoglobin of 9.6 g/dL, serum creatinine of 1.2 mg/dL, with normal serum electrolytes (131/3.6/12 mmol/L) and blood hormones (testosterone <20 ng/dL, 17-OH progesterone 0.365 ng/mL, dehydroepiandrosterone <15 µg/dL). Creatinine clearance was 24.8. Thyroid-stimulating hormone (TSH) and alkaline phosphatase were assessed in view of a widely open

Figure 1 Ambiguous genitalia with a hypertrophied clitoris.

Figure 2 Demonstration of two discrete urinary streams from the duplicated urethra.

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Figure 3 Per operative cystourethrogram demonstrating an incomplete urethral duplication and vesicoureteric reflux.

anterior fontanelle and were both normal. Urine analysis for proteinuria was negative at presentation and on subsequent visits. Ultrasonography (USG) showed bilateral hydroureteronephrosis with a thickened bladder wall and bilateral grade II renal parenchymal changes. A normal appearing uterus was identified, but the ovaries were not visualised. The patient's karyotyping report was consistent with female genotype hence a female

gender was assigned. An MRI of the spine did not show any neurological abnormality. A clinical diagnosis of female pseudohermaphroditism, with female hypospadias causing functional bladder outlet obstruction, was made.

TREATMENT

At cystoscopy, the hypospadiac urethral orifice was visualised 1 cm from the vaginal introitus on the anterior vaginal wall, and it could admit a 7.5 French scope into the bladder. The bladder was trabeculated and suprapubic pressure revealed two discrete urinary streams—one from the vaginal urethral meatus and the other from the tip of the hypertrophied clitoris (figure 2). This accessory phallic urethra could admit a 3 French guide wire. Vaginoscopy revealed a normal vagina and external cervical os. Intraoperative cystourethrogram revealed bilateral grade 5 vesicoureteric reflux and an incomplete urethral duplication (figure 3). A cutaneous vesicostomy was performed to decompress the obstructed system. Postoperatively, a renal cortical scan demonstrated bilateral renal parenchymal dysfunction with scars and a split function of 80% of the left side and 20% on the right.

OUTCOME AND FOLLOW-UP

The child is now 2½ years old, and showing age appropriate growth. She has been on regular follow-up, with no evidence of proteinuria or hypertension. Serum creatinine clearance has improved from 24.8 at presentation to 44.1 at the last follow-up 1 month ago. Subsequent serial USGs have shown a significant decrease in the hydroureteronephrosis and bladder wall thickening (figures 4 and 5).

Figure 4 Ultrasonography images showing the change in the renal pelvic diameters. (A) At admission, (B) 1 week following surgery.

Figure 5 Ultrasonography image demonstrating (A) thickened bladder wall and visible ureters at admission, (B) decrease in bladder wall thickness 1 month following surgery.

DISCUSSION

Urethral duplication is rare in males and almost unheard of in females. Idiopathic female intersex with clitoromegaly, urethral duplication and female hypospadias with non-neurogenic neurogenic bladder is a unique anomaly with only a few cases reported to date.

Female intersex may be classified into five groups, namely:

- Group I—Congenital adrenal hyperplasia
- Group II—Virilisation by maternal androgens (due to drugs or virilising maternal tumours)
- Group III—Idiopathic
- Group IV—Special (idiopathic female intersex with complex caudal malformations)
- Group V—Familial

The idiopathic group, as in our case, consists of similar conditions with distinct features including clitoral hypertrophy, clitoral urethral duplication, hypospadiac vaginal urethra, partial labial fusion and bladder outlet obstruction.¹ Though children in this group have clitoral hypertrophy, other features of masculinisation are absent, as the pathology is attributed to a local rather than a systemic or endocrine cause.

The bladder outlet obstruction described in other cases of Group III was due to stenosis of the hypospadiac meatus.^{2–5} However, in this case, there was no stenosis of the vaginal urethra and obstruction was concluded to be due to a

non-neurogenic neurogenic bladder, the aetiology of which has been documented to be unknown. This is a diagnosis of exclusion that mandates a spinal MRI to rule out other neurological causes.

Various theories have been proposed to discuss the embryogenesis of this condition. Howard and Hinman suggested that, if the Müllerian ducts reach the urogenital sinus further distally than normally, the vestibule and hymen will not develop, and, instead, it will lead to formation of an accessory urethra via the pars phallica.^{6,7} Belis and Hrabovsky⁸ proposed that prolonged androgen exposure leads to increased sensitivity of the genital tubercle and urogenital sinus, resulting in the development of an accessory urethra. However, this is to a lesser degree than that seen in adrenogenital syndrome. More recent data on the subject support this theory. Bellinger and Duckett⁹ believed that, due to abnormal descent of the Müllerian duct, the posterior displacement of the vaginal introitus allowed the accessory phallic urethra to form.

The clinical problems associated with these cases include urinary retention, incontinence secondary to vaginal voiding, urosepsis, renal failure and social issues pertaining to gender assignment. Treatment therefore is aimed at attaining two main therapeutic goals: relieving urinary obstruction, and cosmetic correction of the masculinised external genitalia. Though varying in severity, the obstructive uropathy, if relieved in time, can ensure adequate recovery of renal function. Early gender assignment is warranted by karyotyping, as is laparotomy and gonadal biopsy, to exclude the diagnosis of true hermaphroditism.⁵

As elaborated by Onesti *et al*,¹⁰ the important criteria in establishing a structured diagnostic algorithm include karyotyping, hormonal evaluation and radiological examinations. Karyotyping and serum hormonal assays helped in gender assignment and ruling out of other aetiologies, while USG and cystourethrogram aided in identification of female internal genitalia and urethral duplication with reflux, respectively.

In our case, as an initial step to relieve the bladder outlet obstruction, a cutaneous vesicostomy was performed and the mother was taught how to perform thrice daily clean intermittent catheterisation through the vesicostomy. The future plan is to create a continent catheterisable channel (Mitrofanoff) with closure of the vesicostomy when the patient attains 3–4 years of age. Undiversion earlier would result in non-compliance with clean intermittent catheterisation. Removal of the often non-functional anterior urethra within the hypertrophic clitoris is usually not necessary,⁷ however, feminising genitoplasty with clitoral reduction may be considered at puberty, for cosmesis.

Learning points

- ▶ Idiopathic female pseudohermaphroditism with urethral duplication and a hypospadiac vaginal urethra is extremely rare.
- ▶ It is usually associated with some degree of bladder outlet obstruction as a result of non-neurogenic neurogenic bladder—the reason is still unknown.
- ▶ Adequate initial diversion with creation of a continent catheterisable channel forms the mainstay of treatment in these children.
- ▶ Genital reconstruction may be considered at puberty.

Contributors ARD (corresponding author) was involved in data collection, patient interaction, data write up, analysis, literature search and creation of the manuscript. JJK was involved in formation of the study design, literature review, data analysis and manuscript editing. TJKK was involved in study concept creation, definition of intellectual content, manuscript editing and review.

Competing interests None declared.

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