Posterior Urethral Valves: The Spectrum of Radiological and Clinical Presentations

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Keywords

Urethral obstruction ; prenatal diagnosis ; ultrasonography ; renal failure.

Abstract

Objective

Posterior urethral valves (PUV) are the most common cause of congenital lower urinary tract obstruction (LUTO) and kidney failure with renal replacement (KFRT) in boys. They are suspected on prenatal ultrasound (US) showing bilateral ureterohydronephrosis, megabladder and posterior urethral dilatation. PUV presents with variable clinical severity and radiologic appearance. This study aims to review PUV cases in our center, describe imaging aspects, and assess renal and bladder outcomes of prenatally and postnatally diagnosed cases.

Methods

We reviewed the medical records of all boys who underwent PUV ablation at HUDERF between 2006 and 2021. We recorded prenatal and perioperative US, age and symptoms at diagnosis, cystourethrogram, outcome of renal and bladder function. Prenatal and postnatal diagnosed patients were compared.

Results

We include 50 boys treated for PUV with available antenatal data. Thirty-one patients (62%) had abnormal fetal screening: 90% had the classic antenatal presentation of PUV: bilateral ureterohydronephrosis and megabladder. Three patients had an unusual fetal presentation with unilateral (uretero)hydronephrosis. Nineteen (38%) were diagnosed postnatally with a median age of 9 months. The most common postnatal clinical presentations were urinary tract infection (84%) and voiding disorders (11%). 34% of patients, with similar proportions between antenatally and postnatally diagnosed, reached CKD grade 2-4; 6% progressed to KFRT, all prenatally diagnosed.

Conclusion

This study demonstrates an improvement in fetal screening for PUV. Most fetuses had the classic antenatal presentation, but 10% had unilateral dilatation without signs of LUTO. Children diagnosed antenatally had the worst prognosis in terms of renal and bladder function.

Introduction

Posterior urethral valves (PUV) are tissue leaflets fanning distally from the prostatic urethra to the external urethral sphincter. This pathology is the most common cause of congenital lower urinary tract obstruction (LUTO) affecting 1 in 4,000 male births and it is the leading cause of kidney failure with renal replacement (KFRT) in boys (1-3).

PUV are commonly suspected on prenatal ultrasound (US) revealing bilateral hydroureteronephrosis, bladder wall thickening and proximal urethral dilatation taking the aspect of a keyhole (4, 5). In severe cases, PUV cause a complete bladder obstruction, with oligohydramnios and renal dysplasia (6).

At birth, the elective radiological exam to perform is the voiding cystourethrogram (VCUG), and the diagnosis is confirmed by the presence of proximal urethral dilatation with often a trabeculated bladder and bilateral vesicoureteral reflux (VUR) (4).

PUV may however present with a broad clinical and radiological spectrum with variable severity ranging from early renal failure to late mild picture such as minor lower urinary tract symptoms and recurrent urinary tract infection (UTI).

The aim of this study is to review the PUV cases that occurred in Queen Fabiola Children Hospital, Brussels, in the last 15 years and describe the imaging aspects including uncommon and challenging presentations. The secondary aim is to assess and compare the renal and bladder outcome of children prenatally and postnatally diagnosed of PUV.

Materials and methods

In this descriptive retrospective observational study, we reviewed the medical records of all male patients under 16 years of age who underwent PUV ablation at the Queen Fabiola Children Hospital, Brussels, between January 2006 and March 2021. The following

data were extracted: prenatal US findings, age and symptoms at postnatal diagnosis and preoperative imaging (US and VCUG).

After birth, diagnosis of PUV was based on the VCUG images and reflux, if present, was graded according to the International Reflux Study Committee classification (7). We recorded the age, height and serum creatinine level of the patients 5 years after PUV ablation and at the last follow-up. Renal function was estimated by calculating the glomerular filtration rate (GFR) in ml/min/1.73 m² using the Schwartz formula (8). Renal function was classified according to the KDIGO guideline stages of chronic kidney disease (CKD) (9). KFRT was defined as a stage 5 of CKD (GFR < 15 ml/min/1.73 m²) requiring dialysis or renal transplantation. Renal function 5 years after PUV ablation and at the last follow-up was compared between prenatally and postnatally diagnosed cases. In all children older than 5 years of age, supposedly already fully toilet trained, the presence of voiding disorders (urinary incontinence and urgency, poor urinary stream, or the need of clean intermittent catheterization) was recorded. Categorical variables were compared using chi-square test. A p-value <0.05 was considered statistically significant. The study protocol was reviewed and approved by the Ethics Committee of our institution (reference CEH 30/20).

TABLE 1: Children (Group 1) with abnormal imaging findings at antenatal US screening (N=31).

	No. (%)
Classical presentation	**28 (90%)**
Bilateral ureterohydronephrosis and megabladder	24
Unilateral ureterohydronephrosis, megabladder and keyhole sign	2
Isolated ruptured megabladder with urinary ascites	2
Uncommon presentation	**3 (10%)**
Unilateral hydronephrosis	2
Unilateral ureterohydronephrosis	1

Results

A total of 57 patients with PUV were diagnosed and surgically treated at the pediatric uro-nephrology department of our tertiary center between January 2006 and March 2021. Antenatal data were available for 50 patients (88%), seven patients (12%) with missing data have been excluded from the analysis. The included patients were classified according to their antenatal US findings. Group 1 included 31 patients (62%) with abnormal fetal urinary tract US (Table 1). Group 2 included 19 patients (38%) who had a normal antenatal screening.

Patients with abnormal antenatal screening (Group 1, n=31)

Classical PUV antenatal imaging

28/31 (90%) patients had a classical PUV antenatal imaging (Table 1). Most of them showed a bilateral hydroureteronephrosis associated with a megabladder. Two patients had a major unilateral hydroureteronephrosis with a large bladder and a dilated urethra taking the appearance of a keyhole sign. Two patients presented with a ruptured bladder and urinary ascites. The first patient showed an isolated megabladder at the US of 23 weeks of gestational age. A week later ascites developed secondary to a urinary leakage from the bladder. There was no hydroureteronephrosis, renal dysplasia nor oligohydramnios. A fetal MRI confirmed the US images and showed a megabladder with posterior urethral dilatation appearing as a keyhole sign as well as a large amount of urinary ascites (Figure 1). After birth VCUG confirmed the presence of PUV with bilateral high-grade VUR. The renal function progressed favorably with a plasma creatinine of 0.89 mg/dL at 17 years of age. The second patient showed at the 22nd week of gestational age a severe bilateral hydroureteronephrosis, oligohydramnios and urinary ascites, and at the fetal MRI pulmonary compression by diaphragmatic dome inversion secondary to significant ascites. At birth, the US confirmed the severe bilateral hydroureteronephrosis with renal cortical hyperechogenicity and megabladder, and the VCUG revealed the presence of a stricture in the posterior urethra without VUR (Figure 2). Surprisingly, the patient showed a favorable outcome in terms of both respiratory and renal function with plasma creatinine of 0.73 mg/dL at 13 years of age. Both patients with antenatal urinary ascites progressed favorably also in terms of bladder function and became fully toilet trained before the age of 5 without any medication.

Uncommon PUV antenatal imaging

Three patients (10%) did not present antenatally as a classical PUV (Table 1). One had a unilateral hydroureteronephrosis and two patients presented a unilateral isolated pelvis dilatation.

FIGURE 1: Sagittal fetal magnetic resonance imaging scan. Urethral valve with mega-bladder, keyhole sign and urinary ascites.

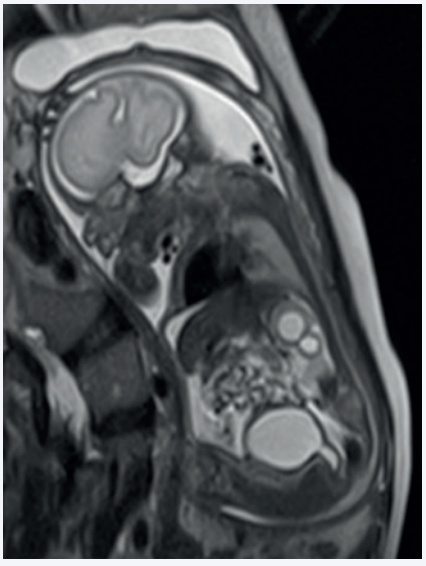
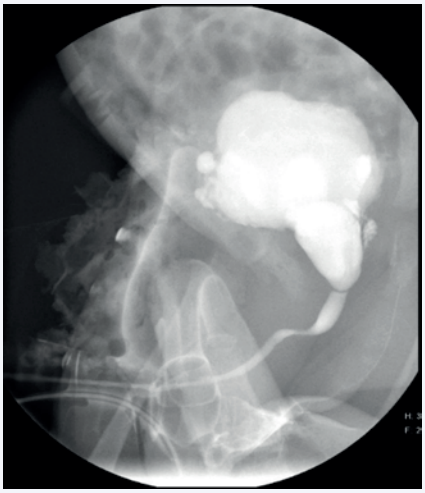


FIGURE 2: Voiding cystourethrogram showing dilatation of the posterior urethra associated with posterior urethral valves, trabeculated bladder and no vesicoureteral reflux.



In the three cases, VCUG after birth surprisingly revealed a PUV. One of these infants rapidly developed a particularly severe clinical outcome with a progressive abdominal distention within the first 10 days of life. US showed a large amount of ascites, left unilateral hydroureteronephrosis and perirenal urinoma. VCUG revealed a dilated posterior urethra, a large trabeculated bladder, high-grade VUR on the left side with peritoneal extravasation of contrast medium.

Patients with normal antenatal screening (Group 2, n=19)

Nineteen patients (38%) had a normal antenatal US. They were diagnosed of PUV during the imaging work-up of urinary tract infection (UTI) in 16 patients (84%) and voiding disorders in 2 patients (11%). One patient was fortuitously discovered during prematurity imaging investigations. Median age at diagnosis was 9 months (IQ range: 3 months to 6 years). Preoperative urinary tract US were normal in 6 children (32%), while different grades of hydronephrosis were found for the remaining 13 patients (68%). The diagnosis of PUV was confirmed by VCUG in all patients and VUR detected in 9 cases (47%).

Long term renal and bladder function

Renal function at last follow-up is reported in Table 2. Median follow-up was 8 years (IQ range 3 to 13 years). A total of 29 patients (58%) had a normal renal function, with the same proportion in Group 1 and 2 (p-value 1). A total of six patients (12%) reached a GFR < 60 ml/min/1.73m², and three children progressed to KFRT, all from Group 1 (p-value 0.07).

The presence of voiding disorders (such as urinary incontinence and/or urgency, poor urinary stream or the need of clean intermittent catheterization), was found in 19 patients (61%) out of the 31 children investigated whom this information was available (20 from Group 1, 11 from Group 2).

In Group 1, 14/20 (64%) children had a voiding disorder: 10 urinary incontinence, 2 poor urinary stream and 2 intermittent catheterization.

In Group 2, 5/11 (45%) children presented a voiding disorder such as urinary incontinence and/or urgency.

Although children in Group 1 tend to have more frequently a voiding disorder as compared to children in Group 2, the difference is not statistically significant.

TABLE 2: Renal function at last follow-up.

1999-2003	Total (n=50)	Group 1 (n=31)	Group 2 (n=19)	p-value
Normal renal function	29 (58%)	18 (58%)	11 (58%)	1
CKD grade 2	15 (30%)	7 (23%)	8 (42%)	0.2
CKD grade 3	2 (4%)	2 (6%)	0	0.07
CKD grade 4	1 (3%)	1 (3%)	0	
RRT	3 (6%)	3 (10%)	0	
Follow-up, median (IQ range)	8 years (3 to 13)	8 years (4 to 13)	8.5 years (3 to 12)	

CKD = chronic kidney disease; GFR = glomerular filtration rate; RRT = renal replacement therapy; £CKD grade 2 (GFR < 90 ml/min/1.73m²); CKD grade 3 (GFR < 60 ml/min/1.73m²); CKD grade 4 (GFR < 30 ml/min/1.73m²).

Discussion

PUV represent the most common cause of congenital lower urinary tract obstruction in boys (1, 2). This pathology constitutes a clinical spectrum ranging from early presentation with severe renal dysplasia to late diagnosis due to mild lower urinary tract symptoms and recurrent UTI (3, 4) .

PUV are commonly suspected on routine prenatal screening US. The classical findings are bilateral hydroureteronephrosis, with enlarged bladder and, occasionally, a dilated posterior urethra taking the aspect of a keyhole (4-6). The prognosis is often relatively easy to predict in severe cases, such as antenatal presentation before 24 weeks, with oligohydramnios and increased cortical echogenicity (10). In those situations perinatal death often occurs secondary to pulmonary hypoplasia and renal failure (6). In partial obstruction, the outcome is less predictable. Fetal urinary electrolytes and β-2 microglobulin are the most used biological markers to predict post-natal renal function. Raised urinary osmolality and a β-2 microglobulin greater than 4 mg/L suggest the worst case scenario (11). The ongoing European ANTENATAL study has been designed to validate fetal urine biochemistry such as proteomics and metabolomics in order to predict postnatal renal function in fetuses with PUV (12). The results of this large multi-centric study are pending.

In developed countries, approximately one-third to one-half of PUV cases are identified by antenatal US (1, 2). A 2014 prospective national cohort study in the UK reported that about one third of PUV cases were diagnosed antenatally, and two third afterwards. Although it was expected that antenatal diagnosis would increase over time, the authors observed that the proportions remained mostly unchanged in the last 30 years (1). In our cohort more than 60% of PUV patients were diagnosed in utero. This better figure of antenatal diagnosis rate is potentially explained by the fact that in Belgium pregnancies are followed with minimum 3 antenatal US.

While the classic antenatal presentation of PUV is bilateral hydroureteronephrosis with enlarged bladder, the proportion of patients showing different images is far less described.

In our cohort, unsurprisingly 90% of antenatally diagnosed cases presented classically.

Noteworthy, two of them presented with bladder rupture and extravasation of urine resulting in urinary ascites. This phenomenon due to the high pressure in the urinary tract has been reported in about 15% of neonates with PUV and is considered a protective pop-off mechanism (13-15). Although we report only two patients, in line with the literature, they both progressed satisfactorily in terms of renal and bladder function after more than 12 years of follow-up.

Moreover, our study shows that 10% of patients had an uncommon antenatal presentation. They were not suspected of PUV as they presented with a unilateral upper urinary tract dilatation without any other signs of LUTO. One of them rapidly developed a major complication soon after birth and before the programmed postnatal US scan.

In our tertiary care center, PUV patients with normal fetal scans represent nearly 40% of the cases. This figure is in accordance with an Australian report (2). However, although UTI was the leading

presentation for 80% of our patients postnatally diagnosed, it only represented 50% in the Australian cohort.

Delayed PUV cases usually present less severe obstructions with minimal impact on the urinary tract and may therefore remain silent for years (3). Brownlee et al. demonstrated that cases diagnosed postnatally have smaller hydronephrosis and less renal dysplasia when compared to antenatally diagnosed obstructions (1).

The median follow-up in our cohort is 8 years. In accordance with a North-American study with a similar median follow-up, the number of patients with normal renal function and very mild CKD, were not significantly different between the antenatally and postnatally diagnosed groups (16). However, when we look at the most severe CKD, the figures are different. In the first group, almost 20% of children reached a GFR < 60 ml/min/1.73m², and 10% progressed to KFRT. During the same follow-up period, none from the postnatally diagnosed group reached a CKD grade 3. Our data are consistent with the literature which shows that about 20% of patients with PUV reach KFRT sometimes even decades after the initial presentations (3). According to Engel et al, patients with later diagnosis progress to KFRT in 10% of cases (17).

In literature, the incidence of bladder dysfunction in PUV patients varies widely, from 13% to 38% and may be suspected in cases of recurrent UTI and/ or voiding dysfunction (4). Infants with valve bladders have detrusor hypertrophy. This will cause poor bladder compliance and detrusor overactivity, reducing functional bladder capacity and causing incontinence. In the more favorable scenario, bladder capacity increases with age and overactivity disappears (18).

In the least favorable scenario, secondary bladder outlet obstruction due to bladder neck hypertrophy will lead to elevated residual bladder volumes and increased storage pressures. This will ultimately lead to myogenic failure (19).

In our cohort, more than 60% of children older than 5 years of age, whom this information was available, presented voiding disorders, slightly more in those diagnosed antenatally. This could be explained by the fact that children diagnosed postnatally have less severe obstructions with minimal impact on the urinary tract.

Conclusions

With 60% of PUV cases diagnosed antenatally, this study shows an improvement in fetal screening for this condition. Although most of those fetuses showed the classic antenatal presentation, 10% presented a unilateral dilatation without any sign of LUTO. While the number of patients with normal renal function and mild CKD did not differ between the antenatally and postnatally diagnosed groups, one fifth of the children in the first group achieved a GFR < 60 ml/min/1.73m² with ten percent of them needing renal replacement therapy. During the same follow-up period, none from the postnatally diagnosed group reached a CKD grade 3. Children diagnosed antenatally showed the most severe prognosis in terms of both renal and bladder function.

The authors have no conflicts of interest to declare with regard to the topic discussed in this manuscript.

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