Original Article

The Long-Term Prognosis of Posterior Urethral Valve in Neonate in North of Iran, a More than Ten Years' Experience from a Tertiary Referral Center

Hamid Mohammadjafari[1] Samaneh Ahangardarabi[2] *Shabnam Shafaee[3]

1- Antimicrobial Resistant Nosocomial Infection Research Center, MazandaranUniversity of Medical Sciences, Sari, Iran
2- Department of Pediatrics, School of Medicine, Mazandaran University of Medical Sciences, Sari, Iran
3- Booali Hospital, School of Medicine, Mazandaran University of Medical Sciences, Sari, Iran

*Shabnamshafai@yahoo.com

(Received: 16 Jan 2015; Revised: 10 Apr 2015; Accepted: 5 May 2015)

Abstract

Background and purpose: Posterior urethral valve (PUV) is one of the most severe urinary tract anomalies presenting as antenatal hydronephrosis that could lead to severe dilatation and functional impairment of one or both kidneys. The aim of this study was to analyze our experience on patients with a diagnosis of PUV.

Materials and Methods: In this prospective study neonates with a diagnosis of PUV were enrolled. The patients were assessed clinically for growth and hypertension and other clinical complaints specially voiding dysfunctions. Urinary tract ultrasonography study, functional renal scan, and voiding cystourethrography performed periodically. The patients were assessed for occurrence of hypertension, growth disturbances, long term urinary tract dilatation, persistence of vesicoureteral reflux (VUR), recurrent urinary tract infection (UTI), nephrolithiasis, voiding dysfunction, scar formation chronic renal failure (CRF) and finally death.

Results: A total of 24 children with PUV were enrolled, 18 (75%) had VUR. The mean standard deviation score for height to age was −0.10. Hydronephrosis was persisted in 22 (86%) of patients. VUR was resolved in 9 (56%). UTI was found in follow-up of 15 patients, 10 of them had recurrent episodes. Nephrolithiasis was found in 8 (33%), persistent renal damage in 14 (70%) and CRF in 9 (37.5%) of patients, 5 of them had end-stage renal disease. Voiding dysfunction was observed in 5 (36%) of patients, enuresis in 3 (21%) of them. Two patients were died in the course of disease.

Conclusion: PUV is an important obstructive process with potential long-term complication with the need to assess the patients for long periods of time.

*[Mohammadjafari H, Ahangardarabi S, *Shafaee Sh*.* **The Long-Term Prognosis of Posterior Urethral Valve in Neonate in North of Iran, a More than Ten Years' Experience from a Tertiary Referral Center**. *IJHS 2015; 3(2): 1-6] http://jhs.mazums.ac.ir*

Key words: Posterior Urethral Valve, Hydronephrosis, Urinary Tract Infection, Scar

1. Introduction

Posterior urethral valve (PUV) is one of the most severe urinary tract anomalies presenting as antenatal hydronephrosis (AH) (1,2). AH may found in 0.5-2% of sonographic studies of pregnant woman, 3.5% of AH is due to PUV (3). The cause of obstruction is presence of a unidirectional valve in PU (4). The valve prevents passage of urine from bladder to distal parts of urethra (5-7). The obstruction could lead to severe dilatation and functional impairment of one or both kidneys (8). The disease may presents at neonatal period as urinary tract infection (UTI) and sepsis, urinary stream disturbances, palpation of distended bladder by parents or physicians and finally renal failure (8,9). But, the most common presentation is prenatal severe bilateral hydronephrosis on gestational ultrasound studies (9). Almost all patients need to early surgical intervention at 1st days of life (8). The long term consequences of PUV are very different (10). The most severe complication is functional renal impairment and hypertension (8). The associated 30-50% prevalence of vesicoureteral reflux (VUR) may lead to UTI (8,11). Another late complication of PUV is voiding dysfunction such as enuresis, incontinence and other difficulties in urination (12-16). In this study, we analyzed our 10 years experiences on patients with diagnosis of PUV.

2. Materials and Methods

This prospective study was approved by the Ethics Committee of Mazandaran University of Medical Sciences, Iran, and was performed between December 2003 and August 2014. All neonates with a diagnosis of PUV were enrolled in the study. We enrolled all neonates with this anomaly and therefore our sample size was the number of patients managed by our center. PUV was clinically suggested by the occurrence of severe bilateral AH, UTI, sepsis or urinary stream impairment and finally palpation of distended bladder by physician or parents. The diagnosis was more suggested by finding bilateral hydroureteronephrosis and bladder hypertrophy and finally was confirmed by voiding cystourethrography (VCUG) and cystoscopic finding of valve. All patients with a clinical diagnosis of PUV were admitted, and appropriate antibiotics were administered intravenously. An ultrasonography study (US) with a siemens G-50 scanner and 2-5 MHz curved-array transducer was performed on all patients. For confirming diagnosis of PUV and VUR, conventional VCUG was performed for all neonates with such history. The diagnosis of PUV was made by finding PU dilatation and valve appearance on voiding phase of graphy. The severity of VUR was classified as Grade 1-5 according to international classification. Kidney scintigraphic imaging by ^{99m}Tc-dimercaptosuccinic acid (DMSA) was used for assessment of parenchymal involvement. The scan was performed using a tomographic gamma camera (Siemens DH E-CAM) with a low-energy high-resolution collimator. We followed patients for long term complications. The patients were visited every 1-3 months. In each visit, the patients were assessed clinically for growth and hypertension and other clinical complaints specially voiding dysfunctions. The imaging studies performed periodically, urinary tract US every 3-6 months and VCUG 12-18 months until complete recovery of VUR and PUV.

We assessed long term complications as occurrence of hypertension, growth disturbances, long term urinary tract dilatation, persistence of VUR, recurrent UTI, nephrolithiasis, voiding dysfunction, scar formation chronic renal failure (CRF) and finally death. Hypertension was defined as systolic or diastolic blood pressure more than 95th percentile based on age, sex and height. Growth assessed by measuring height standard deviation score (SDS) on 1-year of

age. Severity of VUR and hydronephrosis assessed by serial VCUG and US and presents as; worst severity, not changed, improvement and complete recovery. UTI was clinically suggested by the occurrence of fever with or without urinary symptoms, and was confirmed by urinary examination and culture. Urine analysis was considered positive based on the presence of one or more of the following indices: Pyuria, bacteriuria, positive leukocyte esterase, or positive nitrite. UTI was confirmed by positive urine culture, based on the route of urine collection: $>10^5$ colony counts for midstream collection, $>10^3$ colony counts for catheter collection, and any colony count for the suprapubic method of examination. The occurrence of three or more episode of UTI was considered as recurrent UTI. Nephrolithiasis was defined as finding of urinary tract densities with more than 2 mm size and posterior shadow on serial US. Voiding dysfunction and enuresis was assessed by history obtaining from parents or caregiver in more than 6 years old children the scar formation was shown by finding a permanent volume loss on DMSA scan. CRF was defined as glomerular filtration rate <60 ml/min/1.73 m^2 or plasma creatinine more than 1 mg/dl for more than 3 consecutive months. In this study, categorical variables are expressed as percentages, while continuous variables are expressed as mean ± SD or median (25-75th quartiles). All statistical analysis was performed using SPSS software (version 16, SPSS Inc., Chicago, IL, USA).

3. Results

Basic and demographic data 24 children with PUV were enrolled in this study all of them were male. Some basic data were shown in table 1.

The VUR was observed in 18 (75%) of patients, 2 (8%) in right kidney, 2 (8%) in the left kidney and 14 (58%) had bilateral reflux.

UTI was found in the follow-up of 15 patients, 10 of them had recurrent episodes. The most common microorganism was Escherichia coli (Table 2).

Table 1. Clinical findings of patients with PUV

Characteristics	Values
Gestational maturity: N (%)	
Term	20 (83)
Preterm	4 (17)
Type of delivery: N (%)	
Vaginal	0
Cesarian	24
Type of delivery: N (%)	3288 ± 366 g
12 months height to age SDS (Mean ± SD)	-0.42 ± 1.6
Final height to age SDS (Mean ± SD)	-0.76 ± 2.2
Total follow-up time (Mean ± SD)	62.9 ± 38.2 months

PUV: Posterior urethral valve, SD: Standard deviation, SDS: Standard deviation score

Table 2. Some clinical long term complications of patients with posterior urethral valve

Complication	N (%)
UTI number	
0	9 (37)
1	3 (13)
2	2 (8)
3 or more	10 (42)
UTI germ	
E. coli	9 (60)
Coagulase negative staph	3 (20)
Pseudomonas	2 (13)
Klebsiela	1 (7)
Hypertension	4 (17)
Voiding dysfunction	5/14 (36)
Enuresis	3/14 (21)
Nephrolithiasis	8 (33)
Scar on DMSA scan (n=20)	6 (30)
1	0(0)
2	3 (15)
3	1 (5)
4	10 (50)
Chronic renal failure	9 (38)
Death	2 (8)

UTI: Urinary tract infection, E. coli: Escherichia coli, DMSA: Dimercaptosuccinic acid

Hypertension was reported in 4 (17%) of patients, no one had any evidence of end organ damage (Table 2). The mean SDS for height to age centile was -0.42 at 12 months and -0.10 at the end last visit (at the mean age of 63 months) (Table 2).

The long term urinary tract ultrasonographic findings showed that the significant hydronephrosis was persisted in 17 (71%) of patients and 4 (17%) patients had normal sonographic findings without any degree of hydronephrosis (Table 3).

The long term VCUG was available in 16 patients. VUR was resolved in 9 (56%) of patients without antireflux surgery and 7 (44%) patients had persistent VUR (Table 4).

Table 3. First weak and long term sonographic findings of patients with posterior urethral valve

Grade	First postnatal sono (%)	Last postnatal sono (%)
0	2 (8)	4 (17)
1	1 (4)	3 (13)
2	2 (8)	8 (33)
3	5 (21)	5 (21)
4	14 (58)	4 (17)

Table 4. First weak and long term cystographic findings of patients with posterior urethral valve

Grade	First VCUG (n = 24) (%)	Last VCUG (n = 16) (%)
0	6 (25)	9 (56)
1	0(0)	0(0)
2	0(0)	0(0)
3	1 (4)	1 (6)
4	3 (13)	0(0)0
5	14 (58)	6 (38)

VCUG: Voiding cystourethrography

The nephrolithiasis was found in 8 (33%) of patients with a size of 5-7 mm, none of them need to extracorporeal shock wave lithotripsy/surgery.

The DMSA was performed in later months of life for 20 patients in a mean age of 13.2 months. The persistent renal damage (scar) was found in 14 (70%) of patients 11 of them was of severe form, 7 with unilateral scar, 2 with bilateral severe scar and 2 with bilateral scar severe in one side and milder in another kidney. CRF was the late consequence of 9 (37.5%) of patients, 5 of them had end stage renal disease (ESRD). Renal replacement therapy with peritoneal dialysis was planned for 4 patients. Voiding dysfunction was assessed in 5 (36%) of 14 patients with more than 5 years age. 9 children had normal voiding patterns, enuresis was reported in 3 (21%) of them. Two patients were died in the course of disease.

4. Discussion

PUV is an important obstructive process in perinatal period both for acute renal functional impairment and for late complications (17-21). We assessed the course of PUV in our center for more than a decade. Overall the 24 patients in our center had a reasonable growth status, two patients died because of disease process and in one third the obstruction lead to chronic renal function impairment. We reported the prevalence of nephrolithiasis in our patients. 8 of our patients had nephrolithiasis with no need to interventional procedure. The long term status of urinary tract and the potency to UTI development was assessed widely. Kabir et al. in a prospective study included 24 PUV patients who were diagnosed prenatally found that during follow-up, VUR resolved in 4 (16.6%), downgraded in 4 (16.6%), and persisted in 3 (12.5%) patients (22). Caione and Nappo studied 24 more than 18-year-old patients with a history of PUV. He reported that VUR was present in 15 patients (62.5%): Six unilateral, associated with poor renal function and 9 (37.5%) bilateral (15). Ansari et al. assessed the role of patient factors on renal damage in PUV patients and compared those who developed ESRD (Group 1) and those who did not (Group 2). They found that bilateral high-grade VUR (63% vs. 34%) and severe bladder dysfunction which was more prevalent in Group 1 (78% vs. 19%) were risk factors of renal dysfunction progression but recurrent febrile UTI (37% vs. 34%) did not show any negative effect on renal outcome (13). In our study, significant hydronephrosis and VUR was persisted in 17 (71%) and 7 (44%) patients respectively. UTI

was found in follow-up of 15 patients, 10 of them had recurrent infection. We found no significant relation between recurrent UTI and kidney permanent damage. Renal failure development and scar formation is important long term morbidity in the patients. We performed DMSA scan in 20 patients 70% of them had scar formation. 9 patients showed clinical and laboratory findings of CRF 5 of them had ESRD with need to renal replacement therapy. Sarhan et al. at a median follow-up time of 3.6 years in 120 patient with diagnosis of PUV showed that renal failure developed in 44 patients (36.5%) with ESRD in 18. Serum creatinine at hospital admission, nadir serum creatinine, initial creatinine clearance and renal parenchymal echogenicity were significant predictors of the final renal outcome patient age at diagnosis (2 or less vs. >2 years), upper tract dilatation, the presence or absence of VUR, popoff mechanisms and bladder dysfunction had no significant impact on future renal function (16). Among the 24 patients reported by caione, 5 developed ESRD (20.8%): 3 of them (12.5%) received successful renal transplantation. A total of 13 patients (54.1%) had CRF and 9 patients (37.5%) presented systemic arterial hypertension (15). The incidence of ESRD was reported as 12% and 20% in two other studies (12,22). Diurnal and bedtime urinary incontinence is a common functional disorder in PUV patients. f et al. reviewed the records of 59 boys with PUV who underwent renal transplantation. They noted overlapping signs of bladder dysfunction in 18 boys (55%), of whom 11 performed intermittent catheterization or had increased post-void residual urine, 4 had severe urgency, 4 had day time incontinence and 7 had nocturnal incontinence. Bladder dysfunction did not predict increased graft loss (23). Bladder dysfunction was noted in 36 of 102 (35%) toilet trained boys by Sarhan et al. (16). Caione found that lower urinary tract symptoms were observed in 7 out of 24 patients (29.1%). Detrusor over activity and reduced compliance were detected by pressure-flow study in 5 patients (20.8%) (15). Diurnal voiding dysfunction was noted in 5 (36%) of our older patients 3 of them had nocturnal enuresis. PUV is an important obstructive process with potential functional influences on kidney and bladder. It is mandatory to assess the patients for long periods of time.

Acknowledgement

The authors are very grateful to the personnel of pediatric nephrology ward of Booali Hospital for their kindly contribution in the study and the patients and their parents for their helpful participation.

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