Journal of Pediatric Urology (2018) xx, 1.e1–1.e6

Active surveillance for antenatally detected ureteroceles: Predictors of success

V. Andrioli [a,b,c], L. Guerra [a,b,c], M. Keays [a,b,c], D.T. Keefe [a,b], K. Tang [c], K.J. Sullivan [a,c], K. Garland [b], M. Rafikov [a,b], M.P. Leonard [a,b,c]

[a]Division of Urology, Department of Surgery, Children's Hospital of Eastern Ontario, Ottawa, Canada

[b]Faculty of Medicine, University of Ottawa, Ottawa, Canada

[c]Children's Hospital of Eastern Ontario Research Institute, Ottawa, Canada

Correspondence to: M.P. Leonard, Division of Urology, Department of Surgery, Children's Hospital of Eastern Ontario, 401 Smyth Rd, Ottawa, ON K1H 8L1, Canada

mleonard@cheo.on.ca (M.P. Leonard)

Keywords
Ureterocele; Pediatric urology; Duplex system; Conservative management

Received 10 November 2017
Accepted 5 February 2018
Available online xxx

Summary

Introduction
Historically, ureteroceles were surgically treated, as patients were diagnosed after developing symptoms. However, with the advance of fetal medicine, antenatal detection has provided an opportunity to look at the natural history of ureteroceles.

Objectives
With data derived from a retrospective chart review of patients with ureteroceles that were detected antenatally, the current study aimed to determine which group of children would be at risk for failure on active surveillance. It was hypothesized that single system ureteroceles (SSU) and male patients with duplex system ureteroceles (DSU) would be ideal for observation.

Methods
Outcomes were assessed by descriptive statistics. Kaplan–Meier curves were utilized to estimate median duration on active surveillance in both single and duplex cohorts. Breakthrough febrile urinary tract infection (fUTI) and surgery were determined by Cox regression in the duplex system cohort. Surgery was considered surveillance failure.

Results
A total of 102 patients (64 females/38 males) met the criteria: 78 (76.5%) had DSU and 24 (23.5%) SSU. The overall median observation was 1.2 years (range 0.7–3.1). Follow-up ranged from 0.3 to 11.7 years for SSU, and from 0.02 to 17.3 years for DSU. The predictors of failure of active surveillance (AS) in DSU (surgical intervention) were male gender (HR 1.8, 1.0–3.3, $P = 0.037$), or fUTI (HR 3.1, 1.7–5.8, $P = 0.002$). Predictors of fUTI were contralateral hydroureter or ipsilateral hydronephrosis ± hydroureter (OR 9.5, 1.2–71.7, $P = 0.028$). Interestingly, vesicoureteral reflux (VUR) was not a predictor of fUTI. The SSU patients were ideal for AS, while in DSU, surveillance was successful in 30% of patients who were primarily females without contralateral hydroureter or ipsilateral hydronephrosis ± hydroureter. However, in contradiction to the hypothesis, males were at higher risk for surgical intervention in the DSU cohort.

Conclusion
Active surveillance is an option for patients with antenatally detected ureteroceles, but careful long term follow up is mandatory. Parents should be advised that surgical intervention may still be necessary, particularly in males with DSU.

Summary table

Patient characteristics	Total, $n = 102$	SSU, $n = 24$	DSU, $n = 78$
Gender	Female	6	58
	Male	18	20
Circumcision	Yes	5	4
	No	11	13
	Not reported	2	3
Interval on AS	252 days	100 days	7 days to
	to 3.1 years	to 11.2 years	17.2 years
Hydronephrosis of the	No	N/A	11
lower moiety (ipsilateral	Hydronephrosis only	N/A	47
to ureterocele)	Hydroureteronephrosis	N/A	20
Ipsilateral reflux (any grade)		4	34
Surgery	Male	5	17
	Female	0	36

AS, active surveillance; SSU, single system ureterocele; DSU, duplex system ureterocele; N/A, not available.

https://doi.org/10.1016/j.jpurol.2018.02.012

Introduction

Ureteroceles were first described in 1954 by Ericson [1]. They represent a common entity encountered by urologists; however, management is not standardized. The decision of how or whether it is necessary to proceed with surgery for a ureterocele is often left to the discretion of the treating surgeon. Management decisions need to take into consideration multiple factors, including breakthrough febrile UTI (fUTI), VUR, bladder outlet obstruction (BOO) and function/drainage of the renal moiety associated with the ureterocele. Of course, parental preference should also be considered. The goals of management should include: reduction in the number of invasive procedures, prevention of UTI, maintenance of renal function, and promotion of continence and normal bladder function [2].

With the advance of prenatal imaging, genitourinary abnormalities are often identified in utero, which allows urologists to provide counselling and possibly earlier intervention. There has been a shift in management of many urologic conditions to reduce intervention in favor of surveillance. A prime example of this is the management of unilateral hydronephrosis in suspected UPJ obstruction (UPJO). Koff and Campbell showed that neonates with severe hydronephrosis, even with renal scans suggesting obstruction, are unlikely to require intervention and can be safely observed [3]. Recent evidence has shown that surveillance of select patients, including both single and duplex system ureteroceles, may be a safe alternative to surgery [4–7].

The aim of the current study was to identify predictors of successful active surveillance (AS) of patients with antenatally or postnatally incidentally detected ureteroceles. It was hypothesized that single system ureteroceles (SSU) and male patients would be less likely to require surgery, and thus remain on AS.

Material and methods

Study population

This was a retrospective chart review of patients with antenatal hydronephrosis, who were confirmed by postnatal imaging to have ureteroceles, and diagnosed at the current institution between 1990 and 2015. Four different pediatric urologists were involved in the care of these patients during this time interval. This study was approved by the institutional Research Ethics Board.

Inclusion/exclusion criteria

Patients were selected by ICD codes: ICD-9 CM593.9 or ICD-10 N28.9 (disorder of kidney and ureter, unspecified), ICD-9 CM593.5 or ICD-10 N13.4 (hydroureter) and ICD-9 CM753.29 or ICD-10 Q62-64 (congenital obstructive defects of renal pelvis and congenital malformations of ureter). These particular ICD codes were chosen with the intent to include all patients with antenatally detected hydronephrosis.

To be included, patients must have had both postnatal ultrasound (US) and VCUG reports available for review. Hydronephrosis was subjectively reported as 'mild, moderate or severe' by the attending radiologist. Use of the SFU hydronephrosis grading system [8] was not widespread amongst the radiologists at the institution during this time frame, and was therefore not routinely recorded. All patients with duplex systems had some degree of dilatation of the moiety subtended by the ureterocele. Not all patients with SSU had hydronephrosis reported; however, when it was noted, the same criteria mentioned above were used. Patients with BOO or obstruction of a functional ($\geq$10–15% relative renal function) renal moiety associated with the ureterocele were not eligible for AS, and surgical intervention was undertaken in either instance. Patients with multicystic dysplastic kidney (MCDK) subtended by a ureterocele, or those who had fUTI as their initial presentation were also excluded.

Patients who were monitored by AS were initially prescribed antibiotic prophylaxis, which was maintained until toilet training was achieved. Follow-up for VUR was performed with either VCUG or nuclear cystogram. Mercaptoacetyltriglycine (MAG-3) Lasix renal scans were also performed during follow-up when patients developed a significant worsening of the degree of hydronephrosis in any renal unit. DMSA scans were performed to assess differential renal function when clinically indicated.

The primary aim of the current study was to determine which surveillance population failed, and required surgery. The secondary aim was to identify risk factors for developing fUTI while on antibiotic prophylaxis. Febrile UTI was defined as an episode of fever with a positive urine culture obtained by clean catch in patients who were toilet trained, or urine obtained by catheterization in those not yet toilet trained.

Analysis

Kaplan–Meier curves were utilized to compare the probability of need for surgery in patients on AS over time within the SSU and duplex system ureterocele (DSU) cohorts. The log-rank test was used to provide statistical comparison.

To examine predictors of fUTI in the DSU cohort, a multivariable logistic regression model was fitted with three *a priori* independent variables of interest: gender, hydronephrosis status, and VUR. For hydronephrosis, three subgroups, which excluded the status of the renal moiety associated with the ureterocele, were established: 1) contralateral hydroureter or ipsilateral lower moiety hydronephrosis $\pm$ hydroureter; 2) contralateral hydronephrosis without hydroureter; and 3) absence of hydroureteronephrosis. A similar analysis for SSU was not possible, as the number of events were inadequate to perform a proper assessment.

For VUR, two subgroups were created for analysis: presence vs absence. Independent analyses for grades of VUR were not feasible, due to the small number of events within each grade of VUR. Interaction terms were not considered and list-wise deletion of cases was performed where there were missing data on any predictor variables. Following model fitting, lack of significant collinearity and influential observations were verified. Effects from regression were expressed as unstandardized parameter

Please cite this article in press as: Andrioli V, et al., Active surveillance for antenatally detected ureteroceles: Predictors of success, Journal of Pediatric Urology (2018), https://doi.org/10.1016/j.jpurol.2018.02.012