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Long-term impact of unilateral hypo/dysplastic kidney in infants with primary vesicoureteral reflux

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Summary

Introduction
Renal abnormality is not a rare finding in infants with primary VUR. The pathophysiology of the renal abnormality is considered to be congenital or acquired. Congenital hypo/dysplastic kidney is a common finding in infants with primary VUR, especially in boys. However, the long-term impact of unilateral hypo/dysplastic kidney has not been elucidated. The aim of the current study is to clarify the long-term impact of unilateral hypo/dysplastic kidney with primary vesicoureteral reflux diagnosed in infancy.

Material and methods
The medical records of patients with primary VUR detected in infancy with unilateral hypo/dysplastic kidney on initial nuclear renal scan (<40% relative renal function) and no scar on the contralateral kidney were reviewed retrospectively. Among them, 29 patients who were followed for more than 5 years were included in this study. Their clinical outcomes including chronic kidney disease (CKD) stage using estimated glomerular filtration rate (GFR) and the incidences of hypertension and proteinuria were analyzed.

Results
Mean age at final visit was 12.4 years (range 5.9–22.2). Estimated GFR was evaluated in 26 patients at a mean age of 12.0 years (5.9–22.2). CKD stage was 1 in all. According to the guidelines of the Japanese Society of Hypertension, while none exceeded the standard level of systolic blood pressure (BP), two patients slightly exceeded the standard level of diastolic BP. In addition, no significant proteinuria was detected in all patients, although microalbuminemia was detected in 7.7% of patients.

Discussion
The prognosis of reflux nephropathy depends on the remnant renal tissue mass, that is, the number of normal nephrons. The normal congenital solitary kidney is reported to be hyperplastic with normal-sized glomeruli rather than hypertrophic ones with larger nephrons, and to have better long-term outcome regarding renal function. Accordingly, we speculated that patients with unilateral hypo/dysplastic kidney would have a similar number of nephrons to those without hypo/dysplastic kidney who have no or minimal scar as far as the contralateral kidney is well preserved. Long-term outcome of the current retrospective study was consistent with our speculation in terms of estimated GFR, proteinuria, or hypertension.

Conclusions
The present study demonstrated that significant clinical findings related to unilateral hypo/dysplastic kidney detected in infancy were rarely observed in the long term. Accordingly, unilateral hypo/dysplastic kidney seems to be a benign condition. To confirm this finding, further follow-up of these patients is necessary.

Table Clinical outcome in infants with primary VUR and unilateral hypo/dysplastic kidney.

Estimated GFR at final evaluation (n = 26)		92.6–139.6 mL/min/1.73 m^2, (CKD stage was 1 in all)
Hypertension at final evaluation (n = 29)		
	Systolic hypertension	None
	Diastolic hypertension	2
Proteinuria at final evaluation	Proteinuria on dipstick (n = 29)	None
	Microalbuminuria (>30 mg/gCr) (n = 26)	2 (7.7%) (33.6 mg/gCr, 39.0 mg/gCr)

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Introduction

Primary vesicoureteral reflux (VUR) is the most common congenital anomaly of the urinary tract. In infancy, VUR is commonly diagnosed following demonstration of prenatally detected dilatation of the urinary tract or during investigation of urinary tract infection (UTI). Renal abnormality on ultrasonography or a nuclear renal scan has been reported in 12–50% of patients with VUR detected in infancy [1–5]. The pathophysiology of the development of these renal abnormalities is considered to be congenital or acquired [6,7]. Congenital small kidney with decreased renal function is a common finding in infants with high-grade primary VUR, especially in boys. In contrast, focal loss of renal contours of cortical uptake or cortical thinning is considered by many to be an acquired renal scar [6–8]. Whereas acquired renal scarring is recognized to be the result of an acute inflammatory reaction resulting from a febrile urinary tract infection, a congenital renal lesion is known to be a developmental abnormality that is recognized as hypo/dysplastic kidney histologically [6,7,9].

Reflux nephropathy is reported to be an important cause of hypertension, proteinuria, and chronic kidney disease (CKD) with progressive renal failure [7,10]. However, as congenital and acquired renal lesions originate from different pathogeneses, the clinical impacts such as hypertension, proteinuria, and renal function might differ between them in the long term. As a congenital solitary kidney is reported to be hyperplastic, not hypertrophic [11], the kidney contralateral to the unilateral hypo/dysplastic kidney might be hyperplastic. Accordingly, we speculated that patients with unilateral hypo/dysplastic kidney might have a good clinical prognosis under proper management of VUR based on previous literature showing that patients with congenital solitary kidney had better prognoses than those with acquired solitary kidney [12]. Although unilateral hypo/dysplastic kidney with VUR is a relatively common finding, the long-term impact of unilateral hypo/dysplastic kidney with VUR has not been elucidated. In the present study, we evaluated the long-term clinical outcome in infants with primary VUR and unilateral hypo/dysplastic kidney to clarify the impact of unilateral hypo/dysplastic kidney in the long term.

Materials and methods

The medical records of 105 patients with primary VUR detected before 1 year of age who were referred from February 1989 to October 2008 were reviewed retrospectively. They received a routine nuclear renal scan as initial evaluation after VUR was detected. Among them, patients with hypo/dysplastic kidney on the initial nuclear renal scan (<40% relative renal function), with no scar on the kidney contralateral to the hypo/dysplastic kidney confirmed by initial dimercaptosuccinic acid (DMSA) renal scintigraphy with routine single-photon emission computed tomography (SPECT) [13,14], and with more than 5 years follow-up, were included in the present study. Patients who were suspected of having secondary VUR caused by neurogenic bladder or posterior/anterior urethral valve, or who had concomitant congenital solitary kidney or hydronephrosis caused by ureteropelvic junction obstruction or ureterocele, were excluded.

All patients were followed with conservative management with continuous antibiotic prophylaxis (CAP) initially. The timing of discontinuation of CAP varied depending on physician preference and parental opinion, usually at 1–2 years after diagnosis of VUR. Patients were followed through our outpatient clinic at varying intervals, depending on gender, age, and duration since stopping CAP [15]. Regular follow-up was recommended until puberty. Urine analysis and blood pressure were estimated at regular visits. Laboratory investigation and DMSA renal scintigraphy were indicated every 4–6 years unless the patients suffered febrile UTI. The indication for surgical management was recurrent febrile UTI or parents' preference in patients

Table 1 Patient characteristics.

Gender	Boy: 28; girl: 1				
Age at presentation (months)	0.1–9.5 (mean 4.5)				
Presented symptoms	Febrile UTI: 25; abnormality on antenatal ultrasonography: 4				
VUR laterality	Unilateral: 13; bilateral: 16				
Initial VUR grade	I	II	III	IV	V
Hypo/dysplastic unit	2	1	6	8	12
Contralateral unit	3	7	1	2	3
Relative renal function of hypo/dysplastic unit on initial nuclear renal scan (%)	3.0–39.8 (mean 25.7)				
Age at final DMSA renal scintigraphy (years)	3.3–21.2 (mean 10.8)				
Clinical course of VUR	Spontaneous resolution		Open anti-reflux surgery	Subureteral collagen injection	Persisted on final VCUG
Hypo/dysplastic unit	5		7	1 (failed)	16
Contralateral unit	9		2		5
Age at final visit (years)	5.9–22.2 (mean 12.4)				
Follow-up period (years)	5.6–21.6 (mean 12.0)				