Renal outcome of children with unilateral renal agenesis

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The aim of this study was to evaluate associated urological anomalies and renal outcome in children with unilateral renal agenesis (URA). Medical records of 51 cases of URA followed at Şanlıurfa Children's Hospital between January 2009 and December 2012 were reviewed retrospectively. In all patients, diagnosis was made by abdominal ultrasound (US) and confirmed by a radionuclide scan. The children were between 3 months and 17 years of age (median age: 5 years). There were 31 males (60.8%) and 20 females (39.2%). In 33 patients (67.3%), the left kidney was absent. Urological anomalies were found in 12/51 patients (23.5%), including ureterovesical junction obstruction in 4 (7.8%), bladder dysfunction in 2 (3.9%), and vesicoureteral reflux (VUR), ureteropelvic junction obstruction, ureterovesical and ureteropelvic junction obstruction, duplicated collecting system plus grade IV VUR, ectopic kidney plus grade V VUR, and ectopic kidney in 1 patient (2%) each. Chronic renal insufficiency (CRI) developed in 5/51 patients (9.8%) (stage III in 3 patients and stage IV in 2), 4 of whom had additional urological anomaly; in the remaining 1 patient, a 17-year-old female, imaging studies were normal except for a small and hyperechogenic solitary kidney determined on US. A total of 3 patients (5.8%) developed hypertension, and all except one had an associated urological anomaly. Proteinuria was seen in 2 patients (3.8%) with stage IV CRI, one of whom was also hypertensive.

In conclusion, urological anomalies usually accompany URA and should be followed closely to decrease the risk of renal failure.

Key words: unilateral renal agenesis, child, renal failure.

Congenital solitary functioning kidney (CSFK) is among the congenital anomalies of the kidney and urinary tract (CAKUT), which is the leading cause of chronic renal failure in children[1]. CSFK may be due to unilateral renal agenesis (URA), renal aplasia or unilateral multicystic/non-cystic dysplastic kidney (MCDK). URA is defined as the complete absence of renal tissue and a ureter. However, it is known that some cases diagnosed as URA are actually cases of renal aplasia and MCDK that regress spontaneously[2]. URA may be isolated or associated with urological and/or non-urological anomalies[3].

The data based on experimental models of renal mass reduction and clinical observations in patients with solitary kidney show that compensatory renal hypertrophy occurring in the remnant kidney to prevent a decrease in the total glomerular filtration rate (GFR) may predispose to hypertension, proteinuria and premature renal damage. Furthermore, additional urological anomalies in the solitary kidney will accelerate progression to renal failure in early life[4-6].

The objectives of this study were to evaluate associated urological anomalies and renal outcome in children with URA followed in our outpatient clinic.

Material and Methods

The medical records of 51 cases of URA evaluated at Şanlıurfa Children's Hospital between January 2009 and December 2012 were reviewed retrospectively. The diagnosis of renal agenesis was established by ultrasound (US). The absence of renal function was confirmed by a technetium-99m-dimercaptosuccinic acid (DMSA) or Tc-99m-diethylenetriamine penta acetate (DTPA) radionuclide scan. Indications

for a voiding cystourethrogram (VCUG) included the presence of hydronephrosis, hydroureteronephrosis or increased echogenicity of renal parenchyma of the solitary kidney on US and a history of urinary tract infection.

Vesicoureteral reflux (VUR) was graded using the system of the International Reflux Study in Children[7]. Estimated glomerular filtration rate (eGFR) was calculated using the Schwartz formula[8], and levels >90 ml/min/1.73m^2 were considered as normal. In children younger than one year of age, age-specific limits for serum creatinine were used to evaluate renal function[9]. Blood pressure (BP) was measured at each visit. Hypertension was defined as systolic BP and/or diastolic BP ≥95th percentile for sex, age and height on at least three separate occasions or as the use of antihypertensive drugs[10]. Urinalysis was performed in random urine samples by dipstick. If any sample was positive for protein (1"+" or more), protein/creatinine ratio in early morning urine was detected. Values >0.2 mg/mg were considered as positive for proteinuria.

All data are expressed as mean ± standard deviation and median (range) values.

Results

The patient population consisted of 51 children; there were 31 boys (60.8%), with a median age of 60 (range: 3-205) months. Median age at diagnosis was 11 (range: 0-201) months, and median follow-up time was 30 (range: 3-200) months. URA was detected prenatally in 8 patients (15.6%) and incidentally during screening in non-urological anomalies in 9 (17.6%). Presenting symptoms were abdominal pain in 11 (21.5%), urinary tract infection in 7 (13.7%), enuresis in 5 (9.8%), and miscellaneous in the rest of the patients (21.7%). The left kidney was absent in 33 patients (67.3%). A VCUG was performed in 15 cases (29.4%). Urological anomalies were found in 12/51 patients (23.5%), including ureterovesical junction obstruction (UVJO) in 4 (7.8%), bladder dysfunction in 2 (3.9%), and grade III VUR, ureteropelvic junction obstruction (UPJO), UVJO + UPJO, duplicated collecting system + grade IV VUR, ectopic kidney + grade V VUR, and ectopic kidney in 1 patient (2%) each.

Chronic renal insufficiency (CRI) developed in 5/51 patients (9.8%) (stage III in 3 patients and stage IV in 2), 4 of whom had additional urological anomaly: UPJO + UVJO, ectopic solitary kidney + grade V VUR, UVJO, and duplicated collecting system + grade IV VUR in 1 each. In the remaining patient, a 17-year-old female, imaging studies were normal except for a small and hyperechogenic solitary kidney determined on US.

A total of 3 patients (5.8%) developed hypertension, one of whom also had stage IV CRI. In the other patient with grade III VUR, there was a history of recurrent urinary tract infection and renal scarring on DMSA scintigraphy. In the third patient, we did not determine any additional urological anomaly, renal scarring or any factor contributing to the risk of hypertension.

Proteinuria was seen in 2 patients (3.8%) with stage IV CRI, one of whom was also hypertensive (Table I).

Discussion

A significant proportion of the children with CSFK (URA and/or MCDK) have signs of renal injury early in life, such as hypertension, microalbuminuria, or need for renoprotective medications, and they may progress to chronic kidney disease (CKD) in adulthood. The presence of ipsilateral CAKUT increases the risk of progression to CKD[5,6].

In our study, we determined an additional urological anomaly in 12 patients (23%), and three of them had more than one anomaly. Nine patients (9/51) exhibited VUR or obstruction (17.6%). Dursun et al.[3] observed associated urological anomalies in 37% of 87 patients with URA. In this study, the most common urological anomaly was VUR (15%). Song et al.[11] and Cascio et al.[12] found associated urological anomalies in 19 of the 51 patients (37%) and in 22 of the 46 patients (48 %) with URA, respectively. In both series, VUR was more frequent than the other urological anomalies. Calisti et al.[13] observed VUR or obstruction in 11 of 55 patients (19%) with URA (7 VUR, 4 primary megaureter). The incidence of abnormality in that study was similar to ours.

According to the hyperfiltration hypothesis, a reduction in renal mass leads to adaptation

Table I. Demographic, Clinical, and Laboratory Features of Patients

Male (n, %)	31 (60.8)
Median age (month)	60 (3-205)
Median age at diagnosis (month)	11(0-201)
Median follow-up duration (month)	30 (3-200)
Type of anomaly	
UVJO (n, %)	4 (7.8)
Bladder dysfunction (n, %)	2(3.9)
VUR (n, %)	1(2)
UPJO (n, %)	1(2)
UPJO + UVJO (n, %)	1(2)
Renal ectopia + grade V VUR (n, %)	1(2)
Duplicated collecting system +grade IV VUR (n, %)	1(2)
Renal ectopia (n, %)	1(2)
Renal failure (n, %)	5 (9.8)
Hypertension (n, %)	3 (5.8)
Proteinuria (n, %)	2 (3.8)

UPJO: Ureteropelvic junction obstruction. UVJO: Ureterovesical junction obstruction. VUR: Vesicoureteral reflux.

involving a series of structural and functional changes in both glomerular and tubular components in the remaining nephrons. Glomerular hyperperfusion, hyperfiltration, and high capillary pressure eventuate in glomerular sclerosis, predisposing to the risk of progressive azotemia, proteinuria, and systemic hypertension[14,15]. After this hypothesis was established, the studies dealing with CSFK have been increasingly reported in the literature.

Dursun et al.[16] examined 66 children with URA (n=22), unilateral atrophic kidney, and unilateral nephrectomy, with no renal scar or any urinary tract anomaly of the remaining kidney. In the URA group, they found that the prevalence of hypertension and non-dipping phenomenon in ambulatory blood pressure monitoring (ABPM) was 23% (5/22). The mean 24-hour diastolic BP and the diastolic load were higher in the URA group than in the control group (p=0.039 and p=0.012, respectively). There was no statistically significant difference between the urine microalbumin and microalbumin-to-creatinine ratios in the patient and control groups. However, the GFR was lower and the serum creatinine level was higher in the subgroups of patients than those of the control group. They suggested that a mild renal dysfunction might be associated with CSFK with no renal scar or any urinary tract anomaly.

Seeman et al.[17] investigated 29 children with URA, 14 of whom had an abnormal solitary kidney, with mostly scarring. They reported that only children with abnormalities of a solitary kidney had hypertension, proteinuria, or a reduced renal function. In that study, a reduced renal function was found in 43% and hypertension in 57% of the children with abnormal kidneys. In contrast, children with healthy solitary kidneys had BP and renal function similar to those of healthy children.

Wikstad et al.[18] evaluated the long-term prognosis of adult patients born with URA or uni-nephrectomized in childhood. When compared to the controls, no renal insufficiency or marked increase in arterial BP was observed in the patients with a single kidney, but the GFR declined slowly and significantly during the follow-up period, and significant microalbuminuria was detected in 47%, which was more frequent with a longer follow-up period.

In our study, we determined CRI in 9.8%, hypertension in 5.8%, and proteinuria in 3.8% of the patients, with mostly additional urological anomaly. ABPM and microalbuminuria could not be performed due to the limited diagnostic facilities of our hospital. Both additional urological anomalies and signs of renal injury, including hypertension and proteinuria, were found less frequently in our cases. This situation may result from missing or inadequate data due to the retrospective

design of the study. On the other hand, because our hospital is a local center, the patients with more complex malformations and renal parenchymal injury may have been referred to tertiary medical centers.

In conclusion, urological anomalies usually accompany URA and should be followed closely to decrease the risk of renal failure. The patients with URA should also be carefully monitored for early signs of premature renal damage such as hypertension and microalbuminuria.

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