Unilateral multicystic dysplastic kidney in children

Çağla Serpil Doğan[1], Meral Torun-Bayram[1], Mustafa Devran Aybar[2]

[1]Division of Pediatric Nephrology, Department of Pediatrics and [2]Department of Radiology, Şanlıurfa Children's Hospital, Şanlıurfa, Turkey. E-mail: d.caglaserpil@yahoo.com

SUMMARY: Doğan ÇS, Torun-Bayram M, Aybar MD. Unilateral multicystic dysplastic kidney in children. Turk J Pediatr 2014; 56: 75-79.

This study was performed to evaluate the clinical course and renal outcome of patients with unilateral multicystic dysplastic kidney (MCDK). We retrospectively reviewed the medical records of 59 cases with MCDK followed at Şanlıurfa Children's Hospital between January 2009 and February 2013. The median age of the patients (boys 52.5%) was 31 months (range: 6-197) and the median follow-up period was 23 months (range: 6-111). Forty-two (71.2%) patients were diagnosed antenatally. The MCDKs were found more often on the right side (55.9%). The most frequently associated urological abnormality was contralateral vesicoureteral reflux (VUR) (26.6%). A total of 3 (5%) patients developed chronic renal insufficiency (CRI), 2 of whom had grade IV and V VUR; the other patient with CRI had a small and hyperechogenic contralateral kidney, suggesting dysplasia-hypoplasia, without any urological anomalies on imaging studies. The size of MCDK was unchanged in 20 (34%), had regressed in 26 (44%), and had increased in 9 (15.3%) patients. Total involution was documented in 4 (6.7%) patients. Compensatory hypertrophy occurred in 36/45 (80%) patients, with a mean age of 19.2±8.3 months. Proteinuria and hypertension were detected in 1 (1.7 %) patient each.

In conclusion, abnormalities in the contralateral kidney in patients with MCDK increase the risk of renal failure. An initial investigation for associated urinary tract malformations should be done and the growth and function of the contralateral kidney, hypertension, and proteinuria should be monitored in all children with MCDK.

Key words: multicystic dysplastic kidney, urinary tract abnormalities, renal failure.

Unilateral multicystic dysplastic kidney (MCDK), a variant of renal dysplasia, is one of the commonest abnormalities detected antenatally. The incidence ranges from 1 in 2,200 to 1 in 4,300 live births[1,2]. Associated urinary tract abnormalities, such as vesicoureteral reflux (VUR), pelviureteric junction obstruction (PUJO), and ureterovesical junction obstruction (UVJO), have often been reported in patients with MCDK. Although a nephrectomy of the affected kidney due to concern for hypertension and malignant degeneration was standard procedure in the past, because of the low incidence of hypertension and malignancy and the high rates of spontaneous partial or complete involution, a conservative approach has been taken more recently[3].

This study aimed to evaluate the associated urological anomalies and renal outcome in children with unilateral MCDK who were followed in our outpatient clinic.

Material and Methods

We retrospectively reviewed the medical records of 60 patients with unilateral MCDK who were followed at Şanlıurfa Children's Hospital between January 2009 and February 2013. The diagnosis of MCDK was established by the ultrasound (US) appearance of non-communicating cysts of varying number and size, dysplasia, no parenchymal tissue, and a non-medial location of the largest cyst. The absence of renal function was confirmed by a technetium-99m-dimercaptosuccinic acid (DMSA) scintigraphy in all patients. One patient who was nephrectomized with an indeterminate indication at the age of two years was excluded from the study. The patients were assessed every 3-6 months in

the first year of life and yearly thereafter. US of the urinary tract, blood pressure (BP) measurement, urinalysis, plasma creatinine, and electrolytes analysis were evaluated at each visit. A voiding cystourethrogram (VCUG) was performed when the US showed hydronephrosis, hydroureteronephrosis, or increased echogenicity of the renal parenchyma of the contralateral kidney, or when there was a history of urinary tract infection (UTI). VUR was graded using the system of the International Reflux Study in Children[4]. Compensatory hypertrophy of the contralateral kidney was defined as a renal length of >+2 standard deviations of the mean value of normal kidneys[5]. Complete involution was defined as disappearance of MCDK by renal US.

Estimated glomerular filtration rate (eGFR) was calculated using the Schwartz formula (6); levels >90 ml/min/1.73m^2 were considered as normal. BP was measured by an oscillometric device, and 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[7]. Urinalysis was performed in random urine samples by dipstick. If any sample was positive for protein (1"+" or more), the protein/creatinine ratio in early morning urine was determined, and values of >0.2 mg/mg were considered as proteinuria. Hyperfiltration was defined as eGFR >130 ml/1.73m^2/min[8].

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

Results

Our study population consisted of 59 children, 31 (52.5%) boys, with a median age of 31 months (range: 6–197). The median follow-up was 23 months (range: 6–111). MCDK was on the right side in 33 (55.9%) patients. Forty-two (71.2%) patients were diagnosed antenatally (Table I). The median age at the postnatal diagnosis of the remaining 17 children was 46 months (range: 4–174). In these patients, US was performed due to abdominal pain in 6 (35.3%), UTI in 3 (17.6%), and vomiting and decreased renal function in 1 (5.9%). In 7 (41.1%) patients, indications for US could not be determined from their medical records.

Contralateral Abnormalities

A VCUG was performed in 30 (50.8%) cases. The most frequently associated urological abnormality was contralateral VUR (8/30 - 26.6%): 2 cases in grade II, 3 cases in grade III, 1 case in grade IV, and 2 cases in grade V. One of the patients who had contralateral grade V VUR had a history of recurrent UTI and renal parenchymal scarring in DMSA scintigraphy, but normal renal function. The other patient presented with loss of appetite and vomiting, and right-sided MCDK + contralateral grade V VUR + stage II chronic renal insufficiency (CRI) were detected at the time of admission. The case with grade IV VUR also developed stage III CRI. Five of eight refluxing patients had undergone an anti-reflux procedure (3 subureteric injection, 2 ureteroneocystostomy), and the others resolved spontaneously.

The other urological abnormalities included PUJO in 3 (5%) and UVJO in 1 (1.7%). In 1 patient, we determined right-sided MCDK and crossed non-fused ectopic left kidney (Table I).

Renal Function

Estimated GFR was calculated in 44 of 59 patients, with a median eGFR of 104 ml/min/1.73m^2 (range: 15-200). As mentioned above, a total of 3 (5%) patients developed CRI, 2 of whom had grade IV and V VUR; the other patient had stage V CRI + small and hyperechogenic contralateral kidney, suggesting dysplasia-hypoplasia, without any urological anomalies on imaging studies. Two patients had eGFR >160 ml/min/1.73m^2 but without proteinuria.

Rate of Regression

The size of MCDK was unchanged in 20 (34%), had regressed in 26 (44%), and had increased in 9 (15.3%) patients, with a median follow-up duration of 23 months (range: 6-111). Total involution was documented in 4 (6.7%) patients. Initial sizes of the three completely involuted kidneys were 34, 38 and 26 mm. In the other patient, the initial size of MCDK was not known. The patients with increased MCDK size were followed closely without surgical removal.

Compensatory Hypertrophy

Seven patients with delayed diagnosis had already developed compensatory hypertrophy of the contralateral kidney on admission. Lengths of the contralateral kidneys were available in 45 of the remaining 52 children. Compensatory

hypertrophy occurred in 36/45 (80%) patients, with a mean age of 19.2±8.3 months.

Proteinuria - Hypertension

Proteinuria was detected in 1 patient who developed total involution of MCDK at 7 years of age, with compensatory hypertrophy in the contralateral kidney. Hypertension was found only in the patient with hypoplastic-dysplastic contralateral kidney and stage V CRI (1.7%).

Genital abnormalities were found in 4 children: undescended testes in 3 (5%) and imperforate hymen in 1 (1.7%).

None of the patients developed malignancy during the study period.

Discussion

In the present study, we report a retrospective evaluation of our patients with MCDK. In our study, there was a slightly male predominance (52.5%), and MCDK was found on the right side more frequently (55.9%), contrary to the literature[2].

Approximately one in three patients with unilateral MCDK is found to have an associated urinary tract malformation, and those with contralateral urological anomalies have a higher prevalence of CRI. VUR to the contralateral kidney, which is the only functional kidney in patients with MCDK, is the most common urological anomaly[2,3]. The rates of VUR to the contralateral kidney range from 5%-26% in various studies, and 35%-96% of those patients have low grades of reflux (grade I or II)[9-14]. In the largest study, including 202 cases, in which 143 children underwent VCUG, Aslam et al.[10] found the incidence of VUR to the contralateral kidney to be 19%. Mansoor et al.[12] demonstrated a VUR to the contralateral kidney in 17 of 101 (16.8%) patients. In that study, all patients had a VCUG at the time of the diagnosis. In the present study, of 30 (50.8%) patients who underwent a VCUG, we determined VUR to the contralateral kidney in 8 (26.6%) patients. Twenty-five percent of cases with VUR to the contralateral kidney had low grades of reflux. However, since VCUG was not performed routinely in all cases, we may not have identified all the patients with low-grade VUR.

The necessity or not of a screening VCUG in all patients with MCDK is controversial. In some studies, VCUG is only suggested in patients with suspicious findings on US, such as dilatation of the ureter or pelvis, abnormal appearance of the contralateral kidney, or a history of symptomatic UTI[9,10,15,16].

Other urinary tract abnormalities, such as obstruction, have been described often in

Table I. Demographic, Clinical and Laboratory Features of Patients

Sex (male/female)	31/28
Median age (month)	31 (6-197)
Median follow-up duration (month)	23 (6-111)
MCDK location (n , %)	
Right kidney	33 (55.9)
Left kidney	26 (44.1)
Diagnosis (n, %)	
Antenatal	42 (71.2)
Postnatal	17 (28.8)
Type of anomaly (n, %)	
contralateral VUR	8/30 (26.6)
contralateral PUJO	3 (5)
contralateral UVJO	1 (1.7)
crossed ectopic kidney	1 (1.7)
Renal failure (n, %)	3 (5)
Hypertension (n, %)	1 (1.7)
Proteinuria (n, %)	1 (1.7)

MCDK: Multicystic dysplastic kidney. PUJO: Pelviureteric junction obstruction. UVJO: Ureterovesical junction obstruction. VUR: Vesicoureteral reflux.

patients with MCDK. The rate of UPJO has ranged from 4.1%-15% in the previous studies[11,12,16,17]. UVJO is also reported in 1%-6% of patients with MCDK[11,17]. We detected PUJO and UVJO in 5% and 1.7% of our patients, respectively. Furthermore, even if the contralateral kidney appears normal by radiological studies, it may have subclinical microscopic abnormalities such as dysplasia or hypoplasia[10,12].

Complete involution or a reduction in the longitudinal length of MCDK has been reported predominantly in the first five years of life[10-12,18,19]. The studies show that initial MCDK length is the most important factor for predicting complete involution[11,18,19]. Hayes et al.[18] reported that the involution rates in patients with initial MCDK of <5 cm were significantly higher (p=0.0001). Rabelo et al.[19] demonstrated that a renal length of <62 mm on initial US was predictive of complete involution of the MCDK. Tiryaki et al.[11] suggested that the side of MCDK may affect the involution rate. The authors found that a large MCDK on the left had no chance of involution. However, when both variables (initial MCDK length and MCDK side) were used in a multiple regression model, only size showed a significant correlation with the involution rate. In our study, 4 of 59 (6.7%) patients showed complete involution, and the initial length of MCDK had regressed in 26 (44%) patients during the follow-up period.

Compensatory hypertrophy of the contralateral kidney in patients with solitary or functionally solitary kidney begins *in utero* and continues throughout childhood[3,12,17]. Mansoor et al.[12] determined compensatory renal growth in 66 of 89 (74.1%) patients with MCDK. In 37%, hypertrophy occurred in intrauterine life. In the others, except three, compensatory hypertrophy developed by a mean age of 1.8±1 years. Rabelo et al.[13] evaluated 43 patients with MCDK detected prenatally. In that study, 30% of patients reached compensatory renal growth at one year of age. The authors also found that the estimated median time for compensatory hypertrophy was 30 months (95% confidence interval [CI]: 15-45 months). Alaygut et al.[20] demonstrated that compensatory hypertrophy was completed by 17.5 months of age in solitary kidneys (agenesis, multicystic dysplastic kidney) (odds ratio: 5.06). In the present study, compensatory hypertrophy occurred in 36/45 (80%) patients, at a mean age of 19.2±8.3 months.

The risk of hypertension in patients with MCDK ranges from 0% to 7%[9,10,12-14,16]. Kuwertz-Broeking et al.[9] detected hypertension in 5 of 97 patients, and all of them had renal damage such as scarring or dysplastic parenchyma or reduced renal function in the contralateral kidney. Similarly, Mansoor et al.[12] showed that the risk of hypertension in those with abnormalities in the contralateral kidney increased (p<0.001). The authors also showed that the rate of hyperfiltration (32%) and proteinuria (9.8%), as markers of renal injury, was high in patients with no obvious contralateral abnormalities. In our study, we determined hypertension in 1 (1.7 %) patient who already had stage V CRI and proteinuria in 1 (1.7%) patient with compensatory hypertrophy in the contralateral kidney.

The limitations of our study are its retrospective design and the short follow-up period. Thus, we may have underestimated the findings related to MCDK due to missing or inadequate data or the short follow-up.

In conclusion, as abnormalities in the contralateral kidney increase the risk of failure of the solitary functioning kidney, other investigations, such as VCUG, should be done if there is an abnormal US finding or a history of UTI. The growth and function of the contralateral kidney, hypertension and proteinuria should be monitored in all children with MCDK.

REFERENCES

1. Mallik M, Watson AR. Antenatally detected urinary tract abnormalities: more detection but less action. Pediatr Nephrol 2008; 23: 897-904.
2. Schreuder MF, Westland R, van Wijk JA. Unilateral multicystic dysplastic kidney: a meta-analysis of observational studies on the incidence, associated urinary tract malformations and the contralateral kidney. Nephrol Dial Transplant 2009; 24: 1810-1818.
3. Hains DS, Bates CM, Ingraham S, Schwaderer AL. Management and etiology of the unilateral multicystic dysplastic kidney: a review. Pediatr Nephrol 2009; 24: 233-241.

4. Lebowitz RL, Olbing H, Parkkulainen KV, Smellie JM, Tamminen-Möbius TE. International system of radiographic grading of vesicoureteric reflux. International Study in Children. Pediatr Radiol 1985; 15: 105–109.
5. Konuş OL, Ozdemir A, Akkaya A, Erbaş G, Celik H, Işik S. Normal liver, spleen, and kidney dimensions in neonates, infants, and children: evaluation with sonography. AJR Am J Roentgenol 1998; 171: 1693-1698.
6. Schwartz GJ, Haycock GB, Edelmann CM Jr, Spitzer A. Simple estimate of glomerular filtration rate in children derived from body length and plasma creatinine. Pediatrics 1976; 58: 259-263.
7. National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents. Pediatrics 2004; 114: 555–576.
8. Schwartz GJ, Work DF. Measurement and estimation of GFR in children and adolescents. Clin J Am Soc Nephrol 2009; 4: 1832-1843.
9. Kuwertz-Broeking E, Brinkmann OA, Von Lengerke HJ, et al. Unilateral multicystic dysplastic kidney: experience in children. BJU Int 2004; 93: 388-392.
10. Aslam M, Watson AR; Trent & Anglia MCDK Study Group. Unilateral multicystic dysplastic kidney: long term outcomes. Arch Dis Child 2006; 91: 820-823.
11. Tiryaki S, Alkac AY, Serdaroglu E, Bak M, Avanoglu A, Ulman I. Involution of multicystic dysplastic kidney: Is it predictable? J Pediatr Urol 2013; 9: 344-347.
12. Mansoor O, Chandar J, Rodriguez MM, et al. Long-term risk of chronic kidney disease in unilateral multicystic dysplastic kidney. Pediatr Nephrol 2011; 26: 597-603.
13. Rabelo EA, Oliveira EA, Diniz JS, et al. Natural history of multicystic kidney conservatively managed: a prospective study. Pediatr Nephrol 2004; 19: 1102-1107.
14. Miller DC, Rumohr JA, Dunn RL, Bloom DA, Park JM. What is the fate of the refluxing contralateral kidney in children with multicystic dysplastic kidney? J Urol 2004; 172: 1630-1634.
15. Ismaili K, Avni FE, Alexander M, Schulman C, Collier F, Hall M. Routine voiding cystourethrography is of no value in neonates with unilateral multicystic dysplastic kidney. J Pediatr 2005; 146: 759-763.
16. Rahman RC, Amoreo O. Multicystic dysplastic kidney: diagnosis and evolution. Pediatr Nephrol 2005; 20: 1023.
17. John U, Rudnik-Schöneborn S, Zerres K, Misselwitz J. Kidney growth and renal function in unilateral multicystic dysplastic kidney disease. Pediatr Nephrol 1998; 12: 567-571.
18. Hayes WN, Watson AR; Trent & Anglia MCDK Study Group. Unilateral multicystic dysplastic kidney: does initial size matter? Pediatr Nephrol 2012; 27: 1335-1340.
19. Rabelo EA, Oliveira EA, Silva GS, Pezzuti IL, Tatsuo ES. Predictive factors of ultrasonographic involution of prenatally detected multicystic dysplastic kidney. BJU Int 2005; 95: 868-871.
20. Alaygut D, Soylu A, Kasap B, Türkmen M, Cakmakcı H, Kavukcu S. The relationships between renal compensatory hypertrophy etiologic factors and anthropometric development in the pediatric age group. Urology 2013; 82: 442-447.