Microalbumin excretion and outcome in children with multicystic dysplastic kidney

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Aim: To present the long-term follow-up results of children with multicystic dysplastic kidney (MCDK) and urinary microalbumin excretion levels in order to evaluate whether there is an increased risk of renal damage or not.

Materials and methods: Thirty-three children with the diagnosis of MCDK who had been followed up by the nephrology outpatient clinic between 2002 and 2009 were invited to participate in the study. Twenty-six healthy children were investigated as a control group for microalbumin/creatinine ratio (μg/g creatinine). The mean age at diagnosis, the duration of follow-up, accompanying urinary tract abnormalities, attacks of urinary tract infection (UTI), contralateral kidney size, and urinary microalbumin levels were investigated.

Results: The mean age of the patients with MCDK and the mean duration of follow-up were 6.5 ± 3.9 years and 35 months (range 2-96) months, respectively. The most common urinary tract abnormality was vesicoureteral reflux (VUR), with a rate of 34%. Thirty-nine percent of the children experienced UTI during follow-up. The compensatory renal hypertrophy of the contralateral kidney was 24% at 6 months and 68% at 12 months. Sixteen patients (59%) had an increased microalbumin/creatinine ratio (>30 μg/mg creatinine). Microalbumin/creatinine ratio was higher in patients with MCDK than it was in the controls (P = 0.001).

Conclusion: Microalbuminuria and VUR are not rare in children with MCDK. Systematic follow-up of these patients is recommended to identify those at risk of contralateral renal damage.

Key words: Multicystic dysplastic kidney, vesicoureteral reflux, microalbuminuria, contralateral kidney abnormality, outcome

Introduction
Multicystic dysplastic kidney (MCDK) is the most common cystic malformation of the kidney during infancy, with an incidence of 1 in 4000 live births. MCDK is a form of renal dysplasia characterized by the presence of multiple cysts of various sizes and without normal renal parenchyma (1,2). Regarding the high rate of the spontaneous involution of the multicystic kidney, management of MCDK has changed from routine nephrectomy to conservative follow-up (1,3). The important points during nephrological visits are contralateral kidney growth, the level of proteinuria, blood pressure, and renal function tests (4).

Contralateral abnormalities may accompany MCDK in the form of vesicoureteral reflux (VUR), dysplasia, positional abnormality, or ureteropelvic junction with an incidence of 25% (5-9). Feldenberg and Siegel reported on the prognosis of MCDK patients (8). They observed that simple forms of MCDK showed a good prognosis with infrequent UTI attacks. However, in complex forms of MCDK,
defined as either unilateral MCDK with some other urinary tract abnormalities or bilateral MCDK, the overall prognosis was not favorable. The incidences of UTI and chronic renal insufficiency (50%) were higher in them compared with simple forms of MCDK.

In the present study, we analyzed the follow-up results of MCDK patients who were treated conservatively. We also measured urinary microalbumin excretion of these patients to evaluate whether there was an increased risk of renal damage or not.

Materials and methods
Between 2002 and 2009, 33 children were diagnosed with MCDK and prospectively followed up at the Celal Bayar University Hospital and Marmara University Hospital. MCDK was diagnosed based on the presence of multiple, varying sized, noncommunicating cysts on USG, with a nonfunctional kidney on dimercaptosuccinic acid (DMSA) radionuclide scan (3). The urinary microalbumin/creatinine ratio of 26 healthy children was also studied (the control group).

The results of physical examinations of the patients including blood pressure and extrarenal system findings were noted. All patients were investigated with urinalysis, urinary microalbumin, creatinine excretion, and urinary culture. Glomerular filtration rate (GFR) was estimated using the Schwartz formula. Normal urinary albumin excretion was defined as a microalbumin/creatinine ratio (μg/mg) less than 30. Microalbuminuria was defined as a urinary microalbumin/creatinine ratio (μg/mg) greater than 30 (10).

USG examination of the kidneys was performed at baseline, twice in the first year of life, and then once a year. The involution of MCDK and the size of the contralateral kidney were noted. Compensatory hypertrophy of the contralateral kidney was defined as renal length >95 percentile of the mean value of normal kidney according to age (11). Voiding cystourethrography (VCUG) was performed in 29 patients. Antibacterial prophylaxis was used in patients with VUR.

Statistical analysis was performed using SPSS 15.0. Data were expressed as mean ± standard deviation, descriptive analysis was performed for the calculation of frequencies, and comparisons were performed using nonparametric tests. A P value less than 0.05 was considered significant.

Results
The study group consisted of 17 male (52%) and 16 female (48%) children. The ages ranged between 2 months and 13 years, with a mean age of 6.5 ± 3.9 years during the study. The control group consisted of 12 male and 14 female children, with a mean age of 7.7 ± 3.2 years, ranging from 3 to 14 years. The age range was similar between the study group and the control group (P > 0.05).

Seventy-nine percent of the children were diagnosed during the antenatal period. The mean duration of follow-up was 35 months (range 2-96).

The incidence of compensatory hypertrophy was 24% at 6 months and 68% at 1 year.

UTI attacks were observed in 13 of the 33 patients (39%). Most of these UTI attacks were not accompanied by fever or systemic inflammation findings, indicating a lower urinary tract infection. Four attacks (31%) were pyelonephritis. VUR was detected in 10 patients of the 29 in whom VCUG had been performed (34%). Half of them had severe VUR of grades III, IV, and V. Children with severe VUR had recurrent UTI during follow-up. The associated urological and nonurological anomalies in the study group are shown in Table 1.

The mean microalbumin/creatinine ratio (μg/mg creatinine) was 38.4 ± 31 in MCDK patients and 12.9 ± 17.8 in controls, with a statistically significant difference between them (P = 0.001). Sixteen patients of the 27 in whom microalbuminuria was examined (59%) showed an increased microalbumin/creatinine ratio (>30 μg/mg creatinine). There were no differences in microalbumin/creatinine ratio between VUR (+) and VUR (−) patients (P > 0.05) (Table 2). Microalbumin/creatinine ratio was 38.4 ± 36.9 in patients with compensatory hypertrophy of the contralateral kidney and 38 ± 28.7 in patients without compensatory hypertrophy of the contralateral kidney; the difference was not statistically significant.

There was no hypertension according to age, height, or sex in patients with MCDK according to clinical measurements.
During the follow-up 2 patients developed chronic renal insufficiency. One of them was a 2-month-old boy with right MCDK and left grade V VUR. His GFR was 15 mL/min/1.73 m². Right internal carotid artery agenesis was detected by cranial magnetic resonance angiography during the investigation of tonic convulsions (12). The second patient with chronic renal insufficiency was a 13-year-old girl with right MCDK. Her GFR was 68 mL/min/1.73 m² when she was 8 years old, and at the time of writing she has stage III renal failure and her GFR is 44 mL/min/1.73 m². Her follow-up USG scans showed 2 cysts in the corticomedullary junction of the contralateral kidney, without contralateral compensatory hypertrophy. Her family history was remarkable for a sister having bilateral corticomedullary cysts on USG with a normal GFR and a mother with left corticomedullary cysts, increased parenchymal echogenicity, and renal insufficiency. Insulin resistance was detected by oral glucose tolerance test in the proband and her mother. Analysis for hepatocyte nuclear factor-1 mutation with a presumptive diagnosis of nonsyndromic glomerulocystic kidney disease was planned.

One patient with MCDK also had severe ureteropelvic junction obstruction and nephrolithiasis on the contralateral kidney. Pyeloplasty and stone removal were performed.

**Discussion**

MCDK is one of the most common congenital anomalies of the kidney (13-16). The long-term follow-up of these patients displayed a fairly benign course (3,8,14). Our study shows the frequency of accompanying contralateral and extrarenal anomalies, and the presence of associated microalbuminuria, hypertension, and UTI.

VUR was the most common abnormality seen in patients with MCDK. The frequency is quite variable, ranging from 5% to 43% in patients with MCDK (2,6,7,16-18). Some authors recommend routine VCUG for patients with MCDK, because of the high risk of scar formation secondary to acute pyelonephritis or reflux nephropathy in the contralateral kidney. Kuwertz-Broeking et al. reported that VUR was present in 5% of their patients and recommended VCUG for those with a pelvicalyceal dilation on USG or a diagnosis of UTI (6). Aslam and Watson reported VUR in 19% of MCDK patients and considered VCUG unnecessary during routine follow-up (3). In our study VUR was detected in 34% of the patients. Five patients showed a mild degree of reflux (grade I, II) and 5 displayed a severe degree (grade III-V). In contrast to our study, the literature shows that most patients with MCDK...
have a low grade of reflux (grade I, II), ranging from 47% to 96% (3,5,7,14,18). As the most important cause of chronic renal disease in Turkish children is VUR nephropathy, we should take into account the high frequency and high degree of severe reflux in our patients. The decision whether to use VCUG should be considered carefully.

We detected some other associated urological abnormalities in 2 patients. The first patient had grade III VUR in the contralateral ectopic kidney and the second patient had severe ureteropelvic junction obstruction and nephrolithiasis. In a study comprising a group of 90 patients with renal agenesis and MCDK, investigating associated anomalies of the urogenital tract in this group of patients, contralateral renal anomaly and extrarenal anomaly frequency were 22% and 10%, respectively (2). Cardiac and musculoskeletal malformations such as heart disease, inguinal hernia, ovarian cyst, and cryptorchidism predominated in the literature. In our study dilated cardiomyopathy and ichthyosis in 1 patient, patent ductus arteriosus (PDA) in 1 patient, and bilateral congenital dysplastic hip in 1 patient were detected when they were investigated for other anomalies.

During long-term follow-up of MCDK patients, it is shown that while a cystic kidney undergoes spontaneous involution a contralateral kidney exhibits compensatory hypertrophy. In the literature the compensatory hypertrophy rate is 43%-100% (1,2,4,5,18). Our findings correlate with the literature showing that 68% of the study population displays compensatory contralateral hypertrophy at the end of 1 year. Involution of dysplastic kidney was reported in the literature (1,2,20,21). Its frequency was reported as 40%. In a previous study, complete involution rate over 48-month duration was reported as 39% (2).

In previous studies, patients with a solitary kidney were reported to have GFR 75% of normal. This 50% increased capacity results in hyperfiltration, which in turn may cause hypertension, proteinuria, and glomerulosclerosis (22). In a study of MCDK and unilateral renal agenesis, microalbuminuria was found in 23% of patients. Fifty percent of these patients were hypertensive according to their clinical examination (22). In another study, the prevalence of hypertension in patients with a solitary kidney (includes atrophic kidney, renal agenesis, and unilateral nephrectomy) by ambulatory blood pressure monitoring was higher than that in the controls (23). In Seeman's study, hypertensive children with MCDK had significantly higher microalbuminuria than normotensive ones; their hypertension rate was 20% (5 in 25) by ambulatory blood pressure measurement (3). Mansoor et al. (24) reported an increased risk of chronic kidney disease and hypertension in those with contralateral abnormalities, as Feldenberg et al. stated (8). There was a significantly inverse relationship between proteinuria and GFR in their study (24). In our study, increased microalbumin/creatinine ratio frequency was 59%. These results necessitate investigation of microalbuminuria in these patients. Detection of a significantly increased urinary microalbumin/creatinine ratio in patients with MCDK compared to the control group shows us that evaluation of blood pressure and microalbuminuria levels is an important part of the follow-up of these patients; however, we did not detect hypertension in our patients in clinical measurements. When microalbumin/creatinine ratios were evaluated with regard to UTI, presence of vesicoureteral reflux, and compensatory hypertrophy of the contralateral kidney, there was no significant difference.

The results of follow-up of children with conservatively managed MCDK suggest that compensatory hypertrophy of the contralateral kidney begins in the first year of life. However, our data also suggest a higher incidence of contralateral kidney abnormalities like VUR and microalbuminuria in patients with MCDK, which warrants a systematic follow-up to identify patients are at risk of progressive renal damage of the contralateral kidney.
References


