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Conservative management of multicystic dysplastic kidney: clinical course and ultrasound outcome

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Abstract

Objective: The aim of this study was to describe the clinical course and ultrasound outcome of prenatally detected multicystic dysplastic kidney.

Methods: Fifty-three children with unilateral multicystic dysplastic kidney detected by prenatal ultrasound between 1989 and 2004 were included in the analysis. All children were submitted to conservative management with follow-up visits every six months. Follow-up ultrasound examinations were performed at six-month intervals during the first two years of life and yearly thereafter. The following clinical parameters were evaluated: blood pressure, urinary tract infection, renal function, and growth. The following ultrasound parameters were evaluated: involution of multicystic dysplastic kidney and contralateral renal growth.

Results: The mean follow-up time was 68 months. Two children presented hypertension during follow-up and five had urinary tract infection (only one with recurrent episodes). There was no malignant degeneration of multicystic dysplastic kidney. A total of 334 ultrasound scans were analyzed. US scan demonstrated involution of the multicystic dysplastic kidney in 48 (90%) cases, including complete involution in nine (17%). The involution rate was faster in the first 30 months of life. There was progressive compensatory renal hypertrophy of the contralateral renal unit; the rate of growth was greater in the first 24 months of life.

Conclusion: The results of prolonged follow-up of children with conservatively managed multicystic dysplastic kidney suggest that clinical approach is safe, the incidence of complications is small, and that there is a clear tendency for multicystic dysplastic kidney to decrease in size. Our data also suggest that the involution rate of multicystic dysplastic kidney as well as the growth of the contralateral kidney is greater in the first 24 months of life.

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Introduction

Multicystic dysplastic kidney (MDK) is the congenital renal cystic malformation most frequently diagnosed in children, with an estimated incidence of 1:1,000[1] to 1:4,300[2] live births. It is also the most common cystic anomaly detected by fetal ultrasonography and the second most frequent cause of palpable abdominal mass in newborns and infants.[3] Recent improvements regarding the natural history of MDK, especially with regard to prenatal diagnosis and conservative management, have changed the approach to this anomaly. Until the mid-1980s, the management of MDK patients often consisted of nephrectomy. Since then, with the improvements in fetal ultrasonography, such management has been replaced by clinical and echographic

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follow-up of the patients.[2] Some studies have shown that conservative management seems to be a safe option; the prevalence of complications is negligible and most of the affected units have partial or complete involution on ultrasonography.[4,5] Recently, a comparative study between surgical and conservative treatments has not revealed any significant difference in the frequency of complications for the patients.[6]

The aim of the present observational study was to describe the clinical course and ultrasound outcome of a series of patients with prenatally detected MDK, who received conservative treatment and had a long-term follow-up.

Patients and methods

A total of 53 children who had unilateral MDK detected by fetal ultrasonography between 1989 and 2004 participated in the study. The inclusion criteria were the following: 1) echographic diagnosis of MDK according to the criteria proposed by Stuck et al;.[7] 2) at least two ultrasound scans; 3) at least six months of follow-up; and 4) absence of chromosome disorders and association of multiple malformations. The criteria proposed by Stuck et al., which were used to establish the diagnosis of MDK, were: A) presence of interfaces between cysts; B) non-medial location of the largest cyst; C) absence of identifiable renal sinus; D) presence of different-sized, non-communicating multiple cysts and E) absence of identifiable renal parenchyma. Two patients were lost to follow-up and were therefore excluded from the analysis.

Patients were investigated according to a systematic protocol and were followed up prospectively. Clinical, ultrasonographic and laboratory assessments were made every six months during the first two years of life and every year thereafter. Static ^{99m}Tc-DMSA scintigraphy was performed in order to confirm the diagnosis, and voiding cystourethrography was used to investigate other urological disorders. Glomerular filtration rate was estimated using the method proposed by Schwartz et al.[8] Arterial blood pressure was checked according to the Working Group of the National High Blood Pressure Education Program recommendations.[9] Normal arterial blood pressure values and reference values were based on the Second Task Force Report.[10]

Siemens (Sonoline Prima SLC) with 3 to 5 MHz transducers was used for the echographic examination. Renal units were measured using longitudinal sections and cross sections. The following parameters were assessed according to the standards suggested by Dinkel et al.:[11] length, transversal and anteroposterior diameter. The renal volume was calculated based on a formula proposed by Han & Babcock.[12] The values were plotted onto the renal growth charts (renal length *versus* age) according to the reference values obtained by Han & Babcock.[12] Thus, renal units were classified into four groups according to their position on the graph: 1) above the 95th percentile; 2) between the 50th and 95th percentiles; 3) between the 5th and 50th percentiles; and 4) below the 5th percentile. All infants who had complete MDK involution were submitted to at least two ultrasound scans to confirm the absence of cysts.

The descriptive statistical analysis is expressed as mean and standard deviation (SD) of the continuous variables. An informed consent form was signed by parents or surrogates and the study protocol was approved by the Research Ethics Committee of Universidade Federal de Minas Gerais.

Results

During the study, 53 children (29 males) were recruited. Twenty-seven patients (51%) were admitted in the last five years (after 1999). The mean gestational age at diagnosis was 31±4 weeks (range: 21-40). The left kidney was most frequently affected (30; 56.6%). Vesicoureteral reflux (VUR) in the contralateral kidney (CLK) was detected in four patients (7.5%) and mild hydronephrosis in two other cases (3.7%). Static (^{Tc}-DMSA) scintigraphy at admission showed absence of radioisotope uptake in all of the affected renal units. The mean follow-up time was 68 months (range: 7-182); 21 (40%) patients were followed up for over 5 years and 45 (85%) for over 2 years.

Clinical course

The following aspects were taken into account while evaluating the clinical outcome of the followed-up patients: arterial blood pressure, urinary tract infection, renal function, weight and height growth and possible development of malignant degeneration.

Systolic blood pressure in the initial assessment ranged between 70 and 100 mmHg, (mean of 83±8.6 mmHg and diastolic blood pressure, checked in 36 children, ranged from 30 to 65 mmHg (mean of 45±9.5 mmHg). Two female children had systemic hypertension during follow-up. One of them with remarkable increase in blood pressure at four months of life and values persistently above the 95th percentile for age and gender. Nephrectomy of the MDK was recommended at this age, but due to consecutive respiratory infections, the procedure was postponed twice. At 12 months, arterial blood pressure levels returned to normal. Another female patient revealed asymptomatic systemic hypertension, associated with obesity, at five years (weight z score = 3.7; height z score = 0.63; and body mass index = 27.6). Non-pharmacological measures were adopted, but there was low treatment compliance.

Of 53 children, 48 (90%) did not show any episode of urinary tract infection during follow-up. Among the remaining five children, only one patient, who had VUR grade III in the contralateral renal unit, presented recurrent infection (three episodes).

Renal function was assessed in all children during follow-up. All patients showed normal renal function. In the last clinical assessment, the mean serum creatinine was 0.5±0.1 mg/dl and the mean serum urea was 23.5±8.8 mg/dl. Glomerular filtration rate, obtained at the end of follow-up, ranged from 65 to 172 ml/min/1.73 m^2, mean of 119 ml/min/1.73 m^2.

All children had their weight and height growth evaluated at the end of follow-up. The mean weight-for-age z score was 0.05 (range: -2.9 to 3.7) and the median was equivalent to 0.07. The mean height-for-age z score was 0.18 (range: -2.7 to 1.98) and the median was 0.3. Two children had their weight and height z scores below -2.0.

No clinical or ultrasonographic findings suggestive of malignant degeneration were found during the follow-up period.

Ultrasound outcome

A total of 343 ultrasound scans were performed in 53 patients. The mean number of scans per patient was 6.5 (range from 2 to 12). The echographic examinations showed partial involution of MDK in 39 (74%) cases and complete involution in nine (17%). Length of the MDK remained unchanged in five children (9%). One patient (nine scans) was excluded from the subsequent analysis because he had an MDK of approximately 600 cm^3 in volume, making the echographic investigation poorly reliable.

Figure 1 shows the means and two SD of the length of renal units according to the year in which the exam was performed. Notably, there is a continuous decrease in the size of the MDK and a corresponding increase in the CLK. The initial ultrasound scan revealed that the mean length of the MDK was 58.1±21.4 mm and 55.4±7.5 mm for the CLK. For the 17 patients who were followed up for over 10 years, the final mean size of MDK was 15.3±16.8 mm and that of CLK was 120.9±14.4 mm. The size of the MDK tended to decrease in the first 30 months of life (Figure 2a) and, inversely, there was a faster CLK increase in the first 24 months of life (Figure 2b).

The percentile distribution in relation to the longitudinal diameter of MDK/age on the initial ultrasound examination was as follows: 26 units (49%) above the 95th percentile, eight units (15%) between the 50th and 95th percentiles, eight units (15%) between the 5th and 50th percentiles, and 11 units (21%) below the 5th percentile expected for age. After the sixth year of life, all MDK had the expected length for age, below the 5th percentile.

The percentile distribution relative to the length of CLK/age on the first ultrasound examination was as follows: six units (11%) above the 95th percentile, 37 units (70%) between the 50th and 95th percentiles, and 10 units (19%) between the 5th and 50th percentiles expected for age. There was a progressive increase in compensatory renal hypertrophy: at six years, 70% of the contralateral renal units showed a percentile above the 95th and after the tenth year of life, all renal units had this distribution.

Discussion

The present observational study describes the clinical course and ultrasound outcome in patients with intrauterine diagnosis of MDK who had a long-term follow-up. All patients were submitted to a systematic protocol and had a clinical approach. The MDK did not have to be surgically removed during the follow-up period. The incidence of complications was negligible, only one patient had high blood pressure caused by MDK, with spontaneous resolution.[13] Serial ultrasound exams revealed involution of MDK in 48 (90%) cases, of which nine (17%) units became undetectable during the follow-up. After the sixth year of life, all the affected renal units were below the 5th percentile of the renal length expected for age.

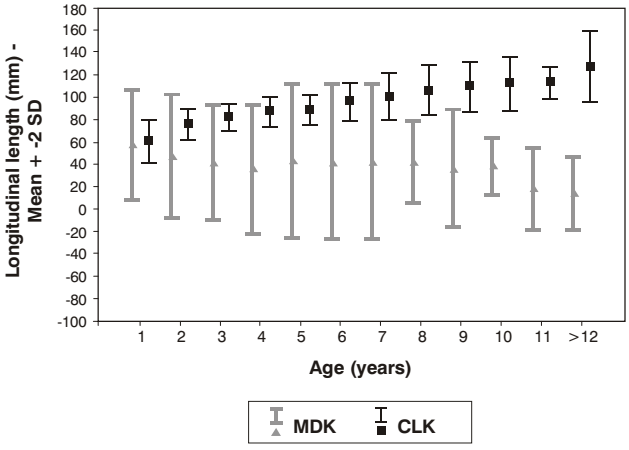

Figure 1 - Means and two SD of the length of the multicystic dysplastic kidney and contralateral kidney according to age

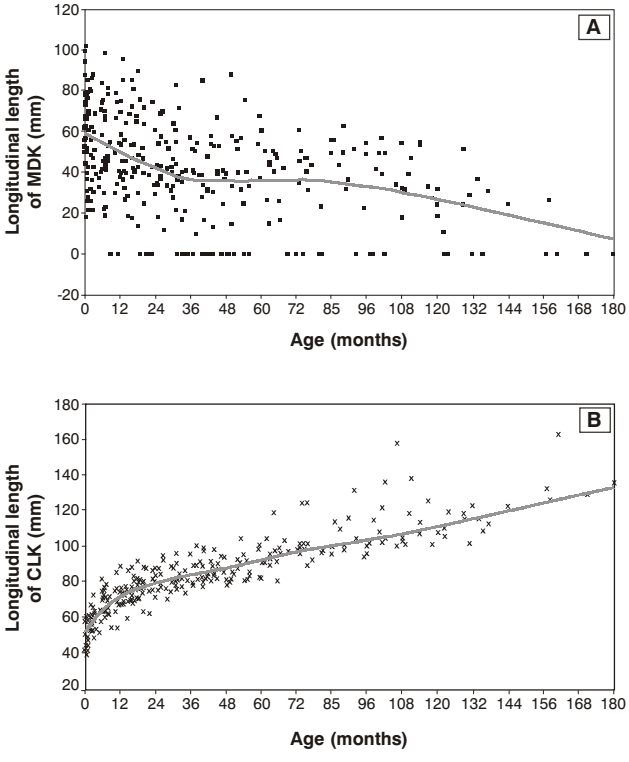

Figure 2 - Graph showing the length of the multicystic dysplastic kidney versus age (**A**), and lenght of contraleteral kidney versus age (**B**). The line represents increase and decrease tendency and rhythm of the renal units

Since the advent of conservative treatment, several studies with MDK patients have been described in the medical literature.[4,6,14-18] Diagnosis was exclusively established in the prenatal period in only two of these studies.[14,16] As with our patient population, there was predominance of male children and compromise of the left side in all of the reported studies. For instance, in the largest patient population described, Wacksman & Phipps[4] stated that in the U.S. multicenter study (n = 441), most of the children were boys (57%) and that the left side was most commonly affected (53%). Renal function remained normal in our population. John et al.,[19] in a study of 33 patients, also showed that the serum creatinine levels remained within normal limits. On the other hand, Rudnik-Schoneborn et al.[6] described creatinine levels above two SD in 19% of the children included in the German multicenter study. Most of those patients had anomalies in their CLK (pyeloureteral obstruction and VUR). In our study, there was a low prevalence of CLK anomalies (11%) in comparison to other studies. Other studies have described percentage values between 4%[14] and 44%,[20] but most of these studies show a percentage around 25%.[4,6,16,17] Reflux in the contralateral renal unit is the most commonly observed anomaly. Most MDK patients have mild VUR and a favorable outcome.[17]

Similarly to our study, the rate of complications reported in the published studies has been negligible. Five cases (2.5%) of hypertension were found during the follow-up of 204 children in the German multicenter study.[6] After extensive literature review, we found only 19 cases of systemic hypertension associated with MDK.[13] In our patient population, as with several studies, there was no report of malignant transformation of MDK. This is a possible complication that has been sporadically described. In a more recent review, Pérez et al.[21] found 17 cases of neoplasms possibly associated with MDK. Of these, 11 were Wilms' tumors, five were renal cell carcinomas and one was a mesothelioma. However, many of the case reports are not properly documented and, quite often, there is no proof that renal cysts do represent MDK.

Several other authors have investigated the ultrasound outcome of MDK. Most studies show that the size of MDK decreases and that some of them disappear during the follow-up period. Quite recently, we reviewed 614 MDK cases in the literature that were conservatively managed and assessed using serial echographic exams. Of 614 renal units, 296 (48%) reduced in size, 121 (20%) disappeared, 157 (26%) remained unchanged and only 40 (6%) increased in size.[22] In the present study, with a longer follow-up period, the rate of reduction and/or disappearance was even higher (91%). In a survival analysis, we estimated that the median time for the disappearance of MDK was 122 months (95%CI = 86-158 months).[22] In our study, the scatter plot (length of MDK vs age) shows that the involution rate varied with patient age (Figure 2). Reduction is greater in the first 30 months and apparently after the tenth year of life. Other authors have reported this finding. Rottenberg et al.[15] followed up 55 children for a mean period of 32 months and showed that the involution rate was inversely proportional to age. The involution rate was -0.5 mm/week in children examined in the first three months of life and -0.02 mm/week in those assessed after the first year of life. Other studies have shown a similar trend.[18,23] The factors related to the reduction in cyst size are still unknown so far. Several variables are associated with this process: initial size of MDK, rate of the reduction, patient age and, obviously, the length of follow-up.[24]

In the present study, there was compensatory renal hypertrophy of the CLK, defined as renal length above the 95th percentile for age during follow-up, in approximately 30% of the renal units assessed in the third year of life, 70% at six years, and in all renal units after the tenth year of life. Compensatory hypertrophy has been observed in patients with a single functioning kidney, although the length and grade of the hypertrophy are controversial. Hill et al.,[25] in a study of 36 fetuses with a single functioning kidney, 22 of which with MDK, demonstrated that compensatory renal hypertrophy was present in 44% of cases after 29 gestational weeks. John et al.,[19] in a study of 33 children with MDK, showed that 24% of contralateral kidneys had a length that exceeded +2 SD at birth. After a mean period of 4.9 years, renal length with more than + 2 SD was observed in 52% of kidneys. In our patient population, growth was faster in the first 24 months of life. Rottenberg et al.[26] showed that the rate of CLK growth was higher in the first months of life, gradually decreasing thereafter. In a study with serial assessments of the renal parenchymal area of 43 children with MDK, Abidari et al.[27] found that solitary kidneys had an accelerated growth up to the 22nd month of life. The compensatory renal hypertrophy mechanism remains still unclear. In older animals, renal growth occurs through compensatory hypertrophy of proximal tubule cells. In young animals, both hyperplasia and hypertrophy occur, which may be accountable for accelerated growth during this period.[28] Some studies have suggested that hyperplasia of nephrons is responsible for most of the growth, but the stimulus behind that is unknown.[29] The detection of intrauterine compensatory hyperplasia implies that this growth does not occur because homeostasis has to be maintained.[26] This stimulus may stem from a renotrophic humoral substance that is produced in response to the reduction in intrauterine functional renal mass and may be intensified by the volume of amniotic fluid produced by the kidneys.[30]

In conclusion, our prospective study children with MDK conservative management demonstrates that the clinical management is safe for this group of patients, the incidence of complications is negligible and there is a clear tendency towards ultrasonographic involution of the affected renal unit. Our data suggest that the involution rate of MDK, similarly to that of the compensatory hypertrophy of the CLK, is greater in the first two years of life.

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