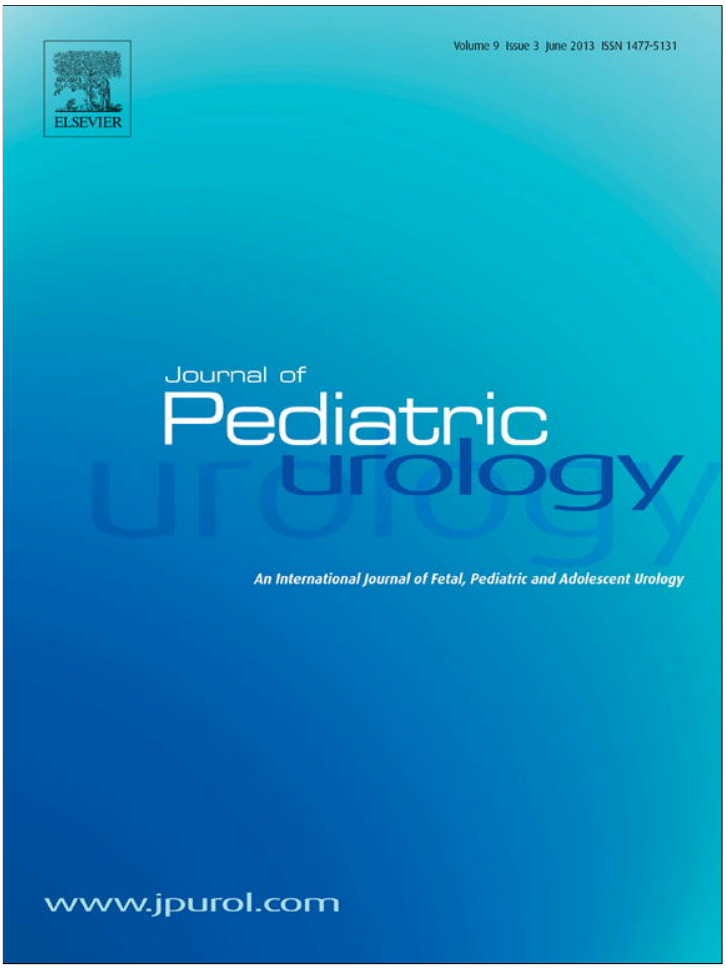

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Involution of multicystic dysplastic kidney: Is it predictable?

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Abstract *Objective:* To evaluate the clinical course of multicystic dysplastic kidney (MCDK) and to reveal any criteria indicating spontaneous involution.
Material methods: Hospital records of patients with MCDK followed in two different institutions in 1994—2009 were reviewed and data were analyzed regarding involution.
Results: Records of 96 patients were reviewed, of whom 46 were diagnosed antenatally and followed for more than 1 year. Fourteen patients had undergone nephrectomy. There was one case of hypertension which resided with nephrectomy. There was no malignancy. Involution rate was 53.6% (15/28) for right-sided and only 16.7% (3/18) for left-sided kidneys. The initial size of the kidney was found to be another predictive parameter for involution. Initial sizes of 43 (15 involuted and 28 non-involuted) kidneys were documented. Mean standard deviation score for involuting and non-involuting kidneys was −3.19 and 3.12, respectively. The chance of involution for a *large* kidney on the *left* was zero; however, involution risk for a small right-sided kidney was 67%.
Conclusion: Reviewing a 15-year period of our patient records conveyed data supporting current literature mainly encouraging non-operative management of MCDK. Further studies are required; however, our two objective indicators, the initial size and side of dysplastic kidney, may contribute to the management.

Introduction

Multicystic dysplastic kidney (MCDK) is the most common form of renal cystic disease in children, reported to occur in 1/2400—1/4300 live births [1]. Reports in the 1970s mentioned MCDK as a rare cause of abdominal mass managed by nephrectomy [2]. The widespread use of ultrasonography (US) has led to an increase in incidence figures for MCDK [3].

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Antenatal US and incidental detection without a palpable mass have provided a better understanding of the course of the disease, which has created a still ongoing controversy. Proponents of nephrectomy argue about hypertension, malignant transformation and improvement of minimally invasive techniques. Non-surgical management, which became more popular recently, is mostly based on high spontaneous resolution rates and the insufficient data about hypertension and malignancy related to MCDK. There is no conclusive evidence supporting any particular approach or predictive data about involution [4]. The aim of this study was to determine the clinical course of MCDK and reveal possible indicators predicting involution in order to constitute a follow-up regimen for all patients with MCDK.

Materials and methods

Hospital records of patients with MCDK followed in two different institutions in Izmir (Ege University Department of Pediatric Surgery and Dr. Behcet Uz Childrens' Hospital Department of Pediatric Nephrology) between the years 1994 and 2009 were reviewed retrospectively. Diagnosis of MCDK was made in the case of documentation of non-communicating cysts randomly distributed throughout the kidney with no identifiable renal parenchyma on US, and no function on renal isotope scan. Data regarding patient demographics, clinical/radiological findings and course of the disease with respect to involution, hypertension and malignancy were collected. Standard deviation score (SDS = (measured value − average value)/standard deviation) of long axis was used to evaluate kidney size. The study by Konus et al. offering age/height-matched normal values for both kidneys individually was used for the average values [5,6]. Contralateral kidney was also evaluated for any accompanying anomaly. Follow-up consisted of urinary US, arterial blood pressure measurement, and blood and urine analyses. Diagnosis of hypertension was made in the case of blood pressure exceeding the 90th percentile for age and sex [7]. Fisher's exact test and logistic regression were used for statistical analyses and ROC (receiver operating characteristic) analysis was done to determine a threshold value for kidney size indicating involution.

Results

A total of 102 MCDK patients were reviewed: 61 boys and 41 girls. Six patients nephrectomized in the earlier years were excluded from the study due to indeterminate nephrectomy indications.

VUR incidence and resolution in MCDK

Voiding cystourethrography (VCUG) was performed in 84 of 96 patients and vesicoureteric reflux (VUR) was detected in 14 (16.7%). Other accompanying urinary tract anomalies were ureteropelvic junction obstruction in 8 patients (8.3%), hypospadias in 2 (2%), duplex system in 2 (2%), and ureterovesical junction obstruction in 1 (0.9%).

Most frequent coexisting urinary abnormality was contralateral VUR. VUR grades were as follows: two cases in grade I, five cases in grade II, six cases in grade III and one case in grade IV. Four out of 14 refluxing patients had undergone an anti-reflux procedure (3 subureteric injection, 1 ureteroneocystostomy) and the others resolved spontaneously. The relationships between hydronephrosis (HN) and urinary tract infection (UTI) and VUR were also evaluated. The presence of both UTI and HN significantly increased the chance of having VUR (57.1%). VUR was significantly more frequent in patients with UTI (45.5%) compared to the ones without UTI (6.5%); however, the relationship between VUR and HN was insignificant (Table 1).

Course of MCDK

Sixty-three patients were diagnosed antenatally. Others were detected during investigations following UTI (10), abdominal pain (9), birth with multiple anomalies (9), discomfort of the baby (3), growth retardation (1) and urinary incontinence (1), with a mean age of 61 months (0—14 years).

Mean follow-up of the whole group was 34.1 months (0—162 months). Hypertension was detected in 1 patient at 6 months of age. No renal parenchymal defect on isotope scan or other urological anomaly was detected and hypertension resolved following nephrectomy. There was no malignancy.

Fourteen patients had undergone nephrectomy at a mean age of 28.5 (1—108) months. Indications were no change in size during follow-up of minimum 2 years (10), increase in size (2), palpable huge mass (1) and hypertension (1).

Total involution of the MCDK was documented in 18 patients including one antenatal involution. Definite time of involution could not be affirmed for all patients because of irregular follow-up; however, 11 of the 18 totally involuted kidneys were known to be involuted before age 3 years.

Total involution in MCDK

Forty-six patients diagnosed antenatally and followed for more than 1 year were assessed in terms of involution and associated factors. Mean follow-up period was 46.7 months (±32.8, 12—162 months). Total involution was documented in 18 of these 46 patients (33%).

No relation with sex or accompanying anomalies (both urinary tract, such as VUR, ureteropelvic junction obstruction, ureterovesical junction obstruction, and non-related anomalies) was detected.

Table 1 Evaluation of VUR and associated factors in 84 patients who underwent VCUG.

	At least one UTI (22)	No UTI (62)	HN on US (23)	No HN (61)	Both UTI and HN (7)	Neither UTI nor HN (45)
VUR%	45.5%	6.5%	21.7%	14.8%	57.1%	6.6%
p	0.000		0.570		0.003	

A relationship between size and side of the kidney, and involution was detected. Fifteen of 18 totally involuted kidneys (83%) were right-sided. Involution rate was 53.6% (15 of 28) for right-sided and only 16.7% (3 of 18) for left-sided kidneys ($p = 0.015$). Initial sizes of 43 (15 involuted and 28 non-involuted) kidneys were documented. Mean SDS for involuting and non-involuting kidneys was −3.19 and 3.12, respectively ($p = 0.001$). SDS of '0' was found to have 86% sensitivity and 68% specificity in terms of prediction of total involution (Fig. 1). Therefore, kidneys were classified as 'big' and 'small' according to '0' SDS. Thirteen of the involuted kidneys were in the 'small' and two were in the 'big' group. Nineteen of the kidneys that did not involute were 'big' and nine were 'small' (Table 2). Unexpectedly, multivariate analyses of the data (with logistic regression test) failed to show a relation with side ($p = 0.096$), although confirming the relation with size ($p = 0.002$).

Discussion

As wider use of ultrasonography continues to increase the rate of diagnosis of MCDK, the controversy around the follow-up of these asymptomatic patients and their unpredictable course becomes more of an issue. The tendency towards conservative management in the last decade has been based on the reported high spontaneous involution rates and lack of evidence for an increased hypertension and malignancy risk [3,4,8]. The aim of this study was to provide some clear information about the natural history of MCDK, mainly focusing on involution.

Coexistent urinary tract abnormalities were not as frequent as formerly believed, which is similar to the current literature data [3,9]. Likewise, the most frequent anomaly of the contralateral kidney was VUR. VUR rate ranges from 4.5% to 28% with a weighted mean of 16% according to Canadian Urological Association guidelines [9]. Our series reveals a VUR rate of 16.7% among the patients who had undergone VCUG and 14.5% overall. Formerly, as a result of higher incidence of VUR, VCUG was mostly accepted as a routine part of the coexistent abnormality search [10]. However, our results indicate that most cases are mild and resolve spontaneously. Some authors state that even mild VUR affects kidney development, but there are few reports about VUR affecting kidney development that mention kidney size [11]. Considering this, we also compared the size of contralateral kidneys at the last sonographic measurement. Mean SDS for kidneys with and without VUR was 3.50 and 3.64, respectively ($p = 0.850$) which did not show any effect of VUR on kidney development, at least in size. Therefore, like some other institutions [1,10], we do not employ VCUG as part of our routine survey any longer. Another finding in our study was the high predictive value of UTI for VUR. We believe that documented UTI is an indication for performing VCUG in MCDK patients; however, HN on US does not indicate VCUG.

In our series, hypertension was detected in only one patient and resided with nephrectomy. We did not encounter any malignancy within a maximum follow-up period of 13 years. Also, histological examination of the nephrectomized kidneys did not result in any findings of nodular blastema, which is reported to progress into Wilms' tumor in approximately 1 in 100 cases [12]. These results

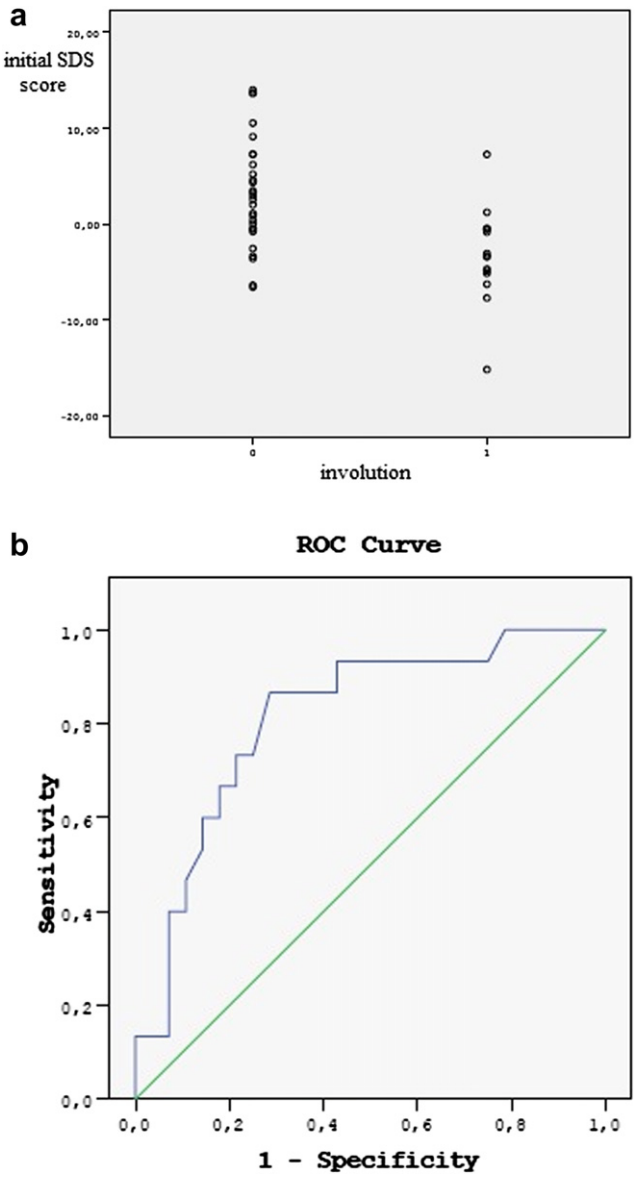

Figure 1 (a) Standard deviation score (SDS) for involuted and non-involuted kidneys ('1' represents totally involuted and '0' represents non-involuted kidneys). (b) ROC curve for SDS '0'.

Table 2 Distribution of antenatally diagnosed patients with more than 1 year follow-up (46) in terms of size and side of kidney.

	Right, big (10)	Right, small (15)	Left, big (12)	Left, small (6)
Involuted 18[a]	2	10	—	3
Non-involuted 28	8	5	12	3

[a] Initial size of kidney was not documented in 3 patients.

support the current literature that MCDK does not increase the risk of either hypertension or malignancy.

Frequencies of the coexistent urinary abnormalities were also similar [1,3,4,7,9,10]. On the other hand, our findings yield an interesting relation with the side and the initial size of the totally involuted kidney. To our knowledge, there is no published data about the relation between side of the multicystic kidney and involution, and there have been scarce reports on size of kidney and involution. As this study mainly focused on complete involution, we concentrated more on this issue.

An elegant study by Rabelo et al. stated that only a renal length of $<$62 mm on initial ultrasonography was associated with faster involution [12]. Unpublished data from Dhillon HK & Wacksman J, London also suggest that a length of 6 cm or greater by the end of the first year was a sign of non-involution [13]. Our series confirms the data about the predictivity of initial size on involution. Also, although not reaching statistical significance, an interesting finding drew our attention to the side of the abnormality. The majority of the non-involuted kidneys were in the big and left-sided group, and in fact the chance of involution for a large kidney on the left was zero; however, the involution risk for a small right-sided kidney was 67% (Table 2). For an objective assessment, only antenatally diagnosed patients with a follow-up of more than 1 year were included in the statistical analyses; however, a glance at the whole group reveals the same result: big left kidneys do not involute! There were 21 big left kidneys in 96 patients and none of these involuted. The side predilection of some genitourinary abnormalities and considerable dominancy of renal agenesis on the left side also encourage us to consider that there might be a relation between side and involution.

Despite the large patient group, our study suffers from being retrospectively constructed. Records of two centers were reviewed to increase the statistical power; however, only antenatally diagnosed patients with a follow-up of more than 1 year were included in the statistical analyses to avoid any bias. Larger series and prospective studies are required to clarify certain issues that we have discussed.

Conclusion

Reviewing a 15-year period of our MCDK patient records conveyed data supporting current literature mainly encouraging non-operative management of the condition. There are not enough data to come to any clear conclusion about the duration and frequency of follow-up; however, the results give a provoking clue to which patients will experience total involution. Further studies with larger series may reveal the relation, and our two objective indicators, the initial size and side of dysplastic kidney, may contribute toward the management strategies chosen, including nephrectomy.

Conflict of interest statement

None of the authors has any kind of financial or personal relationship that could inappropriately influence our work.

Ethical approval

Ethical approval was not required as this was a study based on retrospective review of the hospital records.

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