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Update on Multicystic Dysplastic Kidney

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Abstract Multicystic dysplastic kidney (MCDK) is the most common cause of cystic disease in children. It is characterized by multiple non-communicating cysts of varying sizes with no identifiable normal renal parenchyma. The incidence ranges from 1 in 1000 to 4300 live births, and it is one of the most commonly detected anomalies on prenatal ultrasound. MCDK has been shown to follow a benign course with relatively few sequelae and therefore should be managed conservatively. Currently, the key clinical questions revolve around the detection of anomalies in the contralateral kidney and follow-up imaging. The recent literature suggests that very limited radiographic evaluation of the MCDK is needed. The use of voiding cystourethrogram or nuclear medicine renal scans should be directed by any abnormalities on renal ultrasound or the development of urinary tract infections.

Keywords Multicystic dysplastic kidney · MCDK · Voiding cystourethrogram · VCUG · Nuclear medicine · Natural history

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Introduction

Multicystic dysplastic kidney (MCDK) is a non-heritable developmental anomaly of the kidney and is the most common cause for cystic disease in children. It is characterized by multiple non-communicating cysts of varying sizes with no identifiable normal renal parenchyma [1, 2]. The incidence ranges from 1 in 1000 to 1 in 4300 live births, and MCDK is one of the most commonly detected anomalies on prenatal ultrasound [1, 3]. It most commonly affects the left side, and there is a male predominance.

The literature over the past few years has contributed to answering several key questions surrounding the management of MCDK. After review of the recent literature, we summarize the recommendations regarding the use of serial renal ultrasounds (RUS) for follow-up. Because associated anomalies range from 5 to 48 % in the contralateral kidney, questions remain regarding routine evaluation with voiding cystourethrogram (VCUG) and the role of nuclear medicine (NM) imaging of the kidney.

Etiology

The etiology of the multicystic dysplastic kidney remains a topic of debate; however, there are two predominant theories. The first poses that renal pelvic ureteral atresia leads to severe obstructive hydronephrosis and MCDK [4••]. The other theory suggests that an abnormal interaction between the ureteric bud and the metanephric blastema will cause a failure of these structures to differentiate normally [5]. Other less widely accepted theories include teratogens such as viral infections or medications leading to MCDK [6].

Epidemiology and Diagnosis

MCDK is a congenital genitourinary anomaly that is most frequently identified on prenatal ultrasound (US). According to the literature, 60–80 % cases of unilateral MCDK are detected antenatally [1, 4••]. Cited rates of which renal unit is more commonly affected vary throughout the literature; however, a meta-analysis of 67 studies with approximately 3500 patients found a slight left-sided predominance (53 %) [5].

MCDK is relatively asymptomatic and is commonly detected on antenatal imaging. Postnatal detection of MCDK is less common (20 %), and it is increasingly rare that it presents with clinical symptoms such as an abdominal mass or urinary tract infections (UTIs) [5]. The most significant clinical feature of MCDK is the functionally solitary contralateral kidney; therefore, detection and management of any concomitant anomalies becomes the crux of evaluation.

The incidence of associated anomalies ranges from 5 to 48 % [1, 3, 5–8]. One large meta-analysis with 3500 patients found associated anomalies of the contralateral kidney in 33 % of patients with a rate of vesicoureteral reflux (VUR) of 20 % [5]. The most commonly detected anomalies include contralateral VUR (7–26 %), contralateral ureteropelvic junction (UPJ) obstruction (1.5–5 %), and contralateral ureterovesical junction (UVJ) obstruction (2 %) among other, less frequently described anomalies such as ureterocele and horseshoe kidney [4••, 5, 8–11].

Interestingly, one recent study observed an association of MCDK with the prevalence of unilateral or bilateral undescended testicles (UDTs) to be 12.7 % in a cohort of 165 males with MCDK [4••]. Most of the UDTs were right-sided (57.1 %) or bilateral (33.3 %). Almost all of the UDTs where on the same side as the MCDK (61.9 %) or were bilateral (33.3 %). The authors hypothesize that an association may be due to the abnormal interaction of the ureteric bud with the metanephric mesenchyme and general proximity of the kidney to the testis/gubernaculum during development [4••]. To our knowledge, an association between UDT and MCDK has never been described; a search on PubMed did not yield any other literature with the same conclusions. It will be interesting to evaluate this further in future cohorts of MCDK.

Natural History

Involution

In 2004, Rabelo et al. published a prospective study which included 43 children with MCDK diagnosed on prenatal US, adding to the literature demonstrating the benign clinical course of these patients [12]. Children were followed for a mean of 42 months (range 12–156 months) and underwent regular RUS evaluations every 6 months in the first 2 years then yearly thereafter, a confirmatory nuclear medicine scan and a VCUG. This study demonstrated complete involution in 19 % and partial involution in 70 % [12].

Several other studies have shown the tendency of the MCDK to involute. Involution may occasionally occur prenatally (5 %), soon after birth, or over many years [5]. The rate of involution is reported to range from 35 to 62 %, but it is likely this is an underestimate as MCDK is rarely found in adults [1, 3, 11]. Over short-term follow-up, if complete involution does not occur, the MCDK may decrease in size (30–44 %) or show no change in size (13–34 %) [1, 9, 13]. Eickmeyer et al. set out to identify potential radiographic markers of involution. In this study, the cumulative probability of involution was 9.8 % at 1 year, 38.5 % at 5 years, and 53.5 % at 10 years of age. Baseline MCDK size was the only significant predictor of involution with initial size less than 5–6 cm found to be predictive of complete involution [4••, 14]. In essence, smaller MCDKs were more likely to experience involution and at an earlier age, compared to larger MCDKs [4••].

Contralateral Compensatory Hypertrophy

The contralateral solitary kidney often undergoes compensatory hypertrophy, by mechanisms which have yet to be fully elucidated. Surprisingly, this has been shown to occur in utero. In a study by Mandell et al., measurements on prenatal ultrasound found that solitary kidneys were significantly larger than normal controls [15]. Several studies have shown a rate of compensatory hypertrophy of at least 45–81 % [6, 12]. Indeed, the rate of observed hypertrophy increases over longer periods of observation, with the highest rates reported in studies with up to 10 years follow-up [6]. Eickmeyer et al. used the 95th percentile as the standard for compensatory hypertrophy and reported that 49 % of patients reached these criteria by 1 year of age [4••]. By 5, 10, and 15 years of age, 78, 89, and 95 %, respectively, demonstrated compensatory hypertrophy [4••].

Hypertension

In a systematic review of the literature, Narchi et al. reported the rate of hypertension in children with MCDK as 5.4 per 1000 which was lower than the general population at 4–5 % [16]. Recent studies support a relatively low rate of hypertension with reported rates ranging from 1.5 to 6 % [3, 4••, 9, 11]. A recent large cohort of 300 patients with MCDK reported the incidence of hypertension as 3 % [4••]. Furthermore, nephrectomy performed for hypertension is not always curative. Studies have noted a 25 and 50 % resolution of hypertension following removal of dysplastic and multicystic dysplastic kidneys, respectively [6].

Malignancy

Another potential concern associated with MCDK is the risk of malignant transformation. Fortunately, the published rate of malignancy in children with MCDK is very low. In a systematic review by Narchi et al. which included 1041 patients, the reported rate of Wilms' tumor was zero in all 26 studies [17]. Based on this, the calculated risk of a child with unilateral MCDK developing Wilms' tumor was of course less than 1 in 1041 [16]. Cambio et al. summarized the highest numbers of reported Wilms' and renal cell carcinoma (RCC) citing ten reported cases of Wilms' tumor and six of RCC [18••]. However, they question the accuracy of the cases of RCC diagnosed in association with MCDK since none of the patients had a pre-existing diagnosis of MCDK. They raise the possibility that these may have been cystic RCCs [18••]. More recently, Eickmeyer et al. (2014) reported data on 300 patients over a 30-year period; no malignancy was identified in this cohort either [4••].

Management and Follow-up

Given the benign natural history of MCDK, the minimal risk of hypertension, and almost negligible risk of malignancy, the conservative management of the MCDK is advocated. The topics of debate surrounding MCDK are currently centered on the choice of imaging modalities, frequency, and duration of follow-up imaging studies. The key questions include whether a confirmatory NM renal scan is necessary, whether routine VCUG to evaluate for contralateral VUR is warranted, and finally, whether frequent, long-term follow-up with RUS is necessary.

Confirmatory Nuclear Medicine Studies

In order to minimize exposing children to additional testing, there is increasing literature that questions the necessity of a confirmatory renal scan to confirm the absence of function in the MCDK and to rule out UPJ obstruction. Whittam et al. retrospectively reviewed a cohort of 84 patients, all of whom underwent either Tc-99 m MAG3 or DMSA scan as follow-up to RUS to confirm the diagnosis of MCDK [19]. They found that RUS had a high predictive value in diagnosing MCDK [19]. They concluded that there was no benefit from a renal scan, as their studies confirmed the RUS finding of MCDK in 100 % of patients. Furthermore, they concluded a potential of savings over $200,000 of healthcare expenditures at their institution by forgoing a renal scan over the course of the study [19].

Kalisvaart et al. evaluated magnetic resonance urography (MRU) as an alternative to confirmatory DMSA scan and VCUG proposing this as a single test to determine the anatomy and function of the MCDK and contralateral kidney [20]. However, results indicated that RUS detected most cases of contralateral renal abnormalities compared with MRU; the only difference was the ability to detect the degree of severity. Hollowell and Kogan questioned the benefit of this proposed imaging modality given the sedation required and significantly higher cost associated with MRU [21].

It is our practice not to perform a routine renal scan but to reserve this study for those few cases in which the ultrasound is not clear-cut. Fortunately, as experience and quality of sonography improve, this is necessary less and less often. Not only is this approach much less expensive, it also spares radiation exposure.

The Need for VCUG

Much debate in the MCDK literature revolves around the need to perform routine VCUGs to detect VUR. The reported incidence of VUR in the contralateral solitary kidney ranges from 5 to 47 % of patients diagnosed with MCDK [1, 2, 4••, 6].

The literature highlights that the majority of VUR diagnosed on VCUG is low-grade (grade I–II), most of which resolves spontaneously. In 2005, Ismaili et al. found that in a cohort of 61 patients, if the contralateral kidney was normal on two consecutive comprehensive RUS performed 1 month apart, VCUG revealed low-grade VUR in only 7 % of patients [22••].

Calaway et al. (2014) retrospectively reviewed their series of 133 patients, all of whom had VCUGs performed, and identified VUR in 17 % (10 % contralateral) [23]. In their series, 54 % of those with VUR had low-grade VUR (grade I–II), 29 % had grade III, 14 % had grade IV, and only 4 % had grade V VUR [23]. Only 3 % of patients in this cohort were thought to require ureteral reimplant (one patient with grade II, two patients with grade IV, and one with grade V). Therefore, their conclusion was that routine VCUG in healthy children with MCDK may not be warranted. Potential indications for VCUG in patients diagnosed with MCDK included contralateral hydroureteronephrosis or signs and symptoms of a UTI [23].

Similarly, findings of recent series suggest that screening for VUR with VCUG is unnecessary as most VUR detected on these screening studies is not clinically significant [4••, 22••, 23]. VUR of clinical significance is most likely detected on VCUG prompted by an abnormal RUS.

In our experience, we have seen no clinical UTIs in patients with MCDK and, unless an ultrasound demonstrates a significant abnormality of the contralateral kidney, we would not recommend a VCUG.

Follow-up Imaging Algorithm

Over the past decade, algorithms for follow-up of MCDK have shifted from frequent ultrasound evaluation, confirmatory NM scan, and routine VCUG to less aggressive testing and

follow-up. Previously, published algorithms included follow-up RUS examinations performed at 6-month intervals during the first 2 years of life and yearly thereafter [12]. The rationale for serial RUS follow-up was mainly to assess for development of a renal mass or alternatively, involution, with the theory being that an involuted kidney would have little risk of malignant conversion.

Contemporary studies suggest limiting the number and frequency of RUS evaluations. This is based on the findings that the risk of malignancy arising from the MCDK is virtually negligible. As such, serial RUS evaluations add little to the management of MCDK patients. Furthermore, in 1998, Perez et al. presented a cost benefit analysis based on the follow-up algorithm of performing serial RUS every 6 months in the first 2 years then annually until age 8 in children with MCDK [24]. This analysis estimated a total national charge for serial US from $2.5 to $3 million in a population of 1000, and that was over 15 years ago [24]. As Onal and Kogan note, this estimate did not include any other associated charges (i.e., for an office visit with a urologist). In fact, they conclude that after initial diagnosis, serial RUS provided little clinically significant information and follow-up could be left up to the primary pediatrician to monitor for development of hypertension, an abdominal mass, or UTIs [1].

The current consensus regarding algorithms for evaluation and treatment of MCDK centers around conservative management and limited follow-up. It appears the literature is in agreement that minimizing diagnostic imaging (VCUG and DMSA) and RUS evaluations for follow-up is prudent. Long-term serial RUS follow-up for the purpose of detecting tumors does not seem warranted given the minimal risk of malignant conversion. Furthermore, several authors have suggested that regular follow-up of these children specifically for detection of hypertension does not require urological evaluation since this may be followed by an informed primary care physician [1, 4••].

Recent literature suggests there is no indication for performing serial RUS examinations, a baseline VCUG, or early nephrectomy in MCDK patients. However, initial RUS examination is essential not only for diagnosis but also to evaluate any abnormalities of the contralateral kidney. In order to adequately evaluate the contralateral solitary kidney, one algorithm recommends performing an initial postnatal US and one at 1 year with any further follow-up imaging guided by any abnormality of the contralateral kidney, abnormal blood pressure, or enlarging MCDK [4••].

Indications for Nephrectomy

It is important to note that before robust literature regarding the benign natural history of MCDK and the early detection on prenatal US examination, MCDK was diagnosed upon finding a large abdominal mass and managed by nephrectomy [18••]. However, now that the natural history of MCDK is more clearly understood, nephrectomy is no longer recommended as part of the management algorithm of MCDK.

Conclusion

The consensus of the contemporary literature is that limited radiographic evaluation of the MCDK is not only acceptable but preferable. Furthermore, to address the concern regarding detection of contralateral abnormalities, review of the literature indicates that further workup (i.e., VCUG or nuclear medicine study) should be directed by any abnormalities on RUS or upon development of clinical sequelae (HTN, UTI, palpable abdominal mass).

Compliance with Ethics Guidelines

Conflict of Interest Diana Cardona-Grau and Barry A. Kogan each declare no potential conflicts of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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