ORIGINAL ARTICLE

Unilateral multicystic dysplastic kidney: long term outcomes

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Aims: To report the long term follow up of children with antenatally detected unilateral multicystic dysplastic kidney (MCDK) with documentation of complications, involution rate with time, and renal function at 10 years.

Methods: Data were retrieved from a prospective regional registry of patients with MCDK between 1985 and 2004. Children were followed using a common protocol of investigation with follow up ultrasound scans (USS) at 2 (165 patients), 5 (117 patients), and 10 years (43 patients).

Results: Serial USS showed that 33% of the MCDK kidneys had completely involuted at 2 years of age, 47% at 5 years, and 59% at 10 years. No patients developed hypertension, significant proteinuria, or malignancy, but two developed pelviureteric junction obstruction in the contralateral kidney. Twenty seven of 143 children (19%) had vesicoureteric reflux (VUR) (96% mild to moderate VUR) into the contralateral kidney with no difference in the incidence of urinary tract infections or renal scarring between those with or without VUR. The mean estimated glomerular filtration rate (GFR) was 86.4 ml/min/1.73 m² (range 48–125) in 31 of 43 patients followed to 10 years.

Conclusions: Conservative management of unilateral MCDK is justified with clinical review and infrequent USS but longer term follow up continues in the 41% still with renal remnants at 10 years and those with impaired GFR. It is suggested that the initial micturating cystogram is deferred unless abnormal USS features are present in the contralateral kidney or ureter.

Unilateral multicystic dysplastic kidney (MCDK) is one of the commonest abnormalities detected by antenatal ultrasound with an incidence of approximately 1 in 3640 births.¹ Previous reports have emphasised that most MCDK kidneys undergo involution during the first five years of life.^{2–4} A conservative approach to children with MCDK has therefore been advocated, but others have suggested surgical removal on the basis of risk of hypertension, mass effect, potential for malignant change, and cost of repeated ultrasound examination.^{5–7}

Patients with a unilateral MCDK need to be evaluated for abnormalities in the contralateral kidney, with the reported incidence of vesicoureteric reflux (VUR) being 11–37%.^{2–8–10} Vesicoureteric junction obstruction (VUJ) and, more commonly, pelviureteric junction obstruction (PUJ), has also been reported in the contralateral kidney.^{3–10–11} Children with MCDK therefore need a protocol of initial investigation and regular follow up, even if the MCDK is removed, to determine the growth and function of the contralateral kidney.

We report our long term follow up of children with unilateral MCDK to document complications, involution rate with time, and renal function at 10 years. Although our initial investigation protocol routinely included a micturating cystourethrogram (MCUG) to detect VUR,¹² we also examined the necessity for this procedure by documenting urinary tract infection (UTI) and renal scarring rates in those with or without VUR.

PATIENTS AND METHODS

Since 1985 we have maintained a prospective regional registry of patients with antenatally detected MCDK using a common protocol of investigation and follow up agreed among members of the study group. MCDK was defined on the basis of antenatal and postnatal ultrasound appearance of non-communicating cysts and dysplasia with no function on a dimercaptosuccinic acid (DMSA) radionuclide scan usually performed within three months of birth. A kidney with cystic

dysplasia and function of any degree on the DMSA was excluded from the study.

Infants in this series were not routinely prescribed prophylactic antibiotics from birth. Trimethoprim (2 mg/kg/dose) twice a day for 2 days was prescribed to cover the micturating cystourethrogram (MCUG). If VUR Grade II or greater was detected on the MCUG, children were commenced on prophylactic trimethoprim for 2 years (2 mg/kg nocte). VUR was graded Grades I–V according to the international classification.¹³

Clinical assessment was carried out at 3 months at the time of the DMSA scan and at 6 and 12 months of age with clinic visits. Annual reviews were performed thereafter until 5 years of age and then biannually until 10 years of age. At each clinic visit there was enquiry of clinical symptoms, especially urinary tract infection, with measurement of growth parameters and urinalysis by dipstick. Blood pressure was assessed by Doppler for systolic pressure in young infants or standard mercury or aneroid sphygmomanometer in older children with reference to standard blood pressure centile charts for age and sex.¹⁴ Ultrasound examinations (USS) were performed at 2, 5, and 10 years of age. The USS measurements included an assessment of size of the MCDK and contralateral kidneys in relation to height. Compensatory hypertrophy of the normal contralateral kidney was defined as renal length greater than +2 standard deviations of the mean value of normal kidneys.¹⁵

The involution rate was calculated using life table analysis and Kaplan–Meier statistics. χ^2 analysis was used for comparison of urinary tract infection rates in those with or without vesicoureteric reflux.

Abbreviations: GFR, glomerular filtration rate; MCDK, multicystic dysplastic kidney; MCUG, micturating cystourethrogram; PUJ, pelviureteric junction obstruction; USS, ultrasound scan; UTI, urinary tract infection; VUJ, vesicoureteric junction obstruction; VUR, vesicoureteric reflux

RESULTS

Between 1985 and 2004, 202 cases of unilateral MCDK were registered. The right kidney was involved in 99 cases (49%). In six children the unilateral MCDK was associated with other congenital abnormalities (radial aplasia, Ehlers–Danlos syndrome, bladder diverticulum, hypospadias, CHARGE association, and DiGeorge syndrome). In four families there was a history of a single kidney (two grandmothers, one mother, one elder sibling who died prematurely at 26 weeks). The mean age of the patients under follow up at the time of the study was 8.1 years (range 0.1–19.7 years); 165 had been followed to 2 years, 117 to 5 years, and 43 to 10 years.

A total of 143 children had undergone MCUG; 27 patients (19%) had reflux into the contralateral kidney, with VUR occurring into the atretic ureter of the MCDK in 23 (16%). The grade of VUR into the contralateral kidney was mild (Grade I–II) in 74%, moderate (Grade III) in 22%, and gross (Grade V) in one child where the kidney was small and “globally scarred”. The initial USS in this child showed abnormal kidney structure and ureteric dilatation. Thirteen children with no documented VUR on MCUG had a UTI compared to seven children who also had UTIs while on prophylactic antibiotics for VUR under 2 years of age (not significant). The urinary tract symptoms were those of cystitis; no cases of pyelonephritis or hospitalisation for antibiotic treatment were documented.

Repeat MCUGs and DMSA scans were not performed after the initial investigations. A detailed USS at 2 and 5 years showed no evidence of renal scar formation in children with or without VUR or UTI.¹⁶ No child has had any evidence of proteinuria on dipstick urinalysis to date. No children with hypertension were recorded. No children had symptoms of vomiting or mass effect and no cases of malignancy have been noted.

Two children developed acute renal failure with PUJ obstruction in the contralateral kidney which required pyeloplasty at 9 and 14 months respectively.¹¹ The initial USS in both showed renal pelvic dilatation in the good kidney which merited closer follow up. Nephroureterectomy of the MCDK was performed in 11 children before 2 years of age. Indications included parental anxiety in two, suspicion of benign nephroma in one (histopathology confirmed MCDK only), and failure to reduce in size by 1 year of age in one patient. No indications were clearly specified in the remainder. No patient has undergone nephrectomy in Nottingham regional centre since 1988.

The rate of involution of the MCDKs on serial ultrasound is shown in fig 1. In 11 infants the initial postnatal USS showed disappearance of the MCDK which had been clearly defined antenatally. At 2 years, 34% had completely involuted; this percentage had risen to 47% at 5 years and 59% at 10 years.

Forty three patients have reached 10 years' follow up, with 35 of 43 (81%) demonstrating compensatory hypertrophy of the contralateral kidney. In five patients the kidney was above average size, and in three, size was not recorded. The mean estimated GFR (eGFR) of 31 patients based on height and plasma creatinine¹⁷ was 86.1 ml/min/1.73 m² (range 48–125), with 13 patients having eGFR >90, 16 eGFR 60–90, and two an eGFR <60 ml/min/1.73 m². All children had compensatory hypertrophy (>2 SD) of the contralateral kidney, with abnormal echogenicity suggestive of dysplasia being evident in the two patients with eGFRs of 48 and 59 ml/min/1.73 m² respectively.

DISCUSSION

This study is the largest reported series to date documenting the natural history of patients with MCDK who have been followed with a standard protocol. Paediatric surgeons and physicians have contributed to the registry, and apart from 11

Figure 1 Complete involution rate of MCDK kidneys.

children who underwent nephrectomy during the early years of the study, the follow up has documented the natural history of progressive involution. The lack of any clinical problems justifies conservative management.

Various reports have documented an involution rate of the MCDK of 25–52% between 2.5 and 6.5 years.^{2 18 19} Rabelo *et al*, in a recent paper based on follow up of 43 children from a single centre, suggested a median time of 122 months for the MCDK to become undetectable on USS.²⁰ The current series suggests that 40% of MCDK kidneys completely involute by 5 years and 59% by 10 years. Those that remain visible at 10 years are considerably smaller, with few remaining cysts. We therefore continue to follow these patients into their teenage years to confirm our suspicion that all will eventually involute with time. It is strongly suspected that MCDK is the major contributor to one of the commonest abnormalities in the general population, that of possessing only one visible kidney. Discussion with adult urological colleagues suggests that an MCDK kidney is rarely, if ever, recognised in adult practice.

The contrary view is that nephrectomy for all non-functioning kidneys can easily be performed on an outpatient basis with improvement in the child's insurability.^{7 21} The reasons for advocating nephrectomy of the MCDK are the rare problems of mass effect, hypertension, and potential for malignancy. The MCDK kidney can cause a large mass effect antenatally. However, we are unaware of any patient in our series who had delivery by caesarean section or who underwent postnatal operation for vomiting due to the mass effect.

Hypertension has been reported in children with MCDK and a recent systematic review of 29 studies revealed only six cases in 1115 eligible patients.²² Resolution of hypertension by removal of the affected kidney at 3 months, 23 months, and in a 14 year old patient has been reported,⁵ but hypertension may persist even after operation.²³ Reports have suggested that the hypertension may be renin mediated²⁴ and may be transient in infants where there are difficulties in measurement of blood pressure.^{25 26} It is still uncertain how often and for how long children with a unilateral MCDK need to be assessed for hypertension. Further reports such as ours increase the denominator of patients at risk. Hypertension must be a very rare event when one considers all the other

children with cystic dysplastic elements to their kidneys followed in urology and nephrology clinics.

Concern about potential malignancy in MCDK kidneys has resulted in units adopting a screening programme, as for Wilm's tumour, involving sonography every three months until age 8 years. The costs of 32 ultrasounds over eight years has also been used as justification for early nephrectomy as cost effective treatment for this condition.²⁷ Although nine cases of apparent malignant degeneration in MCDK kidneys have been reported,⁶ there is considerable doubt as to whether MCDK is truly involved as echogenic cysts, nephrogenic rests, cystic partially differentiated nephroblastoma, and cystic Wilm's tumour can be mistaken for a Wilm's tumour in a cystic kidney.²⁸ Our own series, and those of others, have reported no malignant change to date. The UK Cancer Study Registry has documented no cases of Wilm's tumour in MCDK kidneys (personal communication), and a recent systematic review of 26 studies revealed no cases of Wilm's tumour in 1041 eligible children.²⁹ This reinforces our current policy of only performing USS after birth and at 2 years, 5 years, and 10 years except in those patients who in the first two years of life have dilatation of the pelvis on the contralateral side that could evolve into a pelviureteric junction obstruction.¹¹

Abnormalities in the "normal" contralateral kidney are obviously important with one non-functioning MCDK kidney. VUR is the most common problem, with 19% incidence of reflux into the contralateral kidney, and 35% overall including reflux into the atretic ureter. This is similar to the incidence reported by others.⁸⁻¹⁰ However, the grade of reflux was mild to moderate in 96% of these patients, and reflux into the atretic ureter was by definition Grade I using the international classification. We had previously justified the routine use of the initial MCUG on this high pick up rate of VUR. However, only one child had obvious renal scarring on the initial USS and DMSA (in association with Grade IV VUR), and all subsequent USSs showed no evidence of scars in those with or without VUR. The incidence of UTI was also similar between those on prophylactic antibiotics for two years compared to those with no VUR who were followed in the clinic. Most of these urinary infections appear to have been lower urinary tract in nature and no child required intravenous antibiotics or had documented hospitalisation with pyelonephritis. We did not perform DMSA scans on our patients at follow up, but are fairly confident that the USS definition of renal scars is comparable to the DMSA when performed by our experienced radiologists.¹⁶ The MCUG is invasive, carries a high radiation burden, and can be distressing to patients and parents.³⁰

Our analysis has led us to abandon the MCUG on a routine basis in children with MCDK kidneys unless the initial USS is suspicious, such as dilated ureters, calyces, or small or abnormal appearance of the contralateral kidney. This viewpoint has recently been supported by one other group who reported that two successive normal neonatal US scans rendered a neonatal MCUG unnecessary.³¹ Our parents are given information about the possibility of UTIs and we suggest that MCUG is only required in patients who subsequently present at less than 1 year of age with UTI.³²

The lack of significant complications and clinical symptoms, hypertension, or malignancy would suggest that after the annual review at 2 years of age, the next clinical and ultrasound assessment could be carried out at 5 years. Parents should be informed that they should return sooner if the child has urine infections, abdominal complaints, failure to thrive, or headaches. At present we intend continuing follow up of all our patients to at least 10 years to assess renal function. Although the mean GFR in 31 patients followed to 10 years is acceptable at 86.4 ml/min/1.73 m², there is a

What is already known on this topic

- Unilateral MCDK is one of the commonest antenatally recognised urinary tract abnormalities
- Controversy still exists about the intensity of clinical and radiological monitoring with the focus on the risk of hypertension and malignancy

What this study adds

- The majority of MCDK kidneys completely disappear with time and those children with an involuted MCDK and contralateral kidney hypertrophy, normal blood pressure, urinalysis, and estimated glomerular filtration rate can be discharged from regular follow up
- Although 19% of patients had vesicoureteric reflux in the contralateral kidney, this was mild to moderate in degree, with no resultant scarring. The MCUG should no longer be a routine investigation in this group of children

subgroup of young people with lower values that will require long term evaluation. However, those patients with a normal estimated GFR, normal blood pressure, urinalysis, and complete involution of the kidney have now been discharged from long term follow up.

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