Multicystic Dysplastic Kidney

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Multicystic dysplastic kidney (MCDK) is a nonfunctioning kidney that does not undergo normal differentiation and therefore has immature-appearing renal parenchyma with cystic dilations (Fig. 2.1). MCDK is often diagnosed on antenatal ultrasound, where MCDK is the second most common urinary tract abnormality after hydronephrosis. MCDK is almost always unilateral and slightly more frequent in boys and on the left side. MCDK is an uncommon entity with an incidence of 1 in 4,300 births [1]. However, knowledge of MCDK is important for diagnosing and managing these children.

In normal embryogenesis, the ureteric bud undergoes a series of divisions to form the collecting system of the kidney; however, in MCDK the ureteric bud is thought to have abnormal branching into the metanephric blastema resulting in cystic dilations that resembles a bunch of grapes [2]. The dysplastic renal parenchyma frequently occurs in association with an atretic ipsilateral ureter. The "dysplasia" in MCDK refers to renal tissue that fails to undergo the normal process of differentiation to mature functioning nephrons; therefore, the histopathologic appearance is of immature renal parenchyma and cysts of varying sizes. The diagnosis of "dysplasia" should not be confused with the use of "dysplasia" as premalignant in other conditions (e.g., cervical cancer), as the incidence of malignancy in MCDK is exceedingly low.

Key points to remember about MCDK:
- MCDK has essentially no function on renal scan, which is required in establishing the diagnosis.
- "Dysplasia" refers to the failure of development of renal tissue and not to precancerous or malignant dysplasia.
- The contralateral "normal" kidney has a significantly increased risk of vesicoureteral reflux.
- The typical natural history of MCDK is of progressive involution, and nephrectomy is rarely required.

Presentation

The increased use of prenatal ultrasound imaging results in the early detection of most MCDK. Some children present with a palpable abdominal mass or following radiographic imaging at later ages during evaluation of urinary tract infection. Some children remain asymptomatic and are not diagnosed until a much later age. MCDK frequently involutes and some that are diagnosed in utero regress so that the child appears to have unilateral renal agenesis after birth. MCDK is very rarely diagnosed in adults, and thus many

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adults with a solitary kidney may have had an MCDK as a child.

MCDK is typically not associated with symptoms. However, MCDK may present as a palpable abdominal mass in a newborn, and the kidney can rarely be large enough to cause respiratory distress. MCDK is not typically associated with the development of urinary tract infection or hematuria, possibly because the function of the kidney is so low that little, if any, urine is actually produced by the kidney. The contralateral kidney typically has normal function, so presentation as acute renal failure is rare unless ureteropelvic junction obstruction is present in

Fig. 2.1 Nephrectomy specimen of MCDK

the contralateral kidney. Cardiac or neurologic conditions have not been consistently associated with MCDK.

Imaging Studies

The fetal kidney can be visualized on ultrasound at 18 weeks; however, the prenatal diagnosis is usually not made until the third trimester [3]. The antenatal diagnosis of MCDK may be considered based on appearance of the kidney on prenatal ultrasound which is of multiple noncommunicating cysts of various sizes. Because the anatomic detail of prenatal ultrasound is not precise, MCDK may also be labeled as antenatal hydronephrosis.

The postnatal ultrasound appearance of MCDK is of multiple noncommunicating cysts of various sizes that resemble a cluster of grapes (Fig. 2.2). The cysts on ultrasound appear as numerous anechoic (black) circular areas of variable size. The MCDK can be either enlarged or atrophic, and there is loss of the normal reniform shape and an absence of normal renal parenchyma. The contralateral kidney frequently undergoes compensatory hypertrophy resulting in a larger than normal size. Although infrequently obtained, a CT scan of MCDK demonstrates a cystic kidney with

Fig. 2.2 Ultrasound appearance of MCDK with noncommunicating cysts and no parenchyma
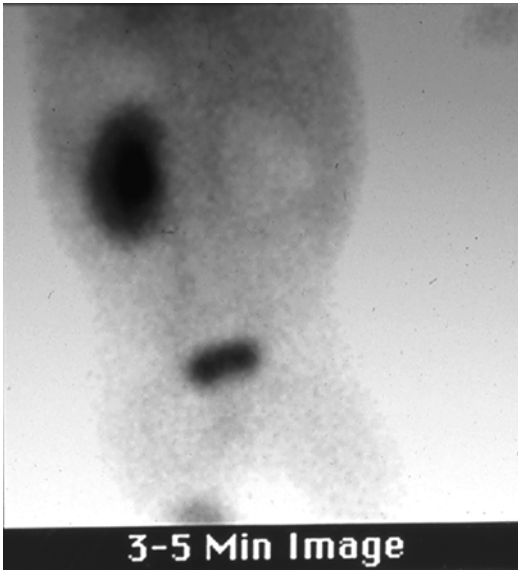
Fig. 2.3 Renal scan demonstrating no function of a right MCDK with an absence of radioisotope uptake, while uptake (*black area*) is seen in the left kidney with excretion to the bladder

Table 2.1 Diagnostic workup of MCDK

- History and physical exam
- Blood pressure measurement
- Serum creatinine
- Urinalysis, urine culture
- Renal ultrasound
- Renal scan (DMSA)
- VCUG

decreased parenchymal thickness and images following administration of intravenous contrast show decreased uptake and excretion in the affected kidney.

A renal scan is performed, usually within the first 3 months of life, to confirm the absence of function in the affected kidney and to rule out the diagnosis of a kidney affected by a severe uretero-pelvic junction obstruction. A renal scan is a nuclear medicine radionuclide study that utilizes intravenous injection of a radioisotope (dimer-captosuccinic acid [DMSA] or mercaptoacetyltri-glycine [MAG-3]) that is taken up and excreted by normally functioning kidneys and provides minimal radiation exposure. In MCDK the kidney shows no or minimal function on renal scan (Fig. 2.3), in contrast to kidneys with hydrone-phrosis which show functioning parenchyma. Table 2.1 outlines the diagnostic workup.

Differential Diagnosis

Several other entities should be considered in the differential diagnosis of MCDK. The modality of choice when evaluating cystic disease of the kidney is ultrasound. Most of the differential diagnoses may be excluded based on the interpre-tation of radiographic images by an experienced radiologist or urologist.

MCDK at times may be difficult to differen-tiate from severe hydronephrosis, which is the most common cause of a palpable abdominal mass in an infant. In hydronephrosis, the overall reniform shape of the kidney is maintained, but the renal collecting system (calyces and renal pelvis) is dilated and can give an appearance suggestive of multiple cysts. However, the "cysts" in hydronephrosis communicate with the renal pelvis. In contrast, with MCDK, the normal shape of the kidney is lost, cysts are non-communicating, and the collecting system is not visualized. On renal scan, a severely hydrone-phrotic kidney will usually show some function, in contrast to a nonfunctioning MCDK.

MCDK also must be differentiated from other forms of cystic kidneys. Simple renal cysts may occasionally be found in children and warrant follow-up ultrasound. Wilm's tumor tends to be solitary and encapsulated, which can be differ-entiated from MCDK based on radiographic appearance. Polycystic kidney can be broken into two groups: autosomal recessive (typically diag-nosed in the perinatal period) and autosomal dominant (diagnosed based on evaluation for known family history or in adulthood as most children are asymptomatic). The pathogenesis for MCDK is different than that of polycystic kidney. In MCDK the ureteric bud does not branch normally and results in dysplasia of the entire kidney, while in autosomal recessive poly-cystic kidney the architecture is destroyed by cystic deformation from dilated collecting ducts,

while the collecting system and reniform shape of the kidney remain normal. In the autosomal dominant variant, the dilation is in all portions of the nephron. Polycystic kidney disease is due to genetic mutations and involves both kidneys.

MCDK that has atrophied and involuted must also be differentiated from an atrophic kidney secondary to a different etiology, such as recurrent pyelonephritis or damage secondary to high-grade vesicoureteral reflux. Kidneys with reflux nephropathy may have poor function and renal dysplasia, but there are no associated cysts.

Associated Urinary Tract Abnormalities

About 15 % of MCDK will have vesicoureteral reflux into the dysplastic kidney, and 15–40 % of children with MCDK have vesicoureteral reflux in the "normal" contralateral kidney [4, 5]. Nineteen percent of children in the MCDK study group had contralateral reflux [5]. We routinely obtain voiding cystourethrogram (VCUG) in all children diagnosed with MCDK; however, some suggest that the initial VCUG can be deferred in children with a normal ultrasound of the contra-lateral kidney [5]. Prophylactic antibiotics and conservative management are used when vesico-ureteral reflux is present in the contralateral kidney, and if breakthrough infections occur, urologists should have a lower threshold for operative intervention due to reflux into a solitary functioning kidney.

Contralateral ureteropelvic junction obstruction can be present in up to 12 % of children with MCDK, which is increased over the risk in the general population [4]. Because the contralateral kidney provides the entire renal function in children with MCDK, those with ureteropelvic junction obstruction can present with acute renal failure.

The risk of future urinary tract infection may at times be used as an indication for nephrectomy, but the true risk of urinary tract infection or pyelonephritis in MCDK is low. One report found only 5 % of children with MCDK had a urinary tract infection during follow-up [6].

Outcome

The overall prognosis for children with unilateral MCDK is excellent. The MCDK can involute, and the kidney can become so small it cannot be identified by ultrasound. The MCDK study group established a prospective follow-up of children with MCDK and reported their findings in 2006, and on follow-up ultrasound the kidney had completely involuted in 47 % of children at 5 years and 59 % at 10 years [5]. Remarkably, in this group of 165 children, no child developed hypertension, significant proteinuria, or malignancy.

Children with MCDK have a favorable prognosis with respect to overall renal function because of compensation (compensatory hyper-trophy) by the contralateral kidney. One study reported that in 81 % of children the contralateral kidney enlarged to greater than 2 standard deviations compared to normal kidney size, and in children followed for 10 years in the MCDK registry, the mean glomerular filtration rate was 86 mL/min/1.73 m^2 (range, 48–125), with only 2 of 31 having an abnormal glomerular filtration rate of <60 [5]. Another report of 80 children found that all children had normal renal function and no proteinuria despite having only one functional kidney [6]. However, we have taken care of a boy who was born with MCDK and severe hydronephrosis of the contralateral kidney who went on to require renal transplant despite prompt treatment of the obstructed functioning kidney in the neonatal period.

Hypertension is a reported infrequent effect of MCDK thought to be renin secreted from ischemic areas of the dysplastic kidney [1]. A systematic review found only 6 cases of hypertension in 1,115 children (0.5 %), which is similar to the risk of hypertension in the general pediatric population [7]. Hypertension has been used as an indication for nephrectomy; however, cases have been reported of hypertension that persists even after nephrectomy [8].

A major concern of parents with regard to children with MCDK is the development of malignancy. While rare case reports of the development of Wilm's tumor in less than 10 children with MCDK have been reported [1, 9],

the concerns for potential malignancy development have not been substantiated by recent reviews. A systematic review of 26 cohort studies found no report of malignancy in 1,041 children [10], and one subsequent large series of 165 patients reported no malignancy identified [5]. One study performed flow cystometry in tissue from 30 MCDKs and found no abnormalities in the number of chromosomes present [11].

Management

All children with MCDK should be referred to a urologist or nephrologist. The management of MCDK has been an area of controversy. The appropriate subsequent follow-up for MCDK remains controversial and heavily debated, with a recent trend toward nonsurgical management and less frequent observation.

Most MCDKs can be managed conservatively with radiographic follow-up, rather than operatively. Nephrectomy remains indicated for cases of respiratory or gastrointestinal compromise (abdominal distension or poor feeding), suspicious solid renal mass, or hypertension. Some parents may seek nephrectomy due to parental anxiety or kidneys that fail to involute during follow-up. In one large series, nephrectomy was required in less than 7 % of children with MCDK [5]. In cases where nephrectomy is required, a laparoscopic approach is feasible if not excluded due to young patient age or large kidney size. Open nephrectomy can be performed through a small incision because cysts can be aspirated intraoperatively to leave only a small kidney for removal. Nephrectomy is generally well tolerated in children with low risk of complications and short hospital stay. In cases where the MCDK is refluxing, a nephroureterectomy may be indicated.

In the management of children with MCDK, some propose that one issue supporting nephrectomy over observation is that insurance companies may be more likely to offer standard insurance rates to a person with an absent kidney as opposed to someone with MCDK. In a survey of the life insurance industry, La Salle reported that 15 % would issue life insurance to a child with MCDK that was observed versus 71 % if treatment had been a nephrectomy [12].

Follow-Up

A consensus among pediatric urologists for radiographic follow-up of MCDK has not been reached. Previous surveillance regimens with frequent ultrasound were based on the false assumption that the development of Wilm's tumor was common in children with MCDK. Our typical recommended plan is radiographic follow-up every 12–18 months until kidney involution, after which radiographic follow-up can be discontinued. Others have recommended less frequent surveillance ultrasound at 2 and 5 years of age and then every 5 years [5]. A consensus has also not been reached regarding the length of follow-up required, with various groups recommending imaging to age 8, adulthood, or complete involution. One group recently commented that follow-up ultrasound provides no clinical benefit and increases parental anxiety and recommended no radiographic follow-up [13]. However, in those children who have contralateral renal pelvic dilation, follow-up ultrasound should be obtained more frequently due to the concern for development of ureteropelvic junction obstruction.

Blood pressure should be measured at clinic visits to assess for hypertension. While our group recommends continued blood pressure follow-up in all children, others have recommended that children with complete involution of the kidney, normal blood pressure, normal creatinine, and normal urinalysis can be discharged from long-term follow-up [5]. Children with MCDK have a solitary functioning contralateral kidney and should be counseled to avoid activities that would place that kidney at risk. This would include avoidance of contact sports and high-risk activities.

References

1. Gordon AC, Thomas DF, Arthur RJ, Irving HC. Multicystic dysplastic kidney: is nephrectomy still appropriate? J Urol. 1988;140(5 Pt 2):1231–4.

2. Bisceglia M, Galliani CA, Senget C, Stallone C, Sessa A. Renal cystic diseases: a review. Adv Anat Pathol. 2006;13(1):26–56.

3. Avni EF, Thoua Y, Lalmand B, Didier F, Droulle P, Schulman C. Multicystic dysplastic kidney: natural history from in utero diagnosis and postnatal followup. J Urol. 1987;138(6):1420–4.

4. Glassberg KI. Renal dysgenesis and cystic disease of the kidney. In: Wein AJ, Kavoussi LR, Novick AC, Partin AW, Peters CA, editors. Campbell-Walsh urology, vol. 4. 9th ed. Philadelphia: Saunders; 2007. p. 3305–58. Chap. 114.

5. Aslam M, Watson AR. Unilateral multicystic dysplastic kidney: long term outcomes. Arch Dis Child. 2006;91(10):820–3.

6. Weinstein A, Goodman TR, Iragorri S. Simple multicystic dysplastic kidney disease: end points for subspecialty follow-up. Pediatr Nephrol. 2008;23(1):111–6.

7. Narchi H. Risk of hypertension with multicystic kidney disease: a systematic review. Arch Dis Child. 2005;90(9):921–4.

8. Snodgrass WT. Hypertension associated with multicystic dysplastic kidney in children. J Urol. 2000;164(2):472–3; discussion 473–4.

9. Homsy YL, Anderson JH, Oudjhane K, Russo P. Wilms tumor and multicystic dysplastic kidney disease. J Urol. 1997;158(6):2256–9; discussion 2259–60.

10. Narchi H. Risk of Wilms' tumour with multicystic kidney disease: a systematic review. Arch Dis Child. 2005;90(2):147–9.

11. Jung WH, Peters CA, Mandell J, Vawter GF, Retik AB. Flow cytometric evaluation of multicystic dysplastic kidneys. J Urol. 1990;144(2 Pt 2):413–5; discussion 422.

12. LaSalle MD, Stock JA, Hanna MK. Insurability of children with congenital urological anomalies. J Urol. 1997;158(3 Pt 2):1312–5.

13. Onal B, Kogan BA. Natural history of patients with multicystic dysplastic kidney-what followup is needed? J Urol. 2006;176(4 Pt 1):1607–11.