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Potential Role of Tc-99m DTPA Diuretic Renal Scan in the Diagnosis of Calyceal Diverticulum in Children

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Abstract: The aim of the study was to assess the usefulness of Technetium-99m diethylene triamine pentaacetic acid (Tc-99m DTPA) diuretic scan to diagnose calyceal diverticulum (CD).

From January 2000 to June 2014, children with evidence of renal cystic lesions of undetermined diagnosis on ultrasound were enrolled. Computed tomography urography (CTU) and Tc-99m DTPA diuretic scan were performed to characterize the precise anatomy. The diagnosis of CD depended on visualization of a renal cystic lesion with filling of contrast material or radiotracer from the collecting system on CTU or diuretic renal scan. Children who had positive findings of CD on 1 or both imaging studies were selected and analyzed.

Both CTU and Tc-99m DTPA diuretic renal scan were performed in 39 children. A total of 9 (23.1%) children with CD were diagnosed. All 9 children had positive diagnosis of CD on diuretic renal scan. Only 6 (66.7%) children could be diagnosed by CTU, and CD was missed by CTU in 3 subjects. The differential renal functions in patients with CD were 46% to 55%. The time of radiotracer appearance in the CD ranged from the 8th to the 24th minute. Seven patients had persistent accumulation of radiotracer in their CD at the end of the study.

Tc-99m DTPA diuretic renal scan seems to be more sensitive than CTU in diagnosing CD. The possible reasons of higher sensitivity are discussed. Additional advantages that Tc-99m DTPA diuretic renal scan provides include the following: continuous monitoring, less radiation doses, and information on renal function, making it an attractive alternative to CTU for diagnosis of CD.

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Abbreviations: CD = calyceal diverticulum, CTU = computed tomography urography, IVP = intravenous pyelography, Tc-99m DTPA = Technetium-99m diethylene triamine pentaacetic acid.

INTRODUCTION

Calyceal diverticulum (CD) is a rare disorder in children, in which a urine-filled cavity is connected to the renal calyx

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or, less commonly, the renal pelvis by a narrow neck or isthmus. CD lining consists of nonsecretory transitional epithelium and the lining is surrounded by muscularis mucosae. Functionally, CD passively fills with retrograde urine flow from the adjacent calyx through the diverticular neck.^{1,2} It may be found at any age, occurs with equal frequency in male and female patients, with no predilection for laterality.³ CD can be congenital resulting from embryological malformation during renal development, likely because of failed degeneration of the third or fourth division of ureteral buds of the Wolffian duct.^{2,3}

Most CD is small or asymptomatic. However, urinary stasis within the diverticulum can be associated with significant sequelae, including stone formation, febrile urinary tract infections, abscess formation, and progressive renal damage.¹⁻⁵ Common presenting features include flank pain, gross hematuria, and recurrent urinary tract infections. With the widespread use of ultrasound, asymptomatic CD is always found incidentally. However, CD is likely underdiagnosed because it often appears as a simple or complex cyst on initial ultrasonography.¹⁻⁶ Multiple or bilateral CD can mimic autosomal dominant polycystic kidney disease.⁵ Other differential diagnoses of CD include parapelvic cyst, hydrocalycosis, renal papillary necrosis, and renal tumors.²⁻⁶ History, physical examination, and laboratory data are not specific to diagnose CD. The key to diagnosis is visualization of a renal cystic lesion with retrograde contrast opacification from the collecting system on intravenous pyelography (IVP), computed tomography urography (CTU), or retrograde pyelography. The connecting channel is usually fine and only occasionally visualized on urography.

Technetium-99m diethylene triamine pentaacetic acid (Tc-99m DTPA) diuretic renal scan is a common nuclear medicine procedure performed in children. It can continuously demonstrate the whole urinary collecting system and provide useful information for the management of children presenting with obstructive uropathies. The procedure is safe, simple, and minimally invasive. Our study aimed to compare Tc-99m DTPA diuretic renal scan with standard CTU in detection of CD in children.

METHODS

The objective of this retrospective study was to assess the role of Tc-99m DTPA diuretic renal scan in the diagnosis of CD in children. Our research was reviewed and approved by Institutional Review Board. From January 2000 to June 2014, children with evidence of renal parenchymal cystic lesions of undetermined diagnosis on ultrasound were enrolled in this study to distinguish between CD and other renal cystic lesions. The inclusion criteria include children presenting with flank pain, cystic infection, gross hematuria, or stone formation within cyst, or renal cystic lesions >1.0 cm at diagnosis or during a follow-up. The exclusion criteria include children with typical presentations or imaging studies of other renal cystic diseases.⁷ For the enrolled patients, both CTU and Tc-99m

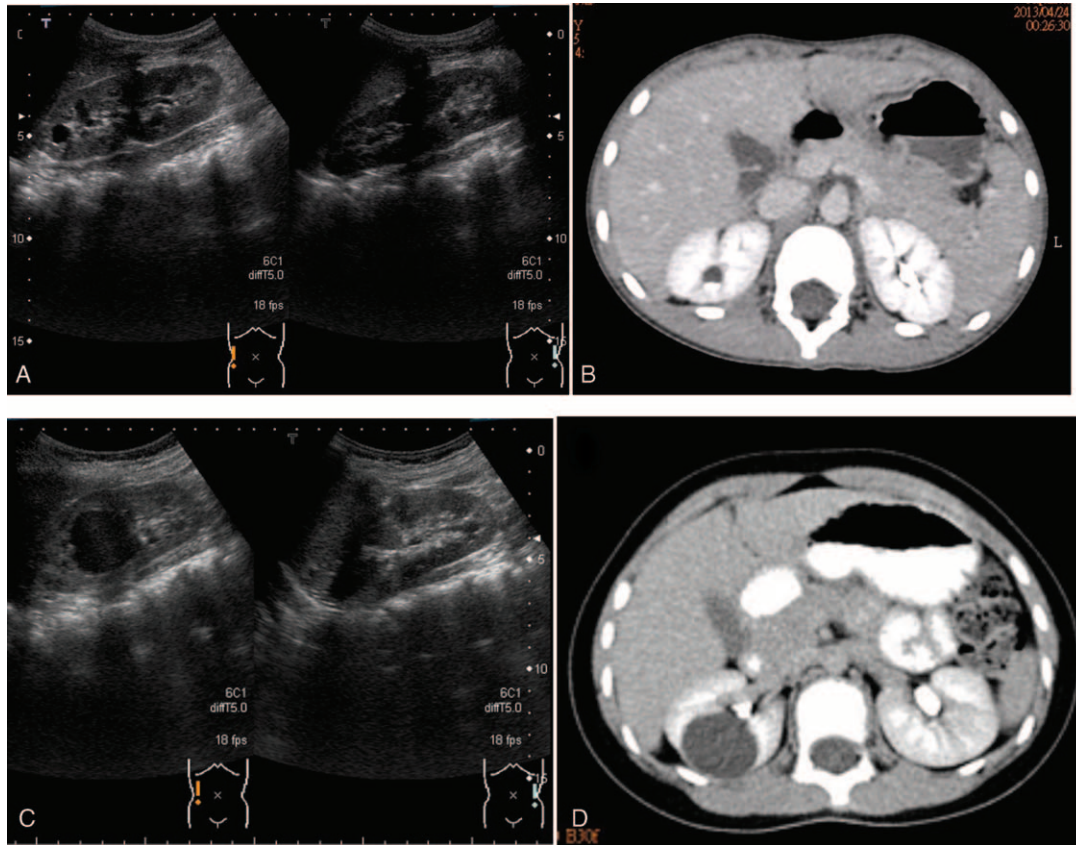


FIGURE 1. A and B, A cystic lesion in the right upper pole is noted on renal ultrasound. Postcontrast CTU image showed a cystic lesion with fluid–fluid level, suggesting a calyceal diverticulum. C and D, Renal ultrasound revealed a cystic lesion in the right kidney. There is a well-defined hypodense lesion without retention of contrast medium on delayed film of CTU, indicating a simple renal cyst. CTU = computed tomography urography.

DTPA diuretic scan were suggested and performed. Informed consent was obtained from parents after they were informed of the aims, potential risks, and benefits of imaging studies.

Water-soluble Ultravist-300 (623 mg of iopromide/6 mL, Bayer) was used as contrast agent for CTU at a dose of 3.0 mL/kg body weight for children ages 2 to 11 years and 1.5 mL/kg body weight for children >11 years. CTU was performed using 5-mm-thickness sections with a 3-phase protocol, including unenhanced, nephrographic phase, and 10-minute excretory phase. The 10-minute excretory phase image was acquired at 10 minutes after the injection of contrast media for each patient. Coronal section images were reconstructed from 10-minute excretory phase. The diagnosis of CD on CTU is based on visualization of a renal cyst with filling of the cavity with contrast material, confirming communication between the cyst and collecting system (Figure 1A,B). If no contrast material was observed in a cyst, the diagnosis of a simple cyst was rendered (Figure 1C, D).

Standard procedures for Tc-99m DTPA diuretic renal scan were performed according to published guidelines.⁸ All children were instructed to have adequate hydration before examinations. Posterior views were obtained from patients in a supine position using a gamma camera (SP-6 HR or Millennium MPR, General Electric Healthcare) equipped with a low energy, parallel-hole all-purpose collimator. After intravenous injection of Tc-99m DTPA in a dose of 0.1 mCi/kg body weight,

sequential 15-second frames were acquired with a dedicated nuclear medicine computer. Furosemide in a dose of 1 mg/kg (up to a maximum of 40 mg) was given, typically 15 to 20 minutes after radiotracer injection, and sequential images were acquired for an additional 20 to 30 minutes. Differential renal function and evidence of obstruction of urinary system were evaluated. The diagnosis of CD on DTPA diuretic renal scan included initial photopenia on the cyst area in the early phase image, followed by gradual intracystic radiotracer accumulation and stasis in the later phase image (Figure 2A). The differential renal function, time of radiotracer appearance in the cyst, and time of radiotracer excretion from the cyst were recorded. If the photopenic area persisted without increased radiotracer in the later phase image, a simple cyst was diagnosed (Figure 2B).

Children who had positive findings of CD on 1 or both imaging studies were further analyzed. Data were extracted from their medical records to determine when the diagnosis was made and the results of imaging studies. Sonographic examinations were reviewed for the following cyst characteristics: location in the kidney, number of cysts, maximum diameter, shape, and whether calcifications or stones were present.

RESULTS

Over the 13.5 years of the study, 42 children with renal parenchymal cystic lesions on ultrasound met entry criteria for

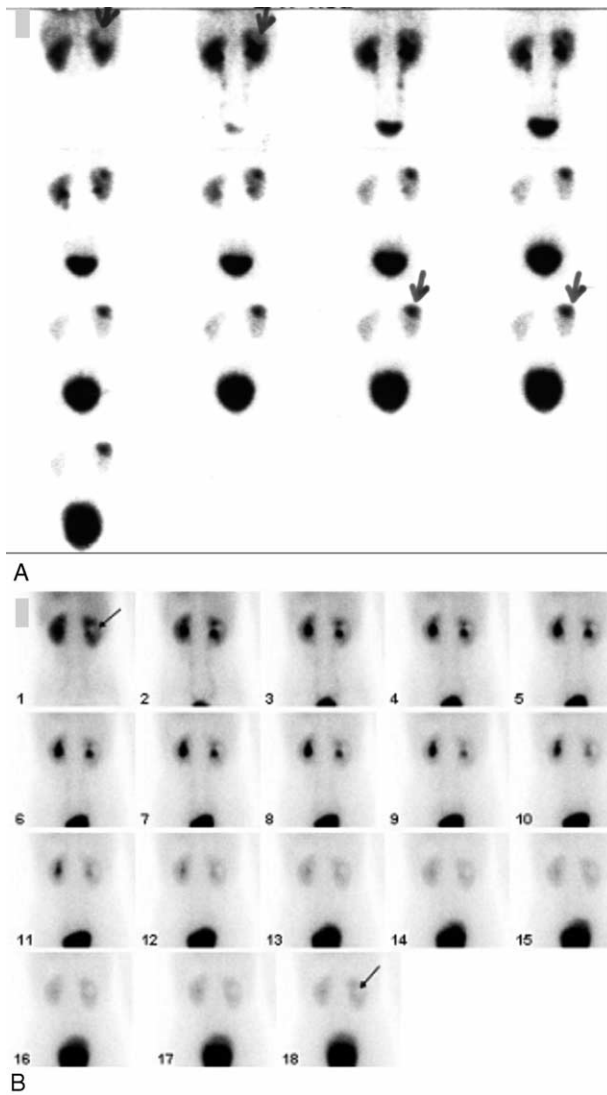


FIGURE 2. A, Calyceal diverticulum detected by Tc-99m DTPA diuretic renal scan. A photopenic area in the right upper pole is seen in the early phase image which shows gradual radiotracer accumulation and stasis in the later phase image. B, Right simple cyst on Tc-99m DTPA diuretic renal scan. The area of photopenia persists and no radiotracer entrance seen during the duration of the imaging period.

evaluation. Both Tc-99m DTPA diuretic renal scan and CTU were performed in 39 children, 20 boys, and 19 girls, ages 3 months to 18 years (mean 7.5 years) in order to characterize the precise anatomy. The 2 examinations were performed within 5 days of each other. Of 39 children, 30 (76.9%) had no evidence of filling of contrast material or radiotracer in the cystic lesion, and therefore the diagnosis of simple cysts was made. A total of 9 (23.1 %) children (6 girls and 3 boys, ages 3–15 years) each with 1 CD were diagnosed by 1 or both imaging studies.

Their clinical presentations and sonographic findings are summarized in Table 1. Eight children had only 1 cystic lesion. One child (patient 5) had 2 cystic lesions in unilateral kidney which were later proved to be 1 CD and 1 simple cyst (Figure 3). Four children initially presented with flank pain related to CD.

TABLE 1. Clinical Presentations and Sonographic Findings in 9 Children With Calyceal Diverticulum

Patient	Sex	Age at Diagnosis	Indication for Ultrasound	Location of Cyst	Shape/Surface	Diameter	Calcification Or Stone
1	F	10 yr	Intermittent abdominal pain, Rt flank knocking pain	Rt middle area	Round/smooth	19 mm	No
2	M	9 yr	Abdominal pain*	Rt middle area	Round/irregular	20 mm	1 stone
3	M	9 yr	Rt flank pain	Rt upper pole	Round/irregular	24 mm	No
4	F	15 yr	Lt flank pain	Lt lower pole	Round/smooth	23 mm	No
5	M	5 yr	Bronchopneumonia with abdominal pain	1 in Rt upper pole 1 in Rt middle area	Round/irregular	23 mm (upper) 16 mm (middle)	No
6	F	3 yr	Nephrotic syndrome	Lt middle area	Round/irregular	17 mm	No
7	F	7 yr	Rt flank pain	Rt upper pole	Round/smooth	40 mm	No
8	F	3 yr	Fever with pyuria†	Rt middle area	Round/smooth	26 mm	1 stone
9	F	9 yr	Precocious puberty	Lt upper pole	Round/smooth	12 mm	No

Lt = left; Rt = right.

* The final diagnosis in patient 2 was acute appendicitis.

† The final diagnosis in patient 8 was viral infection.

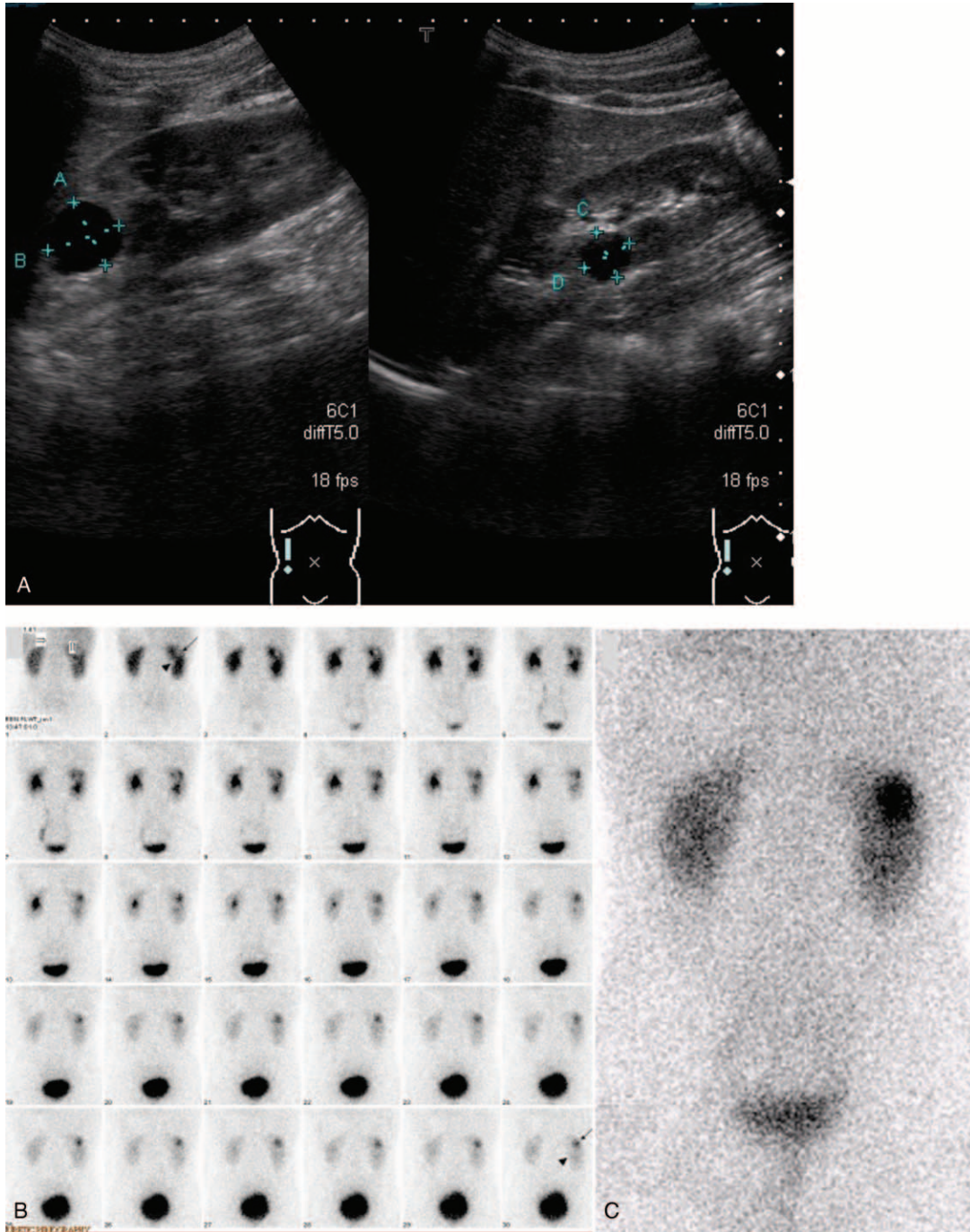


FIGURE 3. Patient 5. A, Renal ultrasound showed 2 cysts in the right upper pole and middle portion. B and C, The Tc-99m DTPA diuretic renal scan revealed a relatively larger sized right kidney with a photopenic area in the superolateral portion, which showed gradual accumulation of radiotracer in the later phase image (arrow), and another photopenic area at middle medial portion without obvious radiotracer accumulation (arrowhead). After injection of furosemide, there was persistent retention of radiotracer in the afore-mentioned lesion at superolateral portion of right kidney.

The other 5 patients were asymptomatic and their renal cystic lesions were noted incidentally on ultrasound for other unrelated reasons, including nephrotic syndrome, precocious puberty, appendicitis, sterile pyuria, and bronchopneumonia-associated abdominal pain. The sonographic findings were

nonspecific, and the lesions were round with a smooth wall in 5 of 9 children (55%) and an irregular wall in the other 4 children (45%). The maximum diameter of CD ranged from 12 to 40 mm. Six CD patients presented with right kidney and 3 with left kidney disease. The anatomic locations within the

TABLE 2. Computed Tomography Urography and Tc-99m DTPA Diuretic Renal Scan Results in 9 Children With CD

Patient	Diagnosis on CTU	Diagnosis on DTPA Diuretic Scan	Differential Renal Function (Rt:Lt) on DTPA Diuretic Scan	Time of Radiotracer Appearing in Cyst on DTPA Diuretic Scan	Time of Radiotracer Excretion From Cyst on DTPA Diuretic Scan
1	Rt CD	Rt CD	49%:51%	8th minute	Incomplete excretion
2	Rt CD	Rt CD	50%:50%	8th minute	Incomplete excretion
3	Rt CD	Rt CD	46%:54%	9th minute	24th minute
4	Lt CD	Lt CD	52%:48%	9th minute	Incomplete excretion
5	Rt 1 CD, 1 cyst	Rt 1 CD, 1 cyst	53%:47%	10th minute	Incomplete excretion
6	Lt CD	Lt CD	53%:47%	9th minute	30th minute
7	Rt renal cyst	Rt CD	48%:52%	9th minute	Incomplete excretion
8	Rt renal cyst with marginal enhancement	Rt CD	50%:50%	24th minute	Incomplete excretion
9	Lt renal cyst	Lt CD	45%:55%	10th minute	Incomplete excretion

CD = calyceal diverticulum; CTU = computed tomography urography; Lt = left; Rt = right.

kidneys varied with 4 in upper, 4 in middle, and 1 in the lower pole of the kidney. Intracystic calculi were found in 2 (22%) of our patients, 1 of whom (patient 2) presented with ipsilateral flank pain. Three patients (patients 1, 4, and 7) underwent surgical procedures to relieve intolerable flank pain during follow-up.

The findings of CTU and Tc-99m DTPA diuretic renal scan are shown in Table 2. All 9 children with CD had a positive Tc-99m DTPA diuretic renal scan. In contrast, 6 of these 9 children were positive for CD by CTU studies (Figure 4). Overall, CD was missed by CTU in 3 of 9 (33.3 %) subjects. No patient had an obstructive curve on diuretic renal scan. The differential renal functions of the kidneys with CD were 46% to 55%, with none of them less than 40%. The time at which radiotracer appeared in the CD ranged from the 8th to the 24th minute. Seven patients had persistent accumulation of radiotracer in the CD at the end of study. Of the 3 children whose CD was seen only by Tc-99m DTPA diuretic renal scan, intracystic radiotracer appeared at the 9th, 10th, and 24th minutes, respectively. CTU in patient 8 revealed marginal enhancement of cystic wall but no definite retention of contrast media in the cystic lesion, and this patient had the longest time until the appearance of radiotracer on Tc-99m DTPA diuretic renal scan (Figure 5).

DISCUSSION

Our studies show that Tc-99m DTPA diuretic renal scan seems to be more sensitive than CTU in diagnosing CD. The management of CD and other renal cystic diseases are different. Accurate diagnosis of CD guides appropriate management and also spares the patients and their families the psychological burden of other renal cystic diseases,⁹ making the discrimination of CD from other renal parenchymal cystic lesions very important.

In our cases, renal cystic lesions were initially suggested on ultrasound studies, and CD were later diagnosed on the basis of filling of contrast material on CTU or radiotracer on Tc-99m DTPA diuretic renal scan. Since ultrasound findings of CD are nonspecific, it fails to distinguish between CD and other causes of renal cysts. As evident from our cases, a CD will generally appear as a well defined, anechoic, smooth or irregular,

thin-walled, parapelvic cystic structure, which may not always be seen to communicate with a calyx.⁶

A mobile calculus is a characteristic finding in CD.^{3,10} When a calculus is found in the cyst, these patients should be scanned in both the supine and prone position to determine the gravitational change of echogenic content. The presence of mobile echogenic content strongly suggests the diagnosis of a CD. On the contrary, calcifications in complex renal cysts present as immobile forms such as mural or septal calcification. In 35% to 50% of adult CD, calculi develop, either in the form of stones or milk of calcium.^{1,3,11} In children, the incidence of stone formation is relatively low, occurring in 13% (3/22) to 29% (7/23) of cases.^{2,5} In our pediatric cases, only 2 of 9 (22%) patients had CD calculus. These results show that ultrasound detection of calculus formation is insensitive as a sole diagnostic modality in children with CD. Therefore, when a CD is suspected, other radiological studies may be needed.

Although CD may be demonstrated on delayed image of IVP, it has limited utility in evaluating other cystic diseases. Previous studies showed minimal role for IVP in evaluating CD, because of the lack of detailed 3D anatomic information and decreased sensitivity for renal stones that commonly complicate CD.^{1,3,5} Due to the increasing use of ultrasound and CTU, IVP is employed less commonly in current practice. On unenhanced CT scan, CD appears as a well defined, thin walled, low density structure. Following intravenous contrast, the structure should gradually fill with contrast, as contrast leaves the normal calyx and fills the diverticulum.¹² On excretory phase scan, prolonged opacification may be observed, as contrast flows slowly out of the diverticulum passing through the narrow neck.^{6,12} Multiplanar reformat images provide valuable anatomical information and delineate the location of the CD and its relationship to the collecting system with better visualization, and inform the planning of percutaneous and open surgical procedures.^{3,12}

However, CTU alone might be insufficient for diagnosis.¹ A recent study reported by Lin et al showed that CTU detected only 75.6% patients with CD complicated by urolithiasis based on imaging at 10-minute excretory phase, after the diagnosis of CD was confirmed by retrograde pyelography or surgery.¹ Retrograde pyelography is recognized as having a higher sensitivity in demonstrating CD, as it allows greater distension

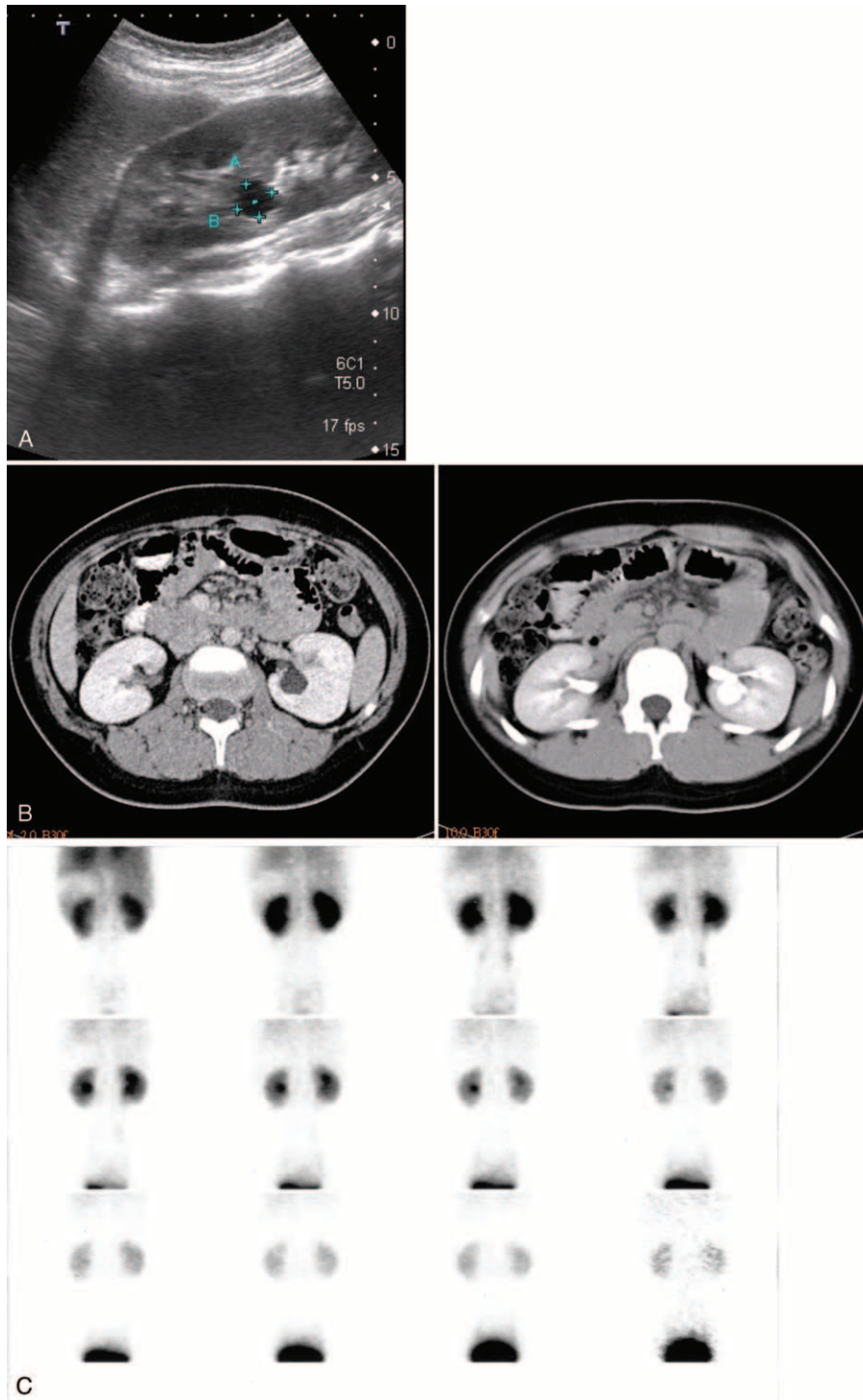
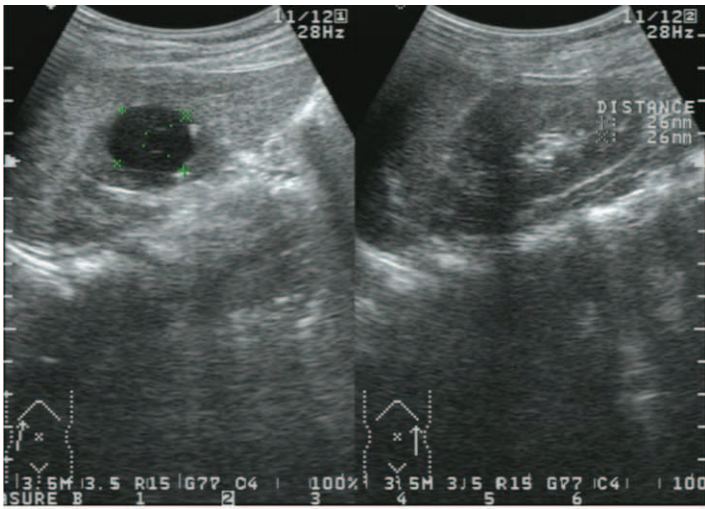


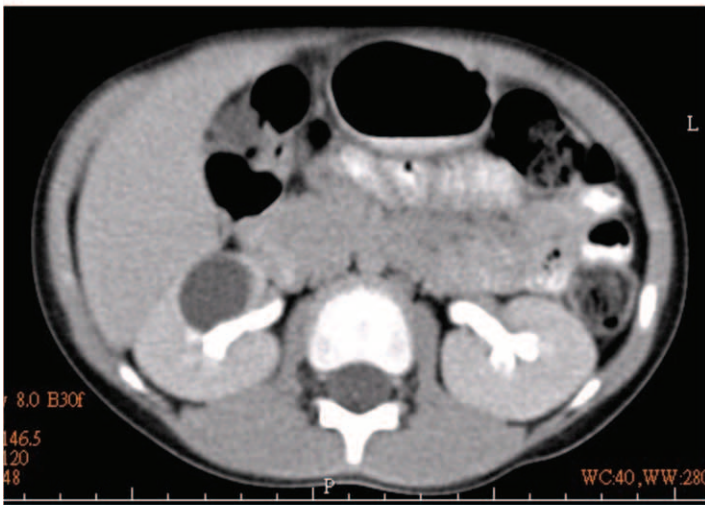
FIGURE 4. Patient 6. A, Renal ultrasound revealed a cystic lesion in left middle portion. B, Computed tomography urography showed a parapelvic cyst with communicating with collecting system, indicating a calyceal diverticulum. C, Tc-99m DTPA diuretic renal scan demonstrated a photopenic area in the middle medial portion of left kidney in the early phase images with later radiotracer accumulation beginning at the 9th minute, followed by excretion at the 30th minute.

of the collecting system than can be attained with IVP.^{1,3,12} The disadvantage of the procedure is that it is invasive and requires cystoscopy and anesthesia. CD and its isthmus may be theoretically shown on magnetic resonance (MR) imaging with a

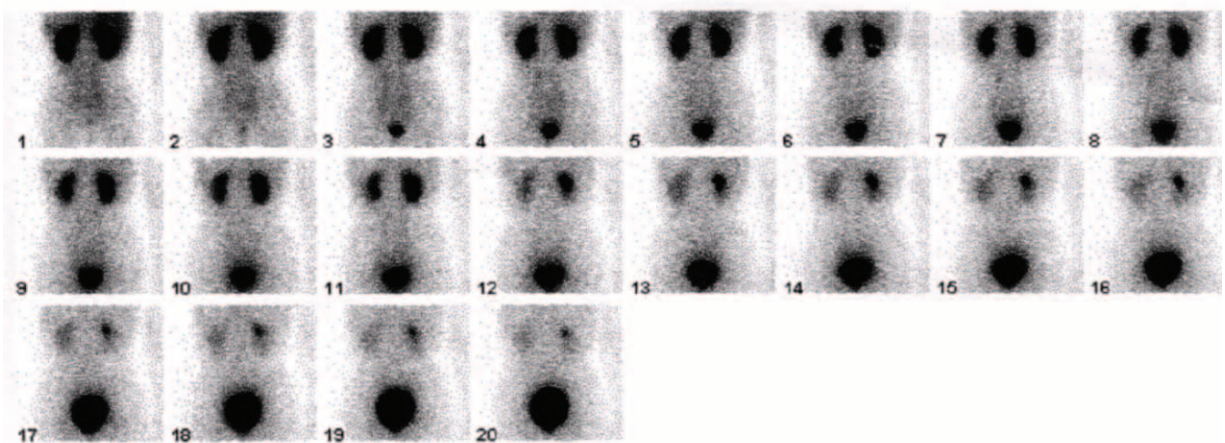
combination of MR urography and delayed contrast-enhanced imaging. However, the reported cases were rare in the literature.³ The role of MR imaging in the diagnosis of CD should be further studied in the future.



A



B



C

FIGURE 5. Case 8. A, Renal ultrasound revealed a cystic lesion with a calcified spot in right middle portion. B, The delayed contrast computed tomography demonstrated marginal enhancement in the cystic lesion but no definite retention of contrast media in the lesion. C, Tc-99m DTPA diuretic renal scan showed local radiotracer stasis in the right kidney after diuretics injection, consistent with calyceal diverticulum.

Three cases of CD in the literature showed renal abnormality first detected incidentally via nuclear medicine studies. Two patients received F-18 FDG PET whole-body scan for cancer screen and esophageal cancer staging, whereupon an abnormal focus of increased activity in the patient's kidneys was found, CD abnormalities were later confirmed by pathology examination and contrast-enhanced CT respectively.^{13,14} A third patient, a 58-year-old female, was being followed up for breast cancer, and a nuclear medicine bone scan showed a focal area of increased tracer uptake in the left kidney. The CD was diagnosed by subsequent ultrasound, CT and IVP.⁶ In addition, Karmazyn et al reported 2 patients with large upper pole CD whose Tc-99m mercaptoacetyl triglycine (MAG3) renal scan mimicked obstructed upper moiety in a duplex kidney.⁵ Turgut et al performed nuclear scan for evaluating the effect of a large pelvic diverticulum on renal function. They concluded that a renal pelvic diverticulum should be thought of when tracer accumulates on Tc-99m DMSA scintigraphy.¹⁵ Together, these studies indicate the potential role of nuclear medicine in the detection and diagnosis of CD.

Tc-99m DTPA diuretic renal scan is a noninvasive, widely available test that can evaluate renal function and urodynamics in a single procedure. The test operating principle depends on high endogenous rate of urine flow stimulated by the administration of diuretics. Interpretation of the results is based on washout of radiopharmaceutical from the collecting system. Our study appears to be the first to describe a series of CD diagnosed by Tc-99m DTPA diuretic renal scan. Early phase images after intravenous injection of Tc-99m DTPA reveal well radiotracer uptake by kidneys with a photopenic lesion on CD area which showed gradual accumulation of radiotracer in the later phase images. After administration of diuretic agent, most of the tracer has been excreted from the urinary pelvis, and then the CD can be clearly visualized when there is delayed elimination of urine from the diverticulum. Our experience has shown that the "cold area" resulting from CD lesion in early phase images may be obscured because of overshadowing by surrounding normal tissue, but after excretion of radiotracer from normal renal tissue in the later phase image, the "hot spot" caused by the presence of a CD becomes readily apparent. Thus, use of diuretics provides additional information and aids in the diagnosis of CD on Tc-99m DTPA renal scan.

Contrast-enhanced CT with delayed image has been suggested as the imaging modality of choice for the diagnosis of CD.⁵ From our study, Tc-99m DTPA diuretic renal scan detected CD with increased sensitivity compared to the 10-minute delayed CTU. Of the 9 children with CD, 3 patients were demonstrated on Tc-99m DTPA diuretic scan but not on the 10-minute delayed CT scan. We do not know the exact reason for the discrepancy in sensitivity for these 2 modes of examination. Urine viscosity and examination duration may play important roles. Since the diverticulum is connected to the pelvicoalyceal system by a thin isthmus and is filled in a retrograde fashion from connecting calyx or renal pelvis, viscosity of contrast material may affect the passive movement of contrast-containing urine. Contrast media viscosity is inversely related to opacification due to its negative impact on flow rate.¹⁶ The contrast media (Ultravist 300) we used in CTU have osmolalities between 610 and 620 mOsm/kg H₂O and viscosity up to 4.6 mPa s at 37°C.¹⁷ Urine viscosity may be elevated considerably and thus retrograde filling may be hindered or delayed;^{18,19} whereas radioisotope used in Tc-99m DTPA diuretic scan is physiologically innocuous and does not result in osmotic overload, nor change urine osmolality and viscosity,

and passes through the isthmus more smoothly. Moreover, the timing of delayed excretory image is another determining factor. Because passive filling of the diverticulum begins from the moment the collecting system becomes filled with contrast-containing urine, there will be a time delay before layering of the contrast material occurs in the diverticulum. The optimal time of examination in the excretory phase CT scan for diagnosing CD is still not known. As the report of Lin et al suggested, examination of the 60-minute delayed image can significantly improve the sensitivity (92.7%) of CTU in diagnosing CD.¹ However, the disadvantage is a prolonged study and attendant higher radiation dose. The 60-minute delayed image may also fail to detect cases with cyst wall thickening and impaired renal function.¹ A thickened wall might be associated with chronic inflammation which constrict and narrow the diverticular neck,¹ requiring more time for the urine to pass through this orifice. This phenomenon may be relevant for our patient 8. Her 10-minute delayed CTU showed cyst wall thickening rather than filling of contrast media, but Tc-99m DTPA diuretic renal scan revealed that radiotracer entered her CD at the 24th minute. As the time required to complete the Tc-99m DTPA diuretic renal scan is about 30 to 40 minutes, and is longer than the 10-minute excretory CT scan, this allows more time for retrograde filling to develop and may lead to higher detection rates. In our 9 cases, all required more than 8 minutes to visualize radiotracer in the diverticulum.

Additional advantages of the Tc-99m DTPA diuretic renal scan include the following: allowing continuous monitoring during the entire procedure, utilizing less radiation, eliminating the risk of contrast nephrotoxicity, and obtaining information on kidney function as well as ureteropelvic drainage. The effective radiation dose for abdomen CT may increase from 10.6 mSv among children <5 years to 14.8 mSv among 10 to 14 year-olds.²⁰ A radiation-induced cancer is estimated to potentially result from every 300 to 390 abdomen CTs performed in girls.²⁰ The effective dose for Tc-99m DTPA renal scan, on the other hand, is only about 0.012 mSv among 5-year-old children and 0.0081 mSv among 10-year-old children.⁸ In addition to imaging the CD, Tc-99m DTPA renal scan can also be used to determine differential renal function, and elucidate the effect of the CD on renal function. Surgical intervention should be considered in children with progressive renal damage.

There are also some disadvantages of Tc-99m DTPA diuretic renal scan. With small CD size, detection with Tc-99m DTPA diuretic renal scan can be difficult and result in a false-negative result. The most criticized shortcoming of diuretic renal scan (as true for IVP) may be its poor anatomic resolution compared to CTU. The precise location of the CD cannot be ascertained, and would not contribute anatomic information if surgical intervention were contemplated.

The limitations of our study include the relatively small sample size and inability to determine the true incidence of CD. At present, there is no gold standard for the diagnosis of CD, and some CD may be missed by both 10-minute CTU and diuretic renal scan. So the true sensitivity and specificity of DTPA diuretic renal scan in diagnosis of CD is not known.

CONCLUSIONS

We successfully diagnosed 9 cases of CD using Tc-99m DTPA diuretic renal scan. From our studies, Tc-99m DTPA diuretic renal scan offers an alternative imaging mode with the advantage of lower radiation exposure and possibly higher sensitivity for detection compared to CTU. Further studies with

larger patient populations are indicated to evaluate the role of DTPA diuretic renal scan in detecting CD.

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