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THE ROLE OF GADOLINIUM ENHANCED MAGNETIC RESONANCE IMAGING FOR CHILDREN WITH SUSPECTED ACUTE PYELONEPHRITIS

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ABSTRACT

Purpose: The diagnosis of pyelonephritis is primarily clinical. However, the history and physical findings can be confusing in children, leading to adjunctive nuclear renal cortical scintigraphic studies (^{99m}technetium dimercapto-succinic acid [DMSA]) to confirm the diagnosis. Nonetheless, ambiguity occurs when differentiating between acute pyelonephritis and chronic scarring. We report our initial experience with gadolinium enhanced inversion recovery magnetic resonance imaging (MRI) to diagnose acute pyelonephritis.

Materials and Methods: Nine patients 7 months to 18 years old (mean age 81 months) underwent MRI to confirm radiographically a clinical suspicion of acute pyelonephritis. All patients had at least 1 prior episode of clinical pyelonephritis. Data were collected to determine whether acute pyelonephritic changes could be differentiated from chronic pyelonephritis on the basis of MRI characteristics.

Results: Of the 9 patients 4 were identified as having acute pyelonephritis on MRI (persistently high signal intensity after gadolinium), 2 demonstrated evidence of postpyelonephritic scar (parenchymal loss without change in signal intensity), 1 had evidence of acute pyelonephritis and chronic changes, and 2 had a completely normal examination (decreased signal intensity after gadolinium). At our institution the billable cost of MRI to the patient is $1,329, while the billable cost of ^{99m}technetium DMSA is $1,459. All patients younger than 6 years required intravenous sedation for MRI, whereas 70% of those younger than 6 years require intravenous sedation for DMSA scanning at our institution. MRI provided greater anatomical detail regarding the renal architecture without radiation exposure, and allowed the unambiguous diagnosis of acute versus chronic pyelonephritis scar in a 1-time (versus often multipart for DMSA) imaging study.

Conclusions: In cases where adjunctive imaging studies are useful to make a diagnosis gadolinium enhanced inversion recovery magnetic resonance imaging allows the detection of acute pyelonephritis rapidly, cost-effectively and safely in the pediatric population.

KEY WORDS: pyelonephritis, magnetic resonance imaging, pediatrics, diagnostic imaging

The diagnosis of acute pyelonephritis is primarily a clinical one. However, securing the diagnosis in infants and children can often be difficult, as the history and physical and laboratory findings are sometimes confusing. It is important to detect acute pyelonephritis early to expedite appropriate therapy and avert the well-known long-term sequelae. Once bacteria enter the papillae of the kidney, an acute inflammatory response occurs in which various enzymes and free radicals are released within the kidney, leading to parenchymal loss and scarring. Evidence of scar formation is present in up to 64% of pediatric kidneys with pyelonephritis.[1] In a small subset of children scarring can ultimately lead to hypertension, toxemia of pregnancy and end-stage renal disease requiring dialysis or transplantation.[2,3] Children who show evidence of renal scarring will need long-term followup of blood pressure and renal function.

Often an adjunctive imaging test is required to make a definitive diagnosis of acute pyelonephritis. Historically, excretory urography was the test of choice to diagnose acute pyelonephritis.[4] Its insensitivity in the detection of acute pyelonephritis led to its replacement with ^{99m}technetium (Tc) dimercapto-succinic acid (DMSA) as the gold standard.[1,4] This imaging modality is reproducible and sensitive, and can assess the functionality of the parenchyma in a dynamic fashion. Nonetheless, the disadvantages of ^{99m}Tc DMSA are well-known—use of ionizing radiation, limited spatial resolution and difficulty differentiating acute pyelonephritis from mature scar, thus, requiring repeat imaging several weeks later. These factors have an enormous impact on the potential long-term outlook for the child as well as the long-term treatment plan.

An imaging modality that would provide morphological and functional data, avoid ionizing radiation, and be reproducible and easily obtained would be ideal. Herein we report our experience with gadolinium enhanced inversion recovery magnetic resonance imaging (MRI) to diagnose acute pyelonephritis.

MATERIALS AND METHODS

Nine patients (8 females and 1 male) 7 months to 18 years old (mean age 81 months) underwent MRI to confirm radiographically a clinical suspicion of pyelonephritis. Clinical suspicion was based on the combination of fever, abdominal or flank pain, dysuria, bacteriuria or pyuria and/or constitutional changes. Two patients had a neurogenic bladder, 1 due to spina bifida and 1 due to a complex anorectal malformation, and were on intermittent catheterization. These pa-

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tients presented with bacteriuria and fever, and their physical examination findings were more difficult to interpret. All patients had at least 1 prior episode of acute pyelonephritis. All examinations were undertaken within 48 hours of the onset of the febrile episode.

MRI of the kidneys was performed with intravenous sedation. MRI of the upper abdomen was obtained with coronal images. Conventional spin echo technique was obtained with T1-weighted images as well as fast spin echo T2-weighted images and fast spin echo inversion recovery images before gadolinium injection. Following gadolinium injection fast spin echo T1 and T2-weighted images were obtained as well as fast spin echo inversion recovery images. Sections were obtained at 3 mm. intervals without interspace.

All images were reviewed by 1 pediatric radiologist (J. L.) looking for evidence of acute pyelonephritis and/or postpyelonephritic scar. In areas of acute pyelonephritis before the administration of gadolinium the kidneys will have high signal intensity on inversion recovery, with lesions of pyelonephritis relatively hyperintense to normal cortex. With the administration of gadolinium, inversion recovery sequences cause the normal kidney parenchyma to become dark (gray to black). This finding is in contrast to areas of acute pyelonephritis, where there will be a lack of concentration of gadolinium secondary to focal ischemia and/or tubular dysfunction. Areas of high signal intensity (bright images) represent the lack of concentration of gadolinium in areas of acute pyelonephritis. A mature renal scar, the aftermath of a previous episode of pyelonephritis, is represented by parenchymal loss of the kidney without any evidence of change in signal intensity with the administration of gadolinium.

RESULTS

Four of the 9 patients had evidence of acute pyelonephritis on MRI (fig. 1). Each of these studies revealed evidence of increased signal intensity on the inversion recovery sequences. Two patients had postpyelonephritic scar without any evidence of acute pyelonephritis (fig. 2), 1 demonstrated acute pyelonephritic changes and postpyelonephritic scar (fig. 3), and 2 showed no evidence of either acute pyelonephritis or postpyelonephritic scar.

All patients younger than 6 years required intravenous sedation. Imaging lasted 30 to 60 minutes. The billable cost of MRI to the patient was $1,329. This price takes into account $1,114 for the study and the reading, and $215 for the gadolinium contrast.

DISCUSSION

The early diagnosis and prompt treatment of acute pyelonephritis are of critical importance. Studies have revealed that early treatment with the appropriate antimicrobial agents can decrease the incidence of renal scarring.[5] We have found upper tract imaging to be helpful in children with a fever of unknown origin without definitive evidence of a urinary infection, patients with chronic bacteriuria secondary to intermittent catheterization, patients with an ambiguous clinical picture, children with known vesicoureteral reflux in whom fever develops during suppressive antimicrobial therapy and children without vesicoureteral reflux but with evidence of recurrent febrile urinary infections.

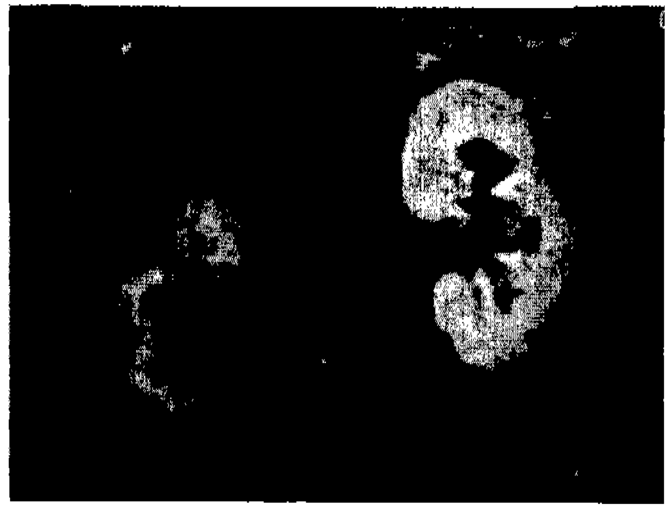

FIG. 2. T1-weighted postgadolinium image demonstrates areas of cortical thinning and scar in right kidney consistent with chronic postpyelonephritic scar. Later inversion recovery images did not show any evidence of acute pyelonephritis.

Although the ^{99m}Tc DMSA radioisotope scan has for years been known as the gold standard to detect pyelonephritis, several limitations are inherent in this modality. Ionizing radiation, poor spatial imaging and the difficulty in differentiating mature scar from acute pyelonephritis are all problems encountered with this technique. The use of MRI for imaging urinary tract pathology has been well documented but has been less described in evaluating the effect of infection.

Studies in animals have demonstrated that MRI can be a sensitive and specific test to diagnose acute pyelonephritis. Pennington et al compared MRI findings with histopathological examination in the diagnosis of experimentally induced pyelonephritis in a piglet model.[6] With contrast enhanced fast multiplanar inversion recovery techniques, the average sensitivity and specificity for the 2 radiologist readers were

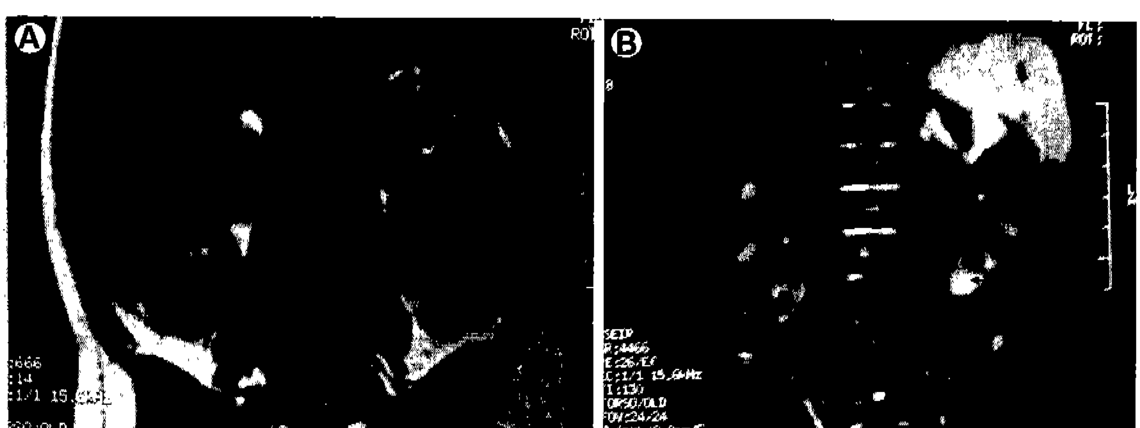

FIG. 1. *A*, T1-weighted postgadolinium image suggests acute pyelonephritis in upper and lower poles of left kidney (wedge-shaped gray areas). *B*, T2-weighted inversion recovery sequence confirms acute pyelonephritis in upper and lower poles of left kidney (arrows, wedge-shaped white areas) along with previously unseen acute pyelonephritis in upper and lower poles of right kidney.

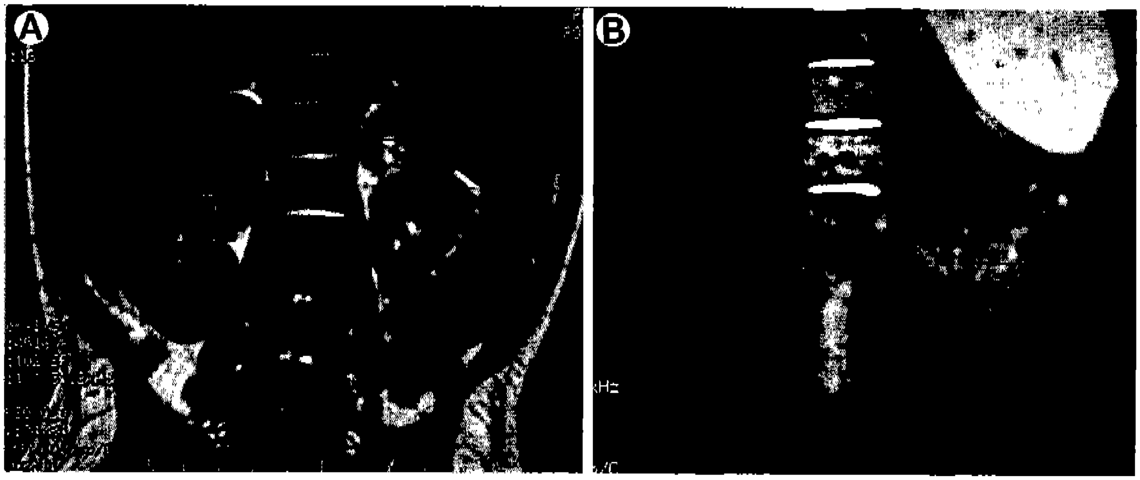

FIG. 3. *A*, T2-weighted post-gadolinium image reveals areas of cortical thinning in upper pole of left kidney (arrows) consistent with previous pyelonephritic scar. *B*, T2-weighted inversion recovery sequence demonstrates previously unseen acute pyelonephritis in upper and lower poles of left kidney (arrows, wedge-shaped gray-white areas).

91% and 93%, respectively, versus pathological examination of the kidneys. Imaging with this technique produced excellent reproducibility and interobserver agreement in their study. In a comprehensive study of acute pyelonephritis in the piglet model Majd et al compared ^{99m}Tc DMSA single photon emission computerized tomography (SPECT), spiral CT, MRI and power Doppler ultrasound in diagnosing and localizing acute pyelonephritis, using histopathological findings as the standard of reference.[7] Statistically, there was no significant difference among SPECT, MRI and conventional CT in the diagnosis of acute pyelonephritis. Power Doppler ultrasound was significantly less accurate than the other modalities.

The widespread availability, ease of use and minimal need for sedation have made spiral CT an attractive imaging modality for the diagnosis of acute pyelonephritis. Spiral CT can rapidly acquire a tremendous amount of data. Administration of intravenous contrast material and imaging of the kidney throughout multiple phases of contrast acquisition are critical. Majd et al found that in some cases cortical phase imaging with CT was normal but parenchymal phase imaging showed acute pyelonephritis.[7] This finding emphasizes the need to image the kidney throughout multiple phases of contrast excretion to diagnose acute pyelonephritis. Disadvantages of CT include ionizing radiation and the need to administer intravenous iodinated contrast material to test properly for acute pyelonephritis.

Lonergan et al found a greater number of pyelonephritic lesions with gadolinium enhanced MRI compared to ^{99m}Tc renal cortical scintigraphy in 37 children with febrile urinary infections.[1] In the absence of histopathological correlation in their study they subjected the discordant studies to more stringent review by their team of 2 radiologists. They found that of the 29 renal zones positive on MRI but negative on scintigraphy 6 were thought to be old scar on scintigraphy instead of acute pyelonephritis, highlighting the difficulty in delineating acute pyelonephritis from mature scar on DMSA scans. Of the 7 renal zones that were positive on scintigraphy and negative on MRI 3 were interpreted as old scar (parenchymal loss without change in signal intensity) on MRI. Of the 37 patients enrolled in the study 5 (14%) had evidence of pyelonephritis on MRI alone. These patients most likely would have had different treatment had they undergone a DMSA scan only. In our series MRI was able to distinguish the absence of an acute process but the presence of scarring from previous infections in 2 children as well as the presence of acute and chronic changes in 1 child. This is an important advantage of this imaging modality over nuclear scintigraphy.

Two of our patients had a neurogenic bladder and were on clean intermittent catheterization. One child presented with fever, nausea, abdominal pain and bacteriuria. Despite this clinical scenario, the child had a completely normal MRI, with no evidence of acute or chronic pyelonephritis. The second child had a complex anorectal malformation, leading to a neurogenic bladder requiring clean intermittent catheterization. She presented with fever and bacteriuria, with no obvious source of infection. MRI in this child revealed evidence of a chronically scarred kidney on the side of known vesicoureteral reflux without any evidence of acute pyelonephritis. Because children with a neurogenic bladder who perform clean intermittent catheterization have chronic bacteriuria, it is often difficult to determine if the urinary tract is the source of the febrile illness. Chan et al studied 24 children with spina bifida and neurogenic bladder or anorectal malformations, children who are at high risk for renal scarring, and compared the results of MRI and DMSA scanning to evaluate for evidence of renal scars.[4] Documented urinary tract infection was present in 10 children at the time of the examination, while 14 had asymptomatic bacteriuria. Using the DMSA scan as the gold standard, MRI carried 100% sensitivity and 78% specificity in the diagnosis of the scarred kidney. Without the presence of histopathological controls, it is difficult to say why this group had more false-positive studies with MRI. No mention was made of the number of kidneys with acute pyelonephritic changes in this study.

A potential disadvantage of MRI is the need for intravenous sedation. In our study all patients younger than 6 years were sedated per protocol. Patients 6 years and older are sedated at the discretion of the radiology and anesthesia teams. Majd et al experienced the need for intravenous sedation in less than 10% of infants and children undergoing DMSA imaging.[7] At our institution approximately 70% of the patients younger than 6 years are sedated for DMSA SPECT. These studies routinely take between 60 and 90 minutes. Our nuclear medicine colleagues believe that the rate of sedation at our institution is so much higher because they have found that in their hands even the slightest bit of motion artifact can impair the results of a DMSA scan. When motion artifact is an issue, the study, specifically the SPECT portion, needs to be repeated with a repeat isotope infusion, incurring greater time and cost to the patient.

Cost is an issue that is often cited as a factor in not choosing MRI as a first line modality in the diagnosis of acute

Billable cost comparison between MRI and DMSA imaging of suspected acute pyelonephritis

Cost	MRI	DMSA
Single study	$ 1,329	$ 1,455
Intravenous sedation/study	$ 1,000*	$ 1,200†
100 Studies	$132,900	$145,500
Intravenous sedation/100 studies	$100,000‡	$ 84,000§
Total cost of 100 studies	$232,900	$229,500

* Based on 45 minutes of intravenous sedation.
† Based on 75 minutes of intravenous sedation.
‡ Based on 100% rate of intravenous sedation.
§ Based on 70% rate of intravenous sedation.

pyelonephritis. As stated previously, the billable cost to the patient at our institution for gadolinium enhanced MRI of the abdomen and pelvis as described in our study is $1,329. This cost is not too different from the $1,455 billable cost to those patients who undergo DMSA SPECT at our institution. At our nuclear medicine department the billable cost of the scan itself is $909 and the isotope is $546. Although the initial anesthesia charge is equivalent for both imaging studies, the remaining balance is based on the amount of time taken by the study based on increments of 15 minutes. Using the average times for MRI of 45 minutes and for DMSA scanning with SPECT of 75 minutes, the billable costs for anesthesia are $1,000 and $1,200, respectively, per study. If one were to figure the billable cost of 100 MRI studies using intravenous sedation 100% of the time versus 100 DMSA studies using intravenous sedation 70% of the time at our institution, the cost comparison is quite interesting. One hundred MRIs with 100% sedation would cost $232,900 versus $229,500 for 100 DMSA scans with 70% of patients sedated (see table). Obviously, the cost of the examinations themselves as well as the amount billed for them will vary from institution to institution. This variation undoubtedly may skew the findings of the cost analysis on an institution by institution basis. Nonetheless, as the availability and use of MRI increase, we believe that the costs involved with the use of MRI will decrease. The cost-effectiveness of MRI in children with pyelonephritis can be further appreciated when considering the cost of a second DMSA scan when the diagnosis of acute pyelonephritis versus mature or evolving scar cannot be made unequivocally. We did not explore cost of CT in our study.

We agree with other authors that the judicious use of imaging studies for the diagnosis of pyelonephritis is warranted.[8, 9] The decision to obtain imaging in a child should be made on a case by case basis depending on the clinical scenario. Imaging studies are helpful in patients with fever of unknown origin and inconclusive evidence of urinary tract infection, patients with chronic bacteriuria (like those on intermittent catheterization) and an uncertain diagnosis of a urinary tract infection, children with known vesicoureteral reflux who seemingly have a febrile urinary infection despite antimicrobial prophylaxis and children without vesicoureteral reflux or demonstrable anatomical urological abnormality who have multiple febrile urinary tract infections.[9]

CONCLUSIONS

The diagnosis of acute pyelonephritis remains primarily a clinical one. Routine use of imaging studies to differentiate between acute lower and upper urinary tract infections is controversial. The decision regarding when to use an imaging study to diagnose acute pyelonephritis should be made on an individual case basis. However, when the diagnosis cannot be readily secured from history and physical and laboratory findings, adjunctive imaging studies can often allow definitive diagnosis of acute pyelonephritis. In these cases gadolinium enhanced inversion recovery magnetic resonance imaging is a useful modality to diagnose acute pyelonephritis. It is rapid, cost-effective and safe in the pediatric population. As the availability, cost and speed of the study increase, we believe that MRI has the potential one day to become the gold standard for renal imaging of acute pyelonephritis.

REFERENCES

1. Lonergan, G. J., Pennington, D. J., Morrison, J. C., Haws, R. M., Grimley, M. S. and Kao, T. C.: Childhood pyelonephritis: comparison of gadolinium-enhanced MR imaging and renal cortical scintigraphy for diagnosis. Radiology, **207:** 377, 1998
2. Jacobson, S. H., Eklof, O., Lins, L. E., Wilkstad, I. and Winberg, J.: Long-term prognosis of post-infectious renal scarring in relation to radiological findings in childhood—a 27-year follow-up. Pediatr Nephrol, **6:** 19, 1992
3. Sacks, S. H., Verrier Jones, K., Roberts, R., Asscher, A. W. and Ledingham, J. G.: Effect of symptomless bacteriuria in childhood on subsequent pregnancy. Lancet, **2:** 991, 1987
4. Chan, Y. L., Chan, K. W., Yeung, C. K., Roebuck, D. J., Chu, W. C., Lee, K. H. et al: Potential utility of MRI in the evaluation of children at risk of renal scarring. Pediatr Radiol, **29:** 856, 1999
5. Winter, A. L., Hardy, B. E., Alton, D. J., Arbus, G. S. and Churchill, B. M.: Acquired renal scars in children. J Urol, **129:** 1190, 1983
6. Pennington, D. J., Lonergan, G. J., Flack, C. E., Waguespack, R. L. and Jackson, C. B.: Experimental pyelonephritis in piglets: diagnosis with MR imaging. Radiology, **201:** 199, 1996
7. Majd, M., Nussbaum Blask, A. R., Markle, B. M., Shalaby-Rana, E., Pohl, H. G., Park, J. S. et al: Acute pyelonephritis: comparison of diagnosis with 99mTc-DMSA, SPECT, spiral CT, MR imaging, and power Doppler US in an experimental pig model. Radiology, **218:** 101, 2001
8. Leonidas, J. C. and Berdon, W. E.: MR imaging of urinary tract infections in children. Radiology, **210:** 582, 1999
9. Lonergan, G. J., Pennington, D. J., Morrison, J. C., Haws, R. M., Grimley, M. S. and Kao, T. C.: Childhood pyelonephritis: comparison of gadolinium-enhanced MR imaging and renal cortical scintigraphy for diagnosis. Radiology, **207:** 377, 1999