Renal scintigraphy using technetium dimercaptosuccinic acid in the diagnosis of pyelonephritis in children: study of 17 cases

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Abstract

Objective: to determine whether the presence of abnormal results in DMSA renal scintigraphy indicates pyelonephritis.

Methods: we performed the washout test in 17 children with urinary tract infection, as a criterion standard, to locate the infection site. All the children underwent DMSA renal scintigraphy in the acute phase of the disease. The results were analyzed by the chi-square test or Fisher test.

Results: DMSA renal scintigraphy revealed changes in all five cases of pyelonephritis, suggesting acute kidney involvement. On the other hand, only one child with cystitis (total = 12 cases) had abnormal results in renal scintigraphy. Sensitivity and specificity were 100% and 92%, respectively.

Conclusion: DMSA renal scintigraphy is a sensitive method for the diagnosis of pyelonephritis in children.


Introduction

There are three types of urinary tract infection (UTI), which are defined according to the location and repercussion of the infection: asymptomatic bacteriuria, cystitis and acute pyelonephritis (APN). Asymptomatic bacteriuria and cystitis are benign infections, and do not cause impairment to renal function. Pyelonephritis, however, may cause progressive and irreversible renal impairment.1-3

The clinical parameters for locating UTI (cystitis or pyelonephritis) are not specific and are difficult to detect, especially in young age groups where there is prevalence of APN with formation of renal scarring.

Direct and indirect methods may be used to locate the infection in the urinary tract. The washout technique, a direct method first described by Fairley et al., in 19674 and modified in 1971,5 consists of bladder washout with non-absorbable antibiotic solution for sterilizing the lower urinary tract, followed by successive washouts with physiological solution for removing antibacterial substance and collecting samples for urine culture. After transitory bladder washouts, the persistence of positive urine culture results indicates contamination of the ureteral urine and, consequently, APN. The application of the washout technique on adults is simple, however, its use on children presents some technical inconveniences especially related to young age and necessity for cooperation during the procedure. In addition, the procedure lasts approximately three hours, is complicated, and requires adequate laboratory support. The washout
technique is preferably recommended for comparative studies since, nowadays, we have less invasive methods for the diagnosis of pyelonephritis.

Among the several indirect methods for locating the UTI site, we have: temporary reduction of urine concentration, increase in urinary enzyme levels (lactic dehydrogenase, beta-glucuronidase, N-acetyl beta-D-glucosaminidase and beta 2-microglobulin), immunoresponse to infection (erythrocyte sedimentation speed, interleukin-6, interleukin-8, C reactive protein); bacterial coating; renal ultrasonography and excretory urography. These tests, however, have low sensitivity and specificity in the diagnosis of acute pyelonephritis.6-10

The diagnosis of APN through imaging has been improved in the last few decades, especially through radioisotope assays. According to Smellie11, the technetium dimercaptosuccinic acid (DMSA) scintigraphy has several advantages over excretory urography: use of radiopharmaceuticals that do not produce allergic reactions; no previous intestinal preparation; lower exposure to radiation; thus preserving the gonads; and high-resolution images, regardless of age.

DMSA is fixed onto proximal tubular cells and onto the upper region of Henle’s ansa, and may directly reach these cells through blood flow or reabsorption of glomerular filtrate. DMSA uptake reflects the functional integrity of the renal parenchyma, especially concerning the cortex. The concentration of DMSA in APN may be affected by an alteration in intrarenal perfusion or in proximal tubular reabsorption.12 During acute pyelonephritis, there is reduced uptake of focal, diffuse, unilateral or bilateral radioisotope, which may be followed by increased renal volume, as observed in the ultrasonography; or attenuation of renal contour, without deformities. These alterations secondary to the inflammatory process may persist for four to six weeks after the treatment of APN, and are not necessarily definitive. When these alterations are early detected by DMSA renal scintigraphy in the acute phase, they may disappear in 50 to 60% of properly treated patients.13-16

Several studies have been conducted on the alterations found in DMSA renal scintigraphy during APN in the last decade.14,16-22 Although these studies differ in terms of population, they are consistent in the following aspects: renal parenchyma impairment is detected by DMSA scintigraphy during acute infection in most patients (50 to 80%), and abnormal DMSA scintigraphy results are rare in children with cystitis.23,24 The present study aims at determining whether the presence of alterations in the DMSA renal scintigraphy during the acute phase of urinary tract infection indicates pyelonephritis.

Methods

We studied 17 female patients with urinary tract infection aged between 3 and 13 years (average = 5.8 years), who were assisted at the Nephrology Unit of the Hospital Santa Casa (São Paulo). All procedures were carried out with the consent of parents or guardians after the objectives of the study were explained and approved by the Medical Ethics Committee. Male patients and also those who were too young were not included in the study since they would not collaborate during the washout procedure.

In the acute phase of UTI, the following procedures were performed: urine sample collection for the confirmation of UTI; washout technique after confirmation of UTI and before initiation of antibiotic therapy; DMSA renal scintigraphy during the first week after the diagnosis of UTI; urine sample collection for control urine culture 48 to 72 hours after the completion of drug therapy. Preferably, intermediate urine jets were collected after adequate asepsis (water and soap). Bladder catheterization was used in female patients with leukorrhea or when patients did not cooperate with the collection of intermediate urine jets. In these cases, chlorhexidine was used for asepsis as recommended by the Nosocomial Infection Service of the Hospital Santa Casa (São Paulo). In both procedures, part of the initial urine was dismissed, thus minimizing the contamination caused by urethral bacteria.25 All of the urine samples were analyzed by the Microbiology and Immunology Laboratory of the Department of Pathology of the Santa Casa de São Paulo School of Medical Sciences. The intermediate samples (collected urine jets) were diluted in 1/1000 and, through bladder catheterization, in 1/100 for inclusion in cystine lactose electrolyte deficient agar (CLED) plates, incubated at 35 to 37°C. The reading was carried out by counting the amount of colonies and multiplying them by 100 or 1000 according to the dilution used. The results were interpreted according to Kass criteria,26 in which values equal or greater than 100,000 (10^5) organisms per ml (UFC/ml) are considered diagnostic of UTI for urine samples collected through intermediate jets, and values equal or greater than 1000 (10^3) organisms per ml (UFC/ml) for urine samples collected through a bladder catheter.

The following procedures were necessary for the use of the washout technique: total bladder voiding through an indwelling catheter, with sample collection for urine culture (flask 1); bladder filling with 0.2% neomycin solution followed by a 40-minute rest; bladder washout with 0.9% physiological solution; bladder filling with 0.9% physiological solution and 20-minute rest followed by bladder voiding and sample collection for urine culture (flask 2); procedure 4 is repeated successively with sample collection for urine culture in flasks 3, 4, 5 and 6, respectively. The total volume for bladder filling is variable, ranging between 5 to 10 ml/kg of body weight, and depends on the age and cooperation of patients. The procedure lasted on average 3 hours. The results of the washout technique are: positive (pyelonephritis) if urine cultures are positive in all flasks; negative (cystitis) in the cases in which urine cultures were negative from the third or fourth flask onwards; and indeterminate if urine cultures were positive but did not show significant colony count.
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DMSA scintigraphy was conducted by the Nuclear Medicine Service of the Arnaldo Vieira de Carvalho Cancer Institute during the acute phase of urinary infection, between the second and fifth day after laboratory confirmation. Metastable technetium-99 dimercaptosuccinic acid (IPEN, São Paulo) was used in the form of sodium pertechnetate in molybdenum generator, in an IV dose of 2mCi. The images were obtained three to six hours after the administration of the radiopharmaceutical in the posterior and obliquely posterior incidences. A consensual report was issued after the evaluation of images by two assistant doctors from the Nuclear Medicine Service. The uptake alterations found in APN-compatible DMSA scintigraphy were focal or diffuse reduced uptake in the renal parenchyma with increased renal volume and/or difference higher than 10% in the relative quantification between kidneys.17,27,28

The chi-square or Fisher test was used for statistical analysis. The significance level was 0.05. The parameters were also assessed using sensitivity, specificity, actual prevalence, estimated prevalence, positive predictive value, negative predictive value, correct classification, and wrong classification.

Results

The washout technique results showed 5 cases of APN and 12 cases of cystitis among the 17 children who participated in the study. The association between APN and alterations in the uptake of DMSA renal scintigraphy was present in all 5 cases while only one child with cystitis showed altered results in DMSA scintigraphy. The Fisher test revealed statistical significance between the presence of alterations in DMSA scintigraphy and the diagnosis of APN. The sensitivity of this association was 100% and the specificity was 92%. The other indices were also satisfactory (Table 1).

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<td>Sensitivity</td>
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<td>Correct classification</td>
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Discussion

The washout technique was successfully performed in all cases of UTI analyzed in this study. We faced some difficulties during the procedure and, based on this, we suggest the following: the catheter used for bladder filling should suit child’s age, preventing the solution from leaking out; the child must remain unagitated throughout bladder filling so that the procedure can be carried out successfully and slowly, preventing early urinary urge; the child must lie down and remain unagitated throughout the rest period so that the desired effect is obtained, while, placing the child in decubital or supine position may facilitate total bladder emptying. It is advisable and of paramount importance that mothers or guardians stay with their children until the completion of the exam. Samples for urine culture should be preferably collected at the end of each bladder voiding procedure. All the results we obtained through the use of this technique were classified as positive washout (APN) or negative washout (cystitis); there were no indeterminate cases.

In the present study, out of the 17 female patients submitted to the washout technique, there were five cases of APN and 12 cases of cystitis. We observed that in the acute phase of urinary tract infection all five children with APN had scintigraphy results that suggested acute renal infection, with a sensitivity of 100% and specificity of 92%. The reduced focal uptake with preservation of renal contour associated with a reduction in the relative uptake of radiopharmaceutical by the affected kidney was the most frequently reported alteration in the DMSA scintigraphy of children with APN. These results are in agreement with those described by Rushton.12

In the eleven cases of cystitis, we had normal uptake of DMSA in the initial scintigraphy, thus eliminating the suspected infectious involvement of the renal parenchyma. Nevertheless, one case of cystitis presented reduced focal uptake of radiopharmaceutical associated with renal contour deformity during the acute phase of infection. The presence of reduced renal uptake of DMSA followed by deformity suggests previous pyelonephritic lesions. The possibility of a new source of APN near the scar region could not be discarded since the area that surrounds the fibrotic area becomes more susceptible to intrarenal reflux in previously affected kidneys, increasing the length of the lesion.12,29 Therefore, even if DMSA renal scintigraphy yields false positive results in a small number of cases, the treatment of APN is recommended once it is difficult to know whether the process originates from previous scarring or if there is a new source of infection next to the pre-established scar.

The early perception of renal scarring signs through DMSA, especially in infants and children younger than five years, is described by several authors.20-22 Rushton and Majd13 followed up 33 children with APN for four to 42 months (average = 10.7 months) and observed that 42% of kidneys presented formation of renal scars or progression.
of existing scars, while the renal parenchyma was totally recovered in 58% of the cases.

The diagnosis of APN has been a challenge in cases of children with UTI. Renal scars that result from late or inadequate treatment, substantially influence the prognosis of kidney diseases in the long run. We believe that the correct diagnosis of UTI, the careful consideration of APN-predisposing factors with occasional scarring, and renal evaluation through DMSA, may favor the early treatment of pyelonephritis as well as the follow-up of its development, reducing the risk of renal function deterioration.

References
