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# Reappraisal of Tc-99m DMSA scintigraphy for follow up in children with vesicoureteral reflux

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We reviewed Tc-99m DMSA scintigraphy in children with vesicoureteral reflux (VUR) in order to assess whether repeated Tc-99m DMSA scans are necessary for the follow up of these patients. Ninety-seven children who were followed up for more than one year (1–7.4 years, average 2.8 years) after the first DMSA scan were included in the study. Fifty-one patients had been diagnosed as primary VUR and 46 as secondary VUR. Age at the first examination ranged from 0 to 14 years (average 5.1 years). Planar images were taken 2 hours after injection. The % renal uptake per injected dose (%RU) was calculated from posterior images. Kidneys in 11 patients (11.3%) changed morphologically during the follow up. Of these, new photon deficient areas (PD) were detected in only 4 patients (4.1%). All of these 4 patients had neurogenic bladder and were managed with self-catheterization. Of the remaining 7 patients, cortical thinning progressed in 5 patients (5.2%) and PDs resolved in 3 patients (3.1%). In one of these 7 patients, PD resolved in one kidney and cortical thinning progressed in the contralateral kidney. Of 97 patients reviewed, % RU decreased more than 20% during the follow up in 6 patients (6.2%). All were diagnosed as secondary VUR due to neurogenic bladder. % RU decreased only in the contracted kidneys at the initial scan. Two of them underwent renal transplantation because of severe renal failure. In conclusion, new PD rarely developed and % RU decreased in only a few patients during the follow up of children with VUR. Repeated Tc-99m DMSA scintigraphy therefore seems to have little benefit in the follow up of children with VUR. It should be performed in selected patients with high risk of urinary tract infection or renal failure.

**Key words:** Tc-99m DMSA, vesicoureteral reflux, urinary tract infection

## INTRODUCTION

Tc-99m DMSA scintigraphy is now recognized as a valid tool for detecting upper urinary tract infections (UTI) and renal scars.[1–9] Reflux pyelonephritis is a major cause of reflux nephropathy and it will possibly lead children with vesicoureteral reflux (VUR) to renal failure. Repeated UTI and increased renal scars are high risk factors for reflux nephropathy. Long term follow up of the patients is therefore necessary to assess whether the children may develop new renal scars or their kidneys remain stable.[10,11] For monitoring renal morphology and function in children with VUR, Tc-99m DMSA scintigraphy is often repeated.

On the other hand, it is known that repeated urinary tract infection or new renal scar formation does not frequently occur in children with VUR under proper medical care such as antibiotic prophylaxis.[12–14] Moreover, the radiation dose to the kidneys from a DMSA scan is even slightly higher than an intravenous urogram.[15,16] In view of this, we need to know if repeated DMSA scans are really necessary for the follow up of children with VUR.

In this study, we reviewed the scintigrams of children with VUR at follow up and investigated how often we

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could find a morphological change in the kidneys during follow up in order to discuss the necessity of repeated DMSA scans.

## MATERIALS AND METHODS

*Patients*

Ninety-seven children (57 boys and 40 girls) who were followed for more than one year after the first scan in our hospital entered the study. Age ranged from 0 to 14 years (average 5.1 ± 3.6 years) at the first examination. They repeated the examinations from 2 to 7 times (average 3.1 ± 1.1 times) during a period of 1–7.4 years (average 2.8 ± 1.6 years). Voiding cystourethrography (VCUG) was performed to detect VUR. Fifty-one had been diagnosed as primary VUR and 46 as secondary VUR (Table 1). Four patients had single kidneys. Reflux of the 169 renal units was graded from 1 to 5 according to the International Reflux Study Classification.[17] Numbers of the units of Grades 1 to 5 were 16, 37, 31, 55 and 30, respectively. Patients were treated with antibiotics for the UTI and maintained on long-term low dose prophylaxis. Anticholinergic agents were given to the primary VUR patients with unstable bladder. Besides instructions for regular frequent voiding, patients with neurogenic bladder were placed on clean intermittent catheterization (CIC) whereas urethral obstruction was managed with transurethral incision. Anticholinergics were also given when they had detrusor hyperreflexia. They were followed up until the disappearance of VUR was confirmed with 3 successive VCUGs. During follow up, 27 patients had at least 1 recurrent urinary tract infection and 7 had on episode of fever of unknown origin. Before the first examination or during follow up, 38 patients underwent anti-reflux surgery for breakthrough UTI.

**Table 1** Patient population

| VUR | Patients No. |
|---|---|
| Primary VUR | 51 |
| Scondary VUR | 46 |
| Neurogenic bladder | 20 |
| Urethral stricture or ring | 12 |
| Urethral valve | 4 |
| Ureterocele | 3 |
| Others | 7 |

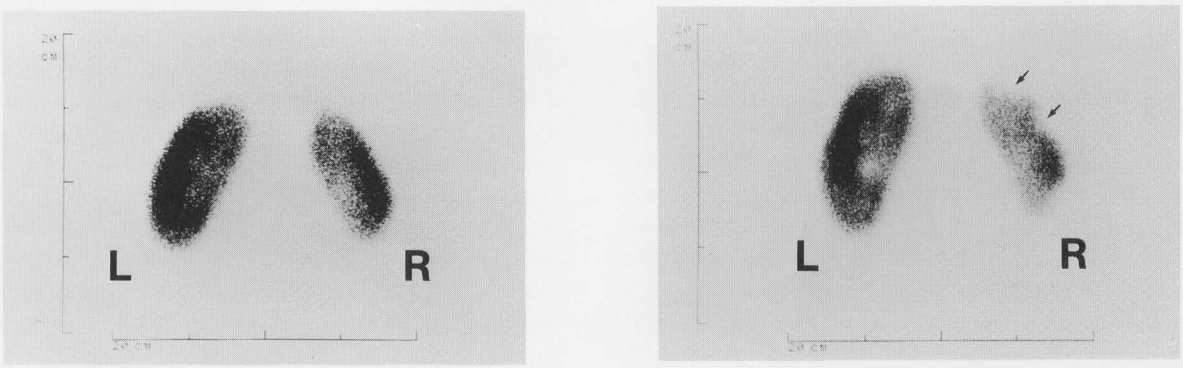
*Scintigraphy*

In all but a few patients with a febrile UTI episode, DMSA scan was performed at least 6 months after the eradication of UTI. All the patients or their parents gave informed consent to the DMSA examination. Patients who were unable to remain stationary during the Tc-99m DMSA study were sedated prior to the study. Tc-99m DMSA was prepared by adding freshly eluted Tc-99m to a commer-

**Table 2** Clinical profile of cases which developed new photon deficient area on Tc-99m DMSA follow up study

| Case | Age/Sex | VUR Grade | | Bew PD | Complication | Recent UTI | Treatment |
|---|---|---|---|---|---|---|---|
| | | R | L | | | | |
| 1 | 7/M | V | IV | R | NB | N | CIC, Ac, Ab |
| 2 | 3/F | I | IV | R | NB, C, Duplex | Y | CIC, Ac, Ab, A-Ope |
| 3 | 0/M | 0 | II | L | NB | Y | CIC, Ac, Ab |
| 4 | 5/M | II | — | R | NB | N | CIC, Ac, Ab, A-Ope |

Abbreviation; NB: neurogenic bladder, UC: ureterocele, CIC: clean intermittent catheterization
Ac: anticholinergic drug, Ab: antibiotics, A-Ope: antireflux operation



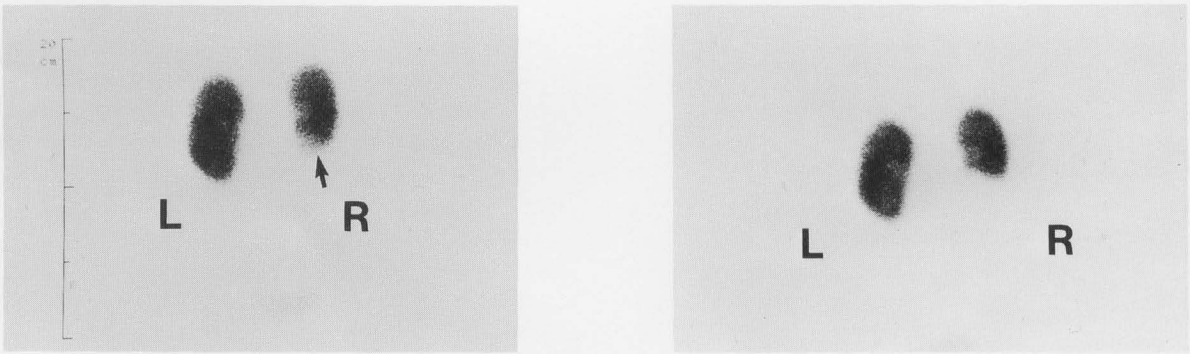

A B

**Fig. 1** A: posterior image of Tc-99m DMSA in a 7-year-old boy (case 1 in Table 2) with neurogenic bladder. B: posterior image in the same boy 2 years later. Note the development of new photon deficient areas in the right kidney.

**Table 3** Clinical profile of cases with progression of cortical thinning on Tc-99m DMSA follow up study

| Case | Age/Sex | VUR Grade | | Cortical thinning | Complication | Recent UTI | Treatment |
|---|---|---|---|---|---|---|---|
| | | R | L | | | | |
| 5 | 7/F | 0 | V | L | NB | N | Ac, Ab |
| 6 | 1/M | II | 0 | R | NB | N | Ac, Ab |
| 7 | 1/M | III | III | L | Primary | Y | Ac, Ab |
| 8 | 9/M | I | I | R, L | Primary | N | Ac, A-Ope |
| 9 | 1/M | V | V | L | AUV | N | Ac, Ab, A-Ope |

Abbreviation; NB: neurogenic bladder, Ac: anticholinergic drug, Ab: antibiotics, A-Ope: antireflux operation




A B

**Fig. 2** A: posterior image of Tc-99m DMSA in a 1-year-old boy (case 6 in Table 3) with neurogenic bladder. B: posterior image in the same boy 7 months later. Note that cortical thinning progressed in lower pole of the right kidney.

cially available freeze-dried kit (Daiichi Radioisotope Lab. Co., Tokyo). A single rotating gamma camera (Toshiba GCA-602A) equipped with a low energy high-resolution parallel-hole collimator was positioned posteriorly to the patient who was in the supine position. Posterior planar images were taken precisely 2 hours after injection with an age-adjusted dose (26–95 MBq) of Tc-99m DMSA for a preset time of 5 minutes on a 512 × 512 matrix. Supplemental posterior oblique images were also obtained in every case. On completion of the planar study, SPECT images were obtained but not used in this study because there was no information in addition to the planar images. % RU of Tc-99m DMSA was calculated from the planar posterior image data by using the equations previously described.[2]

*Evaluation of scintigrams*

Two experienced nuclear physicians (K.I. and E.T.) reviewed and determined with consensus whether there were any changes in the morphology of the kidneys on serial DMSA scans. A photon deficient area (PD) with cortical loss was regarded as an infectious focus or a renal scar.

## RESULTS

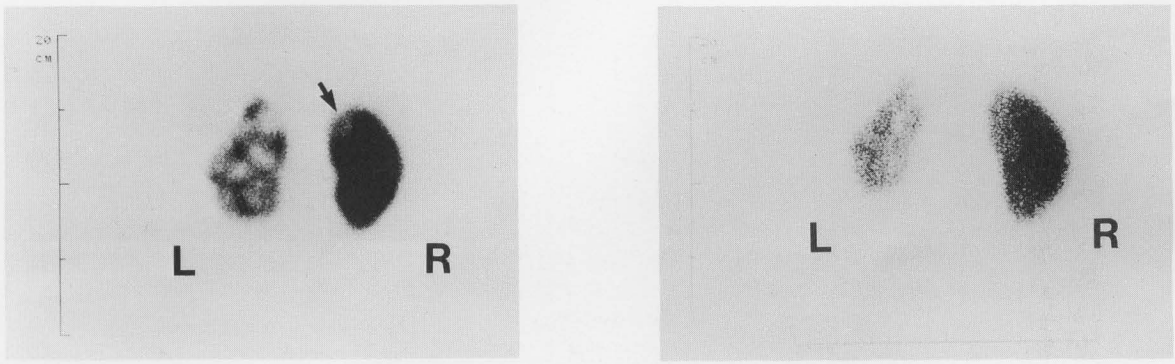
PDs suggestive of infectious foci or renal scars were found in 62 patients (63.9%) on the first examination. Kidneys in 11 (11.3%) of 97 patients changed morphologically during the follow up period. Of these 11 patients, new PDs were detected in 4 patients (4.1%) (Table 2, Fig. 1). All of 4 patients with a new PD had been diagnosed as neurogenic bladder and managed with CIC. Fever due to UTI was evident in 2 patients before the repeated DMSA scan which demonstrated new PDs. A reflux grade greater than grade 3 was found in 3 renal units in 2 patients. Progression of cortical thinning was shown in 5 patients (5.2%) (Table 3, Fig. 2). The lesions resolved in the remaining 2 of the 11 patients (2.1%) and in the kidney of one patient with progression of cortical thinning in the contralateral kidney (Table 4, Fig. 3). All of these 3 patients were under 1 year old at the first examination and had the episode of UTI within 6 months before the examination.

% RU decreased more than 20% during the follow up in 6 patients (6.2%). New PDs were detected in 2 of them. All 6 patients had been diagnosed as having neurogenic bladder. Kidneys in which % RU decreased were all contracted at the first examination. Two of them subsequently underwent renal transplantation preceded by augmentation cystoplasty[18] because of end-stage renal failure.

**Table 4** Clinical profile of cases which showed disappearance of PD on Tc-99m DMSA follow up study

| Case | Age/Sex | VUR Grade | | PD | Complication | Recent UTI | Treatmet |
|---|---|---|---|---|---|---|---|
| | | R | L | | | | |
| 9 | 1/M | V | V | R | AUV | N | Ac, Ab, A-Ope |
| 10 | 1/M | II | II | R | PUV | N | Ab |
| 11 | 1/M | I | V | R, L | UC | Y | Ac, Ab |

Abbreviation; Ac: anticholinergic drug, Ab: antibiotics, A-Ope: antireflux operation
PUV: posterior urethral valve, AUV: anterior urethral valve, UC: ureterocele




A B

**Fig. 3** A: posterior image of Tc-99m DMSA in a 7-year-old boy (case 9 in Table 4) with anterior urethral valve. B: posterior image in the same boy one and half year later. Note that photon deficient area in the right kidney disappeared, and the left kidney is contracted.

## DISCUSSION

This study revealed that new renal scar formation was rarely developed in patients with VUR under proper medical care and treatment. % RU decreased in a few patients. All the patients with new lesions or decreased % RU had neurogenic bladder which may increase the chance of urinary tract infections and high intravesical pressure.

Follow up results for children with VUR have been discussed in many articles. New scar development was reported to be 3–30%[12,19–22] in children with primary VUR and up to 86%[21,22] in children with secondary VUR. Compared to these previous data, our results showed quite a low rate of new scar development. No new scar formation was seen in the children with primary VUR and the rate was very low, even in the children with secondary VUR. Although the population of the patients and methods of evaluation of the renal scars are different, they do not explain this strikingly low rate of new scar development. Different treatment procedures at the centers in the previous articles may partly explain such a difference. Our urologists' principle of maintaining a low pressure urinary system, regular frequent voiding with or without anticholinergics in primary VUR, CIC in neurogenic bladder, and eradication of urethral obstruction with transurethral incision, in the management of VUR is believed to be instrumental in obtaining such a low rate of new scar formation. The fact that they adopted prompt antireflux surgery for breakthrough infection (38 out of 97 patients) whenever those conservative regimens failed must have also played a role. Another possible explanation is the different rate of recurrent urinary tract infection in different countries or in different races, which influences the rate of new scar development. According to the report from the European portion of the international reflux study in children,[23] the incidence of urinary tract infection per patient per month at different centers revealed unexpected differences. It was the lowest in the Finnish (0.005) and the highest in German/Belgian (0.020) centers. There are few reports from Asian centers and our data are limited. We need to accumulate more data from different centers in Asia.

The main purposes of follow up of the children with VUR are preserving their renal function and preventing sequelae of reflux nephropathy such as hypertension. We did not survey for hypertension but found that % RU indicating functioning renal mass decreased in only a few patients during the follow up. The kidneys with decreased % RU were all smaller than the contralateral kidney and associated with neurogenic bladder. We have previously reported that renal scars rarely reduced the functioning renal mass unless they had become relatively small.[24] Others[25,26] also reported that relative kidney size was closely related to renal function in children with VUR. The present data showed that relatively small kidneys

have the potential to progress the renal dysfunction.

Neurogenic bladder appeared to be a risk factor for both new PD formation and decreasing functioning renal mass. Renal damage in children with neurogenic bladder is related to either high intravesical pressure or the association of VUR.[27] Moreover, high intravesical pressure often causes VUR. CIC is the recommended treatment for these children.[28,29] Generally the outcome of CIC in the management of neurogenic bladder has been satisfactory both in the resolution and improvement of VUR and UTI.[30] When this is not the case, either the lack of patient adherence to CIC or poorly compliant bladder to the extent of irreversibility must be considered. The former condition can be corrected by reeducation, whereas the latter may require augmentative cystoplasty with or without antireflux surgery before severe reflux nephropathy occurs.[18] For these reasons, we need a close follow up of the children with neurogenic bladder, and scintigraphic evaluation with Tc-99m DMSA is an effective tool for their management.

The problem in repeating Tc-99m DMSA scan is the high radiation dose to the kidneys. The radiation dose to the kidneys from Tc-99m DMSA is known to be higher than that from intravenous contrast urography. We should consider this disadvantage and therefore select high risk patients for repeated DMSA scintigraphy.

## CONCLUSION

Our results indicated that renal morphology rarely changed and functional renal mass rarely decreased in children with VUR under proper urological care during follow up. Therefore, we should select the high risk subgroup of children with VUR for repeat Tc-99m DMSA renal scintigraphy to prevent unnecessary exposure to radiation.

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