^{99m}Tc dimercaptosuccinic acid (DMSA) scan in patients with established radiological renal scarring

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SUMMARY The findings on ^{99m}Tc dimercaptosuccinic acid (DMSA) scans were examined in 54 patients aged 3 to 33 years in whom renal scarring had been diagnosed radiologically in childhood after urinary tract infection. There was no recent history of infection. Vesicoureteric reflux had been present in 48 patients and had stopped in 23 at the time of the DMSA scan. In six of the 72 radiologically scarred kidneys, the DMSA scan appeared normal but scarring would have been overlooked in only two of the 54 patients. DMSA scan changes are non-specific and underestimated individual scars in 21 kidneys. The intravenous urogram and the DMSA scan showed good correlation but should be regarded as complementary investigations in these patients, giving morphological and functional information, respectively. On DMSA scans the timing of any preceding urinary tract infection must be considered in order to differentiate diffuse potentially reversible defects in isotope uptake after urinary tract infection from those due to permanent renal scarring.

New imaging techniques have been introduced for the investigation of the urinary tract that are less invasive or give less radiation exposure than the established radiological methods. There has been limited parallel evaluation, however, at a time when the new methods are evolving and experience and expertise in their use is being gained.

The radiological features that identify the coarse renal scarring of chronic atrophic pyelonephritis or reflux nephropathy are long established.¹ They include deformity or clubbing of the calyx with thinning of the overlying parenchyma, distributed irregularly through the kidney and particularly affecting the renal poles. When scarring is segmental and not generalised, hypertrophy of the intervening normal tissue produces an irregular renal outline. The overall renal size is usually reduced. These changes correspond closely to the morbid anatomy of the condition. The value of the ^{99m}Tc dimercaptosuccinic acid (DMSA) scan in these patients has been clearly shown: areas of impaired DMSA uptake may indicate a segmental scar.²⁻⁶ In some of these studies, however, the effects of recent infection have not always been excluded.

After noting a number of discrepancies between the radiological and DMSA scan reports in patients with established renal scarring on intravenous urography, we undertook a study of the DMSA scan

findings in a group of such patients in whom there was no recent history of urinary infection.

Patients and methods

We studied 54 patients (10 males, 44 females) who ranged in age from 3 to 33 years. They originally presented with urinary tract infection aged 1 month to 12 years in the paediatric department, University College Hospital, and were found to have chronic atrophic pyelonephritis on intravenous urography. Subsequently all but three had serial follow up films confirming the renal scarring. A micturating cystourethrogram was also carried out in each child.

All the patients were maintained on low dose antibacterial prophylaxis until mid adolescence and were followed up with urine culture, blood pressure, and height measurements at three month intervals; this extended after the age of 15 to six or 12 month intervals. Limited serial radiological investigation was performed every two to three years during the growing years. Patients with outflow obstruction, stones, or complex renal anomalies, including horseshoe kidneys, were excluded from this study.

Renal scarring was bilateral in 18 and unilateral in 36, making a total of 72 scarred kidneys: 42 right and 30 left. There were seven duplex kidneys, five of them scarred, in five patients. Vesicoureteric reflux

was seen in the ureter draining the scarred kidney in 50 patients (67 kidneys) and was presumed to have ceased in four in whom the micturating cystogram had been delayed until over the age of 12 years. In 34 of the 67 kidneys, reflux was severe with dilatation of ureter and renal pelvis. At the time of the DMSA scan, vesicoureteric reflux was known to have ceased in 30 patients, and in 44 ureters draining scarred kidneys. In seven patients (12 ureters) it was corrected surgically and in 23 patients (32 ureters) it stopped spontaneously. Reflux occurred initially into 16 radiologically normal kidneys and had ceased spontaneously in nine.

Three patients had intermittent hypertension and two others were on hypotensive drugs. Plasma creatinine concentrations were in the normal range for age in all patients, but at the upper limit in two. Symptomatic urinary infection had not occurred for at least three months before any of the investigations.

Standard intravenous urograms were taken on the subjects as outpatients. Conray 280 was used for young children and Conray 420 for older children until 1985 when these were replaced by non-ionic contrast media. Since then iohexol 240 or 300 at 2.5 ml/kg for children under 1 year, and iohexol 300 at 2.5–3 ml/kg (up to a maximum of 40 ml) has been used. An initial four film intravenous urogram was carried out over 30 minutes. Follow up at intervals of not less than two years was limited to a single 12 minute film of the renal areas. Tomography was occasionally needed in the youngest children.

The extent and distribution of scarring on intravenous urography were described as follows: *group 1*: one or two polar scars, or a laterally placed scar, or a polar and laterally placed scar; *group 2*: three or more focal scars (multiple); and *group 3*: a uniformly shrunken or globally scarred kidney.

The ^{99m}Tc DMSA scan was performed using an IGE—400T Gamma camera until 1985 when this was replaced by an IGE 400AC Starcan Anga Gamma camera. Posterior and both oblique views were routinely performed four hours after injection of the dose, which was adjusted to the child's body weight and based on a standard adult dose of 150 MBq. In most patients a renogram using ^{99m}Tc diethylenetriamine pentacetic acid (DTPA) was carried out either in combination with the DMSA or on a separate occasion, to exclude obstruction at the vesicoureteric or pelviureteric junction and to measure the proportionate function of each kidney.⁷

The interval between the intravenous urogram and DMSA scan varied but, apart from the adults without recurrent urinary tract infection in whom the findings on intravenous urography had already been shown to be constant, it did not exceed two

years and in the younger children was usually less than three months. The intravenous urogram showing established scarring always preceded the DMSA scan.

The DMSA scans and the intravenous urograms were reviewed individually and blind in each patient. The results were then compared for each kidney and each child both for abnormality and morphological detail. The independent routine reports of the intravenous urogram and DMSA scan were also compared.

Results

REVIEW OF INTRAVENOUS UROGRAMS AND DMSA SCANS FOR RENAL ABNORMALITY

There was good correlation of renal abnormality in 48 of the 54 patients (89%) and in 66 of the 72 radiologically scarred kidneys (92%). In six kidneys, however, no abnormality was reported or noted on review of the DMSA scan. These occurred in six girls, in three of whom radiological scarring was bilateral. The scars that were not recognised on the DMSA scan were localised to the poles in five; four were left kidneys and three kidneys had more than one scar. Although three of the patients had unilateral scarring, this would have been missed in only two patients as the contralateral kidney was reported to be abnormal on the DMSA scan in one of them and further investigation would have followed. The distribution of function between the kidneys in these patients estimated by DTPA and DMSA renography was not helpful as in only one patient, with unilateral scarring, did it differ by more than 10%.

Among 36 patients with unilateral scarring, the DMSA scan suggested an abnormality of three contralateral, radiologically normal, kidneys. On review, two of these appeared to be due to a splenic impression. The third is under continued observation.

DETAILED COMPARISON OF INTRAVENOUS UROGRAMS AND DMSA SCANS

(1) Morphology (table)

In group 1 scarring was confined to one or both poles in 19 kidneys and to the lateral mid zone in two. Eight kidneys had both a polar and a mid zone scar. These three patterns of scarring were considered together. All six disparate kidneys were in this group. The three kidneys that appeared to be small with a smooth outline and without focal defects on the DMSA scan each had bipolar scarring.

There was very close correlation in the interpretation of the appearances on the intravenous urogram

Table Review of the renal findings on the DMSA scan in 54 patients with 72 radiologically scarred kidneys, 42 right and 30 left

Extent of renal scarring on intravenous urography	Renal appearance on DMSA scan						Renal appearance on the DMSA scan compared with intravenous urogram			Total No of scarred kidneys on intravenous urography (right)
	Small	Small with focal defects		Focal defects		Normal	Correla- tion	Under- estimate†	Disagree- ment‡	
		Correla- tion*	Under- estimate†	Correla- tion*	Under- estimate†					
Group 1 1 or 2 polar or mid zone	3	1	1	11	7	6	15	8	6	29 (16)
Group 2 Multiple (≥ 3 scars)	3	5	4	4	9		12	13		25 (12)
Group 3 Global	8	10					18			18 (14)
Totals	14	21		31	6		45	21	6	72 (42)

*=Abnormality on DMSA scan correlating with radiological scarring; †=underestimate of scarred areas; and ‡=disagreement between the findings on the DMSA scan and intravenous urogram.

and DMSA scan in all the kidneys with severe and fairly generalised scarring (group 3). In group 2, 25 kidneys had several scars and multiple focal defects were noted on the DMSA scan in 22 of them. The DMSA scan, however, underestimated the number of scarred areas in 13 kidneys (four right and nine left), which were mainly in the upper or lower pole (table).

Duplex kidneys—among the five patients (two boys) with seven duplex kidneys, the duplex was only recognised on the DMSA scan in two. In one girl a unilateral, scarred duplex kidney contributed 54% of the total function.

(2) Function

The differential renal function assessed on the DMSA scan corresponded closely with the findings in the DTPA renogram. The figure shows the difference in the proportion of total function contributed

Figure Percentage difference in function on isotope renography between right and left kidneys in 54 patients with 72 radiologically scarred kidneys. Scarring was bilateral in 18 patients. No patients had bilateral global scarring.

by each kidney, expressed as a percentage in patients with unilateral and bilateral scarring. There was little disparity in individual renal function in 14 patients, even though 10 of these had unilateral scarring where a greater difference might have been expected. Eighteen patients had one small shrunken kidney and in 13 of them there was considerable disparity in function between the kidneys even in four patients in whom scarring was bilateral.

(3) Age

Renal scarring was first diagnosed on intravenous urography in six of the children under the age of 2 years, in 24 aged 3–6 years, and in 34 aged 7–12 years. Renal scarring was well defined in the initial intravenous urogram of all of them. The first DMSA scan was carried out in two children under the age of 5 years, in nine children between the ages of 6–10 years, and in 13 children between the ages of 11–15 years. The remaining 28 were performed in patients aged 16 or over, mean age 21 years. As the DMSA scan became part of our investigative procedure, most of those performed in young children followed an acute urinary tract infection, and if the interval after this was less than three months, they were excluded from the study. There were thus not sufficient young children in the group to make a satisfactory comparison between age groups.

(4) Vesicoureteric reflux

At the time of the DMSA scan, reflux was assumed to be occurring in 27 scarred kidneys. We found no indication that vesicoureteric reflux, in the absence of infection, affected the appearance of the DMSA scan or the distribution of function.

REVIEW OF REPORTS

There was overall agreement between the intravenous urography and DMSA scan reports in 38 patients (70%) and 54 kidneys (75%) but some disagreement in the remainder. The reports of the DMSA scan would have passed seven patients with radiological scarring as normal.

Discussion

In this population of patients with established radiological scarring, the corresponding kidney was abnormal on the DMSA scan in 92%. Although discrepancies occurred in six patients, three with unilateral and three with bilateral scarring, the scarring would have been missed only in two patients if the intravenous urography had been omitted.

In six kidneys with mainly polar scars the DMSA scan was considered to be normal, but apart from the site of the scarring there were no differences of age, sex, laterality, or presence of vesicoureteric reflux to distinguish them from the other kidneys studied. When the extent, site, and severity of the scarring was considered in the whole group there was very close agreement in 63% of kidneys, but the number of scars was underestimated by the DMSA scan appearances in 30%. No additional scars unsuspected on intravenous urography were detected, even on oblique views by the DMSA scan. Contrary to the observations of Monsour *et al*, who found the left kidney to be scarred more often than the right,⁵ our series included 42 right and 30 left scarred kidneys. On reviewing 119 children with 162 scarred kidneys seen in our department there were 86 right and 76 left kidneys affected. The preponderance of right kidneys in our series is not significant. Interestingly, the three radiologically unscarred kidneys with 'suspicious' DMSA scans were all left kidneys, two due to splenic impressions and one with slight patchy reduction in isotope uptake.

There were few young children in our study population because patients investigated within three months of a urinary tract infection were excluded from the study. The patchy and sometimes extensive impairment of DMSA or ^{99m}Tc glucoheptonate uptake seen after an acute urinary tract infection in a child may be of great importance in identifying those at risk of progressive renal damage and therefore in need of careful supervision, further investigation, and continued antibacterial prophylaxis until the underlying cause has been clarified.^{4 6 8-11} These changes may be transient and probably represent the acute inflammatory stage, which may either resolve or progress to permanent renal scarring. With adequate, rapid treatment the pro-

gress may be arrested as in the piglet and rat models.^{12 13} In these it was shown that by introducing antibacterial treatment soon after infection of the refluxing urinary tract the renal scarring process could be stopped or even prevented. (This is one explanation of the areas of slight parenchymal thinning overlying slightly flattened calyces occasionally seen on intravenous urography in children with vesicoureteric reflux and which do not progress to classical scars.) It is thus of some importance to recognise these potentially reversible inflammatory changes on the DMSA scan and differentiate them from permanent changes due to scarring. Scars may take several months to develop: the exact time is not known clinically, and radiological observations have depended upon the time interval between serial intravenous urograms. Scars will not be immediately apparent on intravenous urography, although evidence of acute inflammation can be recognised by renal enlargement and a locally impaired nephrogram.^{14 15} The presence and severity of vesicoureteric reflux appeared to have no effect on the DMSA scan findings in the absence of recent infection.

Differences in function between the two kidneys were related to the extent of scarring in each kidney. In 10 of the 36 patients with unilateral scarring the difference in function between the two kidneys was less than 10%, indicating that such a small difference does not exclude the presence of scarring. Further, there may be confusion when a unilateral scar involves a duplex kidney as this may still contribute a higher proportion of the total function than the normal kidney. As expected, those with severe unilateral scarring had greater relative differences in renal function, but even when scarring was bilateral there could be a disparity of 40-50% if one kidney was severely scarred. The differential function could thus be helpful in patients with severe scarring and in some with unilateral scarring. Urinary infection can, however, cause a pronounced depression of renal function in a scarred kidney with persistent reflux and where this is unilateral, any difference in function will be accentuated. These observations emphasise the importance of relating functional findings on isotope renography to the clinical history and timing of infection, and of pursuing further investigations if the DMSA scan is abnormal.

The DMSA scan is useful in detecting renal abnormalities in infants and young children when a technically satisfactory intravenous urogram may be difficult to achieve. It will indicate the relative function of the kidneys and there will be less exposure to radiation than from a full intravenous urogram with a large series of films. It is, however,

an expensive and lengthy procedure, often needing day admission, and gives little information about possible contributory causes of urinary tract infection or renal scarring.

On the other hand the intravenous urogram has the advantage to the clinician of providing a morphological renal image that is reproducible for growth assessment. It can also indicate possible factors concerned in the pathogenesis of urinary tract infection and the scarring process, including bowel and bladder function as well as any spinal anomalies. It is a less expensive investigation, still universally available and comparable, and completed in a brief outpatient visit. Radiation exposure can be minimised by careful preparation and by restricting the number of films and focusing on the renal area. The use of non-ionic contrast medium reduces the risk of side effects.

In conclusion we have found the intravenous urogram and the DMSA scan to be complementary investigations in the assessment of patients with renal scarring. The former provides structural and the latter functional information. It is important, however, for the clinician to review both sets of images together, as well as receiving reports of the differential function; any history of recent infection must be taken into account in their interpretation.

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