DMSA findings in the evaluation of pediatric renal allograft

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Owing to their minimally invasive nature, efficiency and availability, radionuclide renal diagnostic studies play an important role in assessing renal transplant function. Various quantitative parameters have been derived from the radionuclide renograms in the follow-up to assess changes in perfusion and function of the transplant kidneys. The aim of this study was to evaluate the changes in renal transplants with technetium-99m dimercaptosuccinic acid scintigraphy. Serial cortical renal scans of 66 patients were reviewed retrospectively. The studies were analyzed regarding the quality of the images and morphology of the kidneys. Cortical renal scintigraphy was unable to provide decisive information for the etiological diagnosis of renal graft dysfunction, thus not allowing a distinction to be made between different clinical situations. Despite being non-specific, it gives information that is not apparent on conventional imaging as well as the extent of pathology, which makes it a sensitive test in the follow-up of transplant pediatric patients. An early scan within the first weeks provides a baseline, which may help in the assessment of future complications.

Key words: Tc-99m DMSA, transplant kidney, pediatrics.

Renal transplantation has become the procedure of choice for the treatment of patients with end stage renal disease, and survival tends to be longer after transplantation compared with dialysis[1,2]. However, successful transplantation is not achieved easily and complications are not uncommon. Acute tubular necrosis (ATN), urinary tract infection (UTI), hypertension (HT) and cyclosporin A (CsA) toxicity are the main problems that increase morbidity in the follow-up[3].

Multiple diagnostic modalities are used since none of them offers total diagnostic specificity. It is sometimes even difficult to distinguish between rejection and immunosuppressor nephrotoxicity on the basis of fine-needle biopsy (FNB) findings[4]. This distinction is essential, because the treatment modalities are quite different. Since it is an invasive method, it is preserved until the other methods fail during the assessment.

Radionuclide renal studies play an important role in the evaluation of renal allograft function, both in the early and late post-transplant period, with the advantage of being minimally invasive. Various quantitative and qualitative studies have been derived from the renograms to evaluate the changes in perfusion and function of the kidneys[5-7]. Technetium-99m dimercaptosuccinic acid (Tc^{99m}DMSA) localizes in the proximal tubular cells of the renal cortex and allows excellent visualization of functioning renal parenchyma. Its role is very well known in the assessment of UTI as well as reflux nephropathy[8-10], but has not been used widely in renal allograft evaluation.

The aim of this study was to evaluate changes in the renal allograft in a pediatric population using Tc^{99m}DMSA and to see if these findings would help in the assessment of the kidney outcome.

Material and Methods

One hundred and five Tc^{99m}DMSA studies performed on 21 female and 45 male children with renal allograft in a period of three years for various reasons during their follow-up were reviewed. The clinical data on all children were retrieved from their hospital charts

and the following information was obtained: age, gender, serum creatinine and CsA level, history of HT, the urine analysis and the consecutive ultrasound (US) findings. Clinical data including immunosuppressive regimen, number of rejection episodes, number of post- transplantation UTI and anti-hypertensive therapy requirement were also recorded.

All patients underwent radionuclide imaging with Tc^{99m}DMSA, 2-4 hours following intravenous injection of the dose adjusted for age (maximum 100 MBq). Images of the transplant kidney in the anterior, posterior, and both anterior and posterior oblique views were acquired with a gamma camera using high resolution collimator. The scintigraphic studies were reviewed by two nuclear medicine physicians without any knowledge of the clinical and laboratory data. The images were analyzed both for quality of the study and function of the kidneys (Tables I and II).

Quality was assessed by the clarity of outline and internal architecture of the kidney with the degree of motion and background activity[8]. The semi-quantitative analysis was based on the preservation or loss of the outline, normal appearance or defects in the parenchyma, central filling defects, as well as visualization of the native kidneys and/or other organs. The interpretation was made judging all views of the kidney with a final conclusion for function as: normal, moderately good, moderate, moderately poor or poor function with or without parenchymal defects and/or central filling defects.

Table I. Data Analysis Regarding Quality Control

	Anterior	Posterior	RAO	LAO	RPO	LPO	Total
OUTLINE							
Clear	65.4%	36%	75%	37%	49%	12%	49%
Slight blurring	5.6%	51%	21%	55%	43%	52%	40%
Excess blurring	29%	13%	4%	8%	8%	36%	11%
INTERNAL ARCHITECTURE							
Well seen	48%	19.6%	69%	34%	35%	4%	38%
Seen	22%	36.4%	16%	34%	40%	28%	30%
Difficult to see	30%	44%	15%	32%	25%	68%	32%
MOVEMENT							
None	47%	63.5%	32%	71%	55%	62%	45%
Slight	6%	36.5%	66%	26%	45%	32%	55%
Excess	47%	–	2%	3%		2%	1%
BACKGROUND							
Low	70%						70%
Moderate	22%						22%
High	8%						8%

RAO: Right anterior oblique, LAO: Left anterior oblique, RPO: Right posterior oblique, LPO: Left posterior oblique.

Table II. Distribution of Tc99mDMSA – Other Organ Uptake

	None (%)	Liver (%)	Spleen (%)	Bone marrow (%)	Native kidney (%)
Anterior	56	42	13	8	12
Posterior	38	57	44	20	42
RAO	67	30	7	4	11
LAO	34	59	33	8	16
RPO	51	62	19	8	40
LPO	34	34	44	4	44
Total	48	47	25	10	26

LAO: Left anterior oblique, RAO: Right anterior oblique, LPO: Left posterior oblique, RPO: Right posterior oblique.

In order to reach etiological diagnosis, FNB findings were obtained in 8 and US results were used for the other 23 patients in addition to the clinical course and laboratory findings within a week of the Tc^{99m}DMSA studies.

Results

Quality Control of the Images

Of the 105 studies, no sedation was used in any case and only 1% of the patients' data revealed excess motion which made the analysis difficult. A clear outline was noted in 49% of the studies and the contrast between the active outer part and the less active inner part was well seen in 38%. The background activity was judged only on the anterior view and was low in 70% of the studies (Table I).

Kidney Analysis

Lower portion of the kidney was better seen on the anterior view and the upper part on the posterior view. The oblique views were found essential, and especially the contralateral oblique views were helpful. Normal function was found in 16% of the studies, while 40% had moderately good, 27% had moderate, 8.4% had moderately poor and 6.6% had poor function. Parenchymal defects were observed in 58.4% and central filling defect was noted in 61.3% of the studies (Fig. 1). In 26% of the studies, native kidneys were seen, while in 47% the liver, in 25% the spleen and in 10% the bone marrow was noticed (Table II).

Clinical Correlation

Some children had more than one clinical diagnosis so the total number is greater than the number of children in the study (Table III). The majority of the studies performed on these patients were due to consequence of UTI (Fig. 2), accompanying problems such as increased creatinine level or proteinuria (n: 46). Parenchymal defects were seen in almost all cases (n: 33), but poor function was rare (n: 2). Patients with a history of rejection were the other largest group (n: 46) (Fig. 3) and most cases were accompanied with UTI. Moderate good to moderate function was observed widely (n: 38) but parenchymal defects were common (n: 30). CsA toxicity was observed in six studies and poor function was seen in three of them, with parenchymal

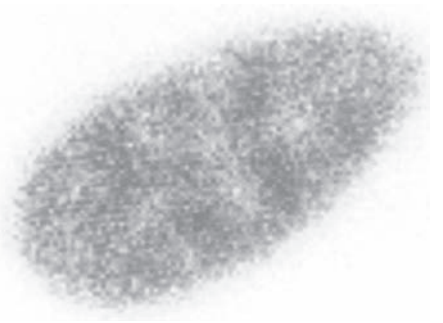

Fig. 1. A 10-year-old male with cystinosis underwent a renal transplant at 9 2/12 years. He had no complications early after the transplant and underwent a routine baseline scan on day 24. The anterior oblique view of the DMSA scan showed good uptake of the radiopharmaceutical with some relatively photopenic areas due to the collecting system, but no evidence of parenchymal defects was observed.

Fig. 2. A 15-year-old female patient with the diagnosis of cloacal anomaly and multiple other congenital anomalies had a living-related renal transplant at age 14 11/12 years. She was treated for UTI on day 12 post-transplant. She was dehydrated and her creatinine level was elevated on day 17. Her DMSA scan was performed on day 22 post-transplant as a routine baseline scan. The right anterior oblique view of the DMSA scan revealed parenchymal defect due to the recent UTI in the lower pole as well as a central filling defect.

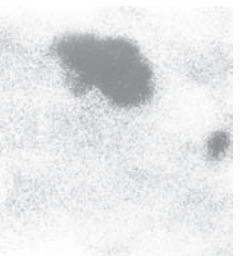

Fig. 3. A 12-year-old male patient with sacral agenesis, neuropathic bladder, and bilateral vesicoureteral reflux underwent a cadaver renal transplant at age 10. He had ATN post- transplant and was treated for rejection on day 9. This anterior view of the DMSA scan, performed postoperative 5 months, showed decreased uptake of the radioactivity in the kidney with high background and a large parenchymal scar in the upper pole with irregular distribution of the activity in the cortex laterally.

Table III. Tc-99m DMSA Findings in Certain Clinical Conditions

Clinical status	Number of studies	Good function	Moderately good function	Moderate function	Moderately poor function	Poor function	PD	CFD
Normal	7	5	1	1			1	4
HT	4	1	2	1			2	3
CsA Tx	4			1		3	2	3
Previous rejection	7	1	4	2			2	3
Previous rejection and CsA Tx	2		1	1			1	
Previous rejection and HT	8		5	3			7	3
Increased creatinine	12	4	2	2	3	1	3	9
Proteinuria	6	1	2	3			4	3
Proteinuria and increased creatinine	3		2	1			2	2
Acute tubular necrosis	3				3		2	1
UTI	8	1	3	3		1	6	6
UTI and previous rejection	29	4	15	7	3		20	17
HT, UTI, proteinuria and increased creatinine	3			1	1	1	1	2
UTI and increased creatinine	6		3	1	2		6	3
Renal artery stenosis	3		2	1			2	1

HT: Hypertension, CSA Tx: Cyclosporin A toxicity, UTI: Urinary tract infection, PD: Parenchymal defects, CFD: Central filling defects.

defects. Three studies were performed in ATN and all showed moderate poor function. Hypertension, either as the only problem or accompanying others, was seen in 15 studies, with moderate to moderate good function in 12 and parenchymal defects in 10.

Of 66 patients, 29 of them had control DMSA studies on the follow-up. Five showed improvement on the scans (all cases with rejection), 10 showed no change [6 with rejection (2 accompanied with UTI), 2 CsA toxicity and 2 with UTI only] and 14 showed deterioration [5 UTI, 1 ATN, 1 CsA toxicity and 7 rejection (2 associated with HT)].

The biopsy findings led to a differential diagnosis between rejection and ATN in 4 cases, showed inflammatory changes in 1, normal findings in 2 and were inconclusive in 1 study. The DMSA findings in these patients were parenchymal defects in cases with rejection and inflammatory changes and normal findings in the rest.

Ultrasonography showed normal findings in 1, collection around the kidney in 1, abscess in 1, loss of blood flow in the lower pole (on Doppler US) in 1, ureteral dilatation in 2, parenchymal injury in 7 and mild pelvicalyceal dilatation in 10 studies. The US findings of pelvicalyceal dilatation and abscess were correlated to 20% of the central photopenic defects of the DMSA studies. Loss of blood flow was seen as parenchymal defect on the DMSA scan and 7 cases with parenchymal injuries were concordant as well.

Discussion

In renal transplant patients, clinical features and laboratory findings are seldom specific to explain the wide range of pathology. Therefore, transplant imaging is a crucial part in the diagnostic process. Renal radionuclide studies are non-invasive, easy to perform and available in most centers, which contribute to their taking an important role in the assessment of function.

Tc^{99m}DMSA localizes in the proximal tubular cells of the renal cortex, thus allowing excellent visualization of the functioning of the proximal tubular mass. There have been a limited number of studies in the literature with conflicting results on its contribution to the diagnosis of renal graft dysfunction[11,12]. This study was performed as a retrospective analysis

of 105 Tc^{99m}DMSA scans of 66 patients who underwent transplant surgery. Analysis was performed on planar scans with the same criteria used by Pusuwan et al.[8]. Use of pinhole collimator or SPECT imaging would undoubtedly improve image quality[13], but the clear renal outlines are a great deal due to the quality of the radiographers who attempt to ensure little or no patient movement. Only 1% of our patients showed excess movement and there was no need for sedation.

In 58.4% of studies, parenchymal defect was observed and in 56% central filling defect was noted. The central filling defect was acknowledged as dilated renal pelvis, explained by a consecutive US in 20% of the studies. On the other hand, 7 out of 23 US studies showed parenchymal injuries, which was not surprising since Tc^{99m}DMSA is known as the gold standard for the evaluation of parenchymal defects[9].

A final decision regarding function was made when all views were taken into consideration and this was correlated to the clinical findings. Contrary to expectation, there were kidneys with deprived function without any significant clinical problem. This can be explained by the fact that even though scans were performed soon after transplantation, a significant portion of the patients had already experienced complications of ATN, rejection, UTI and drug nephrotoxicity, all of which may lead to tubular loss, fibrosis and areas of hypoperfusion causing focal changes.

Budihna et al.[11] showed that clear-cut parenchymal defects were generally related to episodes of rejection. Low values of fractional uptake in rejection were related to lesions in kidney blood vessels and in tubular cells[14]. On the other hand, conflicting results were reported by Cairns et al.[12], who found no defects in 5 patients with rejection proven by FNB. In our group, only 7 studies were with a history of rejection showing moderate to moderate good function while only 2 had parenchymal defects. The majority of the patients with rejection were associated with UTI and it was not possible to clearly identify the main reason for the parenchymal defects.

Post-transplant HT is one of the problems which can be a diagnostic dilemma. Yeo et al.[13] showed that when other diagnostic methods fail to reveal an abnormality, renal cortical SPECT imaging is a valuable tool to show unsuspected renal infarct and areas of segmental perfusion deficit in the evaluation of post-transplant HT in pediatric patients. Likewise, in our group, four studies with HT and 11 with accompanying problems showed parenchymal defects in 12, where US showed positive findings only in two.

These patients are prone to have UTI[16], and Tc^{99m}DMSA was of great value in the evaluation with better recognition of the parenchymal injury. Of 47 studies with UTI either alone or with accompanying problems, 42 of them showed abnormalities on the Tc^{99m}DMSA scans, either areas of cortical tissue with defective uptake or poor function.

Patients undergoing transplantation are under CsA medication and all had poor functioning proximal tubular mass. Kim et al.[17] tried to differentiate ATN from CsA toxicity in rats using renography with enalaprilat and observed deterioration in the CsA group and improvement or unchanged findings in the ATN group after enalaprilat injection. To the best of our knowledge, there is no work in the literature on the evaluation of CsA toxicity using DMSA.

Abnormalities on the transplant kidney have been described in many clinical situations using Tc^{99m}DMSA in our study. This can be explained by the mechanisms of tracer uptake, which requires patent vessels capable of transporting the tracer to the proximal tubules[18,19] and a moderate participation of glomerular filtration[15,19]. Thus, any pathological condition which impairs tubular function or vascular supply reduces the amount of tracer and is seen as a defect on the Tc^{99m}DMSA scan. As a result, many disease states could provoke scintigraphic defects, in particular rejection and immunosuppressor nephrotoxicity, as both cause vascular or tubular lesions[20]. Although Tc^{99m}DMSA imaging does not help to determine the etiology, it enables the estimation of its extent. Detection of focal changes on renal parenchyma scans may give the clinicians important data on clinically unsuspected parenchymal damage, which still can be compensated for with adoptive mechanisms. This in turn should result in careful surveillance of patients at higher risk for deteriorating kidney function due to extensive

scarring and should emphasize the need to optimize long-term immunosuppressive treatment.

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