Journal of Korean Medical Science
Vol. 9, No. 1, 29-34 February 1994

# Poor Renal Uptake of Technetium-99m-DMSA and Technetium-99m-MDP in a Patient with Fanconi Syndrome and Near Normal Glomerular Filtration Rate

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*We present a patient with Fanconi syndrome who demonstrated poor renal uptake of $^{99m}$Tc-DMSA and high urinary concentration of the tracer. A $^{99m}$Tc-DTPA scan was normal and the creatinine clearance only minimally decreased. These findings suggest that $^{99m}$Tc-DMSA may be accumulated in the kidney by glomerular filtration and subsequent tubular reabsorption, with the nonabsorbed fraction appearing in the urine. In Fanconi Syndrome the tubular reabsorption of DMSA may also be reduced, thus explaining the poor renal uptake in this patient. A $^{99m}$Tc-MDP bone scan showed faint renal uptake and diffuse high uptake mainly in the spine, demonstrating that the metabolic bone disease associated with Fanconi Syndrome can be another mechanism for poor renal visualization on bone scan.*

**Key Words :** *DMSA scan, Bone scan, Fanconi syndrome*

## INTRODUCTION

It has been shown that technetium-99m-dimercaptosuccinic acid($^{99m}$Tc-DMSA) concentrates in the proximal tubular cells of the kidney(Willis et al., 1977). Because of the high serum protein binding of $^{99m}$Tc-DMSA (Arnold et al., 1975 ; Yee et al., 1981 ; Vanlic-Razumenic et al., 1984 ; De Lange et al., 1989), it is generally assumed that glomerular filtration of $^{99m}$Tc-DMSA is not signficant and that the localization in the cortical tubular cells occurs by direct uptake from the peritubular capillaries (Chervu and Blaufox, 1982). Recently, some studies have shown evidence that both glomerular filtration and peritubular uptake play a role in the renal handling of $^{99m}$Tc-DMSA (De Lange et al., 1989 ; Van Luijk et al., 1983 ; Van Luijk et al., 1984 ; Kremer Hovinga et al., 1984 ; Peters et al., 1988).

Absent or faint renal uptake on bone scan secondary to rapid and enhanced uptake of tracer by the abnormal bone is associated with various neoplastic, metabolic, and hematologic disorders (Sy et al., 1975 ; Fogelan et al., 1978 ; Kim et al., 1991). Fanconi syndrome is a constellation of transport defects in the proximal renal tubule, including impaired reabsorption of amino acids, glucose, sodium, potassium, calcium, phosphate, bicarbonate, uric acid, and low-molecular-weight (tubular) proteins. When present chronically, metabolic bone disease occurs either as rickets in children or osteomalacia in adults (Brewer et al., 1985).

This report presents a patient with Fanconi syndrome associated with multiple myeloma whose $^{99m}$Tc-DMSA renal imaging study led to clues regarding the mechanism of $^{99m}$Tc-DMSA uptake in the kidney. $^{99m}$Tc-methylene diphosphonate(MDP) bone images in the same patient demonstrated dif-

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fuse high uptake mainly in the spine, with markedly diminished renal uptake despite a relatively well maintained glomerular filtration rate(GFR).

## CASE REPORT

A 56-yr-old woman was admitted to the hospital because of multiple bone pain. The patient had been well until 4 yr earlier, when she developed right lower leg pain. The leg pain worsened gradually, and 8 months before admission she developed multiple bone pain. She could not recall any episodes of trauma. Her height was 150cm and her weight was 39kg. She had a weight loss of 13kg over the previous 8months. Blood pressure was 100/70mmHg, heart rate 102/min, respiration rate 20/min, and body temperature 36.9℃. Motion was limited because of multiple bone pain and tenderness.

Urinalysis showed pH 6.5, albumin 30mg/dl, glucose 1000mg/dl, and was negative for red or white blood cell. Hematocrit was 38.5%, white-cell count $9.3\times10^9$/liter, platelet count $364\times10^9$/liter, and erythrocyte sedimentation rate 55mm/hr. Prothrombin time, partial thromboplastin time, blood glucose, and liver function were normal. Serum calcium was 9.0mg/dl (normal : 8.8-10.5), phosphorus 1.7mg/dl (2.5-4.5), uric acid 1.0mg/dl(2.5-7.0), sodium 139mmol/liter (135-145), potassium 3.1mmol/liter (3.5-5.5), chloride 100mmol/liter (98~110), and carbon dioxide content 19mmol/liter (24-31). Arterial blood pH was 7.37, and calculated bicarbonate level 17mmol/liter. Serum protein was 6.8g/dl (6.0-8.0), albumin 3.8g/dl (3.2-5.2), alkaline phosphatase 472 U/liter (30-115), intact PTH 52.5 pg/ml (10-65), urea nitrogen 5mg/dl (10-26), and creatinine 0.7mg/dl(0.7-14). Creatinine clearance was 69ml/min (75-125). Twenty-four hour urine showed 2740ml volume, 129mmol sodium, 58mmol potassium, 104mmol chloride, 148mg calcium, 500mg phosphorus, 575mg uric acid, 5.8g protein, and 0.4g creatinine. Fractional reabsorption of phosphate was reduced (41%), and fractional excretion of bicarbonate during the bicarbonate loading test was increased (24%). Urine protein electrophoresis showed M-peak in the β region with a M component of 73.5%, and urine protein immunoelectrophoresis showed Bence-Jones proteinuria of kappa light chain type. Urine $\beta_2$-microglobulin was over 40 μg/ml (0.1-0.16). There were increases of urinary asparagine, citrulline, alanine, and ornithine excretion.

Bone marrow examination showed normocellular marrow with increased plasma cells up to 23.5% of all nucleated cells. Bone X-rays showed generalized osteopenia and multiple insufficiency fractures.

Technetium-99m-DMSA images obtained at 3 hours postinjection demonstrated poor uptake in both kidneys together with the presence of a high amount of the tracer in the urinary bladder (Fig. 1). The study was repeated 2 weeks later in order to insure that the scan findings had not been caused by a radiopharmaceutical problem. Again the same findings appeared. No thyroidal or gastric uptake was detectable in this patient and $^{99m}$Tc-DMSA from the same batches gave normal results in other patients.

Technetium-99m-diethylenetriamine pontaacetic acid(DTPA) images revealed normal cortical uptake with only mild retention of the tracer in the pelvocalyceal system (Fig. 2). A $^{99m}$Tc-MDP whole-body bone scan was performed and there was diffuse increased uptake mainly in the spine, with markedly diminished uptake in both kidneys. In additon, there was multifocal increased uptake in the ribs, where the insufflciency fractures were noted on X-ray(Fig. 3).

Fig. 1. $^{99m}$Tc-DMSA scan findings : poor renal uptake in both kidneys.

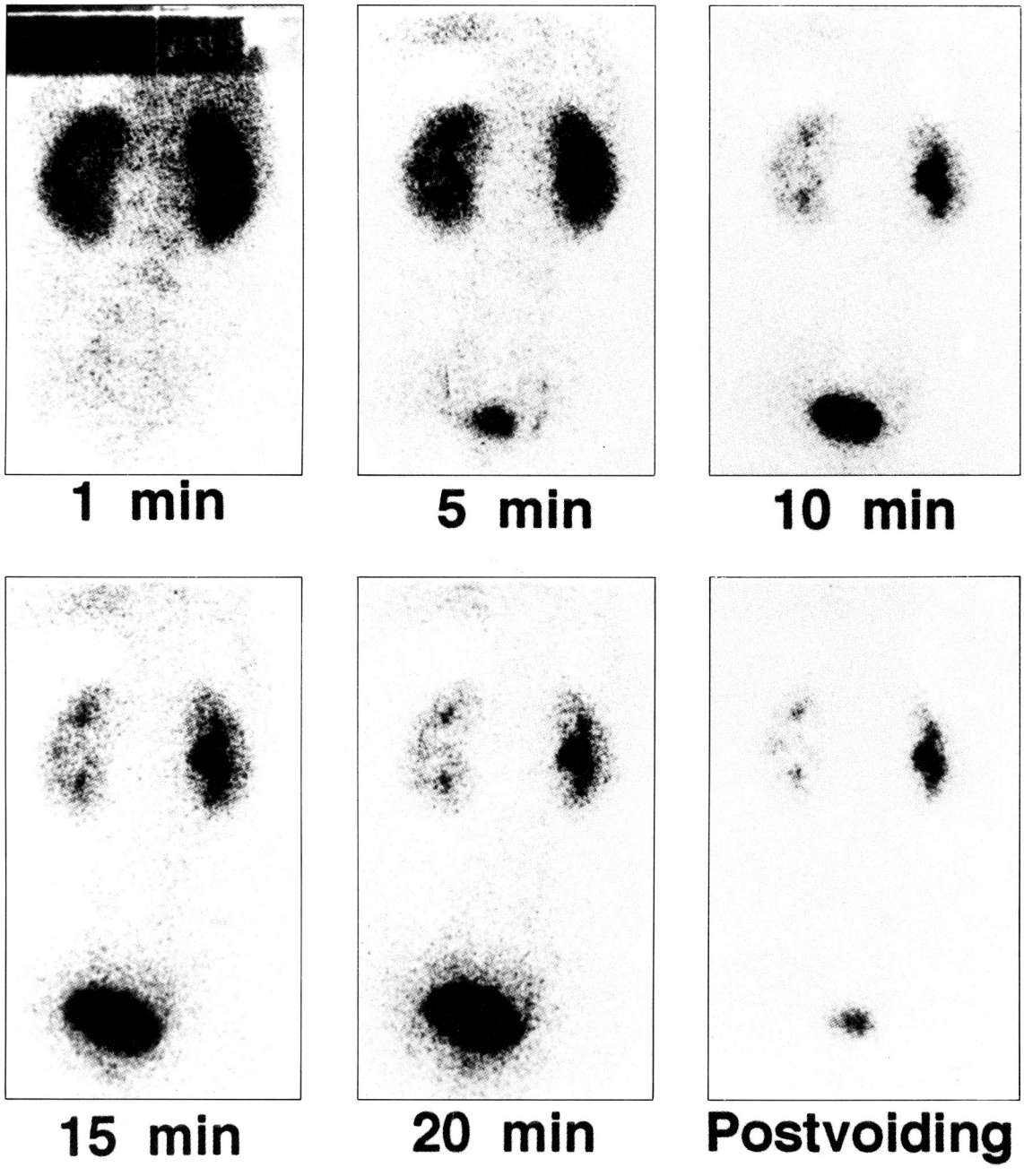


Fig. 2. $^{99m}$Tc-DTPA renal scan findings : normal cortical uptake with mild retention.

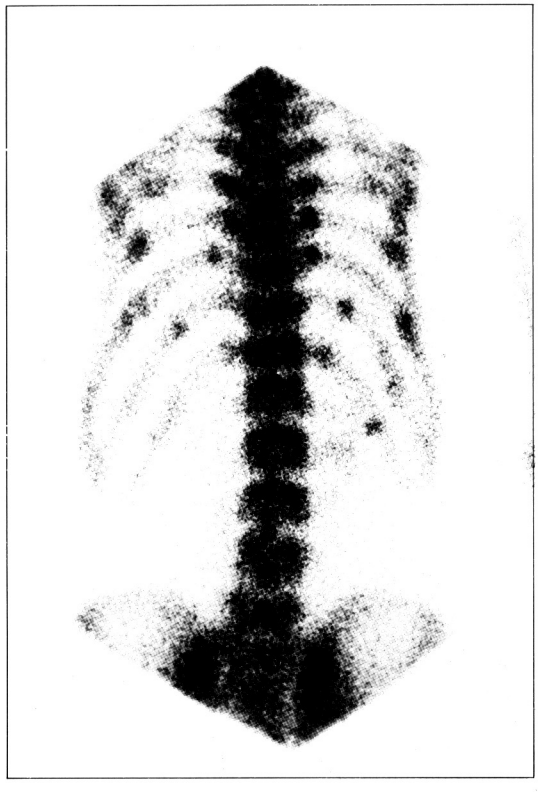

Fig. 3. $^{99m}$Tc-MDP bone scan findings : diffuse increased uptake in spine with diminished uptake in both kidneys.

## DISCUSSION

Technetium-99m-DMSA uptake in the proximal tubular cells may occur either by direct uptake from the peritubular capillaries or by glomerular filtration and subsequent tubular reabsorption. Because $^{99m}$Tc-DMSA is largely bound to serum proteins, it has been suggested that the main route is direct from the peritubular capillaries. Recently, the findings of an increased urinary clearance of the tracer in patients with proximal tubular dysfunction (Van Luijk et al., 1983 ; Van Luijk et al., 1984), and of a decreased renal $^{99m}$Tc-DMSA uptake in patients with renal artery stenosis after captopril treatment (Kremer Hovinga et al., 1984) raised interest in the possibility of glomerular filtration of the tracer. Further evidence for the glomerular filtration was provided by studies based on the measurements of protein binding and clearance of $^{99m}$Tc-DMSA (De Lange et al., 1989 ; Peters et al., 1988).

Normally about 10-20% of $^{99m}$Tc-DMSA excreted in the urine during the first 3 hours after injection (Arnold et al., 1975 : Enlandwe et al., 1974), while the renal uptake is about 40% of the administered dose (Arnold et al., 1975 ; Kim et al., 1990). In the case reported here, despite relatively well maintained GFR as measured by creatinine clearance, a low renal uptake of $^{99m}$Tc-DMSA was found together with a high urinary concentration of the tracer. Biochemical studies showed a picture of multiple transport dysfunctions in the proximal tubule, leading to the diagnosis of Fanconi syndrome. The $^{99m}$Tc-DMSA scan findings in our patient suggest that $^{99m}$Tc-DMSA may be accumulated in the kidney by glomerular filtration and subsequent tubular reabsorption, with the non-reabsorbed fraction appearing in the urine. We have found similar scan findings in a normal infant having immature tubular function (Fig. 4). The possibility of leakage of $^{99m}$Tc-DMSA that has entered the tubular cells by uptake from the peritubular capillaries cannot be excluded in this patient.

This patient showed normal handling of $^{99m}$Tc-DTPA despite a poor renal uptake of $^{99m}$Tc-DMSA. A similar discrepancy has been reported in a patient with tubulointerstitial renal disease (Quinn and Elder,

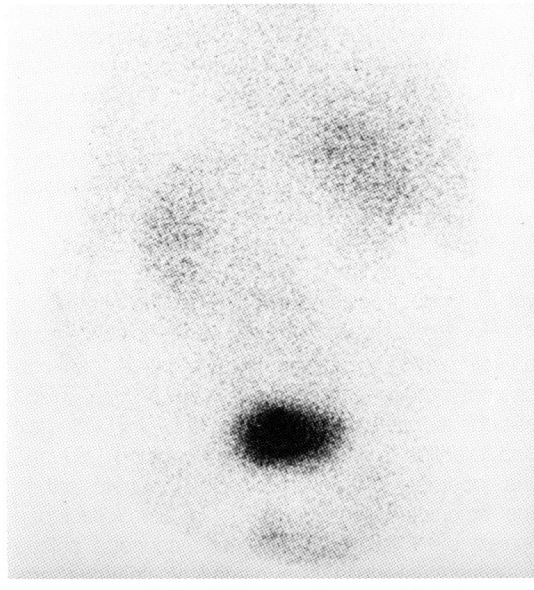

Fig. 4. $^{99m}$Tc-MDSA scan in normal infant.

1991). Technetium-99m-DMSA uptake in the kidney has been shown to correlate well with the effective plasma flow, GFR, and serum creatinine(Kim et al., 1990 ; Kawamura et al., 1978 ; Taylor et al., 1982). However, $^{99m}$Tc-DMSA uptake should be considered as an index of global function : renal blood flow, GFR, tubular extraction efficiency and tubular fixation. This complexity explains why the differential function based on DMSA is not always similar to the differential function, specifically differential GFR based on DTPA(Peters et al., 1988).

Besides a radiopharmaceutical problem, physiological factors such as dehydration and acid-base imbalance can also alter the biodistribution of $^{99m}$Tc-DMSA (Yee et al., 1981). In this patient, systemic acidosis was corrected by medical treatment and only mild acidemia was present at the time of scanning.

Our patients bone scan showed diffuse high uptake mainly in the spine, with a faint renal uptake despite a relatively well maintained GFR. Metabolic bone disease, either rickets in children or osteomalacia in adults, almost always occurs with chronic untreated Fanconi syndrome. Multiple factors may contribute to the pathogenesis of the metabolic bone disease. These include impaired renal tubular synthesis of 1,25-dihydroxyvitamin D, hyperphosphaturia and hypophosphatemia, hypercalciuria, and chronic metabolic acidosis(Brewer et al., 1985). In patients with various neoplastic, metabolic and hematologic disorders rapid and enhanced uptake of bone tracer by the skeletal system takes place (Sy et al., 1975 ; Fogelan et al., 1978 ; Kim et al., 1991). This could be responsible for the poor renal visualization as well as diffuse high uptake most notably in the spine as shown in this patients bone images. This is supported by the persistently elevated alkaline phosphatase level, although this finding may be partially due to the bone fractures and the generalized osteopenia on bone X-rays. Similar bone scan findings have been reported in a patient with distal renal tubular acidosis(Ohashi et al., 1991).

In summary, the findings in our patient suggest that $^{99m}$Tc-DMSA may be accumlated in the kidney by glomerular filtration and subsequent tubular reabsorption, and that differential function based on DMSA studies may not always correlate with that of DTPA studies. In addition, the bone imaging in this patient demonstrates that the metabolic bone disease associated with Fanconi syndrome can be one of the causes of poor renal visualization on bone scan.

## REFERENCES


Arnold RW, Subramanian G, McAfee JG, Blair RJ, Thomas FD : *Comparison of $^{99m}$Tc complexes for renal imaging. J Nucl Med 16 : 357-367, 1975.*

Brewer ED : *The Fanconi syndrome : Clinical disorders : In : Gonick HC, Buckalew VM, eds. Renal tubular disorders : Pathophysiology, diagnosis, and management. New York : Marcel Dekker : 474-544, 1985.*

Chervu LR, Blaufox MD : *Renal radiopharmaceuticals-An update. Semin Nucl Med 12 : 224-245, 1982.*

De Lange MJ, Piers DA, Kosterink JGW, et al. : *Renal handling of technetium-99m DMSA : Evidence for glomerular filtration and peritubular uptake. J Nucl Med 30 : 1219-1223, 1989.*

Enlander D, Weber PM, Dos Remedios LV : *Renal cortical imaging in 35 patients : Superior quality with $^{99m}$Tc-DMSA. J Nucl Med 15 : 743-749, 1974.*

Fogelan I, Mckillop JH, Bessent RG, Boyle IT, Turner JG, Greig WR : *The role of bone scanning in osteomalacia. J Nucl Med 19 : 245-248, 1978.*

Kawamura J, Hosokawa S, Yoshida O, Fujita T, Ishii Y, Torizuka K : *Validity of $^{99m}$Tc dimercaptosuccinic acid renal uptake for an assessment of idividual kidney function. J Urol 1978 ; 119 : 305-3.9, 1978.*

Kim SE, Kim DY, Lee DS, Chung J-K, Lee MC, Koh C-S : *Absent or faint renal uptake on bone scan : Etioliogy and significance in matastatic bone disease. Clin Nucl Med 16 : 545-549, 1991.*

Kim SE, Moon D-H, Lee DS, Han JS, Chung J-K, Lee MC, Lee JS, Koh C-S : *Quantitation of renal function using absolute kidney uptake of $^{99m}$Tc-DMSA. J Korean Med Assoc 33 : 1345-1358, 1990.*

Kremer Hovinga TK, Beukhof JR, Van Luijk WHJ, Piers DA, Donker AJM : *Reversible diminished renal $^{99m}$Tc-DMSA uptake during converting-enzyme inhibition in a patient with renal artery stenosis. Eur J Nucl Med 9 : 144-146, 1984.*

Ohashi K, Smith HS, Jacobs MP : *"Superscan" apperance in distal renal tubular acidosis. Clin Nucl Med 16 : 318-320, 1991.*

Peters AM, Jones AH, Evans K, Gordon I : *Two routes for renal $^{99m}$Tc-DMSA uptake into the renal cortical tubular cell. Eur J Nucl Med 14 : 555-561, 1988.*

Quinn RJ, Elder GJ : *Poor technetium-99m-DMSA renal uptake with near normal technetium-99m-DTPA uptake caused by tubulointerstitial renal disease. J Nucl Med 32 : 2273-2274, 1991.*

Sy WM, Patel D, Faunce H : *Significance of absent or faint kidney sign on bone scan. Eur J Nucl Med 16 : 454-456, 1975.*

Taylor A : *Quantitation of renal function with static imaging agents : Semin Nul Med 12 : 330-344, 1982.*

Van Luijk WJH, Ensing GJ, Meijer AJM, Piers DA : *Is the relative $^{99m}$Tc-DMSA clearance a useful marker of proximal tubular dysfunction. Eur J Nucl Med 9 : 439-442, 1984.*

Van Luijk WHJ, Ensing GJ, Piers DA : *Low renal uptake of $^{99m}$Tc-DMSA in patients with proximal tubular dysfunction. Eur J Nucl Med 8 : 404-405, 1983.*

Vanlic-Razumenic N, Petrovic J, Gorkic D : *Biochemical studies of the renal radiopharmaceutical compound dimercaptosuccinate. IV. Interaction of $^{99m}$Tc-DMS and $^{99m}$Tc-DMS complexes with blood serum proteins. Eur J Nucl Med 9 : 370-373, 1984.*

Willis KW, Martinez DA, Hedley-Whyte ET, Davis MA, Judy PF, Treves S : *Renal localization of $^{99m}$Tc-stannous glucoheptonate and $^{99m}$Tc-stannous dimercaptosuccinate in the rat by frozen section autoradiography. Radiat Res 69 : 475-488, 1977.*

Yee CA, Lee HB, Blaufox MD : *Tc-99m DMSA renal uptake : Influence of biochemical and physiologic factors. J Nucl Med 22 : 1054-1058, 1981.*