Case Report

Differential uptake of Tc-99m DMSA and Tc-99m EC in renal tubular disorders: Report of two cases and review of the literature

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ABSTRACT

Tc-99m DMSA and Tc-99m EC studies are invaluable functional imaging modalities for renal structural and functional assessment. Normally, the relative renal function estimated by the two methods correlates well with each other. We here present two patients with renal tubular acidosis who showed impaired/altered DMSA uptake with normal EC renal dynamic study depicting the pitfall of DMSA imaging in tubular disorders. The two presented cases also depict distinct pattern of Tc-99m DMSA scintigraphic findings in patients with proximal and distal renal tubular acidosis, thus highlighting the factors affecting DMSA kinetics.

Keywords: Fanconi syndrome, Lowe syndrome, renal tubular acidosis, Tc-99m DMSA scan, Tc-99m EC scan

INTRODUCTION

Tc-99m dimercaptosuccinic acid (DMSA) is a routinely utilized radiotracer for renal cortical imaging for the detection of morphological parenchymal abnormalities. Poor DMSA renal uptake with a high blood pool and background activity is almost always associated with deranged RFT's indicating poor renal function. However, renal uptake of DMSA is also influenced by several other factors such as renal blood flow, proximal tubular membrane integrity and urinary acid base balance.[1,2] Tc-99 methylene dicysteine (EC) renal dynamic imaging is another commonly utilized imaging modality for cortical function estimation and drainage assessment.[3] Normally, relative function estimated by the two methods correlates well with each other. We here present the DMSA and EC scintigraphy images depicting differential uptake of these tracers in two children with renal tubular acidosis. The two presented cases also depict distinct pattern of Tc-99m DMSA scintigraphic findings in patients with proximal and distal renal tubular acidosis, thus highlighting the factors affecting DMSA kinetics.

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CASE REPORTS

Case 1

A three and half year old male child was referred to our department for DMSA scintigraphy for evaluation of renal scarring. Renal function tests (RFTs) were within normal limits (Blood Urea Nitrogen: 12 mg/dl, Serum Creatinine: 0.4 mg/dl). Voiding cystourethrogram (VCUG) and renal ultrasonography (USG KUB) were also normal except for mild left hydronephrosis. 60 MBq of Tc-99m DMSA was administered IV after adequate hydration and the scintigraphy was performed 3 hours later. The anterior and posterior images showed no definite delineation of renal cortical outline with high background tracer activity and hence pinhole images could not be acquired [Figure 1a]. The child had no recent history of UTI to suggest any recent acute renal insult. A detailed enquiry then revealed that the child is a suspected case of Lowe's syndrome and had bilateral cataracts operated in his first year of age, history of global developmental delay and abnormal behavioral pattern. Biochemical analysis revealed hyperchloremic normal anion gap metabolic acidosis (NAGMA) and alkaline urine with associated hyperphosphaturia, hypercalciuria, nonselective aminoaciduria, and glycosuria indicative of Fanconi type of proximal renal tubular acidosis. Suspecting the proximal tubular disorder as the cause of the discrepancy, an EC renal dynamic study was performed. Sequential dynamic images were acquired

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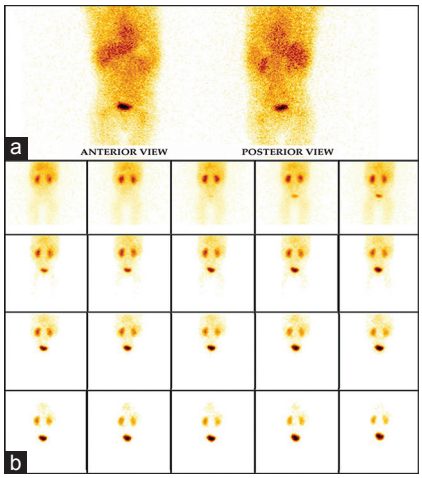

Figure 1: (a) Tc-99m DMSA scintigraphic images revealed significant cardiac, liver blood pool activity and raised background activity. No definite delineation of renal cortical outline could be made suggesting severely impaired tracer uptake. (b) Renal dynamic Tc-99m EC study in posterior view. Sequential dynamic images show adequate cortical tracer uptake in the initial frames in both kidneys with progressive background tracer clearance followed by gradual visualization and intensification of bladder activity. Adequate renal tracer clearance is noted by the end of dynamic study

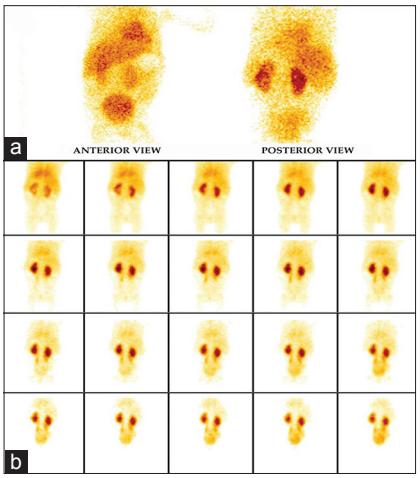

Figure 2: (a) Tc-99m DMSA scintigraphic images revealed raised cardiac blood pool, liver activity and raised background activity. However, definite delineation of renal cortical outline could be made suggesting relatively preserved tracer uptake (as compared to Figure 1a). (b) Sequential dynamic images of Tc -99m EC study show adequate cortical tracer uptake in the initial frames in both kidneys with progressive background tracer clearance followed by adequate renal tracer clearance by the end of dynamic study

in posterior view after intravenous administration of 65 MBq of Tc-99m EC. Dynamic imaging showed adequate perfusion and renal cortical tracer uptake of both kidneys along with adequate background tracer clearance indicating adequate renal function [Figure 1b]. This case depicts the key role of proximal renal tubule membrane integrity in the uptake of DMSA.

Case 2

A 4-year-old male child was referred for DMSA scintigraphy for evaluation of renal scarring. RFTs were within normal limits (Blood Urea Nitrogen: 21 mg/dl, Serum Creatinine: 0.6 mg/dl) and USG KUB was normal except for mild bilateral hydronephrosis. Scintigraphy was performed after 3 h of IV injection of 70 MBq of Tc-99m DMSA. Adequate hydration was ensured prior to tracer administration. The anterior and posterior images showed relatively preserved tracer uptake in both the kidneys along with raised background tracer activity and high cardiac blood pool, liver activity. Possibility of faulty preparation of radiopharmaceutical was ruled out as the other patients injected with the tracer obtained from the same vial on that day showed no abnormal tracer distribution. However, in contrast to the scan of previous child (patient 1), this patient revealed better renal to background ratio and cortical outlines of both kidneys were discernible [Figure 2a]. Detailed history revealed that the child is a known case of distal RTA (hyperchloremic NAGMA, alkaline urine, hypocitraturia) with failure to thrive and knock knees. A Tc-99m EC renal dynamic study of the child was performed for further renal evaluation of function and drainage. Sequential dynamic images were acquired in posterior view after intravenous administration of 75 MBq of Tc-99m EC. Dynamic imaging showed adequate perfusion and renal cortical tracer uptake of both kidneys along with adequate background tracer clearance indicating adequate renal function [Figure 2b]. Note is also made of prompt tracer drainage with a normal renogram curve.

DISCUSSION

Uptake of DMSA by kidneys is an indicator of functional renal tubular mass and this modality is an established radiotracer imaging for structural renal assessment.[4] Renal uptake of DMSA is influenced by several factors such as the renal blood flow, urinary acid base balance.[2] DMSA primarily accumulates in the viable proximal renal tubular epithelial cells.[5] However, the mechanism by which the renal uptake of DMSA occurs, is still the subject of debate. A formerly described mechanism suggested the direct uptake of DMSA by proximal renal tubular cells from adjacent peritubular capillaries which was based on few animal studies, including a micropuncture study of the rat kidneys.[5-7] Recent studies however, indicate the mechanism based on tubular reabsorption following the glomerular filtration.[8] Under physiological conditions, low molecular weight (LMW) proteins are excreted in the urine by glomerular filtration and then reabsorbed by proximal tubular epithelial cells through a process that is mediated by multi-ligand endocytic receptors: Megalin and cubilin. The molecular size of secreted DMSA in the urine is 24-28 kDa, which is well within the range of the LMW proteins. These findings suggest that DMSA is handled by kidneys in the same manner as LMW proteins-i.e. it is filtered in glomeruli and subsequently reabsorbed by proximal tubules via megalin- and cubilin-mediated endocytosis.[8,9]

Organ distribution of DMSA may be altered by the method of tracer preparation, renal blood flow, and acid base disturbances. Yee *et al.*, concluded that acid-base imbalance significantly alters DMSA kinetics in their studies on rats.[1] They showed that acid base imbalance (both alkalosis and acidosis) alters the renal uptake

of the DMSA and acidosis especially is associated with significant rise in the background tracer activity and concomitant increased liver accumulation. Previous studies of DMSA scintigraphy in cases of renal tubular disorders reported similar findings. Lee *et al*., demonstrated markedly decreased renal uptake of Tc-99m DMSA in 13 patients of proximal RTA either due to Lowe syndrome or Dent disease and the decreased uptake was persistent in all serial images.[10] Green *et al*., presented a case of nephropathic cystinosis induced secondary RTA with similar pattern of scintigraphic findings.[11] Caglar *et al*., and Koca *et al*., reported cases of RTA that showed similar pattern of impaired DMSA uptake with normal RFTs which on further evaluation showed a normal Tc-99m mercaptoacetyltriglycine (MAG3) concentration and excretion.[12,13]

The severely impaired uptake of DMSA in the child with Lowe syndrome (patient 1) can be explained by the presence of proximal RTA. Lowe syndrome is characterized by presence of inherited mutation in the gene OCRL1 that encodes a phosphatase, which plays a key role in cellular protein trafficking.[14] Deficiency of this enzyme impairs proper intracellular sorting of various proteins (including megalin and cubilin) especially within polarized cells such as the renal epithelium and the optic lens. This explains the congenital cataracts and renal tubular dysfunction observed in Lowe syndrome.[8,15] This case had all the characteristic features of the Lowe syndrome (oculocerebrorenal syndrome) in the form of bilateral congenital cataracts, global developmental delay, characteristic behavioral pattern and renal Fanconi syndrome. The proximal tubular membrane receptor defect combined with the presence of acidosis explains the severely altered DMSA uptake in this child. In the second child (patient 2), the cause of acidosis was a distal tubular pathology. Thus, the relatively preserved renal uptake of DMSA might be due to intactness of proximal renal tubular membrane integrity which is the key factor in DMSA uptake. Presence of acid base imbalance in the form of acidosis can explain the raised background activity and liver accumulation of DMSA.[1]

EC due to its simplicity of preparation, higher stability, higher renal uptake, lower hepatobiliary activity and lower cost is an effective alternative to Tc-99m MAG3 utilized in previously described cases.[16] Adequate EC uptake and clearance noted in these cases with impaired/altered DMSA uptake is likely due to differences in renal handling of both the tracers.

To conclude, impaired or altered DMSA uptake in the setting of normal renal functional parameters should alert the nuclear medicine physician to the possibility of various pathologic states other than tubular cell loss which may affect the renal uptake as mentioned above. Also, these cases highlight the utility of Tc-99m EC renal dynamic study as a simple alternative tool in such situations due to its different mechanism of renal uptake.

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