Clinical note
Mercaptoacetyltriglycine renal scan for the differential diagnosis of acute tubular necrosis and interstitial nephritis associated to vancomycin

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A B S T R A C T
The differential diagnosis of vancomycin associated renal toxicity includes acute tubular necrosis and interstitial nephritis. We report a case of vancomycin induced renal toxicity shown by Tc-99m mercaptoacetyltriglycine renal scan. Nephrotoxicity was evolved secondary to vancomycin used for treating a patient with meningitis. Tc-99m mercaptoacetyltriglycine renal scan may play a role in differentiation between acute tubular necrosis and tubulointerstitial nephritis of vancomycin associated renal toxicity and can facilitate the clinical decision making.

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Introduction
Vancomycin induced nephrotoxicity has been reported to manifest as acute tubulointerstitial nephritis.1 In patients with preexisting renal disease and sepsis or in the setting of concomitant therapy with aminoglycoside, acute tubular necrosis may also occur.1–3

Dynamic renal scintigraphy is routinely applied in most nuclear medicine departments for the functional evaluation of kidney function and is a useful tool for clinicians. Since its first introduction in 1986, technetium-99m (Tc-99m) mercaptoacetyltriglycine (MAG3), a tubular agent, has replaced the Tc-99m diethylene-triaminepentaacetic acid (DTPA) as a tracer for functional renal studies because of the favorable imaging characteristics of the former one.

Herein we describe a patient with meningitis in whom elevation in blood urea nitrogen and creatinine serum levels were observed after high dose vancomycin administration. Tc-99m MAG3 renal scan revealed diffuse parenchymal retention in both kidneys.

Tubular dysfunction was attributed to vancomycin associated tubular necrosis. Tc-99m MAG3 renal scan played a great role in the differential diagnosis of vancomycin induced renal toxicity. To our knowledge, this is the first report in which findings of MAG3 renal scan in vancomycin associated nephrotoxicity have been demonstrated.

Case
A 6-year-old boy was referred to nuclear medicine department for the assessment of kidney functions with Tc-99m MAG3 renal scan. From his history it was learnt that, he was admitted to our hospital 2 weeks ago suffering from fever, headache and vomiting. In physical examination, neck rigidity was suspicious so lumbar puncture was performed. Cerebrospinal fluid culture was positive for proteus mirabilis. Vancomycin was ordered as 60 mg/kg/day but was misadministered as 4 × 650 mg in a day for 12 days. Four days after the initiation of vancomycin therapy, the patient started to complain about abdominal pain. Renal ultrasound demonstrated enlargement in both kidneys and longitudinal dimensions were 108 mm and 100 mm for left and right kidney, respectively. Bilateral grade 1 increase in parenchyma echogenities were also reported in ultrasonography. Serum concentrations of urea nitrogen (BUN)
and creatinin were 112 mg/dl (normal: 17–43 mg/dl) and 3.3 mg/dl (normal: 0.7–1.2 mg/dl) respectively. Urine work up revealed a density of 1005 (normal: 1015–1025). No eosinophilia was noted and patient was not anuric.

The patient was hydrated with 500 ml of water 30 min before the study in nuclear medicine department. Radionuclide renography was performed supine with the kidneys and bladder in the field of view. Images were acquired with 64 × 64 matrix with a gamma camera (Siemens, ECAM) equipped with low energy general purpose collimator. One hundred and eleven megabecquerel (MBq) Tc-99m MAG3 was administered intravenously. Serial 1-s-per frame digital images were obtained for the first 60 s followed by 15-s-per frame images for a total study duration of 30 min. Perfusion was preserved in both kidneys and Tc-99m MAG3 renal scan revealed gradual increasing of activity in parenchyma of both kidneys (Fig. 1a and b). Background subtracted renal curves showed gradual upsloping during 30 min indicating cortical retention (Fig. 2). Findings in MAG3 renal scan were consistent with acute tubular necrosis and tubular injury was attributed to vancomycin therapy. His condition improved after discontinuation of vancomycin and revision of the antibiotic therapy. One month later, the patient made a full recovery and regained renal function. Serum concentrations of urea nitrogen and creatinine were 35 mg/dl and 0.66 mg/dl, respectively.

Fig. 1. (A) Compressed perfusion images (4 frames per image), which were collected as 1-s-per frame, were obtained for the first 60 s and showed well perfusion in both kidneys. (B) Compressed parenchymal images (1 min per image) revealed gradual accumulation of radioactivity in parenchyma of both kidneys. Cortical retention of radioactivity was observed in both kidneys as well.

Fig. 2. Background subtracted renal parenchymal curves depicted gradual uptake of radiotracer in both kidneys. Maximum uptake \(T_{\text{max}}\), was reached at the end of the study.
Discussion

Drug induced nephrotoxicity, which may manifest as interstitial nephritis, tubular degenerative changes without glomerular pathology, vascular disease or acute tubular necrosis; can be seen after administration of variety of therapeutic agents including cisplatin, aminoglycosides, amphotericin B, radiocontrast agents, diuretics, β-lactam antibiotics and vancomycin. Vancomycin is a frequently used antibiotic in patients with Gram-positive bacterial infections. After the first description of vancomycin induced interstitial nephritis by Eisenberg et al., mechanisms of vancomycin induced nephrotoxicity have been discussed and direct toxic effect of the drug has been suggested in the reported cases. In the kidney biopsies of rabbits, dilation of proximal tubules, destruction of renal tubule cells, swollen mitochondria, increased numbers of vacuoles and abnormal nuclei have been shown after administration of vancomycin. This tubular injury was attributed to the induction of oxidative stress and an increase in free radical generation has been reported.

Although acute renal failure secondary to vancomycin therapy typically presents with interstitial nephritis, patients with biopsy proven acute tubular necrosis have also been presented. Differentiation of acute tubular necrosis from tubulointerstitial nephritis in vancomycin associated nephrotoxicity is a diagnostic challenge and biopsy is commonly used during decision making. Tubulointerstitial nephritis requires steroid therapy but acute tubular necrosis is a self limited disease.

Findings of acute tubular necrosis in renal transplants of single biopsies obtained with Tc-99m MAG3 are well defined and consist of relatively well preserved renal perfusion, progressive uptake of the tracer in the parenchyma and lack of excretion. This classic scintigraphic pattern of acute tubular necrosis in Tc-99m MAG3 renal scan has also been demonstrated in native kidneys. In tubulointerstitial nephritis, however, poor renal uptake has been shown in Tc-99m MAG3 renal scan.

In our patient, Tc-99m MAG3 renal scan revealed preserved perfusion and gradual increasing of activity in parenchyma of both kidneys (Fig. 1a and b). Background subtracted renal curves showed gradual upsloping during 30 min indicating cortical retention (Fig. 2). Scintigraphic findings of our patient were identical with the ones defined in acute tubular necrosis of native kidneys. Since poor renal uptake was not prominent, and also because of the pattern of renal curves and as well as findings on dynamic study, we thought that renal toxicity was evolved secondary to acute tubular necrosis instead of tubulointerstitial nephritis in this patient. Our patient was exposed to larger than ordered dose of vancomycin which most probably contributed to rapid accumulation of vancomycin. Most cases of acute tubular necrosis, especially those resulting from drug toxicity, improve after 3 weeks. Our patient’s renal function was improved after stopping the vancomycin therapy which supports lack of tubulointerstitial nephritis. There was no likely alternate explanation for toxic injury.

By obviating invasive procedures and suggesting no additional investigation, MAG3 renal scan may be valuable for clinicians during decision making and may be a cost-effective management strategy in the differential diagnosis of acute tubular necrosis and tubulointerstitial nephritis caused by vancomycin.

Findings of MAG3 renal scan in vancomycin associated nephrotoxicity have not been shown before. This case illustrates the usefulness of Tc-99m MAG3 renal scan in the management of vancomycin associated renal toxicity.

References