Contrast Nephrotoxicity and the Role of Radionuclide Renal Scan

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Radiographic contrast media-induced nephrotoxicity is an important cause of acute renal failure. The indications of using contrast are usually unavoidable, compelling and continue to expand, especially in the vascular field. When acute renal failure follows such a procedure, it becomes important to establish the presence of contrast nephrotoxicity or an acute occlusive event which may have precipitated the failure. We present two cases of contrast nephrotoxicity in patients with impaired renal function. Radionuclide renal studies with ^{99m}Tc-DTPA (Patient 1) and ^{99m}Tc-MAG3 (Patient 2), confirmed the presence of acute tubular necrosis and excluded major occlusive vascular events. Renal scintigraphy remains an important but underused test which can rule out obvious renal vascular occlusion and/or support the diagnosis of contrast-related acute tubular necrosis, as the cause of renal failure in these patients.

Key Words: iohexol; nephrotoxicity; renogram; renal failure

J Nucl Med 1996; 37:1828–1830

Intravascular infusion of radiographic contrast material is considered to be an important cause of hospital-acquired acute renal failure (*1,2*). The failure induced by contrast media is enhanced by a depletion of intravascular volume, advancing age and presence of underlying renal impairment (*3–5*). Adequate patient preparation such as proper hydration, identification of other iatrogenic factors (NSAIDS, aminoglycosides, ACE inhibitors, etc.) and judicious use of the newer low osmolality contrasts in specific patient subsets can decrease the risks. Based on a better understanding of the pathophysiology of contrast nephrotoxicity, drugs such as dopamine, calcium antagonists, theophylline derivatives and atrial natriuretic peptide are being researched as potential reno-protective agents (*3–5*).

Currently, prevention is the major goal, since management of established toxicity is fairly nonspecific. The single most important clinical axiom for prevention is to limit the use of contrast (*5*). Paradoxically, indications for interventional radiologic procedures requiring intravascular contrast administeration continue to expand especially in the elderly and high risk group (*3,4*). In view of the risks of open surgery in these patients, procedures using percutaneous access and angiographic screening have been developed to address obstructive and other vascular disease. These endovascular procedures range from a simple angioplasty to the placement of complex intravascular prosthetic devices such as stents and endoluminal grafts. Such procedures themselves carry inherent risks (however small) of local and distal vascular complications (*5–8*). Therefore, when renal failure follows such a procedure, it may become important to establish whether the insufficiency is due to contrast-related acute tubular necrosis (ATN) or an acute occlusive vascular event. This distinction is important, since the management could change from an expectant one to a proactive one.

We present two such patients who underwent procedures involving intravascular administration of the contrast agent, iohexol, developed renal failure thereafter and were referred to our department for a radionuclide renal scan.

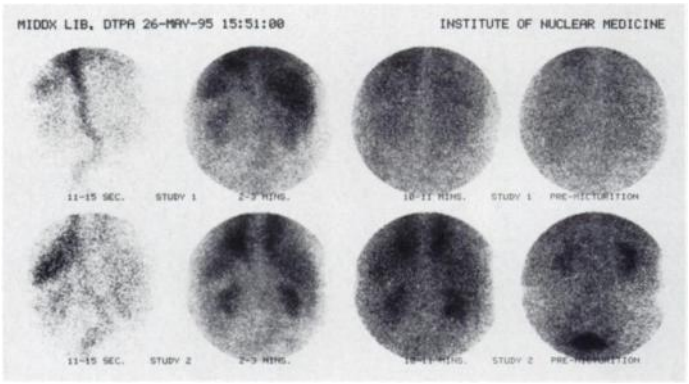

FIGURE 1. Technetium-99m-DTPA renal scan. Top row shows that kidney vascularity was preserved with virtually no concentration or excretion of tracer. After 1 wk of conservative treatment, follow-up ^{99m}Tc-DTPA renal scan (bottom row) showed reasonable tracer concentration and excretion.

CASE REPORTS

Patient 1

A 70-yr-old man, with known hypertension and a prior history of myocardial infarction as well as a preoperative baseline serum creatinine value of 164 μmole/liter, underwent an elective endoluminal repair of an abdominal aortic aneurysm. While the procedure itself was uneventful and the patient remained hemodynamically stable throughout, he received, in the course of the repair, 300 ml iohexol. This intervention also revealed 50% luminal narrowing of the right renal artery. Within 24 hr of the procedure, the patient was oliguric and developed acute renal insufficiency (serum creatinine rising from a baseline preoperative value of 164 μmole/liter to 241 μmole/liter on the first postoperative day). The patient then underwent an ultrasound and Doppler flow study that showed generally poor visibility. The right kidney measured 9 cm, with good flow and Doppler waves, and showed no evidence of pelvi-calyceal dilatation. The left kidney was not visualized. On plain radiograph, there was evidence that the graft had slipped with distal progression. An urgent radionuclide study was requested which was performed with 250 MBq ^{99m}Tc-DTPA administered intravenously. The scan revealed a tortuous abdominal aorta with clear evidence of perfusion to both kidneys (Fig. 1). Subsequent handling of this glomerular tracer by both kidneys was suggestive of acute tubular necrosis (ATN), which in the clinical context was consistent with the diagnosis of contrast induced nephrotoxicity. The patient was managed conservatively with renal support. The serum creatinine values peaked on Day 5 (560 μmole) and began to fall gradually thereafter. He was rescanned after 1 wk when scintigraphic features were consistent with clinical improvement (Fig. 1).

Received Nov. 10, 1995; revision accepted Feb. 28, 1996.
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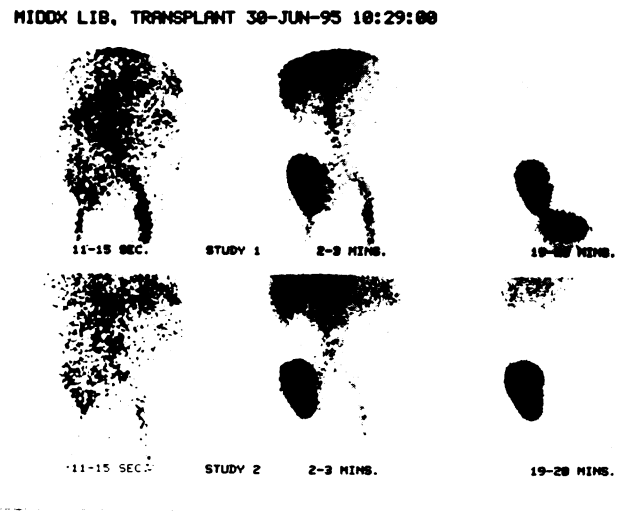

FIGURE 2. Technetium-99-MAG3 study in a renal transplant patient shows a well-functioning right transplanted kidney (top row). Technetium-99m-MAG3 study performed 4 days after a coronary angiogram revealed that the transplanted kidney was perfused but showed a prolonged nephrogenic phase with virtually no tracer excretion (bottom row).

Patient 2

A 57-yr-old man with a cadaveric renal transplant and a baseline serum creatinine of 200 μmole/liter underwent coronary angiography during which he received 150 ml of contrast iohexol. The procedure was uneventful. He was found to have evidence of dilated cardiomyopathy but with normal coronaries. Postangiography, he developed oliguria and his creatinine rose from a baseline level of 200 μmole/liter to 282 μmole/liter on Day 1. The patient was referred for a radionuclide renogram study on Day 4 (as a result of rising serum creatinine level). The scan was performed with 100 MBq ^{99m}Tc-MAG3. The images demonstrated fair perfusion to the transplanted kidney with progressive accumulation of the tubular tracer with a pattern of parenchymal retention consistent with ATN (Fig. 2). In the clinical context, this was compatible with the diagnosis of contrast induced nephrotoxicity. The patient underwent conservative treatment. The serum creatinine peaked on Day 5 at 507 μmole/liter and fell gradually thereafter to 355 μmole/liter on day of discharge (Day 7).

DISCUSSION

The clinical scenarios outlined above share the common denominators of pre-existing impaired renal function, intra-arterial administeration of nonionic contrast (iohexol) and a clinical course quite characteristic of contrast-induced nephrotoxicity (CIN). Both patients, however, were subjected to vascular procedures of varying complexity that carry inherent risks (however small) of renal artery occlusion arising out of thrombotic, embolic, athero-embolic and mechanical events (*5–8*).

Procedures such as placement of an endoluminal aortic graft (Patient 1) have seen considerable refinement over the past few years in technique and prosthetic design. While animal work and initial experience in humans has clearly demonstrated the feasibility of this procedure, it is not without risks. The manipulation of these devices within an aneurysm, the placement of the graft, or its subsequent migration can precipitate an acute renal artery occlusion (*8*). Coronary angiography (Patient 2) on the other hand, is certainly a far less dramatic procedure. In the context of a single-kidney patient, CIN best remains a diagnosis of exclusion despite being the most likely diagnosis. While the prognosis of renal failure arising as a consequence of a vascular event is generally poor, it is dependent on its early recognition and prompt institution of appropriate therapy. Pre-existing collateralization is known to maintain renal viability for varying time intervals just enough to permit recovery upon reperfusion (*9,10*). The lapsed time intervals, however, are best kept to a minimum to allow medical (*11,12*) or surgical treatment (*10,13–15*) a real chance of organ salvage. So, while early recognition is the key, a high index of suspicion is necessary to effect it. The radionuclide renogram, then offers valuable first-pass information to assess the integrity of perfusion, while the subsequent handling of radiotracer can support a diagnosis of contrast-induced ATN to allow for supportive and expectant treatment regimen to continue.

ATN is a clinical entity with a wide pathological spectrum that ranges from frank tubular necrosis to the more common and less dramatic minimal and patchy cell loss. The functional effect of this tubular injury includes a variable rise in intratubular pressure due to sludging of the lumen by cellular debris, the "back leak" of filterate across damaged epithelium, and reabsorptive/secretory dysfunction (*7*). Renal failure in ATN (ischemic or nephrotoxic), however, involves both tubular and vascular events. In fact, sustained intrarenal vasoconstriction is considered to play a central role in the pathogenesis of CIN. Whether these changes in renal hemodynamics are mediated predominantly by tubulo-glomerular feedback or excessive action of endogenous vasoconstrictors is still a matter of debate (*5*). Current research towards specific prophylaxis of CIN is based on the therapeutic modulation of these pathophysiological events (*3–5*). Whatever the initiating and/or predominant mechanism, the final outcome is a profound reduction in glomerular filteration. This net reduction in filteration may be mediated directly by a decrease in blood flow and perfusion, by the raised intraluminal tubular pressure or infact by the tubular "back leak" of filterate (*7*).

In established ATN, a glomerular filtered agent such as DTPA, even if filtered across at all, will tend to "back leak" and scintigraphy with such a tracer will demonstrate a blood-pool image that will gradually fade as the tracer diffuses out into the extracellular space from the vascular space. Whether this is because the filteration marker is not filtered across at all, or because it "back leaks", the net result is of an effective loss of the filteration function. A tubular secreted tracer on the other hand will show progressive accumulation, without any transit to the pelvi-calyceal system, due to the tubular obstruction arising simply out of a diminished intraluminal fluid volume and/or accumulation of debris. This pattern of "parenchymal retention" is seen with agents such as ^{99m}Tc-MAG3 and ^{123}I- and ^{131}I-OIH. The patterns of tracer handling outlined above and illustrated in Figures 1–2 are the hallmarks of typical ATN on a radionuclide scan.

CONCLUSION

Iatrogenic renal failure is of particular concern in patients with pre-existing renal dysfunction undergoing diagnostic or therapeutic vascular procedures. The radionuclide renogram is a simple, nontoxic test, which can provide key diagnostic and prognostic information in this context. Scintigraphy can rule out gross renal vascular compromise or establish ATN to support the diagnosis of CIN as the cause of renal failure.

REFERENCES

1. Hou SH, Bushinsky DA, Wish JB, Cohen JJ, Harrigton JT. Hospital-acquired renal insufficiency: a prospective study. *Am J Med* 1983;74:243–248.
2. Shusterman N, Strom BL, Murray TG, Morrison G, West SL, Maislin G. Risk factors and outcome of hospital acquired ARF. *Am J Med* 1987;83:65–71.
3. Brenden BJ. Contrast nephrotoxicity. *J Am Soc Nephrol* 1994;5:125–137.
4. Porter GA. Radiocontrast-induced nephropathy. *Nephrol Dial Transplant* 1994; 9[suppl:4]:146–156.

5. Rudnick MR, Bern JS, Cohen RM, Goldfarb S. Nephrotoxic risks of renal angiography. Contrast media associated nephrotoxicity and atheroembolism-a critical review. *Am J Kidney Dis* 1994;24:713–727.
6. Smithes M, Cameron JS. Renal failure following reconstuctive arterial surgery. In: Bell PRF, Jamieson CW, Vaughan Ruckley C, eds. *Surgical management of vascular disease*. London: WB Saunders;1992;1027–1048.
7. Brady HR, Brenner BM, Lieberthal W. Acute renal failure. In: Brenner BM, ed. *Brenner's and Rector's the kidney, 5th ed.* Philadelphia: WB Saunders; 1996:1200–1252.
8. Harrison ML. Endovascular grafting for the treatment of abdominal aortic aneurysms. *Surg Clin North Am* 1992;72:959–968.
9. Gerard DF, Dexin JB, Halasz NA, Collins GM. Transplant renal artery thrombosis. Revascularization after 5 1/2 hr after ischemia. *Arch Surg* 1982;117:361–362.
10. Pontemoli R, Rampoldi V, Morbidelli A, Fiorini F, Ranise A, Garibotto G. Acute renal failure due to acute bilateral renal artery thrombosis: successful surgical revascularization after prolonged anuria. *Nephron* 1990;56:322–324.
11. Pineo GF, Thorndyke WC, Steed BL. Spontaneous renal artery thrombosis: successful lysis with streptokinase. *J Urol* 1987;138:1223–1225.
12. Rangel-Abundis A, Olvern R, Cordero J, Cordero E. Postangioplasty renal artery thrombosis treated intraluminally with thrombolysis. A case report. *Gac-Med-Mex* 1991;127:253–256.
13. MacMillan RD, Uldall R, Lipton IH. Simultaneous aortic and renal artery reconstruction for acute arterial occlusion in solitary kidney. *Urology* 1988;31:66–69.
14. Delans RJ, Ramirez G, Farber MS, Shah CP. Renal artery thrombosis: a cause of reversible acute renal failure. *J Urol* 1982;128:1287–1289.
15. Brunetti DR, Sasaki TM, Friedlander G, et al. Successful renal autotransplantation in a patient with bilateral renal artery thrombosis. *Urology* 1994;43:235–237.

Iodine Concentration by the Thymus in Thyroid Carcinoma

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A 14-yr-old boy underwent a total thyroidectomy with bilateral neck dissection for a papillary carcinoma with lymph node metastases. Total-body scanning with 3.7 GBq ^{131}I revealed radioiodine accumulation in the anterior mediastinum. CT and MRI demonstrated a mediastinal mass which corresponded to the area of increased radioactivity. Five months later, another therapeutic dose of ^{131}I was followed by a sternotomy and removal of the thymus because a hand-held radiodetecting surgical probe demonstrated that the thymus was the mediastinal structure which concentrated iodine. Thymus histology was negative for thyroid cancer metastases (as further confirmed by the negative immunostaining) and showed cystic Hassall's bodies. Secondary ion mass spectrometry microscopy demonstrated that iodine was located only in the Hassall's bodies, bound to proteins. This finding suggests that an acquired "thyroid follicle-like" structure, as that observed in cystic Hassall's bodies, could be responsible for the epithelial cell iodine uptake. In conclusion, we have provided evidence for the iodine-trapping property of the cystic Hassall's bodies of the thymus, which may be a possible cause of misleading mediastinal radioiodine uptake.

Key Words: thymus; iodine-131; total-body scanning

J Nucl Med 1996; 37:1830–1831

Total-body scanning with ^{131}I is a sensitive and specific method to localize foci of differentiated thyroid carcinoma. Nonetheless, only two-thirds of distant metastases concentrate radioiodine (*1*). Conversely, uptake of ^{131}I has been reported in nonthyroid lesions such as inflammatory lung diseases, pericardial effusion, ovarian cyst, lymphoepithelial cyst, scrotal hydrocele, skin burn, fungal lesion, primary lung adenocarcinoma, bronchogenic carcinoma, gastric adenocarcinoma, Warthin's tumor and papillary meningioma (*2*).

Thymic uptake of ^{125}I, ^{131}I and ^{123}I has already been reported in rats (*3–5*). Mediastinal uptake observed in young patients has been presumptively attributed to the thymus because thymectomy resulted in the disappearance of the uptake (*5–8*).

In the present study, the mediastinal uptake was investigated by the intraoperative use of a radiodetecting probe, histology and secondary ion mass spectrometry (SIMS) microscopy.

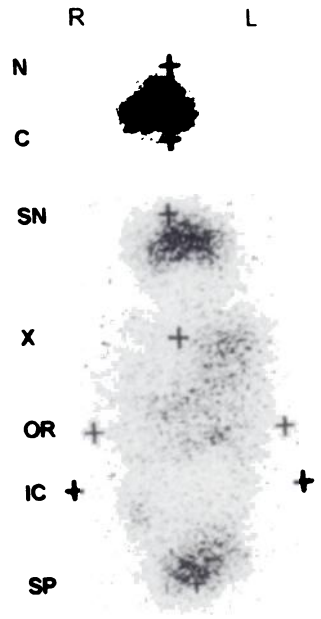

FIGURE 1. Total-body scan performed 5 days after administration of a therapeutic dose of 3.7 GBq ^{131}I (100 mCi) (anterior view). R = right; L = left; N = nose; C = chin; SN = sternal notch X = xyfoid; OR = outer rib; IC = iliac crest; SP = symphysis of pubis.

CASE REPORT

A 14-yr old boy was referred in May 1993 to the nuclear medicine unit of the Gustave Roussy Institute. This patient had undergone total thyroidectomy and bilateral neck dissection because of a papillary thyroid carcinoma with bilateral lymph node metastases. The tumor infiltrated the thyroid in the form of a 5-cm in diameter nodule occupying the entire left lobe and a 3-cm in diameter nodule occupying most of the right lobe. There were seven metastatic neck lymph nodes (four on the right and three on the left). Intraoperatively, it was apparent that the tumor had infiltrated the muscles and the left recurrent nerve.

A ^{131}I total-body scan performed 5 days after the administration of a therapeutic dose of 3.7 GBq ^{131}I (100 mCi) revealed uptake in the anterior mediastinum, which accounted for 0.2% of the admin-

Received Dec. 5, 1995; revision accepted Apr. 4, 1996.
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