Renal Uptake of Technetium-99m Methylene Diphosphonate Following Therapeutic Radiation for Vertebral Metastases

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Radionuclide bone scans in two patients with breast cancer and concurrent chemotherapy treatment revealed increased band-like uptake of [^{99m}Tc]methylene diphosphonate along the medial upper renal cortex corresponding to the portions of the kidneys included within the radiation field. The latency of onset of abnormal uptake was 5 to 9 mo following completion of radiation in one patient, peaked near 13 to 14 mo for both patients, and returned to baseline after 20 to 27 mo. Transient serum creatinine level elevations were also detected. These findings suggest that transient subclinical renal impairment may occur and be detected on bone scans following inadvertent inclusion of renal cortex in radiation fields.

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Injury to the kidneys following therapeutic radiation has been uncommonly identified on diagnostic radiologic studies, including radionuclide and computed tomography (CT) studies (*1–6*). Usually only a small portion of renal parenchyma may be included in radiation fields for skeletal metastases. While such changes may be asymptomatic, we believe that it is important for both diagnostic and therapeutic radiologists to be aware of potential renal injury and its appearance. With this awareness, the extent of renal inclusion in radiation ports can be minimized, and the appearance of any renal changes can be correctly diagnosed and not become mislabeled as renal or adrenal parenchymal metastatic disease.

Case 1

A 46-yr-old white female underwent a modified radical mastectomy for a stage T2 adenocarcinoma of the breast. Bone metastases were diagnosed on technetium-99m methylene diphosphonate ([^{99m}Tc]MDP) bone scan 2 yr later. At that time, no renal abnormalities were present on either bone scan or i.v. bolus contrast enhanced CT. Following one cycle of cytoxan, methotrexate, and 5-fluorouracil, 3,000 rad were administered over 10 days using anterior and posterior opposed fields, with a target depth of 10 cm. The radiation portals included the medial cortex of the upper poles of the kidneys bilaterally (Fig. 1). Subsequent chemo-hormonal therapy included tamoxifen, halotestin, and dibromodulcitol. The progression of postradiation renal uptake of [^{99m}Tc]MDP on follow-up bone scans, and changes in serum creatinine levels are summarized in Table 1. Onset of uptake occurred between 5–9 mo (Fig. 2A), peaked near 13 mo (Fig. 2B), and returned to baseline by 20 mo (Fig. 2C).

An unenhanced abdominal CT scan at 15 mo showed no evidence of renal or adrenal calcification. Following i.v. bolus contrast, decreased enhancement of the upper pole medial cortices was seen (Fig. 3). Transient elevation of serum creatinine from 0.9 to 1.3 mg/dl occurred at 9 mo. No significant changes in blood pressure were detected through the postradiation period. She ultimately died of intraabdominal metastases 4 yr after initial diagnosis.

Case 2

A 46-yr-old white female underwent a modified radical mastectomy for a stage T2 adenocarcinoma of the breast. Vertebral metastasis from T11 to L3 were diagnosed on [^{99m}Tc]MDP bone scan 2 yr later, for which she received 4,000 rad over 21 days, using anterior and posterior opposed fields and a target depth of 10.5 cm. The radiation portals included the medial portions of the upper pole renal cortices. Subsequent chemo-hormonal therapy included tamoxifen, halotestin, and dibromodulcitol. Table 1 summarizes the progression of postradiation renal uptake of bone agent and the changes in serum creatinine levels. Peak uptake occurred by 14 mo and returned to baseline by 27 mo. Transient creatinine elevation from 0.7 to 1.6 mg/dl occurred. Blood pressure was

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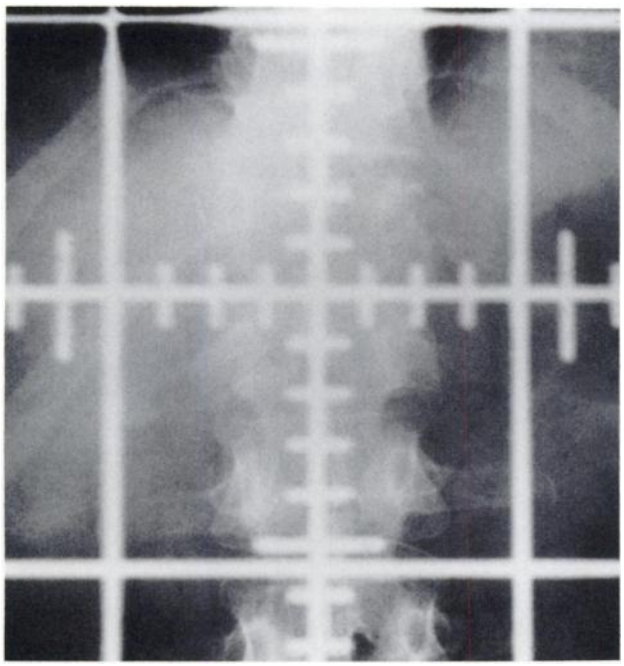

FIGURE 1
A 48-yr-old woman treated with radiation for breast carcinoma metastatic to the lumbar spine. Radiation simulation portals show inclusion of the medial upper renal cortex bilaterally.

essentially unchanged. She ultimately expired 6 yr after initial diagnosis.

DISCUSSION

The clinical, physiologic, and pathologic changes following radiation to the kidney have been extensively described. Luxton (*7*) found that following the administration of at least 2,300 rad, signs and symptoms of "acute" renal abnormalities often developed following a latent period of 6–12 mo. These changes included hypertension, albuminuria, urine casts, and elevation in serum BUN. Many patients continued to progress with continued hypertension and uremia. Of those patients who improved, recovery was seen to begin at ~6 mo after the onset of symptoms. Kunkler et al. (*8*) observed progressive renal failure from radiation doses greater than 2,300 rad delivered over 5 wk to the entire renal volume. If, however, at least one-third of the renal volume was excluded from the radiation field, the risk of renal failure could be minimized. Renal plasma flow has been found to progressively decrease by 36–87% following administration of 2,000 to 2,400 rad, whether or not clinical signs or symptoms are present (*9*). General decreases in tubular function and glomerular filtration rate are also seen (*9*).

TABLE 1
Progression of Postradiation Renal Uptake of Technetium-99m MDP and Serum Creatinine Level

Case 1			Case 2		
t*	Renal uptake	Cr†	t	Renal uptake	Cr
0	Normal	0.9	0	Normal	0.7
5	Normal	0.8	14	Maximal	1.2
9	Unilateral	1.3	16	Minimal	1.2
13	Bilateral	1.2	20	Minimal	1.2
20	Normal	1.1	25	(not imaged)	1.6
			27	Normal	1.4
			34	(not imaged)	1.1

* Time following radiation in months.
† Serum creatinine in mg/dl.

Pathologic changes are primarily that of progressive arteriolonephrosclerosis (*10*). By 6–12 mo following radiation, hyaline obliteration of capillary loops, and necrotic changes of arterioles and interlobular arteries may be seen (*10*), along with tubular atrophy, particularly of the proximal convoluted tubules (*11*).

Radiographically, decreased attenuation along the medial renal cortex may be seen on i.v. bolus enhanced CT scans 3 to 10 mo following 4,100–4,500 rad (*4*). Also, increased attenuation of the medial cortex may be seen on 2-hr delayed enhanced CT, 3 mo following 3,740 rad (*5*). Scintigraphic postradiation renal changes have also been described. Schulman et al. (*6*) noted decreased uptake of ^{203}Hg chlormerodrin 2 to 7 yr following radiation. Hypertensive changes were present in a case that demonstrated globally decreased uptake in both kidneys, whereas localized decreased uptake in another case was not associated with a change in blood pressure (*6*). Technetium-99m pyrophosphate renal uptake has been detected at 6–9 mo following 4,600 rad, and 19 mo following 6,000 rad (*2*). Several reported cases of abnormal [^{99m}Tc]MDP renal uptake have shown a 5–6-mo latency, maximal uptake at 6 mo, and resolution by 10–11 mo (*1,3*).

Our two cases are consistent with the general time course of radiation change regarding latency seen pathologically, and latency, peak, and resolution seen radiographically. Pathologically, vascular sclerosis, with tubular ischemic changes appear to be the primary mechanisms of injury. An ischemic kidney would be expected to show delayed enhancement and prolonged retention of i.v. radiographic contrast, and analogously, renal retention of bone radiopharmaceuticals would be increased 2 hr following injection (*2*). It is interesting that all reported cases with [^{99m}Tc]MDP appear to show resolution. Tubular cells possess regenerative capability (*12*), and resolution of ischemia, either by neovascularization or recanalization could permit tubular regeneration, and hence reversibility seen on bone scans. Thus reports of the appearances of radiation nephritis on CT and scintigraphic studies are consistent with an ischemic model (*1–6*).

It is also interesting that no hypertensive changes were identified among the reports of pyrophosphate or

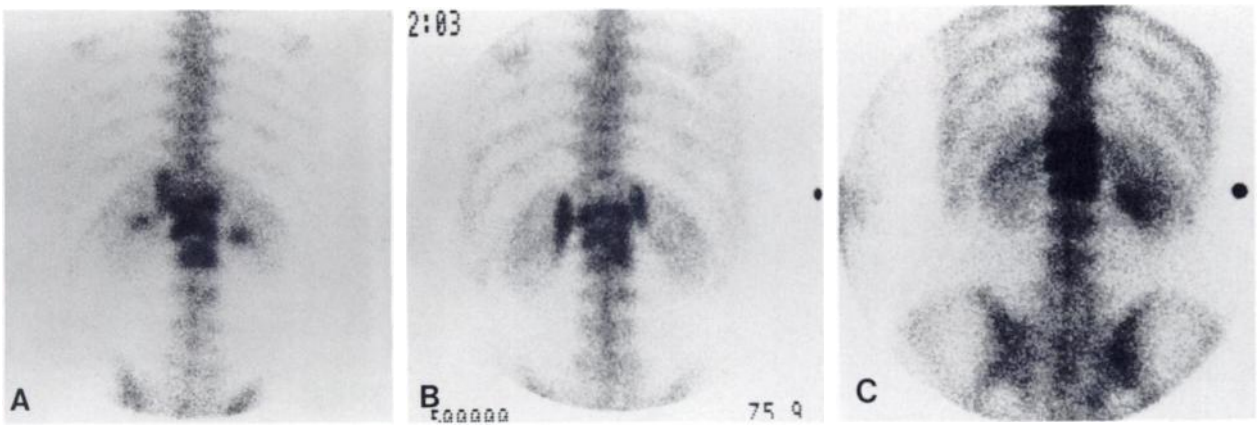

FIGURE 2
A 2-hr posterior image from a [^{99m}Tc]MDP bone scan. (Patients right to readers' left). A: 9 mo following radiation, the right kidney shows abnormal increased activity along the upper medial cortex. B: 13 mo after radiation, bilateral renal changes are evident, corresponding to the portions of the kidneys included in the radiation field. C: 20 mo following radiation, abnormal renal uptake is no longer seen.

diphosphonate bone scan agent uptake. Even with segmental renal cortical ischemia, hypertensive changes might be anticipated. Perhaps the volume of abnormal tissue or the extent of ischemia was insufficient to produce this change. While the nature of the mild elevations in serum creatinine in our patients is not certain, these changes are consistent with subclinical renal injury. Thus, while postradiation changes to the renal parenchyma may not be associated with clinical signs or symptoms, it is possible that repeated exposure or wider fields may have produced hypertensive and azotemic changes. This reemphasizes the necessity of limiting renal volume within radiation fields (*10*). Additionally, radiopotentiation by certain types of concurrent chemotherapy might also enhance the degree of renal injury.

The routine inclusion of transverse processes within radiation fields for palliative treatment of metastases to lower thoracic and upper lumbar vertebral bodies is commonly performed. The width of the treatment field in this region should be the minimum width that is clinically necessary so as to spare the medial renal parenchyma. This observation becomes more important as higher doses of radiation are employed.

Finally, the pattern of uptake seen in these cases could be confused with intrarenal or possible adrenal

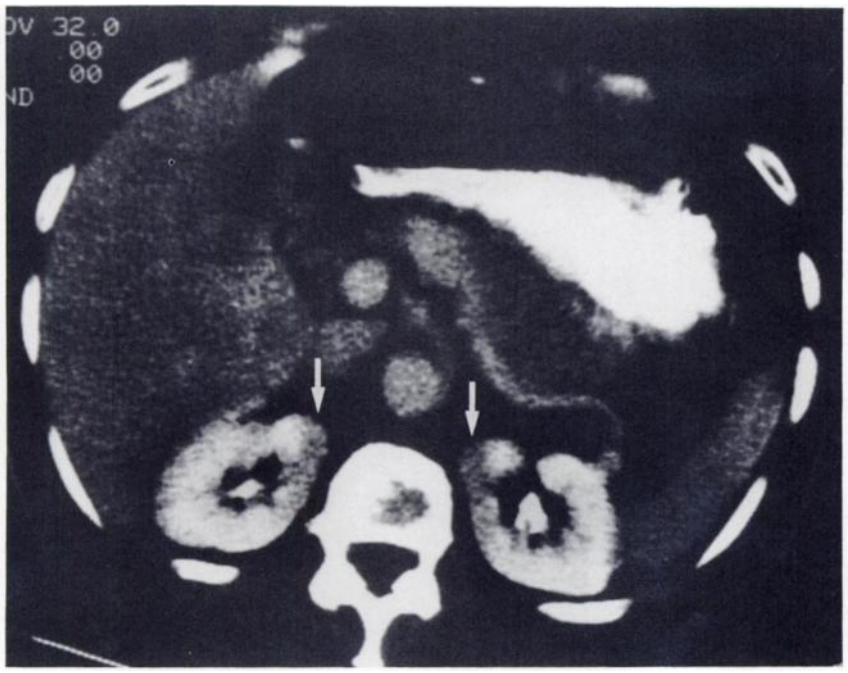

FIGURE 3
Intravenous bolus contrast enhanced CT at 15 mo following radiation shows decreased enhancement of the medial upper pole cortices (arrows).

metastatic disease (*1,3*). Awareness by radiologists of the possibility of renal inclusion within radiation portals will help prevent misdiagnosis.

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