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Incidental DTPA and DMSA uptake during renal scanning in unknown bone metastases

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We report a patient with DTPA and DMSA uptake on unsuspected bone metastases. He had severe pain due to grade 3 hydronephrosis of his left kidney. When Tc-99m DTPA and DMSA renal scanning were performed for preoperative evaluation, abnormal radiopharmaceutical uptake on the iliac area was noted. Pancreatic adenocarcinoma metastases to bone were subsequently defined. This patient is a very demonstrative case in respect of having all DTPA, DMSA and HDP uptakes in bone metastases. The type of the tumor has to be added to the list of extrarenal uptake of DTPA and DMSA as a rare cause.

Key words: DTPA, DMSA, extrarenal uptake, incidental visualization

INTRODUCTION

DYNAMIC AND STATIC RENAL SCANNING are the routine scintigraphic techniques for the preoperative, postoperative and follow-up evaluation of renal functions. In dynamic renal scintigraphy, Tc-99m diethylenetriamine pentaacetic acid (DTPA) and Tc-99m mercaptoacetylglicine (MAG3) are usually used and give information about the renal blood-flow and excretory function. Tc-99m dimercaptosuccinic acid (DMSA) is used for static renal imaging and demonstrates the renal cortical structure as well. In addition to defining aberrations of renal structure, a number of extrarenal abnormalities in the camera field of view may also be surreptitiously detected especially in DTPA studies.[1–13] However, except the pentavalent Tc-99m DMSA studies in which some of the epithelial tumors were visualized, to the best of our knowledge, there are only a few reports concerning extrarenal DMSA uptake.[14–16] Here, we aimed to present the radiopharmaceutical uptake in iliac region of a patient who underwent DTPA and DMSA scintigraphies for the preoperative evaluation of renal function and offered some considerations to the probable reasons for these accumulations with reference to the literature.

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CASE REPORT

Sixty three year-old patient with left flank pain was admitted for routine Tc-99m DTPA and Tc-99m DMSA renal scintigraphies for preoperative evaluation of a grade 3 hydronephrotic left kidney. Radionuclide accumulation on the left iliac area was visualized on both of the scintigraphies in addition to renal pathologies (Figs. 1 and 2). This finding prompted us to perform a pelvic tomography (CT) to show an ectopic kidney. It excluded ectopic kidney and demonstrated clearly the destruction of bony structure of the left and a lesser extent the right ilium suggesting bone metastases (Fig. 3). The patient was thus evaluated for tumoral process. Rectal examination and pelvic USG were normal. Most of the tumor markers were elevated including parathormone (CEA: 407 ng/m*l*, CA-125: 461 U/m*l*, CA-15.3: 526 U/m*l*, AP: 426 U/L, PTH: 196 pg/m*l*). Multiple bone metastases in the ribs, vertebrae, sternum and pelvic bones were determined by Tc-99m HDP whole-body bone scanning (Fig. 4). Tc-99m sestamibi parathyroid scanning excluded parathyroid pathology. When the results of the bone scanning were compared with the renal scanning, the existence of minimal

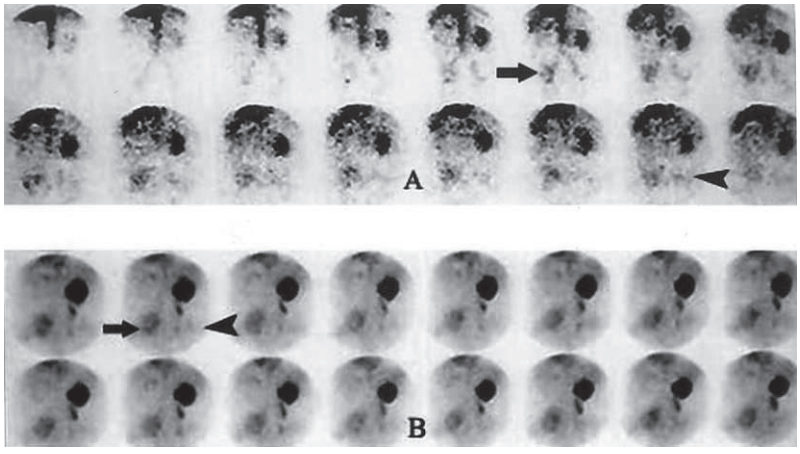

Fig. 1 Sequential DTPA renal images with every 1-second per image (A, First images of the flow phase) and 30 seconds per image (B, Last images of the study). Dynamic imaging lasting 40 minutes on posterior projection after the intravenous injection of 370 MBq (10 mCi) of Tc-99m DTPA demonstrates significant radiopharmaceutical uptake in the left iliac region (*arrow*) in addition to atrophy in the left and pelvicaliectasis in the right kidney. DTPA uptake in the left iliac region begins with the very early flow images and continues to the end of the study without diminishing. Additionally, uptake slightly exists in the right iliac area (*arrowhead*) and T12 vertebra.

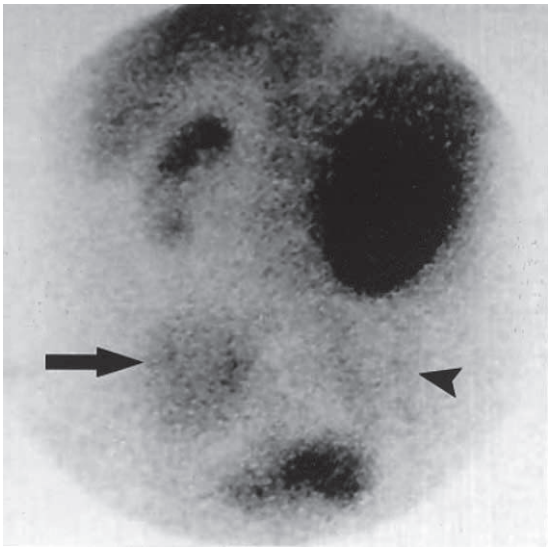

Fig. 2 Posterior image of DMSA study after 3 hours of the intravenous injection of 185 MBq (5 mCi) of Tc-99m DMSA. DMSA uptakes of the right and left kidneys were 20% and 1%, respectively. Significant uptake in the left (*arrow*) and slight uptake in the right (*arrowhead*) iliac region. (Image intensity was increased for better visualization of pathological uptake areas.)

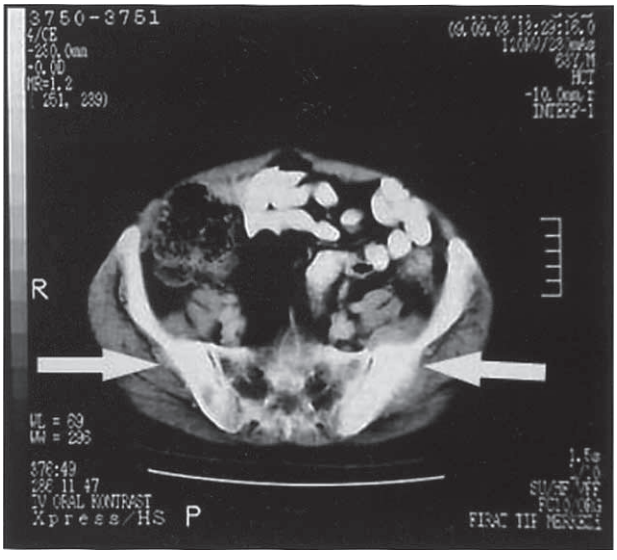

Fig. 3 Pelvic CT demonstrates metastatic involvement on the iliac bones (*arrows*), significantly on the left.

DTPA uptake in the T12 vertebra and right ilium and DMSA uptake in the right ilium were noticed as well. Together with the elevated tumor markers, the bony involvement was highly suggestive of tumor metastases. Findings of scintigraphic and pelvic CT studies were verified by concurrent biopsy of the iliac bone indicating adenocarcinoma metastases. A small tumor focus was defined on abdominal CT. This pancreatic tumor was so small and hidden that it had not been visualized previously in abdominal USG, and it was visualized with difficulty in CT. The patient did not respond to chemotherapy and died 3 mounts after the diagnosis. Pancreatic adenocarcinoma was revealed by the autopsy.

DISCUSSION

Renal scintigraphies are generally the most important imaging methods routinely used for the evaluation of

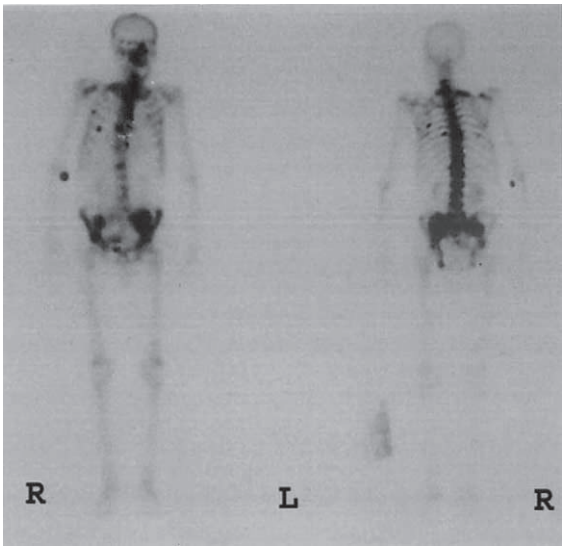

Fig. 4 Tc-99m HDP whole-body bone scanning. Disseminated metastatic bone involvement is visualized.

kidney function. Additionally, the diagnostic information about extrarenal pathology can be obtained simultaneously with renal scintigraphy and this information has a potential benefit for patient management. Especially blood flow phase of the Tc-99m DTPA renal studies has been proved remarkably useful in detecting some extrarenal abnormalities such as splenic, aortic and hepatic pathology.[1]

Tc-99m DTPA is widely used for kidney imaging, and its clearance correlates well with the glomerular filtration rate. Because of its intravascular nature, it is used to demonstrate the perfusion of the kidneys. It is additionally used for the evaluation of peripheral vascular disease, gastrointestinal bleeding and blood-brain barrier integrity. Normally, there is no significant uptake or retention of Tc-99m DTPA in any other organ besides the urinary tract. However, a few anecdotal pathologies in which DTPA accumulated have been reported: cancer metastases,[2,3] plasmacytoma,[2,4] neurofibroma,[17,18] pheochromocytoma,[5,19] angiomyolipoma,[2] soft tissue sarcoma,[20] breast carcinoma,[21] pleural effusion,[6] hepatic hemangioma,[7] Paget's disease,[8] uterine myoma,[9] spleen inflammation,[10] gynecomastia,[22] inflammatory bowel disease,[23,24] bone marrow uptake,[11–13] Grave's ophthalmopathy and pretibial myxoedema.[25] Additionally, Goshen et al. described extrarenal DTPA uptake in some soft tissue pathologies.[26]

Roman et al. evaluated the visualization of left iliac fossa uptake during DTPA renal scanning.[27] They found one malignant reason for the increased uptake in only one of their 41 patients and no pathological increased uptake in the right iliac region. Thus they reported that increased DTPA uptake in the left iliac fossa is a common finding and represents physiological activity or benign conditions in those areas especially concerning descending colon pathologies. However, including in our case, almost all of the reports related to pathological DTPA accumulation in iliac region indicate malignant pathologies, especially when the uptake is in a bony structure.[2–4] The reasons for DTPA accumulation outside the iliac region are generally benign, except for neurofibroma and chondrosarcoma as reported by some authors.[17,18,26]

Skeletal visualization during dynamic renal imaging is a nadir finding and usually corresponds to neoplastic disease. Larcos et al. visualized transient DTPA accumulation on the left iliac region in the flow and immediate blood pool images of a patient with Paget's disease on his ilium and this accumulation diminished with time in the very early phases.[8] They thus suggested that increased arterial vascularity, rather than the underlying disease process, is the major cause of transient DTPA uptake in bone and may be seen in any bone disorder associated with significant skeletal hyperemia. But the DTPA accumulation of our patient was not so transient and DMSA uptake on the lesion was visualized even at the third hour. So the reason for this uptake should not be the hyperemia alone.

Two years after Larcos's report, Goshen et al. did not indicate any correlation between the DTPA uptake and blood flow of some soft tissue pathologies, except lipomas.[26] While lipomas had no DTPA and labeled red blood cell (RBC) accumulation, some of the soft tissue tumors showed DTPA uptake but no RBC accumulation. As expected, both DTPA and RBC accumulation were seen in angioleiomyoma and A-V malformation as well. While we compared the reports of Larcos and Goshen, what we can say is the probability of the existence of some different mechanisms for DTPA uptake between the soft tissue and bone.

Tc-99m DMSA static renal scintigraphy is a well-accepted imaging technique for the evaluation of the renal cortical pathologies in several renal diseases. The handling of the Tc-99m DMSA needs some attention. Four different complexes of Tc-99m DMSA in which the valency of Tc is varied, can be obtained according to the concentration of stannous tin and acidity of the solution. The Tc-99m DMSA complex prepared in acidic solution with a high concentration of stannous tin has +3 Tc valency and is the most proper for the renal imaging. But, if the DMSA is labeled at an alkaline pH and a low concentration of stannous tin, the radiopharmaceutical obtained has a +5 valency. This pentavalent Tc-99m DMSA (DMSA-V) has a different biodistribution and it is used for the tumor imaging. Additionally, Tc-99m DMSA has to be used in a very short time after preparation (usually within 30 minutes) without air exposure. Its structure and also biodistribution alter with time and air contact. Normally, there is only minimal extrarenal excretion of the Tc-99m DMSA and its extrarenal uptake usually originates from kidney rather than preparation problems.

What was the reason for the DMSA uptake in the lesion? First, we want to indicate what reasons are not possible. We are sure that we did not inject DMSA-V to the patient. The preparation of it needs an extremely different procedure and additionally, there was no other patient who showed the scintigraphic findings of DMSA-V either. Free pertechnetate may be another reason but DMSA uptake function of the kidneys was as expected and neither the thyroid gland nor the stomach was visualized at all. Because his blood serum values did not indicate renal insufficiency, we did not suggest the renal insufficiency as a reason either.[15]

Recently, Rondogianni et al. reported multiple areas of DMSA uptake on skeleton in a patient with colorectal carcinoma metastases.[16] They suggested that Tc-99m DMSA could be taken into the cells through the damaged cell membrane, and bind to cytoplasmic proteins and mitochondria, as also showed by Vanlic-Razumenic et al. in 1982, and elevated osteoblastic activity may enhance the accumulation as well.[28]

When we evaluated the DTPA scintigraphy of our patient again with the findings of bone scanning, it was visualized that there was minimal accumulation on the right iliac region and T12 vertebra in addition to the left iliac uptake. But these accumulations were very minor as compared to the left iliac one. Right iliac uptake minimally existed in the DMSA study as well. Mandell et al. performed SPECT study with Tc-99m DTPA to visualize neurofibromas.[29] They could even define some lesions not visualized on planar imaging. If we had a chance to perform SPECT in our patient, we would probably have imaged other metastatic sites and possibly the tumor tissue itself.

In our patient, the early appearance of the radioactivity in the lesions should be because of the increased blood flow as well. In contrast to the report of Prakash et al., DTPA uptake in the lesion did not fade with time.[3] The prolonged retention of DTPA may have resulted from extravasation of the radioactivity within the lesion secondary to altered capillary permeability or slow pooling of the blood.[26] The reason for the persistence of DMSA in the lesion may be the same or different mechanisms could be responsible for this uptake, such as active transport of it through the tumor cells as considered for the uptake by neurofibroma.[26] Taking account of the characteristics of the Tc-99m DMSA, we could hypothesize that chelating of the tracer with a molecule within the abnormal cell membrane or cellular compartment of tumor cell may be another reason for the DMSA uptake. It can be related to increased osteoblastic activity, and the variation of the degree of the uptake in the lesions can be associated to the difference in activity of the cells.

We have to indicate that the uptake in the left iliac region was so significant and similar in shape to a kidney that we oriented for an ectopic kidney. Pelvic CT, recommended after the renal scintigraphies, had a very complementary role in excluding the ectopic tissue and revealing the bone metastases.

The exact mechanism of uptake of DTPA and DMSA is not clear in this pathology. Uptake mechanisms of these radiopharmaceuticals, especially DMSA, warrant further investigation, maybe with animal studies.

In conclusion, considering the literature and our observation, we can say that abnormally increased skeletal activity on DTPA and DMSA scintigraphies are highly suggestive of tumoral pathology. Consulting the additional imaging and laboratory techniques in such situations as soon as possible might provide surprising information and offer an extremely valuable opportunity for the proper management of the patient.

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