

Skeletal Nonvisualization in a Bone Scan Secondary to Intravenous Etidronate Therapy

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Etidronate disodium (EHDP) therapy is often instituted emergently for treatment of hypercalcemia associated with malignancy, and a staging bone scan is part of the evaluation of the patient with extensive metastatic disease. In these patients in whom high dose EHDP therapy has been instituted, uptake of the bone scan agent is markedly diminished. The case presented illustrates this finding: a breast cancer patient who had received two 500-mg intravenous doses of EHDP prior to bone scan staging. No skeletal visualization was present at 3 hr after ^{99m}Tc -MDP injection. Blood-pool activity and uptake in large metastatic sites were observed.

J Nucl Med 1992; 33:748-750

Interfering medications are not usually a major concern in skeletal scintigraphy. We describe the bone scan findings in a 65-yr-old female who was studied shortly after the initiation of intravenous etidronate disodium (EHDP) therapy for hypercalcemia associated with malignancy. Her scan demonstrated essentially no skeletal uptake. Etidronate is a phosphonate used in treatment of Paget's disease, heterotopic ossification, hypercalcemia associated with malignancy and osteoporosis. Principle pharmacologic action is reduction of bone reabsorption and overall decrease in bone turnover. Etidronate competes with ^{99m}Tc -methylene diphosphonate (MDP), a standard bone scanning agent at the skeletal binding site. While false-negative bone scan imaging results after long-term therapy for Paget's disease have been reported, we present scintigraphic abnormalities following acute etidronate administration. Nuclear medicine physicians should be aware of the action of EHDP on the skeleton in order to interpret the bone scan findings in these patients.

CASE REPORT

A 65-yr-old female who was status-post a left radical neck dissection and local radiation therapy for squamous-cell carci-

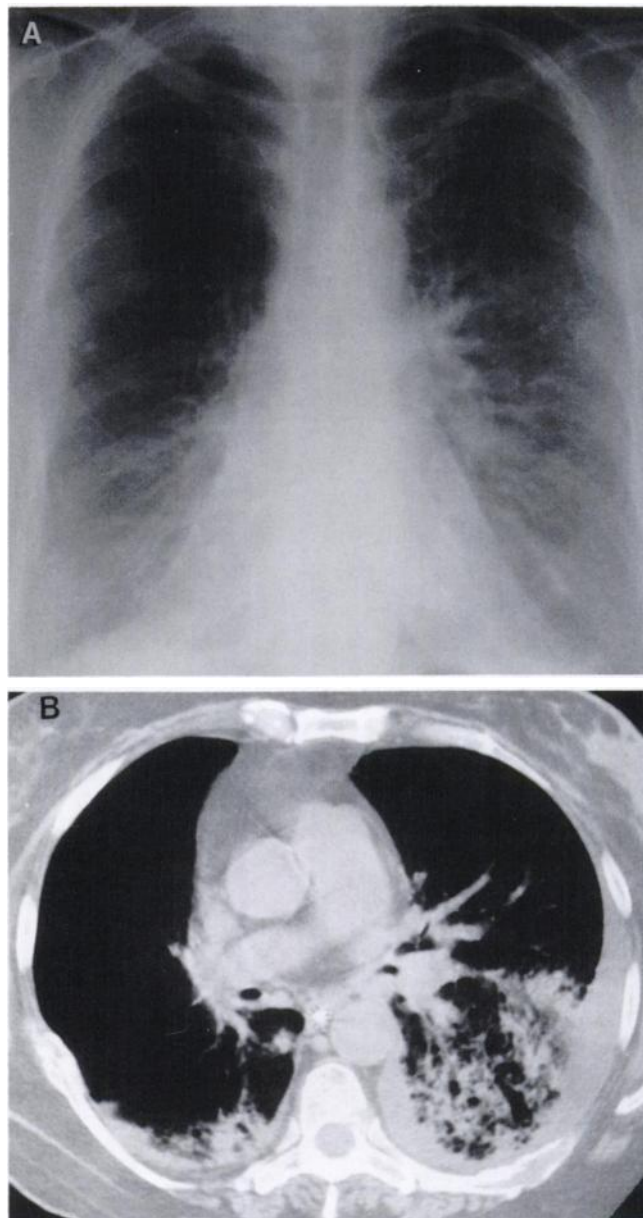


FIGURE 1. (A) Chest x-ray; lytic lesion involving posterior left 7th rib and soft-tissue mass associated with lateral right 6th and 7th rib lesions. (B) Chest CT through the level of the 7th rib; bilateral lytic lesions.

Received Sept. 24, 1991; revision accepted Dec. 4, 1991.

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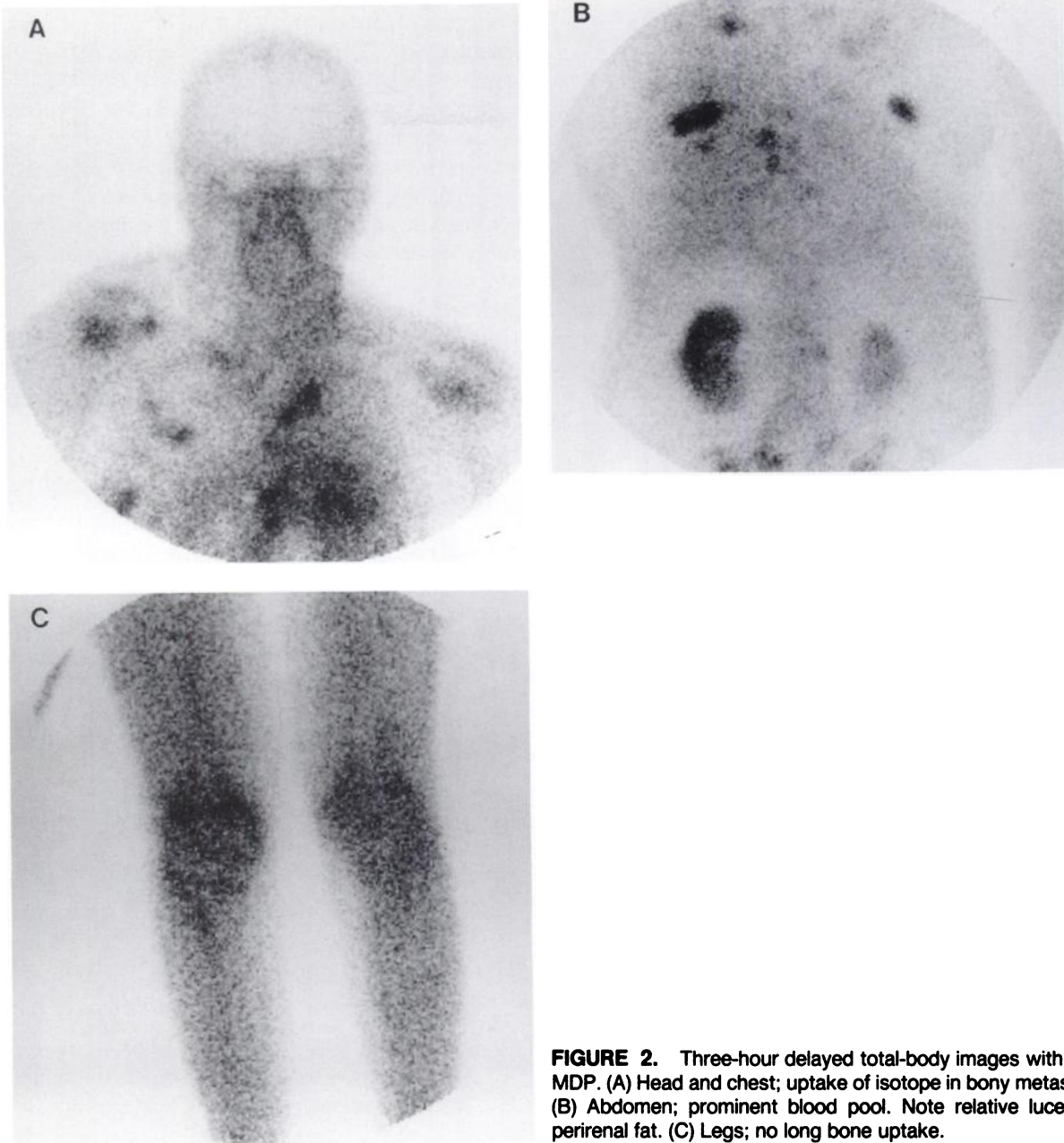


FIGURE 2. Three-hour delayed total-body images with ^{99m}Tc -MDP. (A) Head and chest; uptake of isotope in bony metastases. (B) Abdomen; prominent blood pool. Note relative lucency of perirenal fat. (C) Legs; no long bone uptake.

noma was admitted with general musculoskeletal pain and weakness, increasing fatigue, shortness of breath, episodes of delirium and a serum calcium elevated to 14 mg/dl (normal 8.9–10.2 mg/dl). Several other admission laboratory values were mildly abnormal including a serum creatinine of 1.4 mg/dl and BUN of 24 mg/dl (normal 0.3–1.2 mg/dl and 8–21 mg/dl, respectively). The admission chest film and a follow-up thoracic CT demonstrated a lytic lesion within the posterior left 7th rib and posterolateral pathologic fractures of the right 6th and 7th ribs (Fig. 1), consistent with metastatic disease. Aggressive intravenous hydration and diuretic therapy was begun upon admission to the hospital and EHDP was initiated on hospital Day 2 to lower serum calcium. Two doses of 500 mg EHDP were administered intravenously approximately 12 and 36 hr before the patient arrived at the nuclear medicine department for a total-body bone scan. Other medications included furosemide, amitriptyline, metoprolol, en-

alapril, methylprednisolone, erythromycin, cephtriaxone and nebulized albuterol with atropine.

Skeletal scintigraphy was requested for localization of metastases for possible further radiation therapy. Total-body images acquired 3 hr after injection of 25 mCi ^{99m}Tc -MDP demonstrated extensive soft-tissue, renal and bladder activity (Fig. 2). Sites of uptake were present within metastatic sites in the chest (most intense in the 7th ribs, bilaterally) and right shoulder, however, there was essentially no visualization of the normal skeleton (Fig. 1). Because of this unusual finding, radiopharmacy quality control results of the ^{99m}Tc -MDP scan were reviewed and found to be normal. In addition, no abnormal uptake was demonstrated within the thyroid gland or stomach of this patient as would be expected if the ^{99m}Tc -MDP kit labeling was poor. All other bone scans performed that day using ^{99m}Tc -MDP from the same radiopharmacy were unremarkable.

DISCUSSION

EHDP is a diphosphonate compound with a chemical structure similar to MDP. The central feature of diphosphonates is a phosphorous-carbon-phosphorous (P-C-P) bond which renders the compounds enzymatically stable, such as pyrophosphates (P-O-P), while allowing bone-seeking activity. Interaction of both EHDP and MDP in the skeleton is at the hydroxy apatite crystal surface (1). In fact, EHDP labeled with ^{99m}Tc has been used as a bone imaging agent in the past (2). Current uses for EHDP are therapeutic and limited to symptomatic Paget's disease of bone, heterotopic ossification, hypercalcemia associated with malignancy and experimental protocols for treatment of osteoporosis. EHDP therapy results in slowing of overall bone turnover by reduction of both normal and abnormal bone reabsorption. The mechanism of action is not clear, but appears to be related both to a reduction in number of osteoclasts (3), as well as inhibition of mature osteoclasts that excavate reabsorption pits (4).

Previous reports have demonstrated false-negative bone scan results (6) and decrease in overall activity (5) in patients on relatively long-term (months), low dose (5 mg/kg/day), oral EHDP. Also, acute intravenous administration of EHDP prior to ^{99m}Tc -MDP scanning is known to cause profound changes in skeletal scintigraphy results in experimental animals (7). The overall effect, as demonstrated in rats by Watt et al., is a significant decrease in bone: blood-pool ratio, leading to virtual nonvisualization of the skeleton on the bone scan. The explanation of the unusual images presented here may relate to both the dramatic decrease in overall bone metabolism, as well as

a direct competition for the MDP binding sites already saturated with EHDP with uptake in the more active metastatic deposits being affected less severely than normal bone. As etidronate therapy continues, the uptake in metastases should also decrease. No follow-up scans were obtained on this patient.

For patients receiving long-term etidronate therapy, this information will be documented in the patient chart. The correct explanation of an unusual bone scan in this situation would be less problematic. However, in the patient admitted for hypercalcemia associated with malignancy, both EHDP therapy and ^{99m}Tc bone scanning may be initiated on an emergent basis. Since the structure and action of both the therapeutic and imaging agent are similar, nuclear medicine physicians should be aware of this potential diagnostic pitfall.

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