Cause and Significance of Cold Bone Defects on Indium-111-Labeled Leukocyte Imaging

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Although photon deficient defects on bone scan have received a great deal of interest, such defects in bones on Indium-111 (^{111}In) leukocyte imaging have not been as well recognized. We therefore undertook a retrospective review to determine the frequency and significance of such "cold" defects on ^{111}In-labeled leukocyte imaging. Three hundred thirty-two scans on 290 patients were reviewed and 40 cases of decreased activity involving bone were found, for an incidence of 12%. The causes of the defects were: fracture (eight), nontraumatic avascular necrosis (eight), solid tumor (six), prostheses and other orthopedic hardware (four), advanced age (four), radiation (three), leukemia (two), osteomyelitis (two), myelofibrosis (one), postlaminectomy (one), and idiopathic (one). To determine the frequency of cold defects in osteomyelitis, all 15 cases of osteomyelitis in this series were reviewed and 12 showed increased activity, two were cold, and one was normoactive. Thus, 14% of cases of osteomyelitis presented as cold defects. We conclude that cold bone defects do occur on ^{111}In-labeled leukocyte scans and that the causes of such defects are similar to those reported for bone and bone marrow scanning.

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Indium-111- (^{111}In) labeled leukocytes have been shown to be a sensitive and specific technique for detecting intraabdominal abscesses (*1–4*). Occasionally we have noted areas of decreased bone activity on leukocyte scan. Photon deficient areas on bone scan have been recognized for some time (*6–13*), and are due to a variety of diseases, including osteomyelitis. Osteomyelitis presenting as a "cold" defect is especially worrisome in evaluating patients with suspected occult infection because such defects could be easily overlooked. We undertook a retrospective study to determine the frequency and significance of cold bone defects on ^{111}In-labeled leukocyte imaging, and to determine how frequently osteomyelitis appears as a cold lesion on leukocyte scans.

MATERIALS AND METHODS

Patients

Three hundred thirty-two ^{111}In-labeled leukocyte scans on 290 patients were retrospectively reviewed for photon deficient defects. The charts of the patients whose scans showed cold bone defects, and all patients with osteomyelitis, were then reviewed. The cause of the cold defects was confirmed by history, plain films, computed tomography, bone scan, bone marrow scan, bone and bone marrow biopsy, surgical findings, and culture results.

Leukocyte Labeling

The leukocyte scans were performed using a modification of the method first described by Thakur et al. (*14,15*). Forty-milliliters of blood was collected in a syringe containing 5 ml of acid-citrate-dextrose (ACD) solution. The cells were gravity sedimented for 60 min. The leukocyte-rich supernatant was removed and centrifuged at 350 *g* for 5 min. The white cell button was resuspended in 5 ml of sterile saline to which 1 mCi of ^{111}In oxine was added, and incubated for 30–40 min. Five to 8 ml of leukocyte-poor plasma were added to the suspension of leukocytes, and the mixture centrifuged for 5 min at 450 *g*. Five to 8 ml of the leukocyte-poor plasma were gently added to the labeled white cell button; this was agitated to resuspend the labeled cells. The ^{111}In-labeled leukocytes were then reinjected into the patient.

Imaging Procedure

Patients received ~500 μCi of labeled cells. Imaging was done at 24 hr postinjection using a large field-of-view gamma camera equipped with a medium-energy parallel hole collimator using 20% windows set on the 173- and 247-KeV photopeaks of ^{111}In.

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RESULTS

Overall Incidence

Of 332 scans, 40 cases of decreased activity were found, an incidence of 12%. The causes of cold defects were: fracture (eight) (Fig. 1), nontraumatic avascular necrosis (eight) (Fig. 2), solid tumor (six) (Fig. 3), prostheses and other orthopedic hardware (four), advanced age (four), radiation (three), osteomyelitis (two) (Fig. 4), leukemia (two), myelofibrosis (one), postlaminectomy (one), and idiopathic (one). Thirty of the 40 cases involved significant pathology, representing 75% of cases.

Osteomyelitis Incidence

Fifteen cases of osteomyelitis were found. Twelve cases showed increased uptake on leukocyte scan. Both cases showing decreased uptake were cases of acute osteomyelitis. One case was normal (a false negative); thus, 14% of cases of osteomyelitis presented as cold defects.

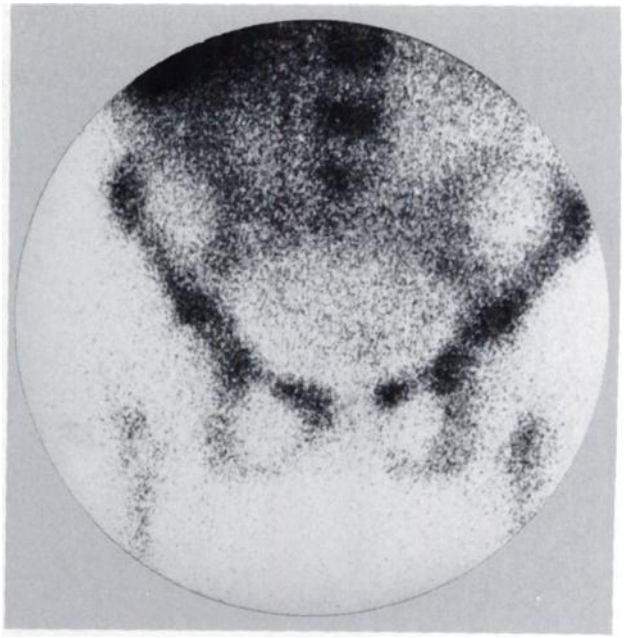

FIGURE 2
A 35-yr-old renal transplant patient who had been on long-term steroid therapy. Decreased activity is present in both femoral heads, most prominent on the right. Plain films showed avascular necrosis.

DISCUSSION

Photon deficient defects on bone scan have received a great deal of interest since their description by Goergen et al. in 1974 (*6–13*). Goergen's cases were due to metastatic tumor and bone infarction secondary to sickle-C disease and subcapital femoral fracture. Other causes have been described, including radiation (*12,13*), osteomyelitis (*9,10*), metallic artifacts, and other rare causes (*11*). In general, the mechanism producing cold defects on bone scan has been interruption of vascular flow (aseptic necrosis, radiation, some tumors) or almost complete replacement of bone (tumor) (*16*).

The normal distribution of labeled leukocytes de-

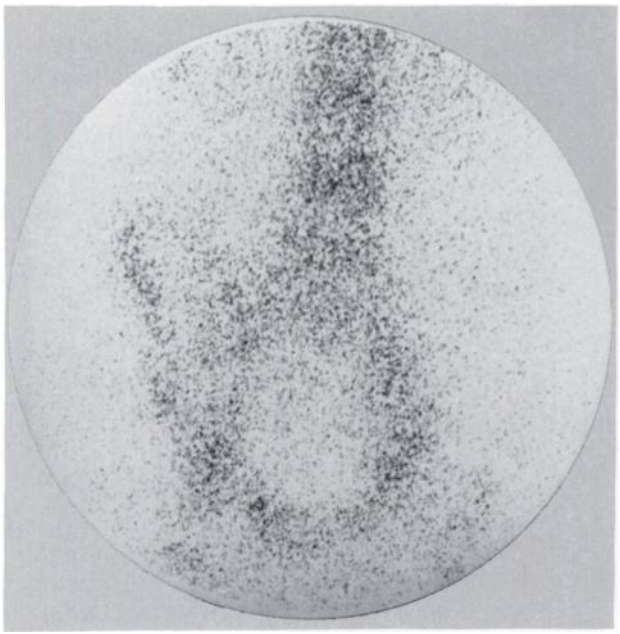

FIGURE 1
A 23-yr-old male who suffered multiple fractures in an automobile accident, including comminuted fracture of the left ileum. View over the anterior pelvis. The right ileum is well visualized. No activity is present in the left ileum.

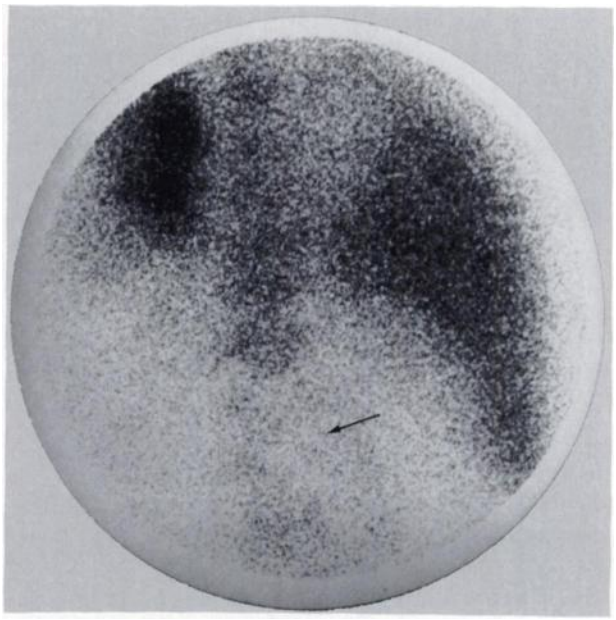

FIGURE 3
A 63-yr-old male with metastatic lung carcinoma. Posterior views over the lower thoracic and lumbar spine. Note decreased uptake in the lumbar spine (arrow). Biopsy revealed tumor involvement.

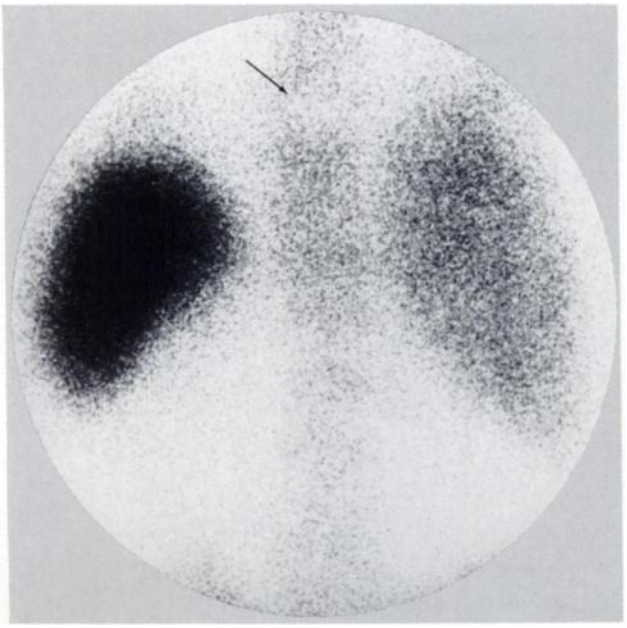

FIGURE 4
A 78-yr-old female with fever and back pain. Posterior view of ^{111}In-labeled leukocyte scan over the lower back shows decreased activity in T9 vertebra (arrow). A bone biopsy was eventually performed, confirming osteomyelitis.

pends on the timing postinjection. Significant lung uptake occurs immediately following injection. By 24 hr, the leukocytes are primarily distributed in the spleen, liver, bone, and bone marrow (*17*).

Cold bone defects on ^{111}In-labeled leukocyte scan have not been well recognized. Coleman describes a case of decreased bone activity of the pelvis on ^{111}In leukocyte scan due to radiation therapy for lymphoma (*5*). In their article, the authors mention that they have also seen diminished uptake of ^{111}In-labeled leukocytes due to large tumor, in treated osteomyelitis, and in disc-space infection following surgery. No discussion of the frequency of cold defects or other details are given. Pu Mok et al. describe four cases of cold defects on ^{111}In leukocyte scan due to similar causes named above (*18*).

We found cold bone defects on ^{111}In-labeled leukocyte scans in 12% of cases. Many of the causes of cold bone defects on ^{111}In-labeled leukocyte scanning are similar to the causes of cold defects described for bone scanning. Advanced age is an exception. Decreased activity in the femoral heads has been described on technetium-99m (^{99m}Tc) sulfur colloid scans in elderly patients (*19–21*). Spencer observed 106 patients undergoing ^{99m}Tc sulfur colloid liver–spleen scans and found that only 37% of individuals 70–79 yr of age had activity in the femoral heads (*20*). Our cases of bilateral and symmetrical femoral decrease of ^{111}In leukocyte uptake were all in patients 70 yr of age or older. ^{111}In-labeled leukocyte activity is associated with both bone and bone marrow (*17,22*), and it is likely that the mechanism for the decreased uptake seen in our elderly patients is similar to that for sulfur colloid. The decreased uptake seen in leukemia and myelofibrosis also is likely to be related to decreased activity in the bone marrow component of the ^{111}In (*23*).

Osteomyelitis is an unusual cause of cold defects on leukocyte scan, accounting for only two of our 40 cases (5%). One case was an osteomyelitis of the thoracic spine; the other involved the ileum. Both were cases of acute osteomyelitis. Of the 15 cases of osteomyelitis we imaged, 14% were cold.

In conclusion, cold bone defects occur on ^{111}In-labeled leukocyte scans more frequently than has been previously appreciated, and indicate significant pathology in 75% of cases. The causes of cold defects on ^{111}In-labeled leukocyte scans are similar to those reported for bone and bone marrow scanning. Osteomyelitis can present as a cold defect on ^{111}In-labeled leukocyte scans.

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