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Skeletal Photopenic Lesions in In-111 WBC Imaging

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Four cases of skeletal photon-deficient areas in In-111 white blood cell (In-111 WBC) images are reported. These were found in patients with lymphoma, vertebral osteomyelitis, and following radiotherapy and extensive surgical procedures. We emphasize that these photopenic lesions, although uncommon, may represent tumor involvement or benign processes, including osteomyelitis. Possible mechanisms to explain this phenomenon are discussed.

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Indium-111 leukocyte scintigraphy is currently used to diagnose or exclude abscesses and to locate sites of focal infection (*1,2*) in patients with a suspected abscess and without localizing signs. Normally the skeleton is well outlined and visualized in an In-111 WBC scintigram. We have encountered four instances of photopenic skeletal lesions. We present our experience and discuss possible mechanisms for these phenomena.

METHODS

Four cases were selected from a group of over 300 In-111 WBC studies obtained for detection of infection. Images are obtained approximately 24 hr after the administration of 500 μCi of In-111-labeled WBCs using a modification of a previously described method (*3*). Gamma camera images are obtained for 200,000 counts or 10 min, whichever comes first, with a medium-energy collimator and 20% windows covering the 173- and 247-keV energy peaks. Bone scintigrams for 500,000 counts were obtained 3 hr after the administration of 20 to 25 mCi of Tc-99m MDP using a gamma camera fitted with an all-purpose straight bore collimator and a 20% window around the 140 keV peak.

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CASE REPORTS

Case 1. A 56-yr-old female was diagnosed as having carcinoma of the cervix, Stage III B, in April, 1981. She received 5000 rad of external radiation to the whole pelvis in May 1981, followed by intracavitary radium therapy in June, 1981. In April, 1983, she presented with numbness and weakness in the left leg. A trans-

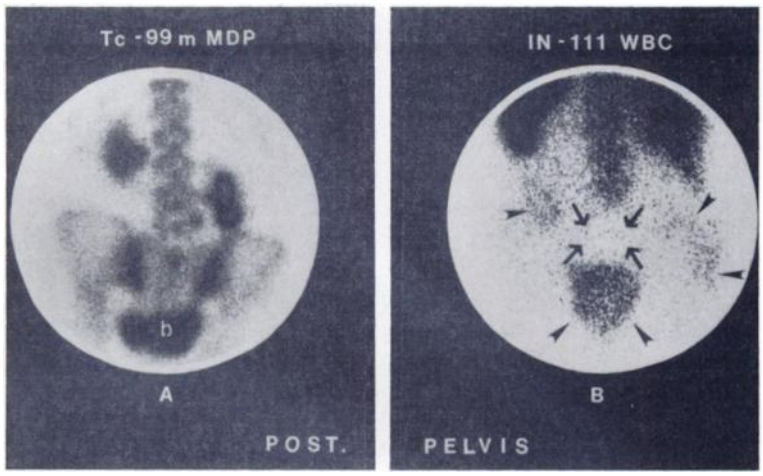

FIG. 1. (Case 1). (A) Bone image showing increased uptake in L5. Mild radionuclide uptake is seen in upper sacrum and sacroiliac joints. Bilateral hydronephrosis and bladder (b) are present. (B) Photopenic area is seen in lower lumbar spine and sacrum on In-111 WBC image (arrows). Note areas of increased uptake in abdomen and lower pelvis (arrowheads) caused by pseudomembranous colitis and pooling of exudated In-111 WBCs in rectum.

mission computerized tomogram showed an erosive lesion of the L4 vertebral body, which was thought to be due to local tumor invasion. A radiograph of the lumbosacral spine showed demineralization of the bony structures but was otherwise unremarkable. White blood cell count and bone profile were normal. A Tc-99m bone image showed areas of increased radionuclide uptake in the sacroiliac joints, at the level of L5 and sacrum attributed to degenerative bone disease (Fig. 1A). Since an abscess of the L4 vertebral body was clinically suspected, an In-111-WBC image was obtained (Fig. 1B), which showed decreased uptake in L5 and the region of the sacrum. There was also tracer uptake in the descending colon, sigmoid, and rectum. The patient subsequently expelled fragments of colonic mucosae, and colonic and rectal uptake was thought to be due to pseudomembraneous colitis. No osteomyelitis was ever demonstrated.

Case 2. A 38-yr-old male previously healthy, was admitted because of rash, adenopathy, and hepatosplenomegaly. Biopsy of a lymph node showed diffuse histiocytic lymphoma. A Tc-99m sulfur colloid liver image and a Tc-99m MDP image (Fig. 2A), ordered for staging purposes, were normal. A Ga-67 study (Fig. 2B) showed abnormally increased uptake in the spine and pelvis and uptake in the lymph nodes of the neck. Fever developed during his

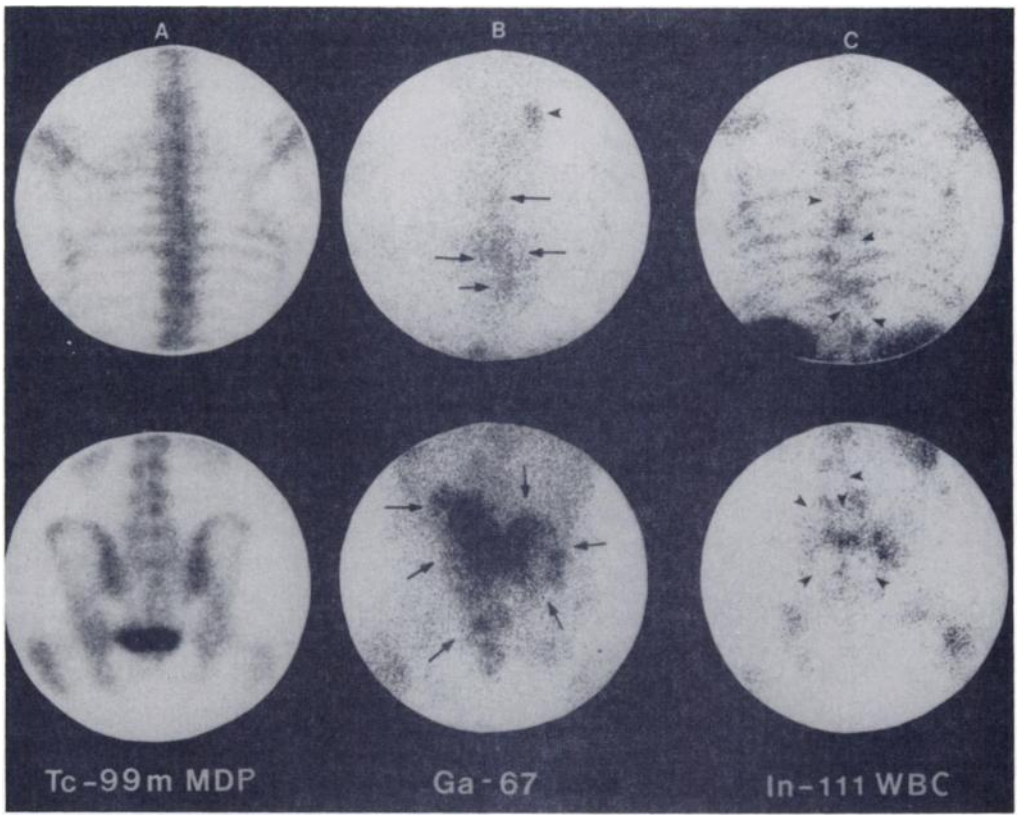

FIG. 2. (Case 2). (A) Bone image is unremarkable. (B) Selected posterior Ga-67 images of chest (upper) and pelvis (lower) show areas of increased uptake in spine and pelvis caused by lymphomatous involvement (arrows). Note involvement of cervical lymph node (arrowhead). (C) Corresponding posterior In-111 WBC images of chest (upper) and pelvis (lower) show irregular radionuclide uptake with multiple photon-deficient areas in spine, ribs and pelvis (arrows).

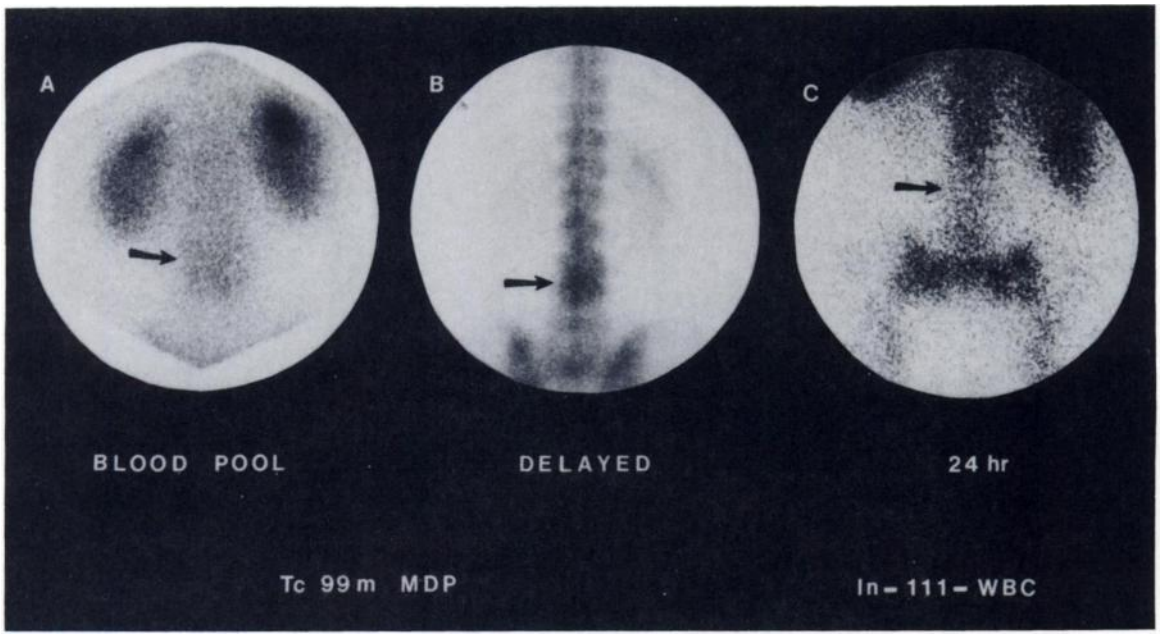

FIG. 3. (Case 3). Increased Tc-99m MDP uptake is seen at L4 in both blood-pool (A) and delayed (B) images (arrows). Corresponding area of decreased tracer uptake is seen in In-111 WBC image (C, arrow).

hospitalization, so an In-111 WBC study was obtained; it showed multiple skeletal photon-deficient areas (Fig. 2C) corresponding to the areas of increased uptake seen in the Ga-67 image. There was no evidence suggesting infection. The patient was treated with chemotherapy, with remission of symptoms.

Case 3. A 46-yr-old female with a past history of i.v. drug abuse had complaints of progressive low back pain and a low-grade fever for 6–8 wk. She was initially seen several times in the emergency room and subsequently admitted for evaluation on August 11, 1982. Physical examination revealed scars from past i.v. drug abuse and diffuse tenderness in the back. Radiographs of the lumbosacral spine, taken on August 26, 1982, during one of the emergency-room visits, were normal. A bone scintigram on that date showed an abnormality at the L4 level (Fig. 3A, B). Repeat radiographs 4 days later disclosed a narrowing of the L3 and L4 space associated with irregularity and destruction of the anteroinferior end plate of L3 and superior end plate of L4 vertebral body. These findings were consistent with disk-space infection and osteomyelitis of L3 and L4. An In-111 WBC study was obtained on September 1, 1982 (Fig. 3C). A Craig-needle aspiration biopsy of L3 and L4 interspace was performed the next day. Culture of the aspirate grew *Pseudomonas aeruginosa*. Biopsy showed acute inflammation and necrosis in fragments of degenerated cartilage in chronic osteomyelitis. The patient was treated with antibiotics.

Case 4. A 43-yr-old male was referred to the nuclear medicine department for Tc-99m bone and In-111 WBC imaging to exclude infection before hip surgery. At age 13, within 3 mo the patient had both a slipped left femoral head and a fracture of the left proximal femur, which required pinning. One year later, pins were removed and a hip prosthesis was placed. In 1969, repositioning of the left hip prosthesis was then removed, resulting in pseudoarthrosis, which was followed by surgical fusion in 1976. After this last operation, chronic *Staphylococcus aureus* infection developed, which required prolonged antibiotic therapy. Residual intermittent pain in the left hip and limitation of function prompted the orthopedist to reevaluate the problem for possible placement of a second prosthesis. Left hip radiographs revealed sclerosis of the acetabulum and left proximal femur. The patient had a Tc-99m bone image (Fig. 4A, B) and an In-111 WBC study (Fig. 4C, D) to search for possible residual infection.

DISCUSSION

Detection of pathological processes in In-111-WBC scintigrams is based upon the demonstration of increased radioactivity in diseased areas through the natural movement of white cells. Normally, 24 hr In-111 WBC images display tracer uptake in the liver, spleen, and skeleton. Hepatic and splenic uptake probably represents removal of damaged cells or cell fragments by the reticuloendothelial system (RES) as well as normal margination and migration of viable labeled cells into these areas (*4*). Outline of the skeleton may represent bone marrow activity that results from deposition of circulating In-111-labeled transferrin (*5*) and also probably from removal of damaged cells by the RES and migration of labeled WBCs.

Photopenic lesions on Tc-99m bone scintigrams are known to occur in processes with a predominantly lytic character and little surrounding vascular reaction (*6*). In other processes, however, compromise of blood supply becomes the mechanism responsible for these photopenic areas.

Occurrence of skeletal photon-deficient lesions in In-111 WBC images is probably uncommon. Out of several hundred In-111 WBC studies, we have encountered only four cases with definite skeletal photopenic lesions. The causes for this are not completely clear, but are speculated to be multifactorial and to include impaired blood supply, death or fibrosis of reticuloendothelial tissue in the involved areas, and substitution of the bone marrow by pathological processes. In Case 1 radiation therapy was given 2 yr before the bone and In-111 WBC studies were obtained. This probably caused vascular injury in the region overlapping the radiation port. Degeneration of the fine vasculature results in inadequate local perfusion, hypoxia, fibrosis (*7*), and loss of bone-marrow tissues (*8*). Depression of reticuloendothelial activity in marrow can be detected by imaging of the bone marrow with Tc-99m sulfur colloid (*8*). Histologic studies indicate that persistent bone-marrow damage almost always occurs with radiation doses of 3,000 rad or more, whereas doses of less than 2,400 rad may not result in permanent damage (*9*). However, bone cortex is well known to be more resistant to radiation than the bone marrow. Hattner et al. found that bone damage as determined by scintigraphy occurred in 60% of the areas receiving radiation doses

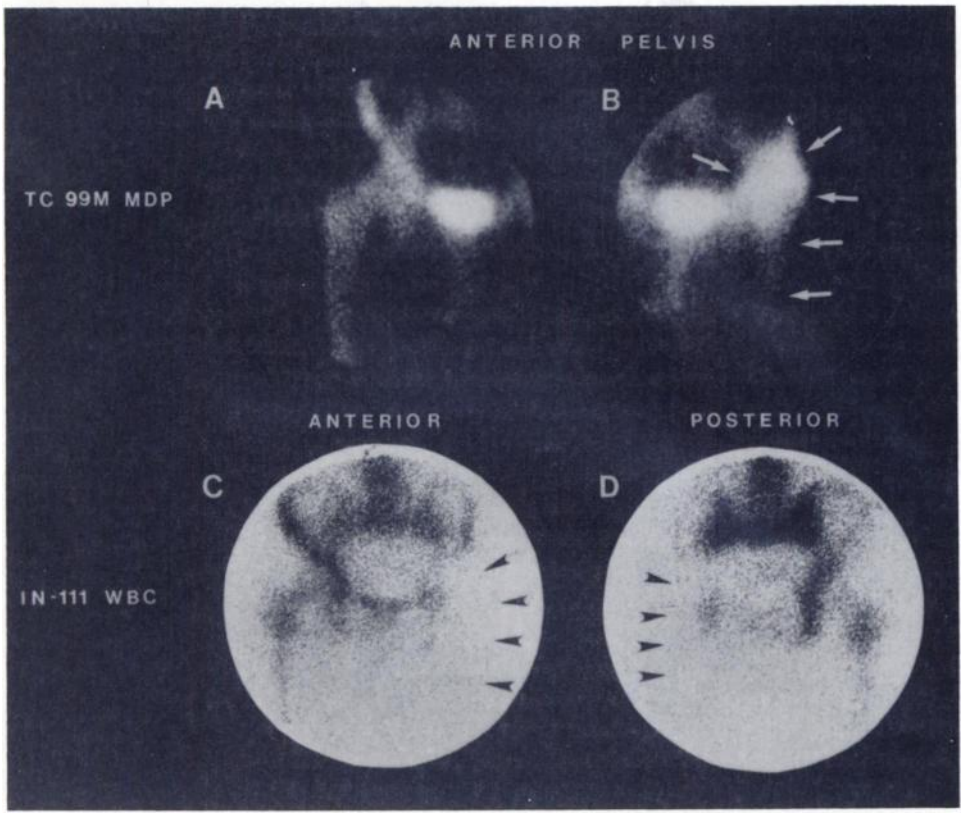

FIG. 4. (Case 4). (A) Normal right hip. (B) Left hip shows increased radionuclide concentration in proximal femur and acetabulum (arrows). (C, D) In-111 WBC images show absence of tracer uptake in left hip and proximal femur (arrows).

of more than 4,500 rad, whereas doses of 2,000 rad or less did not result in photopenic areas (*10*). The Tc-99m MDP bone images in this patient did not show photopenic areas corresponding to the In-111 WBC abnormalities in the lower spine and sacrum. The patient received radiation doses to the pelvis in excess of 5,000 rad, which would be expected to result in photopenic areas on Tc-99m bone images (*10*). This patient, therefore, represents a case of radiation causing damage to the bone marrow but with preservation of osseous tissue. Although the radiation dose was not provided, Siddiqui et al. also reported a similar case with obvious radiation changes on a bone-marrow image, but with a normal bone study (*11*). These discrepancies can be explained by the differing sensitivities of cortex and marrow to radiation (*8*). Bone-marrow damage as determined by marrow scintigrams reflects damage to the reticuloendothelial cells and the microvasculature of the marrow, whereas the damage to the bone tissues as viewed by the Tc-99m scintigrams reflects mainly vascular damage, since the bone tissue itself is more resistant to radiation (*7*).

Marrow-containing skeleton is expected to appear photopenic if invaded by tumor, as illustrated by Case 2. This patient had a histiocytic lymphoma, which, among malignant lymphomas, has a comparatively high incidence of bone and bone-marrow involvement (*12*). In one series, the incidence of bone-marrow involvement was 37% at the time of initial diagnosis (*13*). Interestingly enough, the Tc-99m MDP bone images in Case 2 failed to disclose any significant abnormalities. Cases of biopsy-proven bone-marrow involvement by Hodgkin's and non-Hodgkin's lymphomas with normal bone images are not uncommon (*14,15*). Perhaps foci of lymphoma already involved the bone marrow but had not enlarged enough to erode the contiguous bone, or osseous reaction secondary to marrow involvement was insufficient to be detected by bone scintigraphy (*15*). In our case diffuse bone-marrow involvement by lymphoma was confirmed by increased radionuclide concentration on the Ga-67 study (Fig. 2B) and also by bone-marrow biopsy.

In the patient with acute osteomyelitis (Case 3), the subperiosteal and intraosseous pus may have compressed the microcirculation of the involved bone, with ensuring acute inflammation and necrosis, as shown by biopsy findings, and resulting in a photopenic area (*16*). Occurrence of this phenomenon in varying degrees, resulting in scintigraphic changes ranging from obvious photon-deficient areas to almost normal radionuclide uptake, is expected in infections. This case casts doubt on the usefulness of In-111 WBC studies for the detection of vertebral osteomyelitis in other patients. It should be stressed, however, that most patients with vertebral osteomyelitis seek medical attention late in the course of the disease. They probably represent a chronic stage with little polymorphonuclear exudation. Chronic infections have been found negative in In-111 WBC images (*17,18*).

The absence of skeletal In-111 WBC concentration in Case 4 is more difficult to explain. Several factors may have played a role. These include the previous trauma to the left femoral head, placement of a total hip prosthesis with damage to bone marrow by the femoral intramedulary component, and chronic osteomyelitis. The combination of these factors probably resulted in destruction of the bone marrow itself and its blood supply with subsequent fibrosis. Note that blood supply did not appear to be significantly impaired at the level of bone as suggested by the uptake of Tc-99m MDP. This finding may be explained by the fact that blood supply to the acetabular fossa and proximal femur comes from two femoral circumflex arteries, the superior gluteal artery and the first perforating artery of the profunda. The bone marrow of the femur is supplied by a nutrient artery or arteries derived from the first or second perforating branches of the deep femoral artery (*19*). Therefore, damage to the bone marrow blood supply during previous trauma and surgical interventions may at

least partially explain absence of uptake on In-111 WBC images.

In summary, regardless of the mechanism for the production of photopenic lesions on In-111 WBC studies, it is important to recognize this scintigraphic finding as a manifestation of either neoplastic or benign processes. The possibility of this phenomenon should be kept in mind, especially when imaging the skeleton for detection of infection.

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