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Radionuclide Imaging of Osteomyelitis

Christopher J. Palestro, MD[*,†]

Radionuclide procedures frequently are performed as part of the diagnostic workup of osteomyelitis. Bone scintigraphy accurately diagnoses osteomyelitis in bones not affected by underlying conditions. Degenerative joint disease, fracture, and orthopedic hardware decrease the specificity of the bone scan, making it less useful in these situations. Gallium-67 scintigraphy was often used as an adjunct to bone scintigraphy for diagnosing osteomyelitis. However, now it is used primarily for spinal infections when ^{18}F-FDG imaging cannot be performed. Except for the spine, in vitro–labeled leukocyte imaging is the nuclear medicine test of choice for diagnosing complicating osteomyelitis. Leukocytes accumulate in bone marrow as well as in infection. Performing complementary bone marrow imaging with ^{99m}Tc-sulfur colloid facilitates the differentiation between osteomyelitis and normal marrow and improves test overall accuracy. Antigranulocyte antibodies and antibody fragments, such as ^{99m}Tc-besilesomab and ^{99m}Tc-sulesomab, were developed to eliminate the disadvantages associated with in vitro–labeled leukocytes. These agents, however, have their own shortcomings and are not widely available. As biotin is used as a growth factor by certain bacteria, ^{111}In-biotin is useful to diagnose spinal infections. Radiolabeled synthetic fragments of ubiquicidin, a naturally occurring human antimicrobial peptide that targets bacteria, can differentiate infection from sterile inflammation and may be useful to monitor response to treatment. ^{18}F-FDG is extremely useful in the diagnostic workup of osteomyelitis. Sensitivity in excess of 95% and specificity ranging from 75%-99% have been reported. ^{18}F-FDG is the radionuclide test of choice for spinal infection. The test is sensitive, with a high negative predictive value, and reliably differentiates degenerative from infectious vertebral body end-plate abnormalities. Data on the accuracy of ^{18}F-FDG for diagnosing diabetic pedal osteomyelitis are contradictory, and its role for this indication remains to be determined. Initial investigations suggested that ^{18}F-FDG accurately diagnoses prosthetic joint infection; more recent data indicate that it cannot differentiate infection from other causes of prosthetic failure. Preliminary data on the PET agents gallium-68 and iodine-124 fialuridine indicate that these agents may have a role in diagnosing osteomyelitis.

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Osteomyelitis is an infection of the bone and may be localized or involve periosteum, cortex, marrow, and cancellous tissue. Acute osteomyelitis can arise hematogenously or through inoculation from direct trauma, a contiguous focus of infection, or sepsis following surgery.[1] The diagnosis of osteomyelitis is not always obvious, and radionuclide procedures frequently are performed as part of the diagnostic workup.

*Department of Radiology Hofstra, NorthShore-LIJ School of Medicine, Hempstead, NY.
†Division of Nuclear Medicine and Molecular Imaging, North Shore Long Island Jewish Health System, Manhasset & New Hyde Park, NY.
Address reprint requests to Christopher J. Palestro, MD, Division of Nuclear Medicine and Molecular Imaging, Long Island Jewish Medical Center, 270-05 76th Ave, New Hyde Park, NY 11040. E-mail: palestro@lij.edu

Radiopharmaceuticals

Single-Photon–Emitting Agents

^{99m}Tc-Diphosphonates

Bone scintigraphy usually is performed with technetium-99m-methylene diphosphonate (^{99m}Tc-MDP). Uptake of this radiopharmaceutical, which binds to the hydroxyapatite crystal, depends on blood flow and rate of new bone formation. When osteomyelitis is the indication, a 3-phase bone scan usually is performed. Three-phase bone scintigraphy consists of a dynamic imaging sequence, the flow or perfusion phase, followed immediately by static images of the region of interest, the blood pool or soft tissue phase. The third, or bone, phase consists of images of the area of interest, acquired 2-4 hours after injection. Focal hyperperfusion, focal hyperemia, and focally increased

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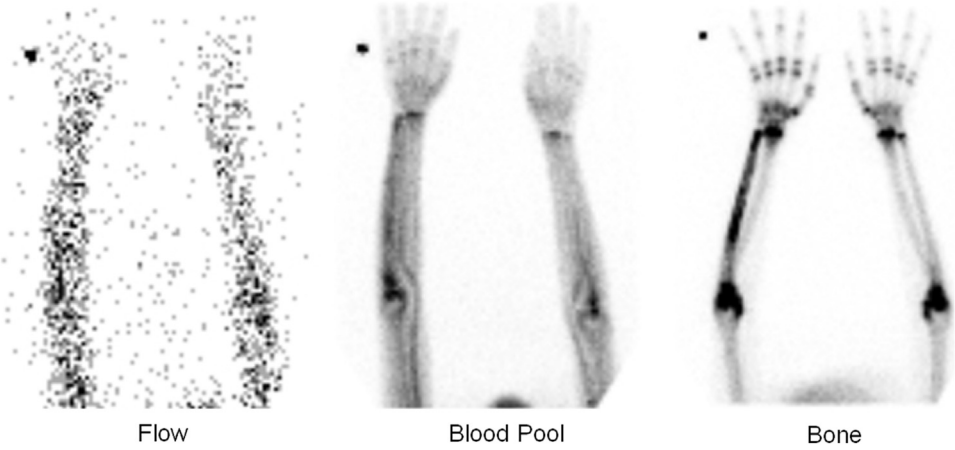

Figure 1 Right ulnar osteomyelitis. There is focal hyperperfusion, focal hyperemia, and focally increased bone uptake of radiopharmaceutical in the right ulna.

bony uptake are the classic presentation of osteomyelitis on a 3-phase bone scan (Fig. 1). The test is both sensitive and specific for diagnosing osteomyelitis in bones not affected by underlying conditions. Abnormalities on bone scintigraphy reflect the rate of new bone formation in general and consequently in the setting of preexisting conditions such as degenerative joint disease, fracture, and orthopedic hardware, the test, because of decreased specificity, is less useful (Fig. 2).[2]

Gallium-67

Several factors contribute to gallium-67 (^{67}Ga) uptake in infection. Approximately 90% of circulating ^{67}Ga is transferrin bound in the plasma. Increased blood flow and vascular membrane permeability result in increased ^{67}Ga delivery and accumulation at infectious foci. ^{67}Ga binds to lactoferrin, which is present in high concentrations in sites of infection. Direct bacterial uptake, complexing with siderophores, and leukocyte transport also may contribute to ^{67}Ga uptake in infection. Imaging generally is performed 18-72 hours after injection.[2] Presently, the role of ^{67}Ga imaging in musculoskeletal infection is limited almost exclusively to the spine (Fig. 3).

In Vitro–Labeled Leukocytes

In vitro leukocyte (white blood cell [WBC]) labeling usually is performed with ^{111}In oxyquinolone (In) or ^{99m}Tc-exametazime (Tc). Uptake depends on intact chemotaxis, number and types of cells labeled, and cellular response in a particular condition. A circulating WBC count of at least 2000 per microliter is needed for satisfactory image quality. Most WBCs labeled usually are neutrophils, and the test is most sensitive for detecting neutrophil-mediated infections.[3]

^{111}In-WBC advantages include label stability; a normal distribution limited to liver, spleen, and bone marrow; and the ability to perform delayed imaging. Complementary bone marrow imaging can be performed during cell labeling, as a simultaneous dual-isotope acquisition, or after ^{111}In-WBC imaging. Disadvantages include low-resolution images and the interval of 16-30 hours between injection and imaging.[3]

The normal distribution of ^{99m}Tc-WBCs is more variable than that of ^{111}In-WBCs. In addition to the reticuloendothelial system, activity normally is present in the urinary tract, large bowel (within 4 hours after injection), and occasionally gall bladder. ^{99m}Tc-WBC advantages include high-resolution images, and the ability to detect abnormalities within a few hours after injection. Disadvantages include label instability and the short half-life of ^{99m}Tc, which limits delayed imaging. When performing bone marrow imaging, there must be an interval of 2-3 days between the 2 procedures.[3]

Leukocytes accumulate in both infection and bone marrow. The normal distribution of hematopoietically active bone

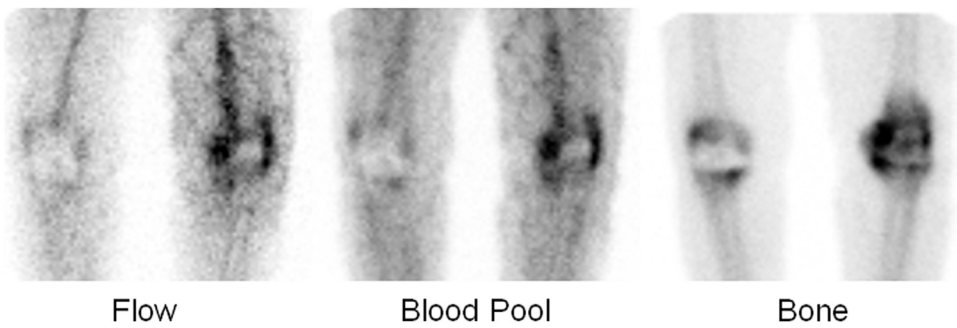

Figure 2 Left knee osteoarthritis. The findings on the 3-phase bone scan in this case mimic those seen in osteomyelitis, illustrating the limitations of bone scintigraphy in individuals with preexisting skeletal abnormalities. This study was performed to evaluate a painful right knee arthroplasty; the left knee was asymptomatic.