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SELF-STUDY TEST

Skeletal Nuclear Medicine

Questions are taken from the *Nuclear Medicine Self-Study Program 1*, published by The Society of Nuclear Medicine

DIRECTIONS

Items 1-3 consist of a question or incomplete statement followed by five lettered answers or completions. Select the *one* lettered answer or completion option that is *best* in each case. Answers may be found on page 814.

- The "flare" phenomenon in bone scintigraphy refers to which *one* of the following?
 - An increase in uptake in healing metastases following therapy.
 - The extended pattern seen with primary bone tumors.
 - The flame-like edge seen in long-bone lesions of Paget's disease.
 - The persisting minimal uptake seen in regressing metastases.
 - The calvarial flame seen in the skull on oblique views.
- Which *one* of the following mechanisms is most important in causing locally increased uptake of a bone-seeking radiopharmaceutical in an osseous lesion?
 - Increased blood flow.
 - Increased compact bone mass.
 - The presence of excessive organic matrix.
 - Increased local alkaline phosphatase activity.
 - Increased surface area of hydroxyapatite crystals per unit volume of bone.
- A 65-year-old man with newly diagnosed carcinoma of the prostate is referred for skeletal scintigraphy. Figure 1 is a posterior image of the pelvis. Based on the scintigraphic findings, the most appropriate next step is which *one* of the following?
 - Obtain a plain radiograph of the pelvis.
 - Repeat the pelvic scintigram after administration of furosemide.
 - Perform SPECT of the pelvis.
 - Perform ^{67}Ga scintigraphy.
 - Obtain a caudal scintigram of the pelvis.

True statements regarding radionuclide imaging of fractures include which of the following?

- Tibial stress fractures and shin splints are generally indistinguishable by $^{99\text{m}}\text{Tc}$ scintigraphy.
- Infected and noninfected hypertrophic pseudoarthroses can be distinguished reliably by the finding of a high concentration of ^{67}Ga at the fracture site.
- The $^{99\text{m}}\text{Tc}$ MDP scintigraphic abnormalities in a fracture often develop more slowly in patients over 70 years of age than in younger patients.
- The finding of normal or minimally increased $^{99\text{m}}\text{Tc}$ MDP uptake at a site of delayed union indicates a high likelihood of healing with piezoelectric stimulation.

- Vertebral compression fractures usually have returned to a normal scintigraphic appearance by 6 months after injury.

Three-phase bone scintigraphy reliably distinguishes

- cellulitis from osteomyelitis.
- periarticular cellulitis from septic arthritis.
- acute osteomyelitis from recent fracture.
- osteomyelitis from osteoid osteoma.
- active Paget's disease from acute osteomyelitis.

True statements concerning the scintigraphic diagnosis of osteomyelitis include which of the following?

- Intense focal concentration of ^{67}Ga in a known region of chronic osteomyelitis is highly suggestive of active infection.
- Imaging with ^{111}In -labeled leukocytes is less sensitive for detecting chronic than acute osteomyelitis.

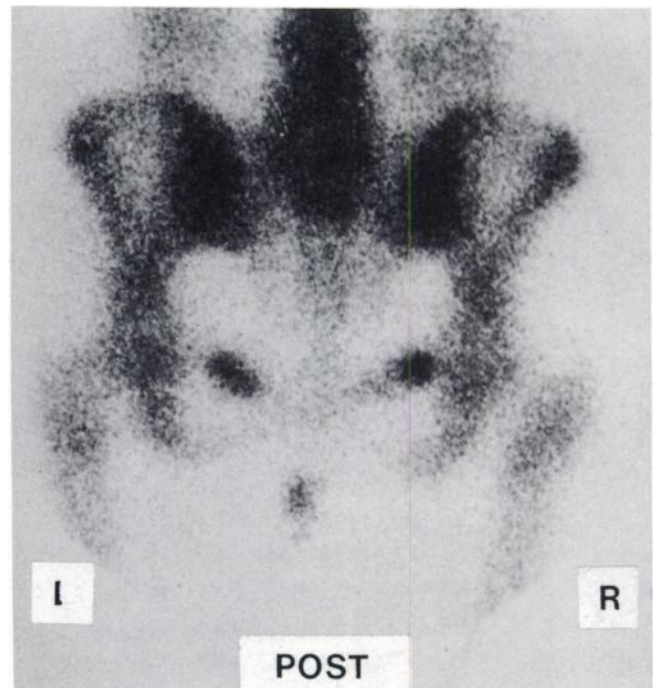


Figure 1

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SELF-STUDY TEST

Skeletal Nuclear Medicine

QUESTIONS (continued)

16. The finding, at the end of a 6-week course of appropriate antibiotic treatment for acute osteomyelitis, that ^{67}Ga uptake has decreased from pretreatment levels, but not to normal, is a strong indication of an unsatisfactory response.
17. Low-grade ^{67}Ga concentration is often seen in chronic osteomyelitis in a distribution that is anatomically similar to that of $^{99\text{m}}\text{Tc}$ MDP.
18. Osteosarcoma and acute osteomyelitis generally can be distinguished by their differential accumulation of ^{67}Ga and $^{99\text{m}}\text{Tc}$ MDP.

SELF-STUDY TEST

Skeletal Nuclear Medicine

ANSWERS

Item 1: "Flare" Phenomenon

Answer: A

The term "flare phenomenon" was originally used by Gillespie et al. to describe the increase in activity seen on $^{87\text{m}}\text{Sr}$ bone scans during treatment of patients with metastatic disease who were responding to chemotherapy. This phenomenon was further characterized by Rossleigh et al. in patients undergoing $^{99\text{m}}\text{Tc}$ MDP bone scintigraphy for evaluation of therapy for breast cancer metastases. They defined the "flare response" as: (1) an increase in tracer uptake or in the apparent size of known metastatic lesions and/or the appearance of new lesions within 6 months of commencing therapy, in the absence of increasing bone pain (in practice, however, pain occurs in some patients responding to therapy); and (2) subsequent decreased uptake in these lesions, without a change in therapy, on repeat scintigraphy within 2-3 months. In this series, ten patients showed a healing "flare response" 6 weeks to 6 months after therapy. Five of the ten patients showed increased uptake in previously demonstrated lesions. In the other five patients, new lesions were identified that previously were undetected. In all of the patients, therapy was not altered during the course of the serial studies, there was a reduction in bone pain or objective tumor responses in other sites, and later follow-up studies showed decreased uptake in the known lesions. In only one of the patients was a radiographic change (sclerosis of a lytic lesion) seen in association with the healing flare. The "flare phenomenon" has been seen in patients with prostate carcinoma and other tumors as well. It also may occur locally in regions undergoing irradiation for metastatic disease. The likelihood of observing the "flare phenomenon" depends on the type of tumor, the type of therapy, the interval after onset of treatment and the frequency of bone scintigraphy.

The "extended pattern" seen with primary bone tumors in long bones is not related to the "flare phenomenon." Patients with primary bone tumors may show increased activity in adjacent joints or along the entire extremity. This increase in activity is usually mild to moder-

ate in degree and is thought to be due either to generalized increased blood flow to the extremity or to a change in the patient's gait. The "extended pattern" is one reason that bone scintigraphy may overestimate the extent of osseous involvement by a primary bone tumor. Similar "extended" findings also occur with inflammatory lesions of the long bones.

When Paget's disease involves long bones, the process may involve the entire bone or it may extend from one end of the bone for a variable length into the diaphysis. Radiographically, the leading edge of the lytic phase of Paget's disease in a long bone has been described as a "flame-like" rarefaction. This also has been characterized as a "blade of grass" appearance.

The persisting minimal uptake seen in regressing metastases is not the "flare phenomenon." This uptake likely reflects continued remodeling of bone after the local tumor deposit has been reduced or eradicated.

On oblique scintigrams of the skull, an area of increased activity in the anterior temporoparietal region is occasionally seen. This has been called a calvarial flame and probably is due to the increased bone thickness of the lateral orbital ridge or the pterion viewed on end in this projection.

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SELF-STUDY TEST

Skeletal Nuclear Medicine

ANSWERS (continued)

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Item 2: Mechanisms of Radiopharmaceutical Uptake in Osseous Lesions

Answer: E

Bone-seeking radiopharmaceuticals are accumulated in greater degree at skeletal sites where there is increased blood flow (thus exposing that bone to more tracer for chemisorption over any given time), and also in sites of new bone formations where there is an increase in the surface area of hydroxyapatite crystals per unit volume of bone. Newly forming hydroxyapatite crystals are of smaller size than mature crystals and provide a relatively greater surface area for chemisorption of the tracer. Although both increased blood flow and new bone formation (with associated increase in crystal surface area) are important, several studies have shown that the magnitude of the change in blood flow is insufficient to account for the substantially increased tracer accumulation in epiphyseal plates, metastatic lesions and healing fractures.

A large mass of compact bone with normal blood flow and hydroxyapatite deposition will not necessarily have increased uptake; e.g., bone islands are not usually noticeably "hot" by scintigraphy.

The organic matrix has rather low affinity for the ^{99m}Tc diphosphate agents when compared with hydroxyapatite crystals. There is little experimental evidence that alkaline phosphatase activity bears a relationship to the localization of bone-seeking radiopharmaceuticals.

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Item 3: Caudal Imaging of the Pelvis

Answer: E

Figure 1 shows bilateral focal uptake in the pubic area, which could be due to metastases or insufficiency fractures; however, retained urine in bladder diverticula is more likely. The true nature of the focal uptake is most easily demonstrated by performing a caudal

scintigram of the pelvis, which can separate activity in the bladder from that in the pubis. In this patient, the pubic bones are normal and the activity is in the bladder diverticula. Additional delayed views the next day are also helpful to separate osseous lesions from activity in the urinary bladder, especially in patients who are unable to void fully at the time of initial imaging.

Imaging after furosemide is used to distinguish obstructive from nonobstructive pelvicalyceal dilatation, but not to evaluate lower urinary tract lesions. It is not indicated in this case, although a change in bladder configuration conceivably could result. Although SPECT of the pelvis would distinguish pubic from bladder activity, the question in this patient is more easily and less expensively resolved by a caudal scintigram. Plain radiography would be of value to distinguish metastases from insufficiency fractures, but it would not be appropriate until an osseous localization of the increased activity is confirmed. Gallium scintigraphy would involve additional expense, radiation exposure, and an unnecessary delay in diagnosis. Because ⁶⁷Ga uptake in metastatic lesions of prostatic cancer is often poor, the absence of definite abnormalities would not help greatly to distinguish metastases from fractures or true osseous lesions from bladder activity.

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Items 4-8: Scintigraphy of Fractures

Answers: 4, F; 5, F; 6, T; 7, F; 8, F

Tibial stress fractures are characterized by focal, fusiform accumulations of increased uptake of ^{99m}Tc MDP, whereas shin splints exhibit more diffuse uptake extending over a large length of bone, usually along the posterior cortical surface. The two usually are distinguishable scintigraphically.

Focally increased uptake of ^{99m}Tc MDP is usually apparent soon after an acute fracture, and nearly always by 72 hours after injury. However, Matin has shown that this response may be delayed in elderly patients, with some fractures not clearly apparent scintigraphically at one week.

Both sterile and infected hypertrophic pseudarthroses concentrate both ^{99m}Tc MDP and ⁶⁷Ga. Therefore, they are very difficult to distinguish by scintigraphy with these agents. The absence of ⁶⁷Ga uptake favors the absence of infection, but increased ⁶⁷Ga uptake is not necessarily due to infection. More recent studies indicate that ¹¹¹In white cell scintigraphy is more reliable for diagnosing infection in nonunion fractures.

The finding of normal or minimally increased ^{99m}Tc MDP uptake at a site of delayed union reflects a poor capacity to heal; in this situation piezoelectric stimulation does not promote effective healing. If there is a high concentration of the tracer about the fracture site, and if the gap between the fracture fragments is not large enough to be resolved by scintigraphy, the chances of stimulated healing are greater.

On average, ^{99m}Tc MDP images of vertebral compression fractures

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SELF-STUDY TEST

Skeletal Nuclear Medicine

ANSWERS (continued)

usually return to normal 12-18 months after injury.

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Items 9-13: Three-phase Bone Scintigraphy

Answers: 9, T; 10, F; 11, F; 12, F; 13, F

Focally increased perfusion and enhanced "blood-pool" activity of ^{99m}Tc MDP is common to both acute osteomyelitis and cellulitis. The distinction between osseous and soft-tissue infection is made on the delayed images where focally increased activity in bone favors osteomyelitis, whereas normal activity distribution or low-grade diffuse uptake in the underlying bone signifies adjacent cellulitis.

Recent traumatic fracture, osteomyelitis, Paget's disease, and osteoid osteoma show increased activity in all three phases and, thus, cannot be differentiated readily by three-phase scintigraphy.

Periarticular cellulitis and septic arthritis both exhibit hyperperfusion and hyperemia about the joint and cannot be distinguished by these criteria alone.

As indicated by the above, three-phase bone scintigraphy is of primary use in distinguishing an osseous lesion from a soft-tissue abnormality, but is of relatively little value in differentiating between various types of active osseous lesions.

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Items 14-18: Scintigraphy in Osteomyelitis

Answers: 14, T; 15, T; 16, F; 17, T; 18, F

The reduction of ⁶⁷Ga uptake to levels still above normal after treatment of acute osteomyelitis is seen frequently and is not a harbinger of chronic osteomyelitis. It probably represents the sterile component of bone repair. The corresponding ^{99m}Tc MDP images often continue to show intense activity after the infection passes from the septic phase to the bone repair phase. In chronic osteomyelitis, on the other hand, low-grade ⁶⁷Ga concentration often is seen in the same distribution as ^{99m}Tc MDP. In this setting, infection is more reliably diagnosed when the ⁶⁷Ga uptake is much greater than that of ^{99m}Tc MDP, or when intense focal ⁶⁷Ga uptake is seen within the larger region of remodeling depicted by bone scintigraphy.

Although literature reports exist to the contrary, the consensus is that ¹¹¹In leukocyte scintigraphy generally is less sensitive for detecting chronic than acute osteomyelitis, presumably reflecting the greater fraction of mononuclear cells rather than polymorphonuclear leukocytes, in the inflammatory response with chronic infection.

Both osteosarcomas and acute osteomyelitis avidly concentrate ⁶⁷Ga and ^{99m}Tc MDP, so that they cannot be distinguished on that basis alone. However, osteosarcoma more likely will show extension of the accumulation of the two radiopharmaceuticals into the adjacent soft tissues.

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For further in-depth information, refer to the syllabus pages in Nuclear Medicine Self-Study I.