Scintigraphic Evaluation of Diabetic Osteomyelitis: Concise Communication

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We have reviewed the three-phase bone scans, radiographs, and histologic findings of 39 diabetic patients with serious foot problems. The sensitivity and specificity of bone scans were 83% and 75%, respectively, for osteomyelitis of the small bones of the foot. The positive and negative predictive values were 87% and 69%, respectively. The radiographs were less sensitive (62%) and less specific (69%), with predictive values of 80% (positive) and 47% (negative).

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Patients with diabetes mellitus are predisposed to a variety of inflammatory processes, among which infections account for major morbidity (*1*). Optimal management of diabetic foot infections requires knowledge of the extent of the infection and specifically whether the bone is involved. Neuropathic bone disease, so-called osteoarthropathy, should also be distinguished from osteomyelitis, since their treatments are different (*1,2*).

Bone scanning using technetium-99m phosphonates is a very sensitive tool in detecting various skeletal abnormalities. Its greater sensitivity over radiographs plays an important role, especially in the early diagnosis of osteomyelitis (*3,4*). It has been shown that comparison of blood-pool images obtained soon after injection with bone images obtained a few hours later can help differentiate cellulitis from osteomyelitis (*5,6*).

We have reported our earlier experience with three-phase bone scanning of the diabetic foot (*7*). That study showed a more intense uptake of technetium-99m MDP in the focus of proved osteomyelitis than in degenerative bone disease.

This retrospective investigation was undertaken to evaluate the efficacy of the three-phase bone scanning in diagnosing osteomyelitis in a larger number of patients with diabetic foot problems, all with histologic confirmation. We also compared the sensitivity and specificity of the foot radiographs and the bone scans in these patients.

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MATERIALS AND METHODS

Subjects. Thirty-nine diabetic patients who had radiographs, three-phase bone scans, and histologic confirmation of the diagnosis were included in this study. These patients, with a variety of infections and/or ischemic problems: cellulitis, gangrene, abscess, and ulcers, required bone biopsy to exclude osteomyelitis or bone debridement or amputation. Patients were excluded if the surgical procedure was performed more than 4 wk after the bone scan. Proper antibotic treatment was given whenever indicated clinically.

Bone-scan technique. The scans were obtained following an intravenous injection of approximately 20 mCi of Tc-99m methylene diphosphonate. With the patient supine, a gamma camera was placed under the plantar aspect of the feet. A flexible lead shield was placed over the feet to prevent any interference from the activity in other parts of the body. Following the injection of the radiopharmaceutical, 12 serial 3-sec images (Phase 1) were obtained. The camera was started when the bolus was first visualized in the persistence scope. Between 5 and 10 min after injection, with the feet remaining in position, the blood-pool image was obtained (Phase 2), recording 500,000 counts on an 8- by 10-inch transparent film. Bone images were obtained at least 2½ hr later

TABLE 1. INTERPRETATION OF THREE-PHASE BONE SCANNING (Tc-99m MDP) IN DIABETIC FOOT

Degree of activity* in			
Phase 1	Phase 2	Phase 3	Interpretation
2+ 3+	2+ 3+	2+ 3+	Acute osteomyelitis
2+ 3+	2+ 3+	1+	Cellulitis
1+	1+	2+ 3+	Osteoarthropathy, degenerative bone
−1	−1	−1	Absent flow

* Tc-99m MDP uptake was graded in five levels (−1, 0, 1+, 2+, 3+) for each phase, "0" being the normal activity in the forefoot: 1+, minimal increase beyond the normal bone activity; 2+, moderate increase beyond the normal bone activity; 3+, marked increase beyond the normal bone activity; −1, total lack of activity.

(Phase 3) in plantar projection. When necessary, additional dorsal or lateral images were obtained to visualize the lesion better.

Histologic studies. The specimens obtained were from trephine needle biopsy in five patients, from debrided bone in three, and from amputated bone in 31. Decalcification was done with a commercial preparation without prior formalin fixation. Histologic studies of the removed bone were performed without knowledge of the clinical, radiographic, or bone-scan findings, and in most of the cases the surgical pathology report was accepted as the final diagnosis. In one patient with Charcot's joint, the histology showed active inflammation and bone necrosis. The subsequent clinical course, however, was not that of an acute osteomyelitis and the bone culture was negative. This case was considered not to have osteomyelitis.

Radiographic interpretation. One of us read all the radiographs in one sitting, without knowledge of the histologic or bone-scan findings. Previous radiographs were also reviewed whenever available. Cortical defects associated with soft-tissue swelling or subcutaneous gas were considered to represent osteomyelitis.

Bone-scan interpretation. Three of the authors, with at least 7 yr experience each in nuclear medicine, interpreted the scans independently without knowledge of the radiographic or histologic findings. An example of a foot scan showing varying amounts of uptake (−1, 0, 1+, 2+, 3+) was used as a reference in the grading of patients' scans, with "0" being the normal activity in the forefoot. Studies were interpreted according to the scheme shown in Table 1. Examples of various abnormalities are shown in Figs. 1 and 2. If Phase 3 showed focal 2+ or 3+ uptake and Phases 1 and 2 showed more-diffuse uptake beyond the bone structure (Fig. 1, left foot), the scan was read as osteomyelitis with superimposed cellulitis. When there was disagreement among readers, the majority opinion was taken as the final interpretation.

RESULTS

The results of the bone-scan findings are summarized

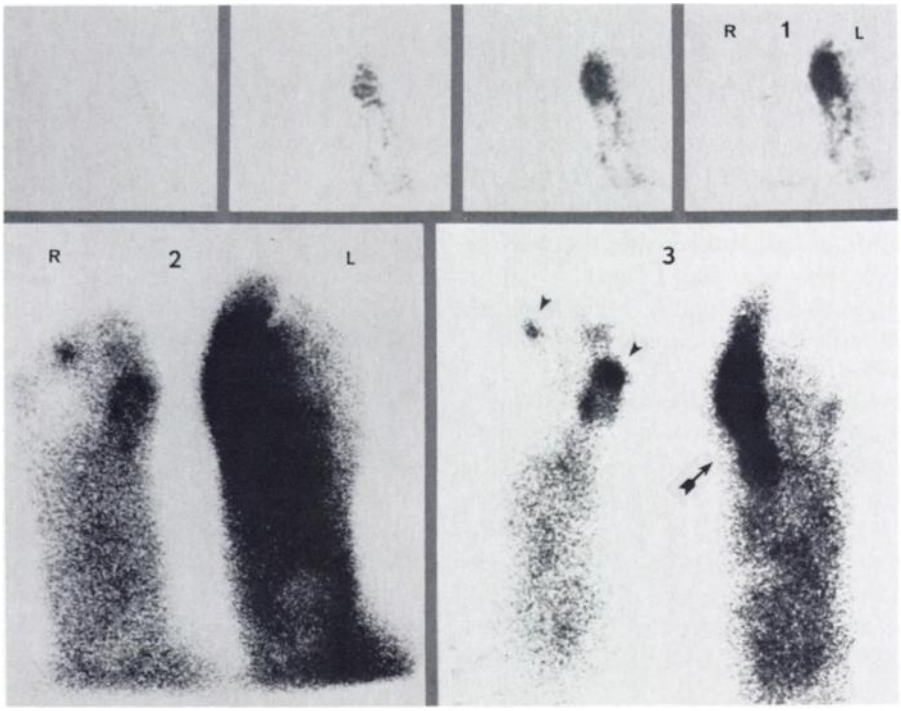

FIG. 1. Three-phase bone scan of diabetic foot illustrating osteomyelitis superimposed upon cellulitis (left foot, arrow). Note greatly increased flow, blood-pool, and bone uptake in lesion. In degenerative bone lesions (right foot, arrow heads) uptake is minimal in Phases 1 and 2.

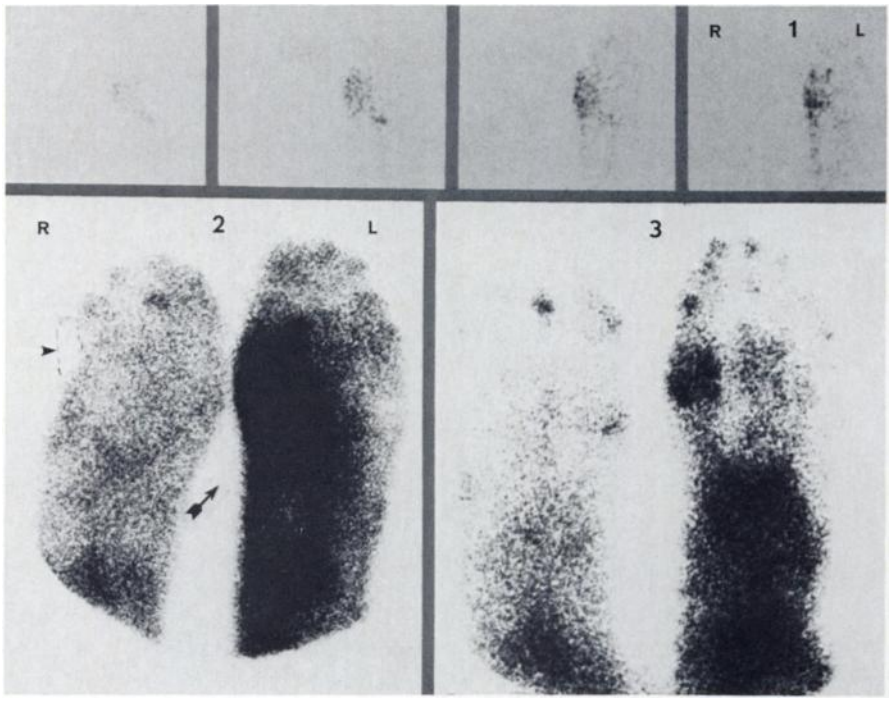

FIG. 2. Three-phase bone scan of diabetic foot illustrating cellulitis without osteomyelitis (left foot, arrow). Note that uptake in Phase 3 is much less than in Phase 2. Gangrenous toe (right fifth, arrow head) shows absent flow.

in Table 2. There were three cases with absent blood flow in the toe, with clinical evidence of ischemia. Absent flow may be secondary to either intrinsic vascular disease or to compression due to osteomyelitis (*4*). The two cannot be distinguished scintigraphically, but the finding of absent flow is important clinically. Thus, a separate category was established to include such cases. Histology of the three cases in this category showed evidence of acute osteomyelitis in two and no pathologic change in one. These three were excluded from the further statistical analysis.

Of the remaining 36, 21 patients had histologic evidence of acute osteomyelitis. Twenty of the 21 patients had positive scans (95% sensitivity), and the one with the false-negative scan had x-ray evidence of osteomyelitis. Three cases with the histological evidence of "mild chronic" or "chronic" inflammation showed only minimal uptake in the bone phase, which was interpreted to be consistent with degenerative bone changes. Radiographs were also negative in two of these three.

Among 12 patients without osteomyelitis, the bone scan was negative in nine (75% specificity). In the remaining three patients with false-positive scans, one had Charcot joint and two had no pathologic changes in their bone biopsies. When both acute and chronic osteomyelitis were combined, the sensitivity and specificity of the bone scanning for osteomyelitis were 83.3% (20/24) and 75% (9/12), respectively (Table 2). The positive predictive value was 87% (20/23) and the negative predictive value was 69% (9/13).

The interobserver agreement in scan interpretation was excellent: 95% for "osteomyelitis," 93% for "no osteomyelitis," and 100% for "absent flow."

The correlation between radiographic findings and the final diagnosis is shown in Table 3. The sensitivity and

TABLE 2. SCINTIGRAPHIC FINDINGS IN DIABETIC OSTEOMYELITIS OF THE FOOT

	Final diagnosis		
	No osteomyelitis	Acute osteomyelitis	Chronic osteomyelitis
Scintigraphic findings			
No osteomyelitis	9	1	3
Osteomyelitis	3	20	0
Absent flow	1	2	0

TABLE 3. RADIOGRAPHIC FINDINGS IN DIABETIC OSTEOMYELITIS OF THE FOOT

	Final diagnosis		
	No osteomyelitis	Acute osteomyelitis	Chronic osteomyelitis
Radiographic findings			
No osteomyelitis	9	8	2
Osteomyelitis	4	15	1

specificity of radiographs were 62% (16/26) and 69% (9/13), respectively. The positive predictive value was 80% (16/20) and the negative predictive value was 47% (9/19).

DISCUSSION

The foot of the diabetic is subject to three main insults: ischemic, septic, and neurotrophic. The presenting lesion may be caused by any or a combination of these (*8*). In the evaluation of diabetic foot lesions, one needs to know whether the patient has cellulitis, osteomyelitis, diabetic osteoarthropathy, or any combination of these (*1*). Recently, some effort has been made to use noninvasive methods to differentiate these conditions (*8,9*). However, no single noninvasive test is known to be satisfactory in providing precise diagnostic information. Bacterial cultures from the ulcer or sinus tract do not necessarily represent organisms in the bone. A comparative study showed that only 44% of the sinus-tract cultures contained the pathogens in the infected bones (*10*).

Radiographs provide information about the structures of foot bones involved with diabetic osteoarthropathy (*11*), but are insensitive in early diagnosis of osteomyelitis. In our study the sensitivity of radiographs was only 62%.

We have previously reported that three-phase bone scanning may be useful in detecting early diabetic foot problems and in differentiating osteomyelitis from degenerative bone changes (*7*). The present study confirms those impressions and also shows that bone scans are more accurate than the radiographs in diagnosing osteomyelitis. Three-phase bone scanning, however, has limitations. As shown in one case in this study, an exceedingly destructive type of joint lesion (Charcot joint) could not be distinguished from acute osteomyelitis. Also, histologically mild or chronic inflammation could not be diagnosed.

Since bone uptake relies on perfusion, a question is often raised as to the effect of nearby hyperemia. We and others (*12*) have noted that the increased bone uptake caused by hyperemia alone is low in intensity and diffuse in location (Fig. 2).

The overall accuracy of three-phase bone scanning in the diagnosis of osteomyelitis in the diabetic foot (acute and chronic combined) was 80% (29/36) in this series. This is somewhat less than one would like to see. Some of the factors one may question include the role of antibiotic therapy, the appropriateness of the biopsy specimen, and the effect of diabetic angiopathy on the delivery of radiotracer. It has been reported that with proper antibiotic therapy the flow may return to normal whereas the static scan remains abnormal much longer (*13*). This may result in a false-negative scan. Thus, scanning early in the course is very important.

Apart from Charcot joint, bone and joint diseases that may mimic acute osteomyelitis in three-phase bone scans are acute septic arthritis, acute gouty arthritis, recent fracture, osteoid osteoma, fibrous dysplasia, and osteosarcoma. Radiographic and clinical features assist in distinguishing some of these conditions from osteomyelitis.

In summary, three-phase bone scanning in conjunction with radiographs provides useful information in the evaluation of diabetic foot problems. This study, however, was limited to patients with more serious foot problems needing surgery. The role of three-phase bone scanning in the evaluation of patients with milder foot problems requires further study.

As an adjunct to bone scanning, Ga-67 citrate imaging has been used to confirm or to guide the course of therapy (*4,14*). More recent reports caution against such an approach. Glynn reported marked gallium accumulation in neurogenic (Charcot's) arthropathy (*15*). Kolyvas et al. (*16*) found that Ga-67 uptake may persist in many cases for six or more weeks despite complete clinical resolution of osteomyelitis.

Another promising preparation in a search for inflammation is In-111 leukocytes (*17–20*). We are in the process of evaluating In-111-granulocyte imaging for detecting inflammatory lesions, including osteomyelitis.

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