# Indium-111-Leukocyte/Technetium-99m-MDP Bone and Magnetic Resonance Imaging: Difficulty of Diagnosing Osteomyelitis in Patients with Neuropathic Osteoarthropathy

James E. Seabold, Frederick W. Flickinger, Simon C.S. Kao, Theodore J. Gleason, Daniel Kahn, James V. Nepola, and J. Lawrence Marsh

Departments of Radiology and Orthopaedic Surgery, The University of Iowa College of Medicine, Iowa City, Iowa

Fourteen patients (16 sites) with clinical and/or radiographic evidence of neuropathic osteoarthropathy (Charcot joints) were evaluated with combined indium-111-leukocyte (111 In-WBC) and technetium-99m-methylene diphosphonate (99mTc-MDP) bone imaging for suspected osteomyelitis. Magnetic resonance (MR) images were obtained in seven patients. Using a positive bone culture as the criterion for the presence of osteomyelitis, there were four true-positive studies, six true-negative sites, and one false-negative 111In-WBC study. Five of 16 sites (31%) had false-positive 111 In-WBC uptake at noninfected sites. There were four true-positive and three false-positive MR studies. All false-positives showed at least moderately abnormal findings by both techniques at sites of rapidly progressing osteoarthropathy of recent onset. In this preliminary study, both techniques appear to be sensitive for detection of osteomyelitis, and a negative study makes osteomyelitis unlikely. However, the findings of 111 In-WBC/99mTc-MDP and MR images at sites of rapidly progressing, noninfected neuropathic osteoarthropathy may be indistinguishable from those of osteomyelitis.

J Nucl Med 1990; 31:549-556

euorpathic osteoarthropathy (Charcot joint disease) refers to the bone and joint changes occurring in patients with an underlying spinal or peripheral neuropathy (1-5). It is not uncommon for osteomyelitis to occur in or adjacent to sites affected by neuropathic osteoarthropathy. Many of the clinical and radiographic findings of neuro-osteoarthropathy, especially in rapidly progressing cases (4), are also seen in patients with a primary bone and/or joint infection (1,2,5).

Three-phase bone scintigraphy and/or combined gallium-67 (67Ga)/technetium-99m-methylene diphos-

Received Sept. 21, 1989; revision accepted Dec. 21, 1989. For reprints contact: J. E. Seabold, MD, Department of Radiology, The University of Iowa Hospitals and Clinics, Iowa City, IA 52242. phonate (99mTc-MDP) bone imaging do not have sufficient specificity to establish the diagnosis of osteomyelitis involving Charcot joints (6-8). Recent articles suggest that indium-111-leukocyte (111In-WBC) imaging appears promising for detection of infected Charcot joints (8-10). This retrospective study compares the results of plain radiographs, combined 111In-WBC/99mTc-MDP bone imaging, and magnetic resonance imaging (MRI) with bone culture results and radiographic follow-up in patients with suspected osteomyelitis in or adjacent to neuropathic joints to evaluate the accuracy of these techniques in the detection of osteomyelitis. The problems encountered in interpretation of the various diagnostic imaging techniques are discussed.

# **MATERIALS AND METHODS**

A retrospective analysis was performed on the diagnostic imaging studies obtained in 14 patients who underwent combined <sup>111</sup>In-WBC/<sup>99m</sup>Tc-MDP imaging between January 1985 and January 1989 for high clinical suspicion of osteomyelitis in or around neuropathic joint(s).

## **Patient Population**

Fourteen patients (16 sites) with documented peripheral neuropathies had combined 111In-WBC/99mTc-MDP imaging for suspected osteomyelitis in or around Charcot joint(s). None of the patients had received intravenous (i.v.) antibiotics for at least 3 wk before the imaging studies and bone cultures. All cultures were obtained within 1-2 wk of imaging. Bone cultures were not obtained in one patient (Case 13). This patient stabilized radiographically within 3 mo without antibiotic therapy and has shown no evidence of osteomyelitis after 10 mo of follow-up. Five patients (six sites) were evaluated for osteomyelitis adjacent to large joints (Cases 1-5, see Table 1). Two patients presented with recent onset of signs and symptoms of an inflamed ankle. In this study, each foot was considered one site regardless of the number of joints affected by neuropathic osteoarthropathy. Two other patients (three sites) had neuropathic joint changes on serial plain films and were being evaluated for suspected osteomyelitis in or TABLE 1 atient Data Summary

			Patient Data Summary	summary			
Case/Age/Sex	Symptoms	Radiographic findings	Bone scan findings	111 In-WBC localization	MR results	Culture results	Final diagnosis
1, 37, F dlabetic	Pain and swelling R ankle × 3 mo	Osteolytic destruction, R subtalar jt, fx and osteolysis distal R fi- bula in 2 wk	H and ↑ uptake R anke R anke and calcaneus	Marked pos [FP]	Not done	Neg bone and joint aspirates	Rapidiy progress Charcot Rankle & subtalar joints × 4 mo
2, 57, M alcoholic	Pain and swelling L ankle and foot, plantar ulcer 6-9 mo	Mixed O and H tarsal, ant. talus and calca- neus, neg L ankle jt	H and ↑ uptake L anke and midfoot calcaneus tarsals and prox MT	Marked pos bone [FP] and adj soft tissue	Pos bone [FP] and adj soft tissue	L BKA, neg none Staph a in soft tissue	<ol> <li>Cellulitis L ankle and midfoot</li> <li>Charcot L midfoot × 1.5 yr</li> <li>Plantar ulcer × 9 mo</li> </ol>
3, 47, M cerebral palsy	Progress R hip pain and loss of motion within 1 vr	Mixed O and H, marked destruction and loss jt space R hip	H and ↑ uptake R acetabulum and prox femur	Neg [TN]	Not done	Neg aspirates	Charcot R hip × 14 yr w/ recent progression
4, 27, M paraplegic	Chronic R per- rectal ulcer	Hypertrophic hips soft- tissue calcif, medul- lary rod L femur with osteopenic callus, R ischlotomy defect	H and ↑ uptake both hips, midshaft L femur & R ischium	Marked pos: L hip and femur, [TP] neg: R hip [TN]	Not done	Open bx: L femur, Staph a	Osteomyelitis L hip & L femur     L femur     Charcot hips × 8 yr     Osteotomy R ischium × 2 yr (not infected)
5, 59, F diabetic	Nonunited fx L wrist × 1.5 yr	Fx nonunion distal L radius, osteopenic L wrist	H and † uptake at fx site and adj wrist	Moderate pos [FP]	Not done	Open bx: acute in- flammation w/ neg cul- ture	<ol> <li>Noninfected nonun- ion L radius × 1.5 yr</li> <li>Inflammatory process L wrist, probable early Charcot × 3 mo</li> </ol>
6,68, F diabetic	Chronic foot ulcers × 8 mo	Bilat destruction of tarsals, osteolysis distal L 5th MT, cortical erosion and fx, adj	H and ↑ uptake mid- tarsals and both feet L 5th MT	L foot marked pos soft tissue and bone [TP] R foot neg [TN]	Pos L foot soft tissue and bone [TP]	Staph a., E. coll, group D entero-coccus	Osteomyelitis L 5th     MT and adj cellulitis     Charcot bilat mid and     hindfeet for 3–5 yr
7, 56, M diabetic	Ucer midlateral R foot × 1 yr	Mixed O and H of tarsals, synostosis MT, osteolysis prox 5th MT and absent 5th MT head	H and ↑ uptake R tar- sals	Marked pos [TP]	Pos bone [TP]	B-hemolytic streptococ- cus	<ol> <li>Osteomyelitis R 5th</li> <li>MT</li> <li>Chronic Charcot R</li> <li>tarsal bones × 6 yr</li> </ol>
8, 64, M diabetic	Draining ulcer L foot $\times$ 2 wk	Hypertrophic, sclerotic L subtation It, pan-MT amputations	No hyperemia † uptake L talus and subtalar region	[NL] BeN	Not done	Neg	<ol> <li>Poor healing L plantar utcer</li> <li>Charcot L subtalar jt x 3 vr</li> </ol>
9, 58, M diabetic	Draining utoer and pain L midfoot × 6 mo	Hypertrophic, sclerotic and collapsed ant: tarsals except for cuboid	H and ↑ uptake L midfoot	Marked pos [FP]	Pos bone [FP]	Neg	Rapidly progressing Charcot L midfoot × 4 mo

TABLE 1 (Continued)
Patient Data Summary

Bone scan findings in the scalization in the scalization in the scalization is selected by the scalization in the scalization is selected by the scalization is soft that is and sub-constituted by the scalization is soft in the scalization in the scalization is soft in the scalization in the scalization in the scalization is soft in the scalization in the scalization in the scalization is soft in the scalization in the scale in				Patient Data Summary	ummary			
Swelling & ey- Mixed O and H of sub- H and † uptake 1st heap bone [FN], Pos bone secens, tasken and soft period in the factor of	Case/Age/Sex	Symptoms	Radiographic findings	Bone scan findings	111 In-WBC localization	MR results	Culture results	Final diagnosis
midtateral R marked periostical foot X 6 wk, reaction prox 4th curefrom toox 4th MTP plus TWJ it narrowing M Midplantar ul- Cortical erosion, J if and and soft and s	10, 53, M diabetic	Swelling & ery- thema L 1st and 5th toes	Mixed O and H of subtalar and mid-TMT its, diffuse osteopenia, pan mid-MT amputations	H and ↑ uptake 1st MT, talus and sub- talar jts	Neg bone [FN], pos soft tissue	Pos bone and soft tissue [TP]	Serratia mar- cescens, Staph a.	1. Cellulitis 1st and 5th toes 2. Osteomyelitis L 1st MT 3. Charcot L subtalar and mid-MT jts × 2
Midplantar ul- Cortical erosion, J it Focal hyperemia and ore L BKA, Staph  cer L foot × space and subluxa- † uptake 2nd-5th L pos soft tissue and subluxa- ton L 2nd-4th MTP	11, 24, M dlabetic	Draining ulcer midlateral R foot × 6 wk, TMJ jt nar- rowing	Nonunited fx and marked periosteal reaction prox 4th and 5th MT plus TMT jt narrowing	H and ↑ uptake 3rd, 5th MT, and lateral cuneiform	Moderate pos bone and soft tissue [TP]	Pos bone and soft tissue [TP]	Group D enterococcus	Osteomyelitis R 3rd and 5th MT and adj cellulitis     Early Charcot R midfoot
Pain and swell- Mixed H and O 1—4 H and ↑ uptake 1 st- ing L ankle MT jts and fx 1 st- and midfoot 3rd MT within 6 wk, forms and diffuse calcaneus [FP] tissue and soft gradual and midfoot 3rd MT within 6 wk, forms and diffuse calcaneus [FP] tissue resolution x 6 wk  X	12, 51, M diabetic	Midplantar ulcer L foot × 6 wk	Cortical erosion, ↓ jt space and subluxation L 2nd-4th MTP jts, distal amputation 1st MT	Focal hyperemia and † uptake 2nd–5th L MTP jts	Neg bone [TN] pos soft tissue	Not done	L BKA, <i>Staph</i> a. plantar ulcer, bone neg	Chronic infected     plantar ulcer L foot     Charcot L midfoot × 2-3 yr
Chronic ulcer L Soft-tissue swelling, Focal hyperemia L Neg bone [TN], Not done Staph a. from heel and in- plantar ulcer L mid- midfoot and dif- marked pos famed L calf foot, marked H and fusely L calf, ↑ up- soft tissue take all tarsals and of tarsals, subluxa- prox 4–5th MT tion of TMT its, atrophy of 5th MT and adj soft-tissue calcif	13, 29, F diabetic	Pain and swelling L ankle and midfoot	Mixed H and O 1-4 MT jts and fx 1st- 3rd MT within 6 wk,	H and † uptake 1st- 3rd MT, adj cunei- forms and diffuse posterior healing fx L calcaneus	Marked pos bone and soft tissue calcaneus [FP]	Pos bone and soft tissue [FP]	Not done; gradual resolution within 9 mo	Rapidly progress Charcot L midfoot × 9 mo
	diabetic	Chronic ulcer L heel and in- flamed L calf × 2 wk	Soft-tissue swelling, plantar utcer L midfoot, marked H and O and compression of tarsals, subluxation of TMT jts, atrophy of 5th MT and adj soft-tissue calcif	Focal hyperemia L midfoot and dif- fusely L calf, ↑ up- take all tarsals and prox 4–5th MT	Neg bone [TN], marked pos soft tissue	Not done	Staph a. from ulcer, neg bone	Chronic ulcer L heel     Cellulitis L calf and     foot     Charcot L midfoot ×     6 yr

Note: ( ) = type of peripheral neuropathy affecting the evaluated limbs; BKA = below knee amputation; calc = calcaneus; H = hyperemia; fx = fracture; adj = adjacent; jt = joint; MT = metatarsal; O and H = osteolytic and hypertrophic sclerotic changes; f = increased; TMT = tarso-metatarsal; MTP = metatarso-phalangeal; calcif = calcification; pos = positive; neg = negative; bx = biopsy; prox = proximal; and progression.

adjacent to these joints. The fifth patient was undergoing preoperative evaluation for possible osteomyelitis at an atrophic nonunited wrist fracture.

Nine patients (10 sites) with diabetic neuropathy presented with draining foot ulcers or evidence of soft-tissue infection of the feet. Eight patients had plain film findings of Charcot changes in multiple joints of the feet and one (Case 13) developed radiographic abnormalities in the ensuing 6-wk interval. Two of these had clinical and radiographic findings of Charcot joints in both feet. In both cases, cultures were obtained from one foot only, since the contralateral foot remained stable and asymptomatic by clinical and radiographic follow-up.

# **Scintigraphy**

Each patient underwent three-phase bone scintigraphy after 20 mCi (740 MBq) of i.v. <sup>99m</sup>Tc-MDP. Delayed bone images were acquired for 2,000 i.d./cm<sup>2</sup> using a large field-of-view gamma camera, equipped with a high-resolution collimator, and a 15% window centered at 140 keV. White blood cell (WBC) labeling with <sup>111</sup>In-oxine was accomplished using a modification (11) of the technique reported by Thakur et al. (12). Combined 5-min <sup>99m</sup>Tc-MDP bone and 15-min <sup>111</sup>In-WBC scintigraphs were obtained 18-24 hr after i.v. injection of 400-500 µCi (14.8-18.5 MBq) of <sup>111</sup>In-WBCs. A mediumenergy collimator was used for image acquisition. A 10% window centered at 140 keV was used for <sup>99m</sup>Tc-MDP images, and a 5% window centered at the 173-keV photopeak and a 20% window at the 247-keV photopeak were used for the <sup>111</sup>In-WBC images (13).

The scintigraphic images were interpreted in conjunction with plain films by four of the authors (J.E.S., F.W.F., D.K., and S.C.S.K.) independently without knowledge of patient histories, culture results, and/or clinical course. Duplicate copies of the paired "IIn-WBC/99mTc-MDP images in each projection were utilized so that the "IIn-WBC images could be superimposed over the corresponding 99mTc-MDP bone images, to determine if labeled leukocytes were localized to bone and/or to soft tissue (13). Indium-111-WBC/technetium 99m-MDP images were judged positive for osteomyelitis if "IIIn-WBC uptake corresponded to abnormal bone remodeling and was greater than that of the adjacent or contralateral normal bone marrow. The "IIIn-WBC localization was graded mild, moderate, or marked.

# **Magnetic Resonance Imaging**

The MR studies were interpreted independently in conjuction with the plain films but without the scintigraphs by three of the authors (F.W.F., T.J.G., and S.C.S.K). Magnetic resonance studies were considered positive for osteomyelitis if there was decreased signal intensity on T1-weighted images and increased signal on either T2-weighted or short-tau inversion recovery (STIR) images within the bone marrow compared to normal marrow signal. All MR examinations were performed with either a 0.5-T or a 1.5-T superconductive unit. At least one T1-weighted [recovery time (TR) 400-600 msec. echo time (TE) 20-26 msec] and STIR [TR 2,250-2,450 msec, inversion time (TI) 125-150 msec] or one T2-weighted [TR 1,800-2,300 msec, TE 80-100 msec] pulse sequence were obtained in each MR examination. The slice thickness was 5 mm. Magnetic resonance images were obtained within 1-3 wk of scintigraphy.

#### RESULTS

The clinical and diagnostic imaging results are summarized in Table 1. Two patients (Cases 1 and 2) had false-positive <sup>111</sup>In-WBC/<sup>99m</sup>Tc-MDP images at culture-negative but acutely inflamed ankle and adjacent joints of the foot (Fig. 1). A third patient (Case 3) had a true-negative <sup>111</sup>In-WBC/<sup>99m</sup>Tc-MDP study of a symptomatic right hip joint that had shown recent plain film progression of Charcot changes. Another patient (Case 4) with a perirectal ulcer had serial plain films that showed Charcot changes in both hips and had had prior episodes of osteomyelitis in the right ischium. Scintigraphy of the pelvis and left femur showed true-positive findings at a culture-positive left hip joint and at mid-



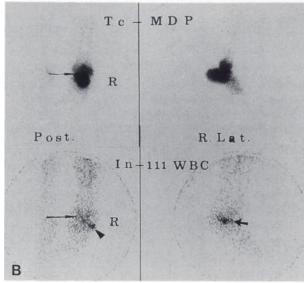


FIGURE 1

A 37-yr-old diabetic (Case 1) with peripheral neuropathy and intermittent pain, swelling, and erythema of right ankle for 3 mo. (A) Radiograph shows soft-tissue swelling of right ankle plus osteolytic destruction of right subtalar joint. Radiographs taken 2 wk previously had shown only soft-tissue swelling. (B) False-positive combined 111 ln-WBC (lower)/99mTc-MDP bone (upper) images show 111 ln-WBC localization corresponding to the abnormal bone remodeling in left subtalar joint (short arrow) and adjacent soft tissue (arrowhead) also extending medially and superiorly into ankle joint (long arrow).

femoral fracture. Both sites were not clinically suspected to have osteomyelitis. The right hip and the prior osteotomy site in the right ischium were true-negative sites.

Case 5, suspected of having early neuropathic osteoarthropathy of the right wrist, showed <sup>111</sup>In-WBC localization at a noninfected, atrophic nonunited fracture (pseudoarthrosis), and at the adjacent wrist joint. Cultures of both sites were negative, but the synovial biopsies of the pseudoarthrosis and adjacent wrist joint

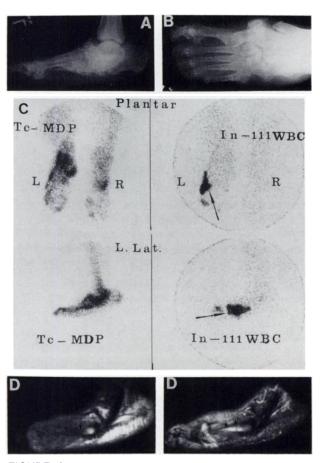


FIGURE 2

A 68-yr-old diabetic (Case 6) with peripheral neuropathy and chronic ulcer over lateral left midfoot for 1 vr. (A) Left lateral and (B) plantar radiographs of left foot show marked destruction and disorganization of tarsal bone and joints (noted on prior radiographs for 6 yr), osteolysis, cortical erosion, and fractures of 5th metatarsal and adjacent soft-tissue calcification. (C) True-positive combined 111In-WBC/99mTc-MDP bone images show abnormal tracer localization along an infected left 5th metatarsal. The 111In-WBC localization corresponds to the abnormal bone tracer uptake along the 5th metatarsal as well as in the adjacent soft tissue (arrows). Note the absence of 111In-WBC localization in the tarsal regions of both feet, which show chronic neuropathic changes on plain films and abnormal bone tracer localization. (D) True-positive MR images show decreased bone marrow signal (arrows) on T1 (left) and increased signal (arrows) on T2 (right) images in left 5th metatarsal. There is also increased signal on T2 images in adjacent dorsal and lateral soft tissues.

revealed inflammatory infiltrates. Unfortunately, this patient expired within a few months from a myocardial infarction, and follow-up radiographs could not be obtained.

Nine patients (11 sites) were evaluated for osteomyelitis involving one or both feet. Two patients (Cases 6 and 7) had true-positive studies on <sup>111</sup>In-WBC/<sup>99m</sup>Tc-MDP images at sites of osteomyelitis and showed no <sup>111</sup>In-WBC localization in adjacent and contralateral chronic Charcot joints (Fig. 2). Case 6 had serial plain film neuropathic changes for 3 yr and Case 7 for 6 yr. Case 11 had true-positive <sup>111</sup>In-WBC uptake at sites of osteomyelitis in the right foot, which had only recently developed neuropathic changes on plain films. In another patient (Case 10) with recent onset of osteoarthropathy, osteomyelitis involving the first metatarsal was not detected on <sup>111</sup>In-WBC/<sup>99m</sup>Tc-MDP imaging (false-negative).

Three patients (Cases 8, 12, and 14) with chronic foot ulcers had true-negative studies at sites in or adjacent to joints showing serial plain film neuropathic changes for 3, 1.5-2, and 6 yr, respectively. One patient (Case 9) had false-positive 111In-WBC localization corresponding to noninfected bone and joints of the left midfoot. Prior plain films had been negative, but additional films showed progressive neuropathic changes during the ensuing 4 mo. One other patient without foot ulcers (Case 13) presented with pain and swelling of the left foot and lower leg. Initial radiographs revealed a healing left calcaneal fracture and narrowing of the first to third tarso-metatarsal joints. Indium-111-WBC/ technetium-99m-MDP images showed moderately abnormal localization at the tarso-metatarsal joints and adjacent soft tissue. Follow-up radiographs within 3 mo showed progressive Charcot changes in the intertarsal and tarso-metatarsal joints as well as additional fractures. Although cultures were not obtained in this case, there has been no evidence of infection during 11 mo of clinical and radiographic follow-up. Furthermore, the patient was stabilized with casting and never received antibiotic treatment. (Subsequently, a second patient has shown very similar clinical and radiographic findings during 6 mo of follow-up.)

Seven of the 14 patients had MRI and all seven showed decreased signal intensity on T1 images and increased signal on T2 and/or STIR images in joint(s) and adjacent bone marrow (Fig. 3). Four of these patients (Cases 6, 7, 10, and 11) had positive bone cultures obtained from these sites. However, the three remaining studies showed identical MR findings at culture-negative sites in patients with recent onset, rapidly progressing Charcot osteoarthropathy (Cases 2, 9, and 13). In contrast, the T2-weighted and STIR images of chronic noninfected Charcot joints did not show increased signal intensity. In addition, these joint space(s) were not well delineated.

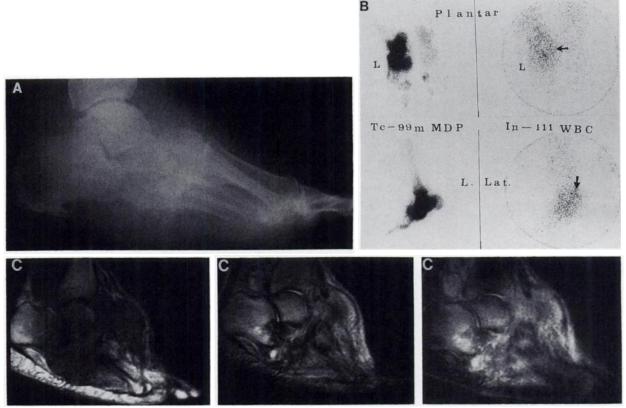


FIGURE 3

A 57-yr-old alcoholic (Case 2) with severe peripheral neuropathy, who presented with pain and swelling of left ankle and foot, plus a dry ulcer on the plantar aspect of the foot for 6–9 mo. Multiple bone aspirations and biopsies were culture negative. (A) Radiograph of right foot and ankle shows soft-tissue swelling and mixed osteolytic and hypertrophic sclerotic changes of anterior talus, anterior calcaneus, and tarsal bones. These findings were less severe in radiographs taken 4 and 15 mo previously. (B) False-positive combined <sup>111</sup>In-WBC (right)/<sup>99m</sup>Tc-MDP bone (left) images show marked bone remodeling manifested by increased uptake in the left ankle and midfoot on the bone images. There is also diffuse <sup>111</sup>In-WBC localization in the corresponding regions, which extends into the adjacent soft tissue (arrows). (C) False-positive MR images show decreased bone marrow signal on T1 (left) and increased signal on T2 (middle) and STIR (right) images in anterior calcaneus and tarsal bones of right midfoot as well as adjacent soft tissue.

## DISCUSSION

Neuropathic osteoarthropathy usually occurs in limbs affected by peripheral somatic and autonomic neurologic deficits. Sympathetic denervation of arterioles causes vasodilatation and arteriovenous shunting, which increases blood flow to the limb (1,4). This is associated with the development of osteopenia, which predisposes bone to stress fractures (1,14). Loss of motor innervation results in muscle weakness and wasting, leading to abnormal weight distribution on adjacent bone and joints (1,4). Ligaments and joint capsules frequently become stretched, resulting in joint instability and subluxation. Loss of normal pain response mechanisms often leads to additional mechanical injury to the region. Thus, relatively minor trauma can initiate rather marked inflammation and destructive changes in susceptible bones and joints.

Radiographically, there are two forms of neuropathic joints: hypertrophic and atrophic (1). The hypertrophic

form is found most frequently in the tarso-metatarsal, metatarso-phalangeal, ankle, and subtalar joints. It is characterized predominantly by destructive and reparative changes: joint narrowing, subluxation and dislocation, bone fragmentation, erosion, fracture, sclerosis, periosteal new-bone formation, and soft-tissue calcification. The atrophic form is most commonly identified in the upper limbs and usually shows resorption of bone at the joint margins.

Three-phase bone scintigraphy is extremely sensitive for detection of early Charcot bone changes, but cannot differentiate between neuropathic osteoarthropathy and osteomyelitis (6,8). Both Charcot osteoarthropathy and osteomyelitis cause considerable bone remodeling, which results in increased radiophosphate accumulation. Combined <sup>67</sup>Ga/bone imaging is not reliable for establishing a diagnosis of osteomyelitis because <sup>67</sup>Ga also accumulates in sterile Charcot osteoarthropathy (7,8).

Recent publications suggest that 111In-WBC/99mTc-

MDP imaging appears promising for identifying infected Charcot osteoarthropathy (8-10,15,16). Schauwecker et al. (16,17) have reported better results using <sup>111</sup>In-WBC/<sup>99m</sup>Tc-MDP imaging for detection of coexisting osteomyelitis in neuropathic feet rather than osteomyelitis at other sites. This was attributed to two factors: less surrounding soft-tissue background activity and the lack of active <sup>111</sup>In-WBC uptake in the normal bone marrow of the feet. Two of their false-positive studies resulted from active overlying soft-tissue infection (16).

In our series, five false-positive studies occurred in patients with recent-onset, rapidly progressing Charcot osteoarthropathy. Furthermore, two of the four cases with little or no plain film findings to suggest Charcot osteoarthropathy were initially thought to have thrombophlebitis because of the marked swelling and erythema extending into the calf. It is likely that sites of rapidly progressing Charcot have a greater degree of active inflammation and/or reparative changes than sites with long-standing Charcot osteoarthropathy. In addition, 111In-WBC localization occurs at noninfected acute fracture sites (9,10,18). Stress or insufficiency fractures frequently occur at sites of neuropathic osteoarthropathy and may not be seen on plain-film radiographs. Increased bone remodeling, fibro-osseous metaplasia, periosteal callus, and heterotopic soft-tissue ossification can also cause 111In-WBC localization (13, 18). The poor spatial resolution afforded by radiotracer techniques is another factor that can make it difficult to determine if osteomyelitis is present at sites that have adjacent soft-tissue infection.

Three-dimensional imaging with MR has proved useful in differentiating between bone and soft-tissue infection (19-23). The accuracy of MRI for detection of osteomyelitis complicating Charcot osteoarthropathy has not been reported. In this series, four of seven patients had true-positive MRI studies for osteomyelitis. However, three patients with sites of noninfected, rapidly progressing Charcot showed findings indistinguishable from those observed in the culture-positive cases (Fig. 3).

Magnetic resonance imaging has been shown to have high sensitivity and specificity for detecting osteomyelitis when there are no concurrent fractures (24). However, signal changes that occur after recent surgery or healing fracture are difficult to differentiate from active osteomyelitis within the medullary cavity (19,23). The signal intensity of healing granulation tissue can be similar to that of osteomyelitis for 3-6 mo after an acute fracture (23). Berquist et al. (19) reported <sup>111</sup>In-WBC imaging to be more useful than MRI for diagnosing infection at fracture sites. Yuh et al. (25) recently reported false-positive MR marrow findings in the feet of diabetic patients who had recent fractures or surgery. In addition, early stress fractures not visible on radio-

graphs may cause marrow signal changes on MRI.

In summary, the findings of <sup>111</sup>In-WBC/<sup>99m</sup>Tc-MDP and MR imaging at sites of noninfected, rapidly progressing neuropathic osteoarthropathy may be indistinguishable from those of osteomyelitis. Thus, radiologic and/or scintigraphic findings of osteomyelitis in patients with peripheral neuropathy may indicate the onset of noninfected, rapidly progressing Charcot osteoarthropathy.

#### **ACKNOWLEDGMENTS**

Presented in part at the 36th Annual Meeting of the Society of Nuclear Medicine, St. Louis, MO, June 13–16, 1989.

The authors thank Jan Widmer and LuAnn Osdoba for secretarial assistance, Phyllis Bergman for editorial assistance, John Bricker for technical assistance, and John Johnson for photographic assistance in the preparation of this manuscript.

### REFERENCES

- Bruckner FE, Howell A. Neuropathic joints. Semin Arthritis Rheum 1972; 2:47-69.
- Goldman F. Identification, treatment, and prognosis of Charcot joint in diabetes mellitus. J Am Podiatry Assoc 1982; 72:485-490.
- Brooks AP. The neuropathic foot in diabetes. Part II: Charcot's neuroarthropathy. New York: John Wiley & Sons; 1986: 116-118.
- Edmonds ME. The diabetic foot: pathophysiology and treatment. Clin Endocrinol Metab 1986; 15:889-916.
- Frykberg RG, Kozak GP. The diabetic charcot foot. In: Kozak GP, Hoar SC, Rowbatham JL, et al, eds. Management of diabetic foot problems. Philadelphia: WB Saunders; 1984: 103-112.
- Park H, Wheat LJ, Siddiqiri AR, et al. Scintigraphic evaluation of diabetic osteomyelitis: concise communication. *J Nucl Med* 1982; 23:569–573.
- Glynn TP Jr. Marked gallium accumulation in neurogenic arthropathy [Letter]. J Nucl Med 1981; 22:1016-1017.
- Knight D, Gray HW, McKillop JH, Bessent RG. Imaging for infection: caution required with the charcot joint. Eur J Nucl Med 1988: 13:523-526.
- Nostrand DV, Abreu SH, Callaghan JJ, Atkins FB, Stoops HC, Savory CG. In-111-labeled white blood cell uptake in noninfected closed fracture in humans: prospective study. *Radiology* 1988; 167:495-498.
- McCarthy K, Velchik MG, Alavi A, Mandell GA, Esterhai JL, Goll S. Indium-111-labeled white blood cells in the detection of osteomyelitis complicated by a pre-existing condition. J Nucl Med 1988; 29:1015-1021.
- Ponto JA, Seabold JE. Time course of indium-111 oxine labelling of human leukocytes. *Nucl Med Commun* 1984; 5:769-733.
- 12. Thakur ML, Coleman RE, Mayhill CG, et al. Preparation and evaluation of In-111 labeled leukocytes as an abscess imaging agent in doses. *Radiology* 1976; 119:731-732.
- Seabold JE, Nepola JV, Conrad GR, et al. Detection of osteomyelitis at fracture nonunion sites: comparison of two scintigraphic methods. AJR 1989; 152:1021-1027.
- Brady TF, Edmonds ME, Watkins PJ. Osteopaenia and metatarsal fractures in diabetic neuropathy. *Diabetic Med* 1985; 2:461-464.

- Maurer AH, Millmond SH, Knight LC, et al. Infection in diabetic osteoarthropathy: use of indium-labeled leukocytes for diagnosis. *Radiology* 1986; 161:221-225.
- Schauwecker DS, Park HM, Burt RW, Mock BH, Wellman HN. Combined bone scintigraphy and indium-111 leukocyte scans in neuropathic foot disease. J Nucl Med 1988; 29:1651.
- Schauwecker DS. Osteomyelitis: diagnosis with In-111-labeled leukocytes. *Radiology* 1989; 171:141-146.
- Kim EE, Pjura GA, Lowry PA, Gobuty AH, Traina JF. Osteomyelitis complicating fracture: pitfalls of <sup>111</sup>In leukocyte scintigraphy. AJR 1987; 148:927-930.
- Berquist TH, Brown ML, Fitzgerald RH, May GR. Magnetic resonance imaging: application in musculoskeletal infection. *Magn Reson Imaging* 1985; 3:219-230.
- Modic MT, Feiglin DH, Piraino DW, et al. Vertebral osteomyelitis: assessment using MR. Radiology 1985; 157:157– 166.

- Modic MT, Pflanze W, Feiglin DH, Belhobek G. Magnetic resonance imaging of musculoskeletal infections. *Radiol Clin* North Am 1986; 24:247-258.
- Beltran J, Noto AM, McGhee RB, Freedy RM, McCalla MS. Infections of the musculoskeletal system: high-field-strength MR imaging. *Radiology* 1987; 164:449-454.
- Berquist TH. The musculoskeletal system. In: Higgins CB, Hricak H, eds. Magnetic resonance imaging of the body. New York: Raven Press; 1987:469-489.
- Beltran J, McGhee RB, Shaffer PB, et al. Experimental infections of the musculoskeletal system: evaluation with MR imaging and Tc-99m MDP and Ga-67 scintigraphy. *Radiology* 1988; 167:167-172.
- 25. Yuh WTC, Corson JD, Baraniewski HM, et al. Osteomyelitis of the foot in diabetic patients: evaluation with plain film, 99mTc-MDP bone scintigraphy, and MR imaging. AJR 1989; 152:795-800.

(continued from page 3A)

## ANSWERS TO THE MAY QUIZ

Five Blessings (wu fu) of the Chinese Long Life; Wealth (Health); Tranquility (Virtue); Love; and a Peaceful End.

Five Books of Moses (Pentateuch) that comprise the Old Testament Genesis; Exodus; Leviticus; Numbers; Deutoronomy. On the fifth day, birds and fish were created.

Five Days of the work week Monday-Day of the Moon; Tuesday-Day of Mars (OHG Ziesdag-Zues Day); Wednesday-Wodens day-Day of Mercury; Thursday-Day of Thor-(Day of thunder); Friday-Named for Odin's wife-Frigg. Friday is also called Hangman's Day since many hangings were carried out on Friday.

Five Cardinal Relations between Men (Confucianism) Price and Officer; Father and Son; Elder and Younger Brother; Husband and Wife; Friend and Friend.

**Five Nations** The five American Indian tribes making up the Iroquois Confederation-Cayuga; Mohawk; Oneida; Onondaga; Seneca.

**Five Sacred Wounds** The wounds made by the nails and the soldier's spears in the body of the crucified Christ.

Five Senses Sight; Sound; Touch; Smell; and Taste.

Fifth Column Subversive, Sabotour.

**Fifth Estate** Scientists—The first four estates are the Clergy, the Noblemen, the Serfs, and the Press.

**Fifth House** One of the 12 sectors of the horoscope dealing with the houses of the earth—the Fifth House deals with offspring, pleasures, and speculation.

Fifth Wheel An extra part (e.g., spare tire).

**Fifth Business** In old repetory theatres, a minor role which is essential to the plot or the individual given such a role.

Fifth Dimension A popular singing group.

Fifth Element Boron.