CHAPTER 54

Imaging of the Infected Foot Fact or Fancy?

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"The scientific basis and the artful usage of medical knowledge may be distant in the clinical practice," (personal communication, LS Reyilleni, 1990).

The virtue of diagnostic imaging in foot infections is nebulous. Despite the continual sophistication of technology, the diagnosis and treatment of suspected osteomyelitis in the foot remain a complex clinical challenge. The challenge is multifaceted and encompasses many considerations confronted in clinical medicine today. Assessment of foot infections is often a multidisciplinary task and may require coordination of appropriate contributions from infectious disease specialists, radiologists, internists, and vascular surgeons. Effective evaluation of patients with foot infections demands skill and judgment. Treatment of osteomyelitis potentially involves long-term antibiotic therapy, prolonged hospital stays, and surgical intervention.

Many diagnostic efforts revolve around recent developments in nuclear medicine and radiology. A tendency exists for practitioners to expect new modalities to readily solve difficult cases of questionable osteomyelitis. The clinical reality is they do not necessarily provide the answers desired. All medical professionals must renew a spirit of critical inquiry concerning the role of imaging in suspected osteomyelitis. Are the conclusions of the scientific literature germane to lower extremity pathology and readily applicable in the local community hospital or private practice? Translation of current medical research or technological advances into tangible adjuncts that refine and economize patient care is the essence of the challenge.

A tenet of quality scientific research is accountability for identifiable variables. Likewise, the practical application of such research demands cognizance of those inherent variables. Comprehension of the imaging literature and its clinical relevance to podiatric medicine and surgery are the issues.

The anatomy of osseous tissue and the pathogenesis of osteomyelitis are key factors in new imaging theories; specifically, this concerns the skeletal location and marrow content. The central or axial skeleton, such as the spine, contains predominantly red or active bone marrow. The peripheral or appendicular skeleton contains more yellow or inactive marrow. These differences are the basis for the localization of certain radionuclides. The etiology of the disease process, such as hematogenous spread and direct invasion from contiguous soft tissue infection, or temporal factors such as acute and chronic conditions selectively improve the efficacy of certain techniques.

The modalities used to investigate osteomyelitis may be divided into two principal groups. Techniques such as plain films, computed tomography, magnetic resonance imaging, and ultrasound identify morphological or structural change in bone as evidence of infection. The radiopharmaceuticals seek to identify lesions that are inflammatory or infectious by cellular response. There is a general lack of standardization in the technical production of these modalities. Materials and methods vary considerably among institutions. Disparity in qualifications of investigators adds further subjectivity to the studies. Last, the effective management of problematic subsets of patients with lower extremity pathology requires extrapolation of conclusions. The physician must incorporate all variables into each treatment plan. Imaging in osteomyelitis should be undertaken with an appreciation of technological progress, but tempered by practical thought processes that enable the physician to optimally manage difficult cases.

ANALYSIS OF THE LITERATURE

Endeavors to diagnose osteomyelitis with imaging techniques hinge on an interplay between radiographic studies and scintigraphy, and, recently, radioimmunoscintigraphy. To summarize the current thought is a herculean task. Methods are discussed monthly in the radiographic, orthopedic, podiatric, and nuclear medical literature in an effort to more effectively diagnose osteomyelitis by noninvasive measures.

Generally, the imaging modalities are fairly sensitive, poorly specific, and exhibit wide variability. Sensitivity is the ability of a test to detect all patients with the disease. It is the true positive results divided by the sum of the true positives and false-negatives. Specificity is the ability of a test to determine those patients without disease. It is the true negative results divided by the sum of the true negatives and false-positives.[1] Advocates and detractors debate the validity of every modality for the diagnosis of osteomyelitis.

Computed tomography has been sporadically used as an aid in the evaluation of the diabetic foot.[2] Favorable reports indicate that computed tomography provides effective identification of the sequestra and cloaca of chronic osteomyelitis and depicts intraosseous gas, an infrequent but reliable sign of osteomyelitis.[3–8] Conversely, limited contrast discrimination of computed tomography underscores the difficulty in reliably distinguishing between infection and abnormal soft tissue densities.[9, 10] The gradual transition between infected and normal soft tissues on computed tomography images increases the degree of subjectivity in defining the proximal margin of disease.[9] Contrast-enhanced computed tomography has been somewhat useful in diagnosing subperiosteal abscesses and osteomyelitis in sickle cell patients. Some authors believe it the preferred modality for the evaluation of suspected soft tissue and bone infection.[11–13]

Magnetic resonance imaging has become the standard imaging technique for discerning spatial and soft tissue contrast and resolution.[14–16] Subtle inflammatory changes within the marrow are now easily appreciated.[17–20] The intramedullary fluid signal of acute hematogenous osteomyelitis manifests as decreased signal intensity on T1 images and hyperintensity on T2 images.[3, 7, 15, 16, 20–26] However, there is considerable debate over the ability of magnetic resonance imaging to differentiate osteomyelitis from healing fractures, stress fractures, previous surgery, infarction, osteonecrosis, tumor, metastasis, acute progressive neuroarthropathy, and gout.[21, 24, 25, 27–33] Conflicting reports exist regarding magnetic resonance imaging findings in acute versus chronic Charcot disease, active infectious foci in chronic osteomyelitis, and bone contiguous to septic arthritis.[25] Further refinements that may enhance this technique include gadolinium enhancement and variations of the standard spin echo images.[6, 16, 17, 20–22, 29, 34–39] Fat suppression techniques, such as Short Tau Inversion Recovery, selective nonexcitation water imaging, and the chemical shift selective Dixon method, further improve contrast between normal and abnormal tissue.[15, 18, 23, 29, 40–42]

Other authors have cautioned against overconfidence in these sequences and claimed that T1 is as sensitive as Short Tau Inversion Recovery in peripheral marrow.[21, 23, 25, 43] Magnetic resonance imaging is not completely specific for the diagnosis of bone infection.[25, 44, 45] Reports concerning magnetic resonance imaging scans are diluted by a diversity of field strengths, pulse sequences, and diagnostic criteria. Factors like positioning, surface coil selection, and partial volume effects add further difficulty when comparing results or attempting to standardize methods between studies.[3, 23, 25, 31, 46] The most enlightening contributions of magnetic resonance imaging appear to be in facilitating surgical planning, establishing anatomical extensions of pathologic processes, and having an impact on clinical management.

The documentation of ultrasound as an imaging technique for bone infection is limited and not specifically correlated to the foot.[47–49] The small surface area of the bones of the foot makes ultrasound studies difficult.[31]

Radionuclide skeletal scintigraphy was popularized with ^{99m}Tc and then ^{67}Ga for earlier detection of osteomyelitis than conventional skeletal radiography.[1, 50–53] While the scans are generally sensitive, difficulty in differentiating bone infection from nonosseous inflammatory disease means that these studies are nonspecific.[54–63] False-positive and false-negative results are reported in as many as 40% of cases because of the superimposed abnormalities, such as neuropathic joint disease, trauma, arthritides, metabolic disorders, metastasis, and chronic soft tissue change.[1, 14, 21, 24, 54, 57, 59, 64–71] Technetium-99m

localization is dependent on osteoblastic activity as well as tracer delivery and therefore may fail to demonstrate positive results in proven osteomyelitis caused by infarction or reduced blood flow.[72–75] Technetium-99m uptake ceases at 4 hr in lamellar bone and persists for 24 hr in the woven bone affected by osteomyelitis.[71] Images taken at 24 hr increase specificity for bone infection, particularly in patients with peripheral vascular disease.[1, 7, 71]

Gallium-67 also localizes at sites of noninfective osseous reactive lesions, such as tumors, healing fractures, noninfected orthopedic implants, pseudarthroses, previously treated osteomyelitis, osteoarthritis, and gout.[1, 61, 63, 76–80] Accumulation in sterile Charcot osteoarthropathy occurs, and bone imaging enhanced with ^{67}Ga and ^{99m}Tc is a reliable indicator in only 25% to 33% of patients with infection.[63, 64, 81] An accuracy rate of only 70% is reported.[82, 83] Even the best results from radionuclide scanning often provide inadequate spatial resolution in the foot with the attendant difficulty of precisely localizing an infectious process.[27, 30]

Leukocytes labeled with ^{111}In or Tc-HMPAO were introduced in an attempt to overcome the limitations of other isotope-based scanning techniques.[84–86] A compilation of 16 studies using ^{111}In-labeled leukocyte scans disclosed a sensitivity of 88% and specificity of 85% for osteomyelitis.[14] Generally, pitfalls with ^{111}In-labeled white blood cells include the visualization of aseptic soft tissue or bone inflammation, hyperemia, and inflammatory arthritis.[49, 55, 87]

Specific false-positive results have been reported in noninfected acute closed fractures, stress fractures, diabetic neuropathic osteopathy, rheumatoid arthritis, noninfected prostheses, synovitis, neuromas, and tumors[30, 49, 55, 89–98] Similarly, chronic or indolent infectious processes that consist predominantly of lymphocytic populations further reduce the sensitivity for this modality.[61, 63, 93, 94, 99] Impaired leukocyte responsiveness secondary to tissue necrosis, poor blood supply, and avascular bone marrow may all create additional false-negatives results.[49, 99, 100] Furthermore, the extent of soft tissue uptake of leukocytes compared with the adjacent bone is difficult to determine in locations with minimally active bone marrow like the foot.[100] Lastly, indium scanning is time consuming, costly, and requires meticulous technique and considerable experience.[49, 101, 102] Technetium hexamethylpropylenamineoxime-labeled leukocytes have been used in evaluating various inflammatory conditions and adolescent osteomyelitis with some favorable results.[103–105] Distinct advantages over ^{111}In are the availability of the radionuclide and a higher sensitivity caused by an increased radioactivity.[14] False-positive and false-negative results are similar to ^{111}In.[105–111] Radiocolloid bone marrow imaging with ^{99m}Tc-labeled sulfur or albumin colloid has also been used in conjunction with ^{111}In. The combination of agents has resulted in a number of false-positive studies and increased the diagnostic accuracy of ^{111}In white blood cells alone for the detection of musculoskeletal infection.[19, 112–115]

Indium-111 oxine chloride has also been advocated for imaging adult chronic osteomyelitis.[116] However, in comparisons with ^{111}In leukocytes, no significant difference was found between these two techniques.[73, 117] Indium-111 chloride shows some utility when compared with ^{99m}Tc in imaging experimental osteomyelitis and detecting infection around prostheses.[62, 118] Its major limitation is the difficulty of separating bony involvement from adjacent soft tissue infection.

Preliminary radioimmunoscintigraphy studies have shown some promise, but are unrefined. Newer modalities include ^{99m}Tc or ^{123}iodine-labeled mouse monoclonal antibodies, ^{99m}Tc, or indium-labeled polyclonal nonspecific human immunoglobulin and ^{99m}Tc-labeled antigranulocyte antibodies.[119–125] The human antibody technique is preferred because of a human antimouse antibody reaction observed in some studies.[14, 120] The advantages of these new modalities are less technical and time-consuming nuclide preparation. However, the techniques do not completely eliminate the poor specificity of differentiating aseptic inflammation, nonspecific arthritis, osteotomies, or fracture healing from bone or joint infection.[13, 120, 121, 126, 127] Further comprehensive clinical studies are needed.[121, 128]

On the horizon, an enzyme-linked immunosorbant assay to measure the antibody response to exocellular protein antigens of *Staphylococcus aureus* in bone infection is under investigation.[129]

The clinical pertinence of all of these modalities to the average podiatric medical practice is not clear. Some of these techniques are used to evaluate infectious foci in different anatomical areas of the body. Therefore, caution must be exercised in interpreting the conclusions of such studies and extrapolating their results relative to the foot and ankle.

Another factor to consider is that experimental design and research study control are more

easily standardized in major university settings. Accordingly, the results may not be reproducible in smaller community hospitals where many podiatrists practice. The imaging techniques may not even be performed in a practitioner's local hospital exactly as they were in the institution that produced the literature. Variations in methodology, such as radionuclide handling, preparation technique, scintillation camera intensities, and a multitude of protocols, are complicating variables among the diagnostic imaging modalities.[14, 21, 73]

In an ideal world, the perfect imaging technique would localize the infectious process in a cellular manner, visualize the bone marrow accurately, and detect structural changes in the bone. This perfect modality does not exist. No nuclear imaging method clearly distinguishes inflammation from infection. Even when the most specific modalities are used, such as monoclonal antibodies against infecting organisms, the major cause of localization of the imaging agent may be a nonspecific one.[128, 130] Paradoxically, the challenge of defining the role of imaging in osteomyelitis in the foot is heightened by the proliferation and evolution of imaging technology.

CLINICAL SUBSTANTIATION

The intent of this presentation is to determine the practical utility of imaging techniques for the diagnosis of osteomyelitis in the foot and ankle. The authors will specifically 1) identify realistic applications and expectations of the imaging modalities available; 2) depict the limitations of these studies as they pertain to the diagnosis of infection; 3) emphasize that bone biopsy and culture remain essential in the diagnosis of osteomyelitis; and 4) delineate a guideline for the rational and cost-effective use of the imaging modalities in private practice. These objectives are readily illustrated and substantiated by clinical examples.

Why are imaging techniques used so frequently? Simply stated, the modalities presumably aid in the diagnosis of osteomyelitis. Accurate and prompt identification of bone infection is critical. A differential diagnosis for this affliction includes soft tissue infection, bone or joint infection, postoperative or traumatic sequelae, diabetic neuroarthropathy, and rheumatologic or neoplastic processes.

A number of case studies will be used to demonstrate the uses and misuses of the imaging modalities in the effort to identify osteomyelitis. This collection represents a cross sample of patients potentially seen in a typical podiatric medical practice.

Case 1

A 75-year-old cachectic female presented with exquisite pain and pregangrenous changes of the fifth toe. Cellulitis originating at the site extended above the ankle. She resisted efforts to inspect the interspace. A ^{99m}Tc scan revealed no activity on the first or angiogram phase for nearly 45 sec. The comparison of the third *versus* fourth bone phases showed an increase of less than one integer and was determined to be doubtful for osteomyelitis by the radiologist. However, eventual inspection of the fourth interspace under a local field block revealed the partially eroded head of the proximal phalanx of the fifth toe protruding through the skin. Additional vascular studies changed the surgeon's plan from fifth toe resection to a below the knee amputation.

Case 2

An 83-year-old bedridden male presented with a chronic ulcer beneath the fifth metatarsal head. The bone could be probed through the ulcer. Plain films showed obvious dissolution and destruction of the fifth metatarsal head and proximal phalanx (Fig. 1A). A ^{99m}Tc scan revealed no uptake in this region. However, there was activity at the first and second digits but no integumentary compromise (Fig. 1B).

Case 3

A 57-year-old diabetic female presented with thermal burns of each hallux from a heating pad (Fig. 2A). The distal phalangeal tufts were exposed bilaterally. Her surgical history included a first metatarsophalangeal implant arthroplasty and a fifth metatarsal osteotomy for tailor's bunion correction 2 years earlier (Fig. 2B). An initial ^{99m}Tc scan did not show appreciable changes between the 3-hr and 24-hr phases for either hallux and was therefore interpreted as "doubtful for osteomyelitis" by the radiologist (Fig. 2C). Bone biopsies and cultures revealed fungal osteomyelitis of the left distal phalanx and no osteomyelitis of the right distal phalanx. The well healed fifth metatarsal osteotomy showed more intense radionuclide uptake 2 years after surgery than either hallux.

Plain film radiographic studies are predomi-

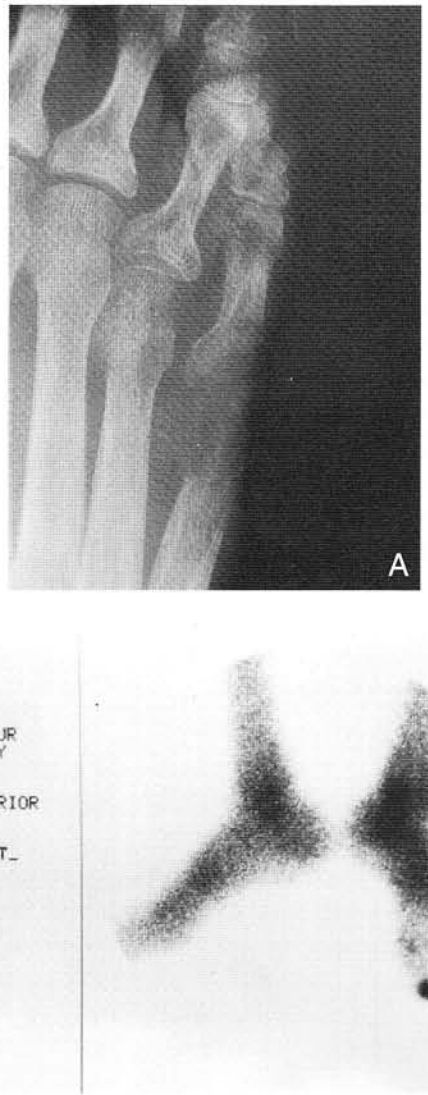

Figure 1. A, Gross dissolution of the fifth metatarsal head and the base of proximal phalanx. **B,** Technetium-99m scan shows focal activity on the first and second digits, but not on the fifth digit.

nantly valuable as a baseline record for future reference. Soft tissue evaluation is certainly nonspecific, but may be enhanced with the use of mammography films or xeroradiography. Osseous dissolution may be seen as early as 5 to 7 days, but the classic signs of osteomyelitis will take longer.[131] Any destructive bone process, regardless of the etiology, may appear similar on plain films. Additionally, plain films are poor indicators of the course of disease. A patient may improve clinically while showing x-ray signs of progressive disease.[62]

Technetium-99 methylene diphosphate bone scintigraphy serves as a metabolic marker binding to hydroxyapatite within the collagen lattice network. Any condition that promotes osseous activity will create a positive ^{99m}Tc scan if the blood supply is adequate for tracer delivery. Technetium scan-

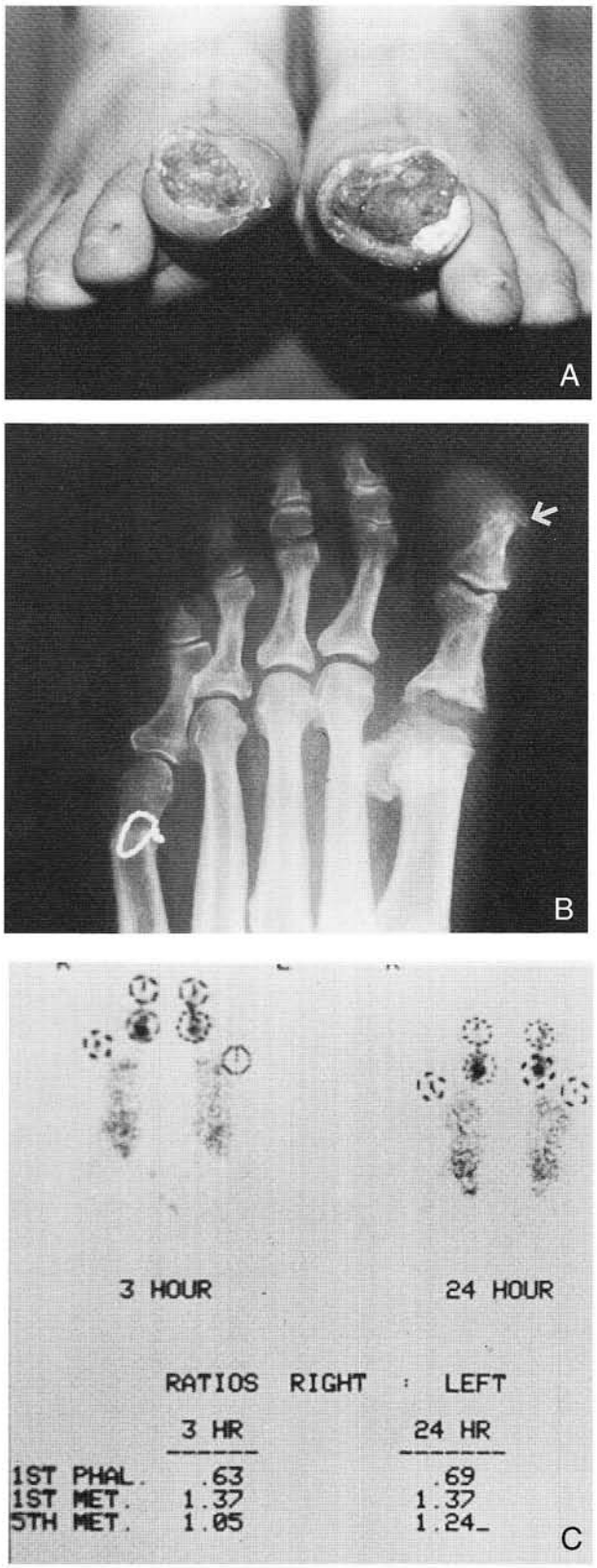

Figure 2. A, Bilateral thermal burns. The white deposit on the left hallux is *Candida albicans.* **B,** The hallucal tuft is exposed (arrow). The fifth metatarsal osteotomy is now 2 years old. **C,** Twenty-four-hour intensity is greater for the fifth metatarsal osteotomy than for the osteomyelitic left hallux.

ning consists of four phases, with the first two phases serving practically as evaluators of vascularity. The third phase, 3 to 5 hr after injection, is called the bone phase. A 24-hr or fourth phase of technetium scanning is also available. It does increase the specificity of the image for osseous involvement, but not osteomyelitis, in comparison with the 3-hr phase. An integer count representing the activity of the region of interest is obtained and compared with the background count. An increase between the third and fourth phase of greater than one whole number is reportedly diagnostic of bone infection. A decrease by greater than one reportedly excludes osteomyelitis and any number in between is labeled indeterminate.[132]

Cases 1 to 3 depict the inherent limitations of the ^{99m}Tc scan and its poor specificity regarding lower extremity infection. Inconsistencies in the vascular supply of individual patients are a frequent drawback. In a healthy patient without vascular compromise, uptake is immediate. The presence of peripheral vascular disease may account for false-negative results, as in cases 1 and 2. Extreme reservation is advised when attempting to assess bone involvement in similar patients. The authors' clinical experience indicates that the third *versus* fourth phase ratios are inconsistent and completely unreliable in diagnosing osteomyelitis, as in cases 1 to 3. The authors have obtained numerous negative bone biopsies after positive fourth phase scans and positive biopsies after negative technetium scans.

Case 4

A middle-aged healthy male was seen 3 weeks after bilateral bunionectomies with forefoot cellulitis. The infectious disease consultant ordered a ^{99m}Tc scan to "rule out osteomyelitis." Not surprisingly, the bone phase showed intense uptake caused by the recent osseous surgery. The 24-hr phase demonstrated an increased uptake that was greater than one integer count bilaterally and the radiologist declared this definitive for osteomyelitis (Fig. 3). Subsequent bone biopsies and bone cultures were negative.

Case 5

A 45-year-old female underwent proximal interphalangeal joint arthroplasty and a phenol nail procedure of the second digit with cheilectomy of the first metatarsophalangeal joint. Her initial postoperative period was uneventful. However, 2 weeks after surgery, she presented to the emergency department of a separate hospital with complaints of chest pain. The internist on call noticed drainage and erythema of the second digit and nail area and ordered a ^{99m}Tc study. The scan revealed focal activity of the first and second digits, which the internist interpreted as osteomyelitis (Fig. 4). Despite the recent osseous surgery, which would account for the positive scan, a 6-week course of intravenous vancomycin was initiated. The patient subsequently developed ototoxicity and renal complications in addition to enduring the expense and inconvenience of this unwarranted treatment.

Case 6

A 43-year-old female suffered residual pain and swelling over the second metatarsal of the right foot 3 months after a plantar condylectomy was performed. The plain films showed metaphyseal dissolution and destruction, but preservation of the

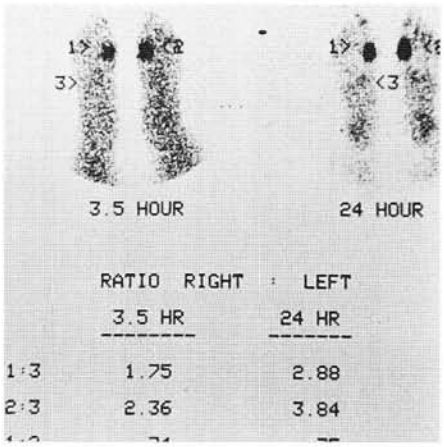

Figure 3. Marked increase in intensity at 24 hr for both first metatarsal heads compared with the uninvolved area.

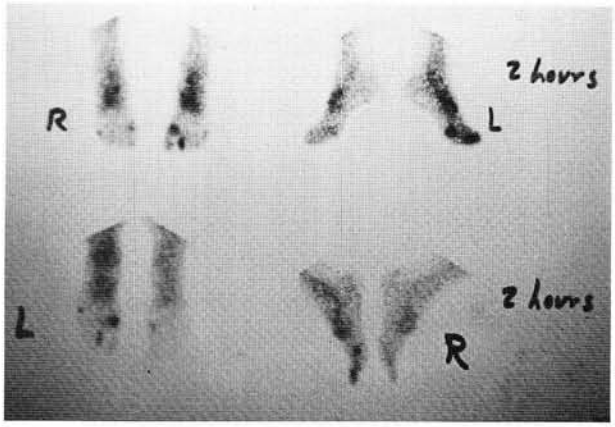

Figure 4. Focal uptake noted on the ^{99m}Tc scan at the second digit and first metatarsal head.

articular surface (Fig. 5A). A positive ^{99m}Tc scan in conjunction with the plain film changes was believed to be indicative of osteomyelitis, despite the recent surgery (Fig. 5B). A complete metatarsal head resection was performed. The microscopic evaluation revealed osteonecrosis that probably represented a Freiberg's infraction, not osteomyelitis.

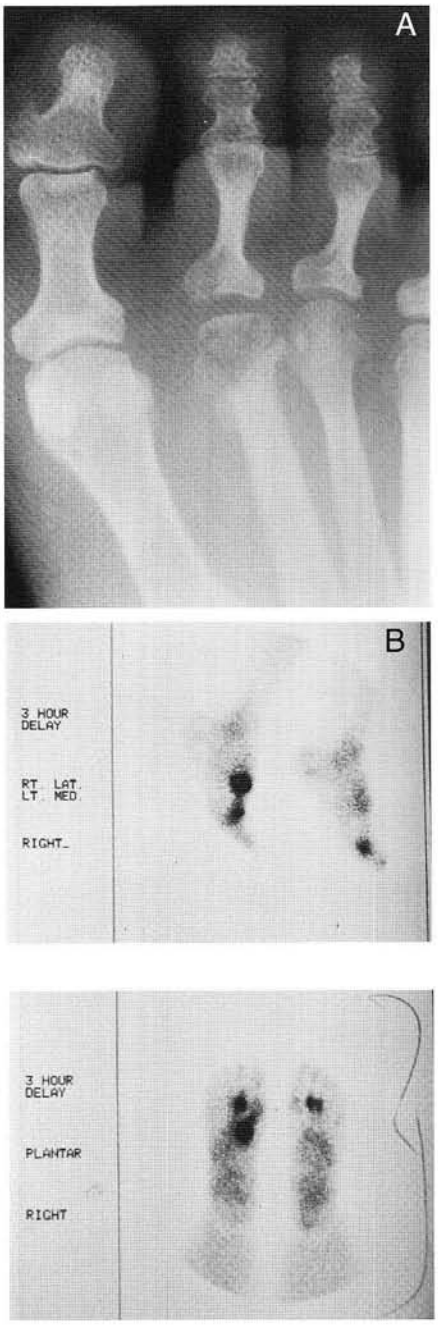

Figure 5. A, Metaphyseal dissolution with articular preservation of the second metatarsal head. B, Technetium-99m scan showing intense activity bilaterally.

Case 7

A patient was convalescing from bilateral Silver bunionectomies and developed dehiscence, erythema, and pain. Erosive changes were seen on the plain films of the first metatarsal head (Fig. 6A and B). He was admitted to the hospital for evaluation and to rule out osteomyelitis. The infectious disease consultant recommended a ^{67}Ga scan that was equivocal and a ^{99m}Tc scan that was positive (Fig. 6C and D). During

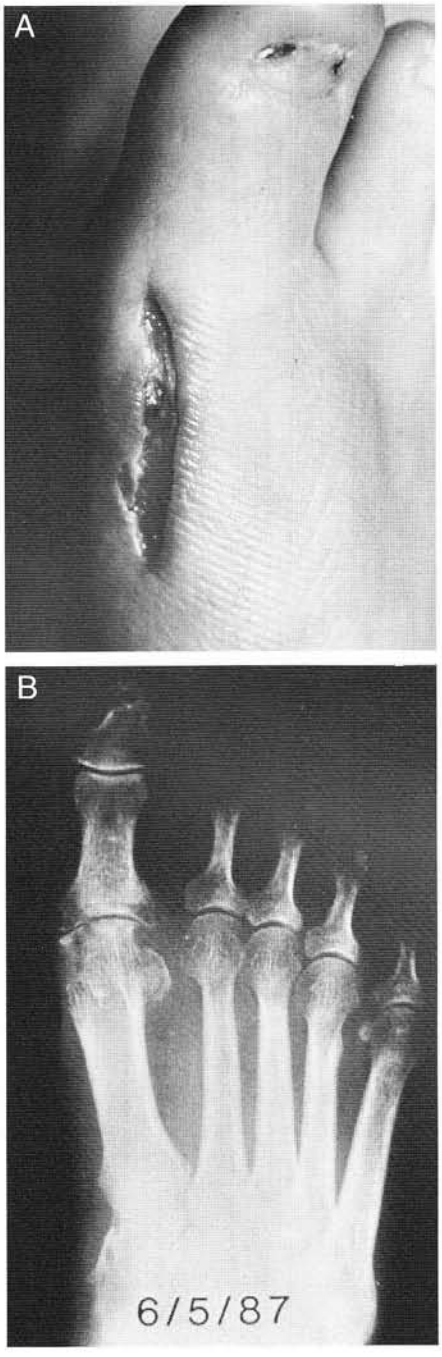

Figure 6. A, Indurated, erythematous surgical incision with dehiscence. B, Erosions of the medial aspect of the first metatarsal head and phalanx.

subsequent open biopsy, tophaceous deposits were encountered and later confirmed as uric acid crystals. This patient suffered a postoperative gout attack and biopsies were negative for osteomyelitis.

Case 8

A 28-year-old healthy male was admitted to the hospital with a postoperative infection after an interdigital neurectomy. He initially responded to incision and drainage and intravenous antibiotics, but the cellulitis recurred 10 days later. There was a concern that perhaps osteomyelitis had developed through contiguous spread from a soft tissue infection. Plain radiographs were negative for any osseous insult and a ^{99m}Tc scan was obtained. Intense uptake was evident on the early blood flow phases consistent with cellulitis (Fig. 7A). The 3-hr and 24-hr delay bone phases were negative, essentially excluding any bone involvement (Fig. 7B). The patient subsequently responded completely to repeat incision and drainage of a remaining abscess and intravenous antibiotics.

Cases 4 to 8 introduce additional factors to those inherent limitations of the ^{99m}Tc scan already illustrated. A ^{99m}Tc scan does not accurately depict the presence or absence of an infectious process when recent osseous surgery has been performed, as in cases 4 to 7. Bone scans ordered in this context will undoubtedly be positive and indeterminate. The nonspecific focal uptake of gallium seen in case 8 merely confirms soft tissue infection. The ^{99m}Tc scan was positive as expected. In this instance, the imaging modalities, in concert with recommendations from consultants, inaccurately suggested that there was osteomyelitis. The only use of the technetium scan in postoperative infections is where surgery was restricted to the soft tissues. A negative delayed phase can then basically rule out bone infection (case 8). Technetium scanning is the most frequently used and inadequately interpreted modality. It requires use in the appropriate context and must serve to affect the eventual treatment of the patient.

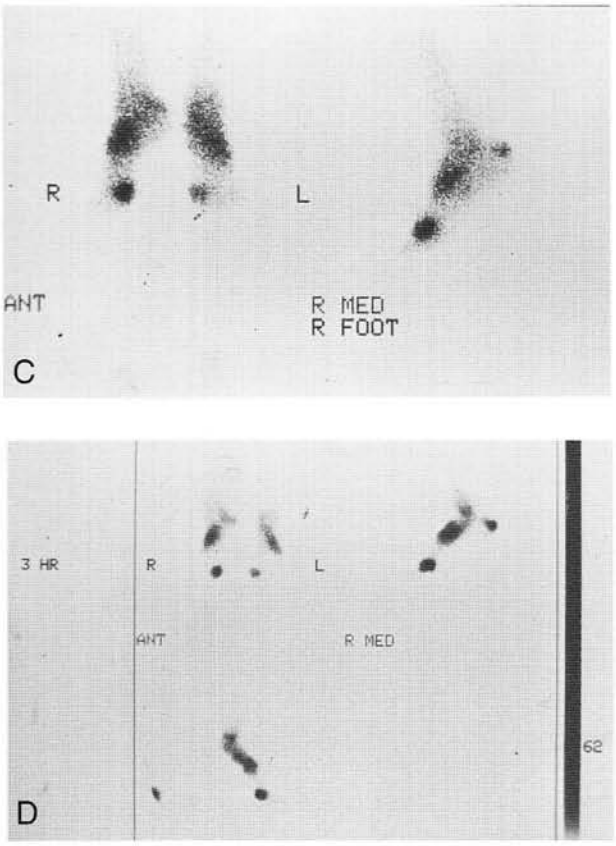

Figure 6. C, Gallium scan showing intense activity at the first metatarsal head. D, Technetium-99m scan showing marked activity at the first metatarsal head.

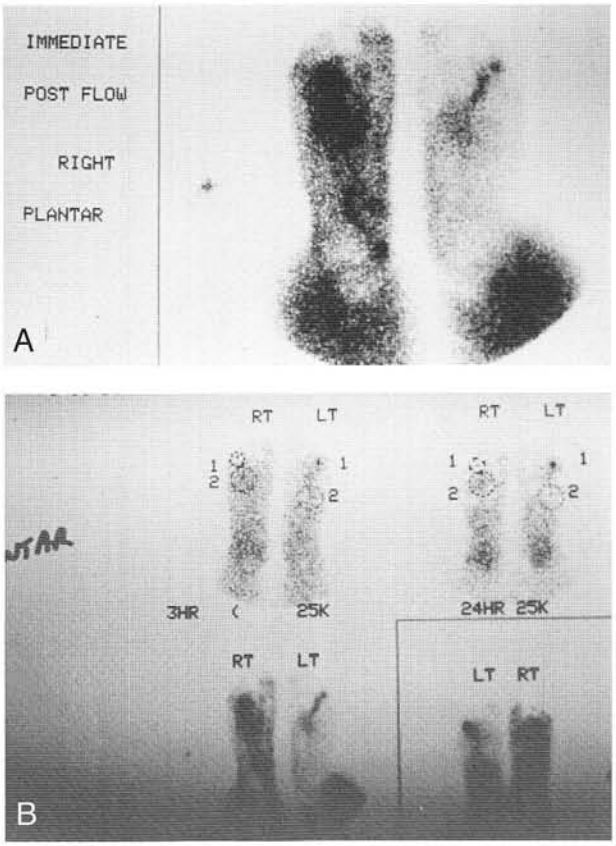

Figure 7. A, Technetium-99m scan showing diffuse intense uptake on the blood flow phase. B, The negative 24-hr scan.

Case 9

A 67-year-old diabetic male developed an infected ulceration under the second digit and metatarsophalangeal joint with concomitant erythema and edema of the midfoot. Plain films showed Charcot changes at the second metatarsophalangeal and Lisfranc joint levels (Fig. 8A). The infectious disease consultant requested a ^{99m}Tc scan, which was significantly positive between the 3-hr and 24-hr phases with the integer count increasing by greater than one (Fig. 8B). The radiologist diagnosed definitive osteomyelitis, and infectious disease personnel recommended a Syme or below the knee amputation. However, because of the documented low specificity of technetium scanning, particularly in light of active Charcot disease, a magnetic resonance image was ordered. A T1 image was the only sequence available for review. This was a suboptimal study and equivocal for osteomyelitis. Multiple metatarsal and cuneiform biopsies were performed instead of amputation and read as negative for osteomyelitis. Three years postoperatively, the patient is active and walking with a functional foot.

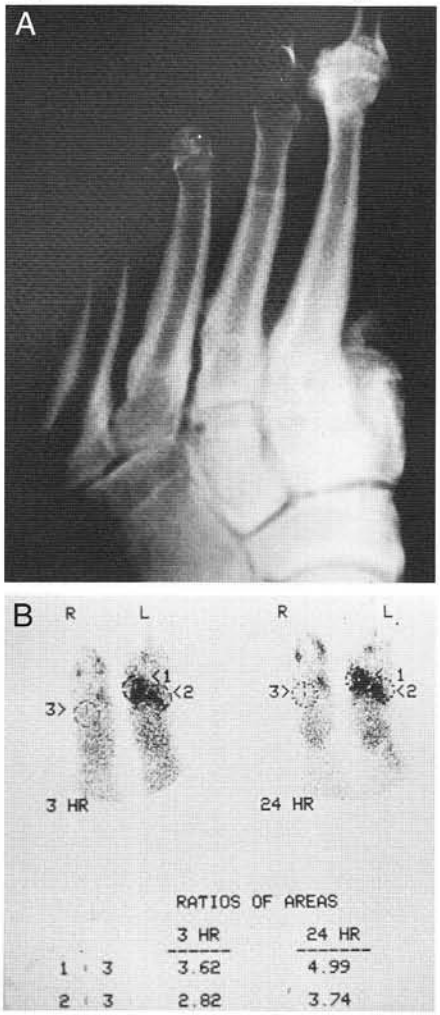

Figure 8. A, Advanced Charcot changes at the second metatarsophalangeal joint and early appearance at the Lisfranc joint. B, Technetium-99m scan showing extremely intense activity between the 3-hr. and 24-hr. phases

Case 10

A patient presented with a swollen, erythematous, and cellulitic forefoot and midfoot. She recounted a history of recent trauma. Plain films were essentially unremarkable and an infectious etiology was suspected. Technetium-99 methylene diphosphate and ^{111}In scans identified activity in the digits and the patient was treated with 6 weeks of intravenous antibiotics for presumptive osteomyelitis (Fig. 9) Subsequent plain films revealed a fracture of the fourth toe.

Case 11

A plantar condylectomy of the second metatarsal was performed to alleviate a plantar ulceration on a diabetic patient. Postoperatively, the patient developed cellulitis, drainage, and dehiscence. An ^{111}In scan obtained in an effort to define the extent of infection was judged equivocal. A ^{99m}Tc scan was questionably positive at the plantar condylectomy site. The 24-hr ratio comparison showed a slight

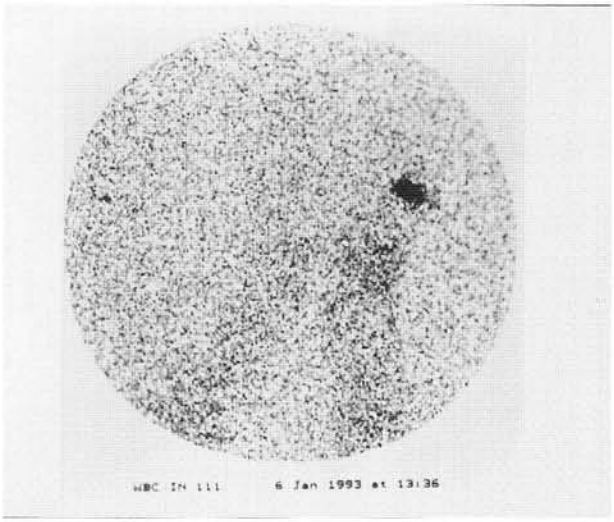

Figure 9. Indium-111 scan showed localized activity presumably at the digital level and corresponded with activity on the ^{99m}Tc scan. This was a false-positive result caused by a fracture.

increase in activity. Eventual bone biopsy and culture were negative for osseous infection.

Case 12

A 35-year-old diabetic female's second toe and metatarsal head were amputated because of osteomyelitis after a nail puncture wound (Fig. 10A). She subsequently presented with a 3-year-old, nonhealing ulcer under the third metatarsal head. Technetium-99 methylene diphosphate, ^{111}In, and magnetic resonance images were all determined to be negative for osteomyelitis (Fig. 10B). A repeat ^{99m}Tc scan was scheduled, but the surgeon intervened and removed the third metatarsal head. Biopsies and cultures were negative for osteomyelitis.

Cases 9 to 12 further broaden the ambiguity of the imaging modalities in relation to osteomyelitis of the foot. Charcot foot deformity or diabetic neuroarthropathy is the classic diagnostic challenge in patients with a suspected bone infection. The hyperemia of the Charcot state and the osseous changes secondary to infection or neuropathy provide for a wide range of sensitivities and specificities for most imaging modalities. Indium-111 oxine scanning is frequently unenlightening for the numerous reasons stated earlier. False-positive results such as the fracture in case 10 are common. False-negative studies are seen in patients with vascular insufficiency or gangrenous changes. Furthermore, the spatial resolution of ^{111}In and other radionuclides is marginal because of the number, size, and close proximity of the pedal bones.

Most importantly, these cases illustrate a prevalent tendency toward the use of multiple modalities despite plausible gain. In case 12, three imaging studies indicated the absence of osteomyelitis. Surgical cultures and biopsy confirmed this. Despite the accuracy of the scans on this occurrence, they still failed to affect the treatment. The patient required osseous resection to eradicate the plantar ulcer.

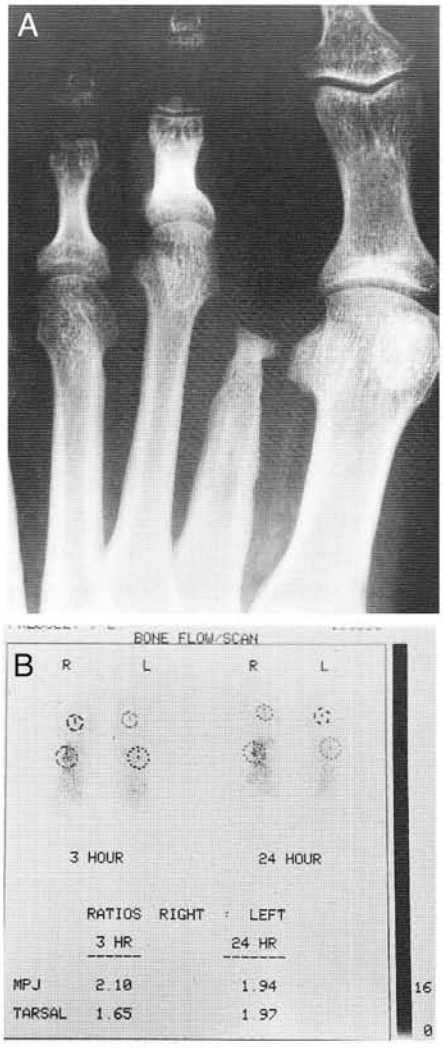

Figure 10. A, The third metatarsal does not appear disrupted. B, Negative 24-hr. ^{99m}Tc scan.

Case 13

A 55-year-old male developed a postoperative infection after surgical intervention for a fractured ankle and dislocated subtalar joint. Questionable plain film changes 9 months later prompted a magnetic resonance imaging to rule out osteomyelitis

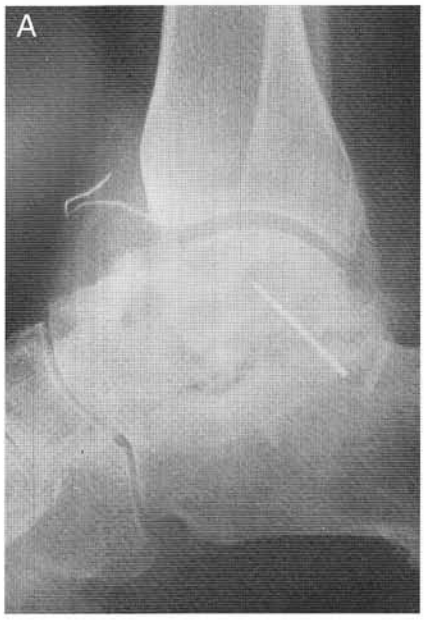

Figure 11. A, Areas of patchy radiolucency throughout the entire talus.

(Fig. 11A). This revealed findings consistent with osteomyelitis and associated osteonecrosis (Fig. 11B and C). Subsequent bone biopsy and culture revealed only avascular necrosis of the talus, and 5 months later, the patient underwent a successful pantalar arthrodesis.

Case 14

A 70-year-old female suffered continued pain, erythema, and swelling of the left first metatarsophalangeal joint after an Austin and Keller bunionectomy.

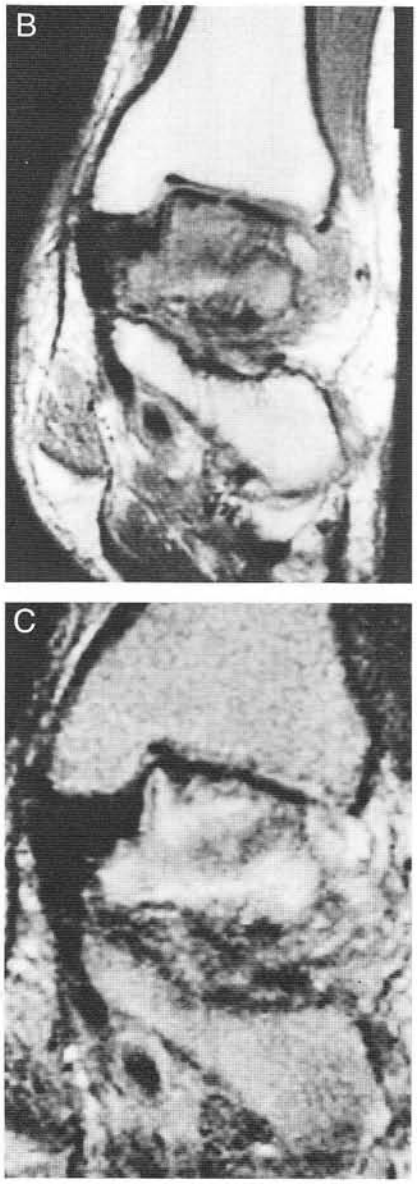

Figure 11. B, Magnetic resonance image (T1) demonstrating nonhomogeneous decrease signal within the talar body. C, T2 image showing variable areas of increased and decreased intensity.

Three weeks after the initial surgery, a second procedure had been performed to relocate the metatarsal head, which had displaced. Six months after surgery, the plain films showed gross destruction of the metatarsal head and early dissolution at the base of the proximal phalanx (Fig. 12A). Magnetic resonance imaging showing hypointensity on the T1 image and variable increases and

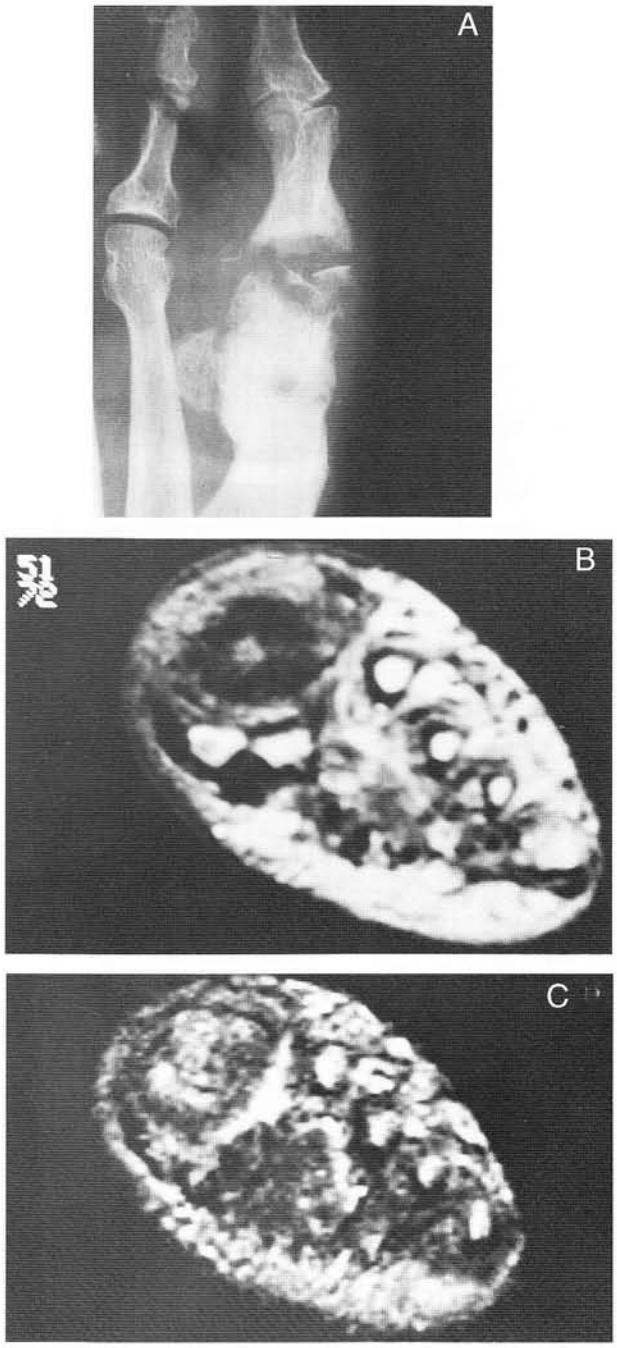

Figure 12. A, Radiograph 6 months postoperatively. B, Magnetic resonance image. T1 coronal slice at level of sesmoids reveals marked hypointensity of metatarsal head. C, Proton density image at level just proximal to Fig. 12B showing areas of hypo- and hyperintensity.

decreases on the T2 image was read as probable osteomyelitis by the radiologist (Fig. 12B and C). Subsequent bone biopsy of the first metatarsal revealed avascular necrosis of the first metatarsal and viable bone of the proximal phalanx and proximal first metatarsal.

Case 15

A 37-year-old male presented 3 months after open reduction and internal fixation of a calcaneal fracture with a nonhealing lateral wound and exposed hardware. Removal of the hardware and aggressive local wound care failed to heal the incision and 1 month later, a magnetic resonance imaging was performed. Because of an extreme signal abnormality and a communicating sinus tract, the radiologist suspected osteomyelitis (Fig. 13A). Bone cultures were negative and bone biopsy revealed osteonecrosis. A Papineau graft and free muscle flap were performed for soft tissue coverage, but 11 months after the original fracture, a draining area developed at the surgical wound. A repeat magnetic resonance imaging was performed and showed an abnormal area of increased signal intensity in the calcaneal tuberosity consistent with healing granulation tissue, yet suspicious for infection as well (Fig. 13B). A computed tomography-guided calcaneal aspiration revealed negative cultures and cytology (Fig. 13C).

Case 16

A 45-year-old female presented 5 days after bilateral partial hallux nail avulsions. A localized paronychia was evident on the right foot and ascending cellulitis on the left foot (Fig. 14A). Plain radiographs were unremarkable (Fig. 14B). A ^{99m}Tc scan revealed focal uptake on the 3-hr phase. The 24-hr phase decreased significantly and the integer count comparison eliminated suspicion of bone infection (Fig. 14C). The patient initially responded to incision and drainage and a course of intravenous antibiotics. A delayed primary closure was performed 4 days later. She was discharged on oral antibiotics.

She returned 1 week later with recurrent cellulitis, dehiscence, and drainage. Repeat plain films revealed marked narrowing of the interphalangeal joint and osteolysis of the distal and proximal phalanges (Fig. 14D). A presumptive diagnosis of indolent septic arthritis with progression to contiguous spread osteomyelitis on both sides of the joint was made. Magnetic resonance imaging was performed and demonstrated low intramedullary intensity on the T1 image and bright signal intensity on the T2 images involving both phalanges (Fig. 14E and F). Because of the aggressive nature of the process and the resistance to

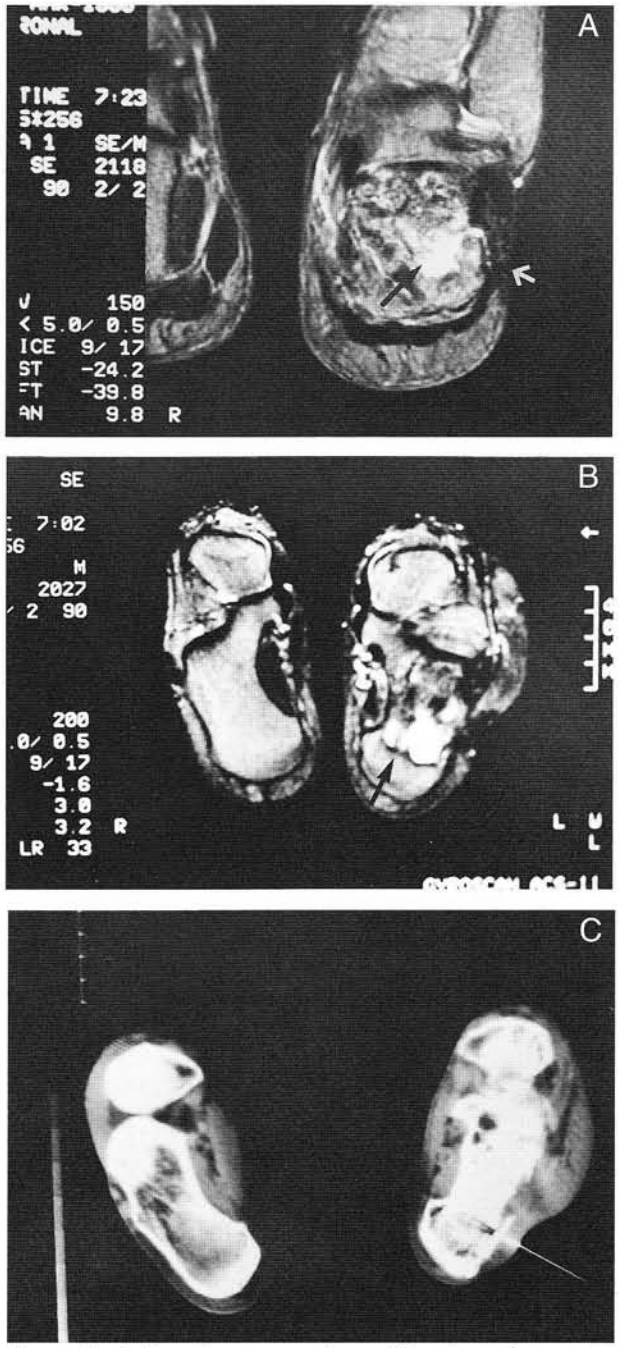

Figure 13. A, Magnetic resonance image T2 at 5 months postoperatively. Signal abnormality is more than would be expected for uncomplicated fracture healing. Note: sinus tract (arrow) leads to area of focal hyperintensity. B, T2 image, 13 months after original injury and 7 months after insertion of bone graft. A focal aea of increased signal (arrow) is evident on the T2 image just lateral to the graft. C, Computed tomography-directed calcaneal biopsy of focal area identified in Fig. B.

previous antibiotic therapy, the patient opted for a hallux amputation. Simultaneous first metatarsal biopsy and culture were negative for osteomyelitis.

Magnetic resonance imaging appears to be the most accurate nonoperative modality for the diagnosis of osseous infection. By virtue of its exquisite sensitivity to tissue hydration states, it can differentiate subtle bone marrow changes and intraosseous disease from surrounding soft tissue pathology. Superb contrast resolution provides excellent anatomical detail and defines corticomedullary involvement. However, the intramedullary fluid changes of osteomyelitis are quite similar and often inseparable from those secondary to surgery or traumatic injury to bone marrow. Magnetic resonance imaging does facilitate surgical planning, yet

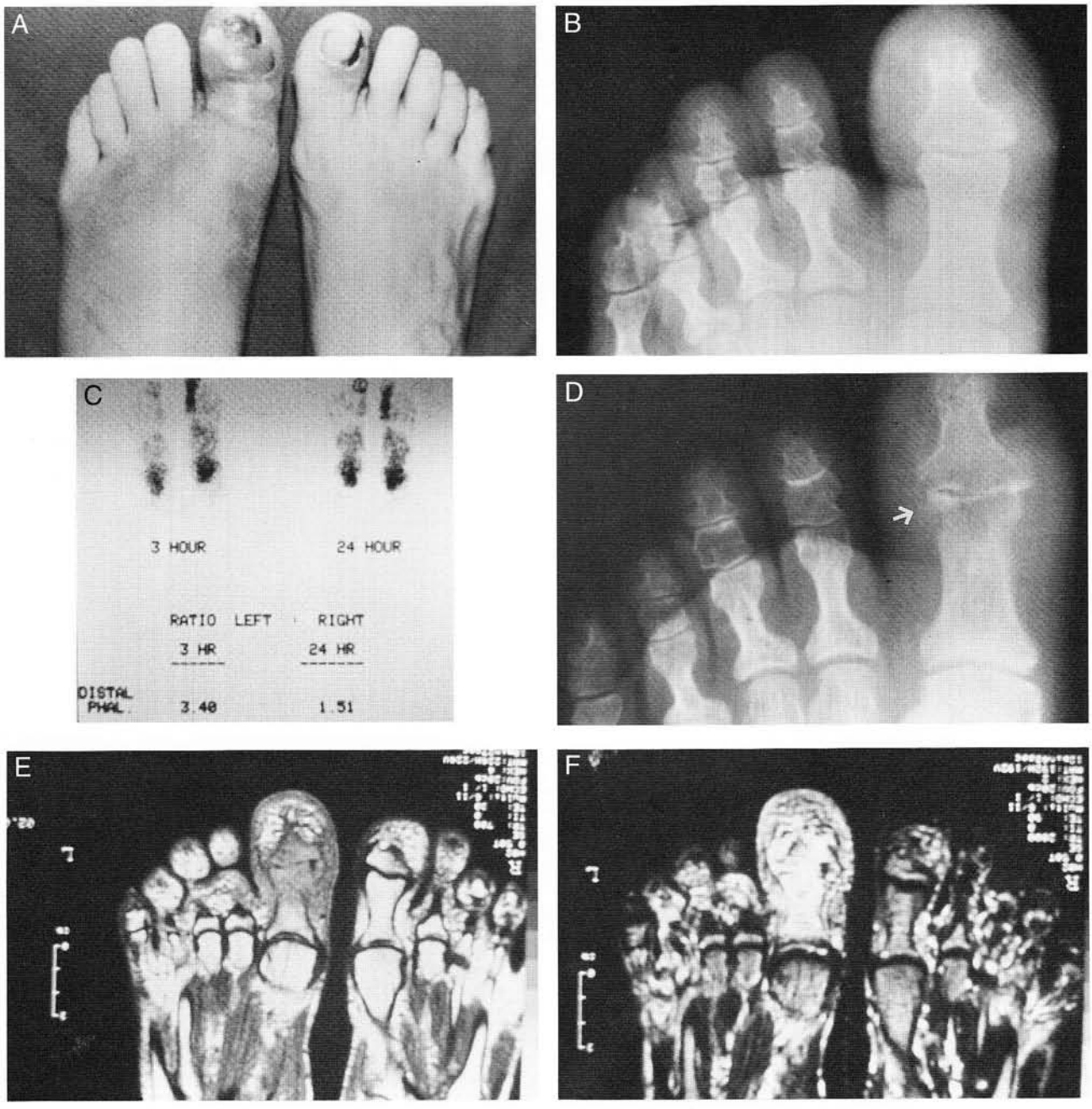

Figure 14. A, Initial presentation. B, Plain films are unremarkable. C, Technetium-99m bone phase, although positive, decreases significantly by 24 hr. D, Repeat plain films 10 days later. In comparison with Fig. B, note irregular joint narrowing, osteolysis, and dissolution of the distal lateral proximal phalanx (arrow). E and F, T1 and T2 magnetic resonance images, respectively, reveal calssic osteomyelitis, gross destruction of the distal and proximal phalanx evidenced by hypointensity on the T1 and hypertensity on the T2. Favorably, the subchondral bone plate of the base of the proximal phalanx is intact.

rarely obviates the need for a bone biopsy and must be used prudently. Long-term antibiotic therapy was avoided in cases 13 to 16.

Medical Economics

One final case will emphasize the financial burden created by the overuse of imaging modalities. This case is chosen for its simplicity, as only one modality was used and the treatment and hospitalization were relatively short and uncomplicated. The clinical presentation is extremely typical of a large population of diabetic patients seen by podiatric medical physicians. A male presented with an interdigital ulcer over the proximal interphalangeal joint of the second toe, which had been present for 3 months (Fig. 15A). Plain films showed erosive changes of the proximal and middle phalanges (Fig. 15B). A technetium scan was read as indeterminate for osteomyelitis by the radiologist (Fig. 15C). Subsequent bone cultures and biopsy revealed chronic osteomyelitis of the excised bone. A clean, viable margin on the proximal phalanx was confirmed histologically.

The bone scan did not influence the treatment. Despite plain film changes underlying the ulcer, the bone scan was considered indeterminate and the spatial resolution was insufficient to determine the anatomical extent of infection. A simple cost analysis was performed on the premise that the ^{99m}Tc scan was unnecessary and needlessly extended the patient's hospitalization and in-house intravenous antibiotic therapy from 3 days to 8 days. When hospital charges for the room, pharmacy, medical supplies, and nuclear medicine services were discounted for the 5-day differential, the total bill was reduced by 51% from $12,950 to $6,350. This is a mere microcosm of the additional expense incurred nationwide on a daily basis when patients are treated in this manner. Typically, treatment consists of multiple imaging modalities, long-term intravenous antibiotic therapy, and even more costly medical or surgical services.

Discussion

Accurate bone culture and biopsy are the definitive standard for detecting osteomyelitis. The microscopic analysis of osseous specimens is purely diagnostic. Bone cultures are most representative of the causative organisms and may direct antibiotic therapy as sinus tract cultures are proven to correlate poorly with the infecting pathogen.[133]

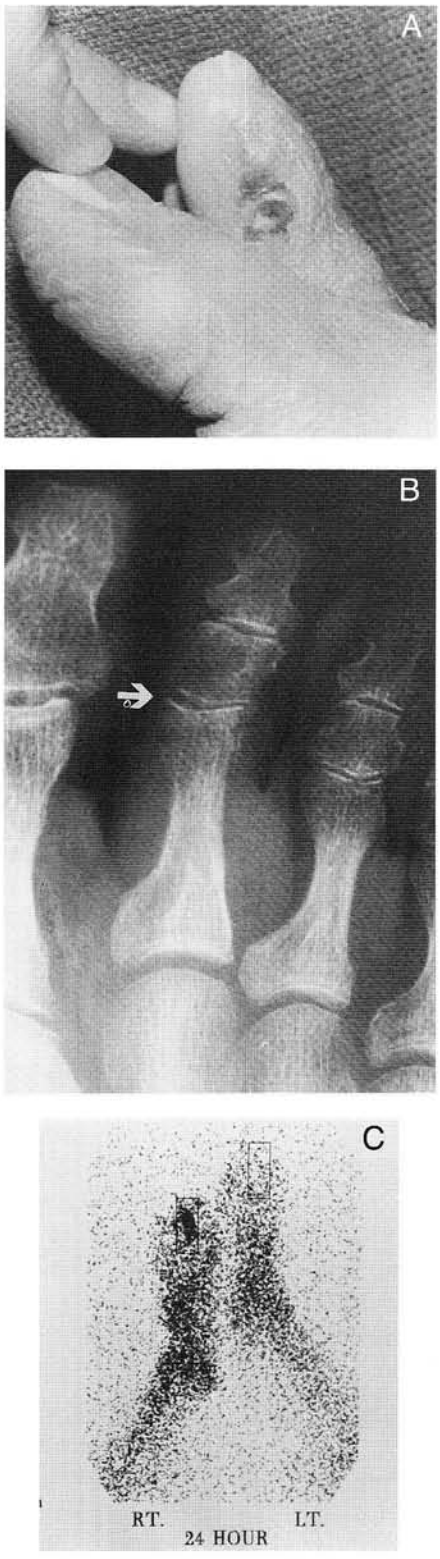

Figure 15. A, Ulcer on the medial aspect of the second digit. B, Cortical erosions are evident at the medial aspect of the proximal and middle phalanx (arrow). C, Focal uptake is present on the second digit at 24 hr. The integer count increased by 0.67 and was considered indeterminate.

The majority of practitioners who suspect bone infection frequently exhaust the imaging modalities first, ultimately turning to surgical treatment when considered necessary. The authors' approach to the infected foot is the opposite. The authors initially consider bone biopsy and culture, then assess whether an imaging modality may obviate the need for surgery or guide the surgical plan. The imaging studies are recurrently equivocal and often unessential. The bones of the foot are readily accessible and most surgery can be done under local anesthetic or intravenous sedation, if there is prompt diagnosis.[134]

The first consideration is whether the patient belongs to that problematic subset so commonly seen with diabetes, osteoarthropathy, previous surgery, trauma, or other medical conditions. If not, a technetium scan might reasonably eliminate the need for bone biopsy and culture. However, a majority of patients have concomitant pathology that obscures the accuracy of the imaging techniques. In treating this more difficult set of patients, the authors occasionally consider a magnetic resonance image. It is the sole study that bridges the gap between merely depicting morphologic changes in bone or identifying the inflammatory nature of disease. To some extent, it does both. Magnetic resonance imaging may be useful in the diabetic fetid foot with rampant infection. Much of the osteomyelitis within the foot is derived from contiguous infection and not hematogenously derived. However, if acute osteitis is present but the marrow is not yet involved, the accuracy of magnetic resonance imaging for bone infection may diminish. The strength of magnetic resonance imaging is detailing intramedullary and soft tissue involvement. The authors use this modality with reservation and only when it will direct the surgical plan, and very rarely to diagnose.

Immediate bone biopsy and culture are recommended through needful open exposure when an ulcer overlies the area in question and it is doubtful the ulcer will heal without osseous resection. The quality of bone is assessed intraoperatively and an appropriate level of resection or biopsy determined. This is almost universally the case with long-standing digital and submetatarsal diabetic ulcers. Foot ulcers serve as a portal of entry for bone infection, and in one prospective study were found to overlie 94% of diabetic pedal osteomyelitis.[135] The conclusion was that the majority of diabetic foot ulcers have an underlying osteomyelitis that is clinically unsuspected. The usual clinical manifestations of infection may not be present because of neuropathy, immunopathy, and vasculopathy.[136] Osseous resection can provide timely diagnosis, alleviate deformity, and reduce the potential for infectious extension.

Common Concerns

Certain inquiries continually recur regarding this topic. Potential implantation of bacteria from the soft tissue into bone during biopsy is possible. Preferably, specimens are obtained through clean open exposure that does not traverse inflamed or infected tissue. False-negative bone specimens are possible with needle aspirates as a result of sampling error and inadequate size.[131, 137]

The popular caution regarding bone biopsy in diabetics because of blood supply and poor healing response is overstated.[21, 100, 136] The majority of diabetics will have adequate peripheral perfusion.[138, 139] Those with advanced autonomic neuropathy and medial calcification will exhibit increased blood flow.[138, 140–142] Those who do have occlusive disease and distal gangrene will, in all likelihood, need revascularization or resection proximal to the site of osteomyelitis.

Many practitioners believe the radionuclide methods can identify the anatomical extent of disease. The spatial resolution of these scans among the numerous bones and joints of the foot is inadequate. It is extremely difficult to unequivocally resolve the exact margins of osseous involvement, thus making the accuracy of these modalities inconsequential.

Conclusion

The evaluation of a patient with complaints of an infectious nature must be systematic and comprehensive. The history and physical examination remain preeminently important. Nevertheless, plain radiographic studies and a variety of imaging modalities are available. In imaging osteomyelitis, the assessment of disease activity, disease extent, and the differential diagnosis are the questions to be answered.

It is evident that none of the imaging modalities are entirely specific for osteomyelitis. The critical realization must be that all the modalities image is inflammation, not infection. Certainly inflammation

acompanies infection; the differentiation of the two is the unmet challenge. Nowhere is this better exemplified than in the problematic subset of patients seen with foot and ankle pathology. The central question remains: is the result of the test trusted to favorably influence the treatment? If not, the test is clinically irrelevant, medically unnecessary, adds unneeded expense, and offers no therapeutic return.

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