Gallium-67 Scintigraphy in Tuberculous and Nontuberculous Infectious Spondylitis

R. Lisbona, V. Derbekyan, J. Novales-Diaz and A. Veksler

Departments of Nuclear Medicine and Radiology, Royal Victoria Hospital, Montreal, Canada

Vertebral osteomyelitis is a difficult condition to diagnose clinically. A retrospective review of 21 cases of infectious spondylitis (6 tuberculous, 15 nontuberculous) confirmed the utility of ^{67}Ga scintigraphy in imaging this process. Gallium-67 scans were positive at all sites of disease in this patient population. They anticipated the presence of spondylar infection in 23% of regions where radiographic abnormalities were originally lacking, while confirming a current and ongoing septic process at the other sites where vertebral destruction was already present on x-ray. Gallium-67 studies, as compared to the ^{99m}Tc-MDP bone scans, also provided important information as to the extent of disease by documenting the presence of eight paraspinal abscesses and the location of remote extraspinal foci of infection both in soft tissues and in bone. The relative merits of all radiologic imaging procedures are discussed. A diagnostic algorithm is also suggested.

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Infectious spondylitis is an infrequent entity, accounting for as little as 2%–4% of all cases of osteomyelitis, which may still be associated with serious neurological disturbances and high mortality (*1–3*). It is a difficult condition to diagnose at an early stage since the clinical presentation of patients with vertebral osteomyelitis may be perplexing while the radiographic manifestations of the infection may be noncharacteristic or significantly delayed (*1,4,5*). The advent of computed tomography (CT) scanning and magnetic resonance imaging (MRI) has helped bridge the lapse between the onset of symptoms and the final diagnosis of the spinal infection (*6,7*). It is our experience that ^{67}Ga scintigraphy can also play a useful role in establishing the early presence of infectious spondylitis, in documenting the multicentricity of the infection and in monitoring its response to therapy.

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For correspondence or reprints contact: Dr. Robert Lisbona, Department of Nuclear Medicine, Royal Victoria Hospital, 687 Pine Avenue West, Montreal, Quebec, Canada H3A 1A1.

PATIENTS AND METHODS

A retrospective analysis of scintigraphic findings was carried out in 21 patients with culture-proven infectious spondylitis who were studied over the past 10 yr, in the course of their clinical investigation, by sequential imaging with ^{99m}Tc-phosphate complex and ^{67}Ga. There were 11 males and 10 females ranging in age from 14 to 84 yr. None of the patients had had previous back surgery. Bone scans of the spine were obtained 3 hr after the intravenous injection of 20 mCi of ^{99m}Tc-methylene diphosphonate (MDP). Upon completion of the imaging procedure, 5.0 mCi of ^{67}Ga citrate were administered intravenously to the patients, while the spinal region of interest was scanned 48 hr later. More extensive body imaging with ^{99m}Tc-MDP and ^{67}Ga was also undertaken in eight patients because of clinical suspicions for extraspinal sepsis. In all instances, appropriate radiographic examinations were available for comparison. These had been obtained within 48 hr of the nuclear studies. All sites of infection were finally identified through the integrated interpretation of all imaging tests, as well as the clinical presentation and evolution of the disease process, including its response to antibiotic therapy.

RESULTS

Fifteen patients had infectious nontuberculous spondylitis (Tables 1 and 2), whereas the remaining six suffered from tuberculous spondylitis (Table 3). Examples of both conditions are illustrated in Figures 1–4.

Nontuberculous Infectious Spondylitis

Staphylococcus aureus was the most common organism for pyogenic spondylitis, accounting for 10 of 15 or 67% of cases (Table 1). Overall, there were 17 levels of spinal involvement, one in each patient, except for two

TABLE 1
Causative Organisms of Nontuberculous Infectious Spondylitis

Total number of cases	n = 15
Individual organisms	
Staphylococcus aureus	n = 10
Escheria coli	n = 1
Salmonella	n = 1
Aspergillus	n = 1
Candida albicans	n = 1
Gram-negative bacillus (not further identified)	n = 1

TABLE 2
Nontuberculous Infectious Spondylitis

No. of patients	No. of spinal sites	Gallium-67 scintigraphy		^{99m}Tc-MDP bone scan		
		Spinal sites	Extraspinal sites	Spinal sites	Extraspinal sites	Spinal radiographs
15	17	Positive at all 17 sites	Positive at four sites (sternum, MCP joint, knee, elbow crease)	Positive at 16 sites	Positive at two sites (sternum, MCP joint)	Normal or nonspecific for infection at four sites
		Six para-spinal abscesses identified				Disk space narrowing and end plate destruction at 13 sites

patients who had two sites of disease. There were two septic foci in the cervical spine, six in the thoracic spine, one at the dorso-lumbar junction and eight in the lumbar spine. The gallium scans were positive in all instances of nontuberculous spondylitis, whereas ^{99m}Tc-MDP bone scanning identified 16 of 17 spinal sites. Gallium-67 scintigraphy also disclosed six paraspinal abscesses arising from infected bone. Furthermore, the ^{67}Ga study revealed additional sites of sepsis in the sternum, knee, small joint of the hand and the elbow crease in three different patients. The radiographic studies showed destruction of the spine at 13 sites, as characterized by disk space narrowing and end plate destruction. The radiographs were initially normal or nonspecific for infection at four sites.

Tuberculous Spondylitis

Four of the six patients with tuberculous spondylitis had one level of involvement while two patients had multicentric disease of the spine. Overall, there were nine vertebral sites of tuberculous osteomyelitis. There were two foci in the cervical spine, three in the dorsal spine, one at the dorso-lumbar junction and three in the lumbar spine. Those regions with spinal osseous tuberculosis were detected on ^{67}Ga imaging; scintigraphy also revealed paraspinal masses in two patients. The bone scan was categorically abnormal at six sites, while the findings were more subtle at three remaining sites. Two additional skeletal foci of tuberculosis, one in the sternum and the other in a sacroiliac joint, were present. Both were strikingly evident on the ^{67}Ga images. The bone scan identified only the sternal focus of disease and failed to detect tuberculous sacroiliitis. Gallium-67 scans also revealed two extraspinal sites of soft-tissue involvement in two different patients, one in the pre-auricular region and the other in the parainguinal area. Gallium-67 scans of the thorax, obtained in five patients with tuberculosis, showed no evidence of thoracic uptake of radiotracer to suggest pulmonary infection by mycobacterium tuberculosis. Radiographic studies were abnormal in all patients, but missed two of three sites of disease at C3 and L1 in a patient with multicentric tuberculous spondylitis.

DISCUSSION

Infectious spondylitis is one of the infrequent causes of back pain with clinical manifestations which may be of a nonspecific and indolent nature (*8*). It is commonly a blood-borne infection arising from a remote primary focus elsewhere in the body. It is usually caused by *Staphylococcus aureus*, *Staphylococcus epidermis*, *Streptococcus* group B, *Salmonella*, *Escheria coli* and *Myobacterium tuberculosis* (*1*). Generally, the causative organism seeds hematogenously into the richly vascularized subchondral vertebral end plates with eventual progression of the infection to involve the adjacent but relatively avascular intervertebral disk (*1,9*). At other times, during childhood adolescence, the infection is triggered by or-

TABLE 3
Tuberculous Spondylitis

No. of patients	No. of spinal sites	Gallium-67 scintigraphy			^{99m}Tc-MDP bone scans		
		Spinal sites	Extraspinal sites	Lungs and mediastinum	Spinal sites	Extraspinal sites	Spinal radiographs
6	9	Positive at all nine sites	Positive at two skeletal sites (sternum, sacroiliac joint)	Negative in all five patients whose thorax was imaged	Markedly positive at six spinal sites	Positive at one site (sternum)	Abnormal at seven of nine sites
		Two paraspinal abscesses identified	Two soft-tissue sites (pre-auricular region, inguinal node)		Subtly positive at three other sites		

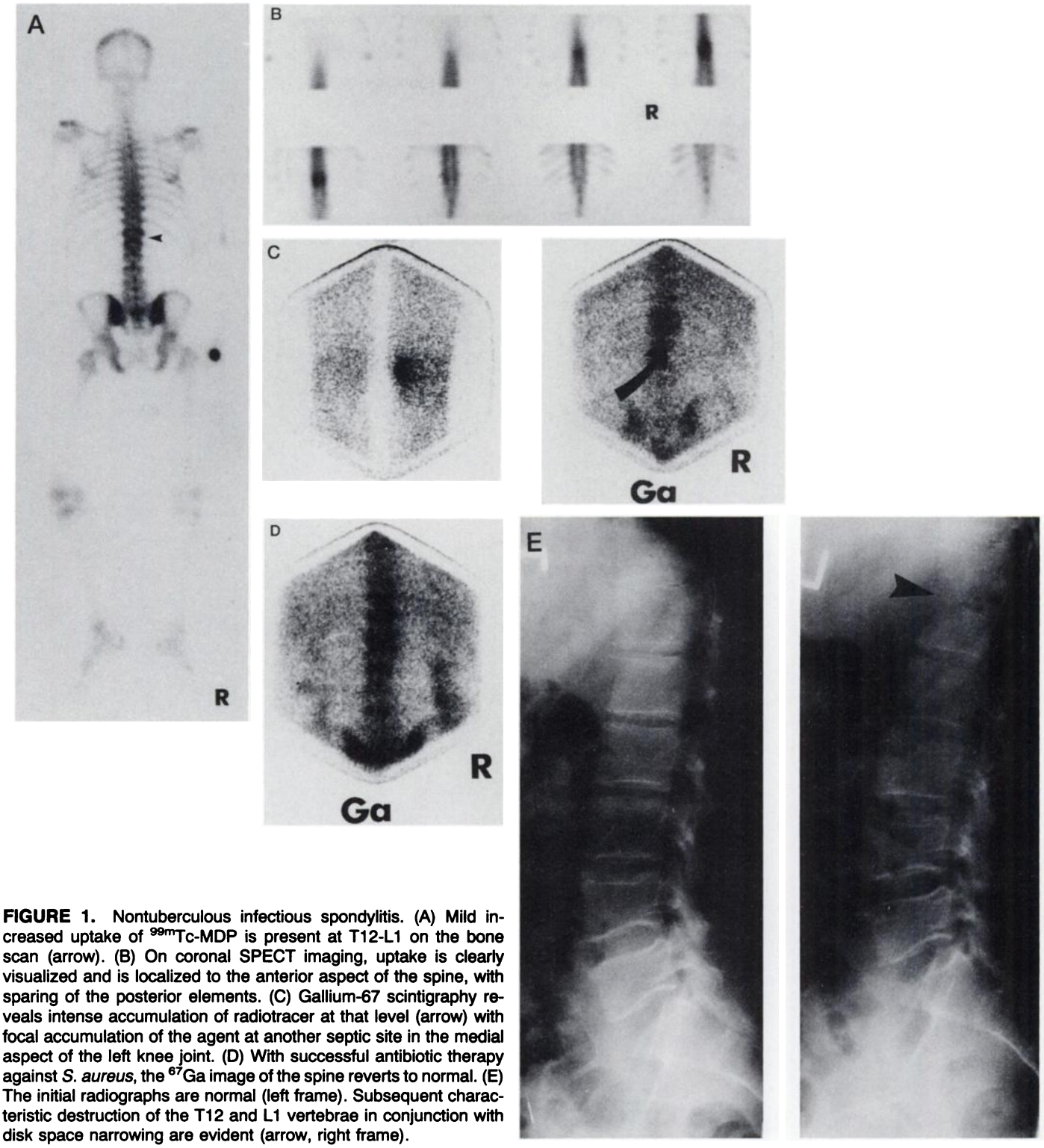
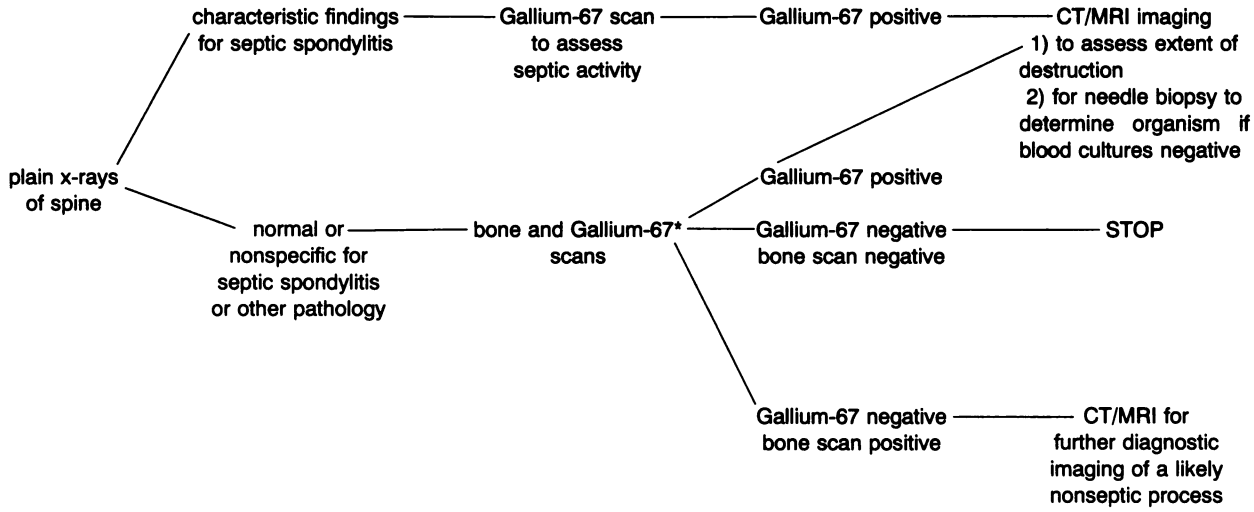


FIGURE 1. Nontuberculous infectious spondylitis. (A) Mild increased uptake of ^{99m}Tc-MDP is present at T12-L1 on the bone scan (arrow). (B) On coronal SPECT imaging, uptake is clearly visualized and is localized to the anterior aspect of the spine, with sparing of the posterior elements. (C) Gallium-67 scintigraphy reveals intense accumulation of radiotracer at that level (arrow) with focal accumulation of the agent at another septic site in the medial aspect of the left knee joint. (D) With successful antibiotic therapy against *S. aureus*, the ^{67}Ga image of the spine reverts to normal. (E) The initial radiographs are normal (left frame). Subsequent characteristic destruction of the T12 and L1 vertebrae in conjunction with disk space narrowing are evident (arrow, right frame).

ganisms that travel to disks already nourished by smaller perforating vessels (*6*). Ultimately, local spread of the infection ensues and these pathological events translate into end plate destruction and disk space narrowing and collapse which become evident on radiological imaging. On conventional radiography, however, these findings usually manifest later and sometimes only weeks after the onset of symptoms. They may even be obscured because of degenerative changes or skeletal hyperostosis (*3,4,10*). Plain film radiographs have been documented as having a sensitivity of 82%, specificity of 57% and an accuracy of 73% in vertebral osteomyelitis (*7*). In fact, however,

TABLE 4
Diagnostic Algorithm for the Investigation of Septic Spondylitis



*Whole-body imaging should be done if a systemic or multicentric process is suspected.
SPECT imaging increases the sensitivity and localizing properties of the bone scan study.

these numbers are very much dependent on the patient population since back pain is also a common denominator for many more prevalent conditions unrelated to infectious spondylitis.

CT and MRI

CT and MRI will disclose morphological abnormalities of vertebral osteomyelitis earlier than plain film radiography and shorten the lag between patient presentation and final diagnosis. These modalities will also emphasize the full extent of destruction and potential for spinal instability.

Reliable CT criteria have been elaborated for the specific diagnosis of infectious spondylitis (*4*). For pyogenic infection, these criteria have included diffuse destruction by a process about an intervertebral disk, complete prevertebral soft-tissue involvement and gas in bone and soft tissue. On CT, nonpyogenic infection is identified by focal lytic bone involvement and marginal sclerosis. The

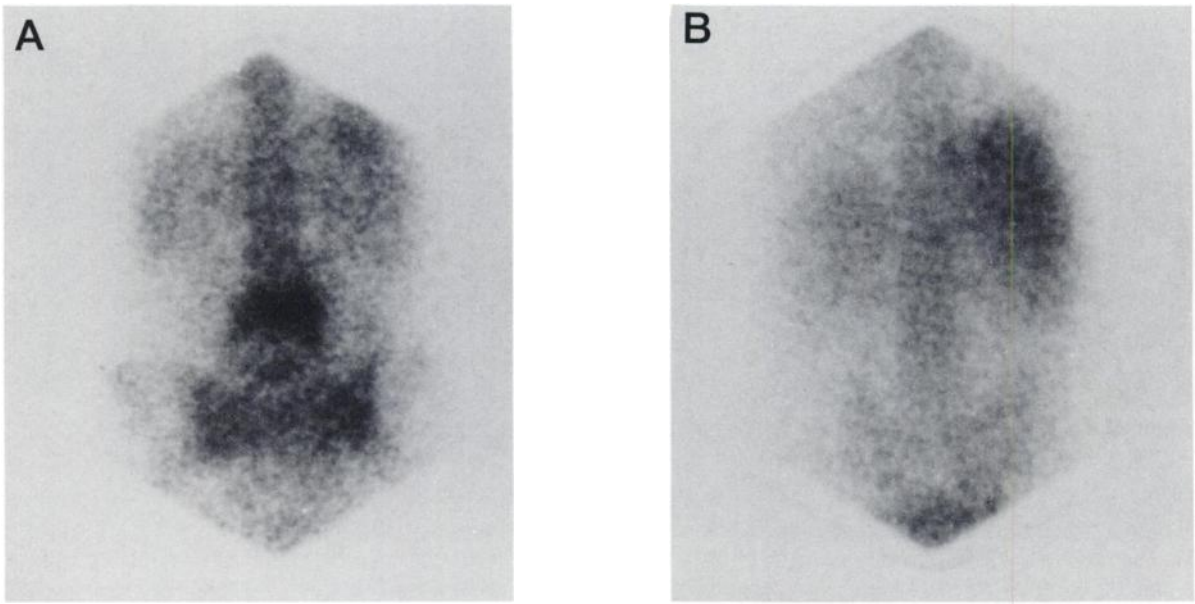


FIGURE 2. Nontuberculous infectious spondylitis. Gallium-67 accumulation at L4 with overspill of radioactivity in the paraspinal spaces results in a "butterfly" pattern indicating vertebral osteomyelitis with spinal abscesses (Fig. A). The abnormality resolves after successful therapy (Fig. B).

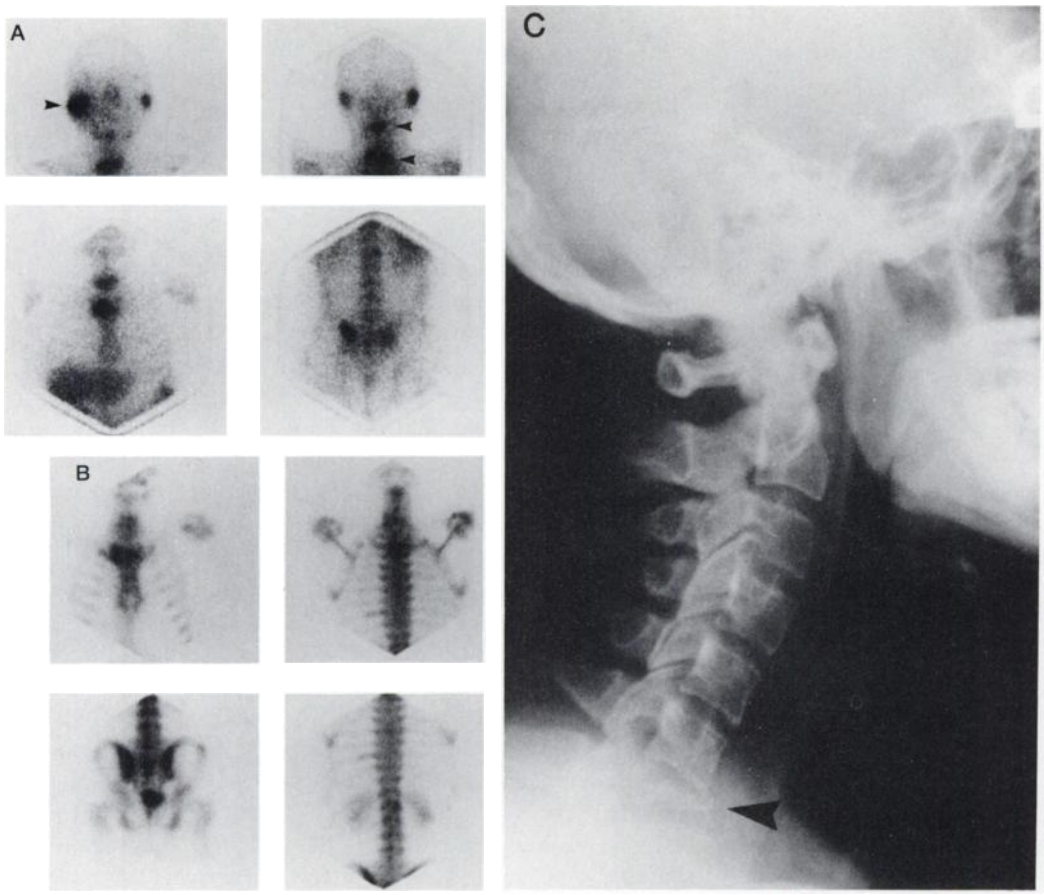


FIGURE 3. Tuberculous spondylitis. (A) Intense ^{67}Ga accumulation is noted in the right periauricular region on the anterior view of the head (arrow, left upper frame) with equally intense ^{67}Ga uptake at C3 and C7 on the posterior images of the head and neck areas (arrow, right upper frame). Gallium-67 uptake in the sternum indicates sternal osteomyelitis on the anterior view of the thorax (left lower frame). Intense ^{67}Ga accumulation in the left sacro-iliac joint and milder uptake on the right side of the L1 indicate further dissemination of the tuberculous infection (right lower frame). After therapy, all ^{67}Ga images reverted to normal. (B) On the bone scan, increased uptake of ^{99m}Tc-MDP is noted in the sternum (left upper frame) with only mild accumulation at C3 and C7 (right upper frame). The left sacroiliac joint has a normal appearance (left lower frame) and mild ^{99m}Tc-MDP uptake is present on the right side of L1 (right lower frame). (C) Lateral radiographs of the C spine at the time of diagnosis show destruction of C7 (arrow), whereas C3 has a normal appearance.

classic CT findings of tuberculous spondylitis are a large paraspinal soft-tissue mass which is frequently calcified with an irregularly enhancing rim and anterior vertebral body destruction. The destruction, however, progresses much more slowly than in pyogenic spondylitis. Although sensitivities and specificities have been generated for individual CT signs in proven vertebral osteomyelitis, it is more difficult to obtain these statistics for CT diagnosis of the condition in the general population in view of the retrospective nature of many of the studies. In many centers, MRI is superceding CT in the diagnosis of septic spondylitis.

A characteristic appearance of vertebral osteomyelitis has been defined as confluently diminished signal intensity of the involved vertebral bodies and disks on a T1-weighted MR image. With T2-weighted sequences, an abnormal configuration and signal intensity of the disk with enhanced signal intensity of the adjacent vertebral bodies can also be elicited. These diagnostic criteria have resulted in a sensitivity of 96%, specificity of 92% and accuracy of 94% in identifying vertebral osteomyelitis (*7*).

Both CT and MRI provide more accurate anatomical detail than scintigraphy, and involvement of the vertebral bodies, disks and paravertebral regions as distinct structures is better highlighted by these modalities (*4,7*). In particular, the thecal sac and neural structures can also be assessed well by MRI. Nevertheless these morphological abnormalities depicted on CT and MRI do not always distinguish between a burnt out infection and an ongoing one, since the destructive changes of the process tend to remain permanent in some fashion. Furthermore, CT and MRI permit only regional assessment of a septic process, which in fact may be widespread and systemic in nature.

Scintigraphy

The original scintigraphic approach to the diagnosis of osteomyelitis, as a rule, has entailed imaging of the condition with bone tracers such as ^{99m}Tc-phosphate complexes. Although exquisitely sensitive, this technique is, by itself, frequently nonspecific, thus necessitating supplementary scanning with ^{111}In-labeled white blood cells (WBCs) or ^{67}Ga. So far the ^{111}In-WBC technique has proven disappointing for imaging the spine (*9,11*).

Indium-111-WBC Imaging. A large review series of ^{111}In-labeled leukocyte images on 71 patients with suspected vertebral osteomyelitis was recently published (*9*). It determined that septic spondylitis could manifest on ^{111}In-WBC scintigraphy as a focus of increased or dimin-

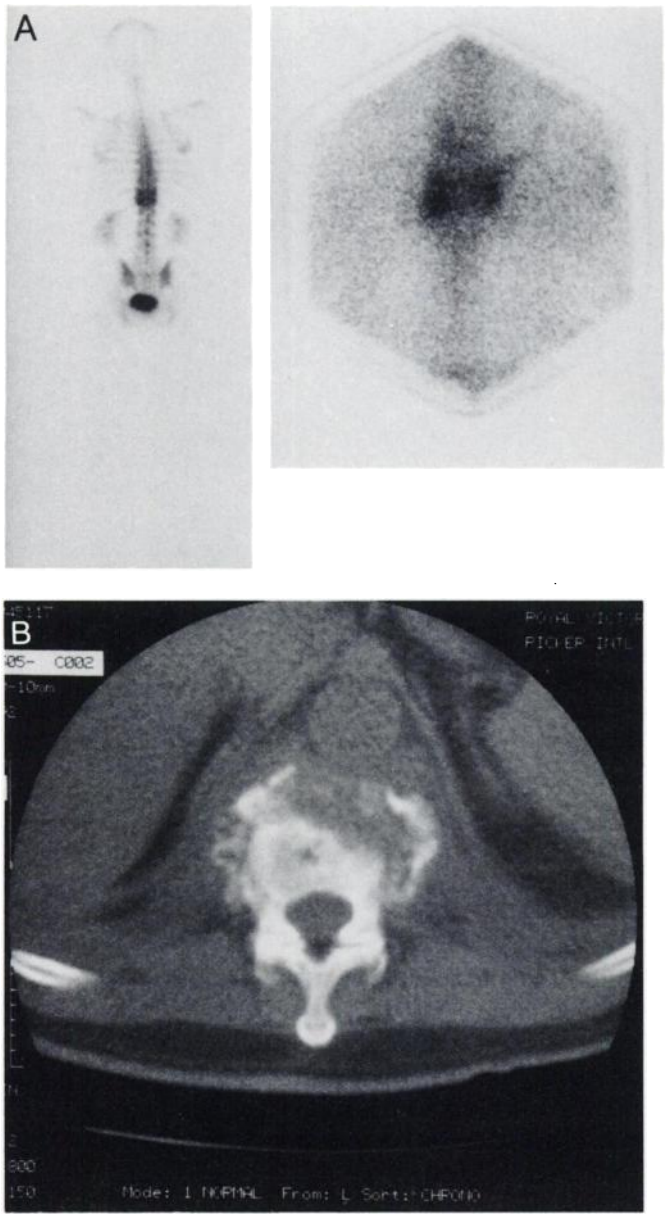


FIGURE 4. (A) A solitary lesion centered at T11-T12 is present on the whole-body bone scan. Gallium scintigraphy of that site reveals the infectious nature of the process in the vertebrae and overspill of the infection into the paraspinal soft tissues. (B) Confirmatory destructive changes at T11-T12 are seen on the CT scan, which also documents swelling of the soft tissues surrounding the spine.

ished accumulation of the labeled cells. Although enhanced deposition of ^{111}In-WBC was associated with a high specificity of 98% for the condition, it was notoriously insensitive at 39%. Also, an area of photopenia exhibited neither sensitivity (54%) nor specificity (52%) as a marker of infectious spondylitis. Overall, the accuracy of leukocyte imaging for diagnosing vertebral osteomyelitis was 66% when either increased or decreased activity were used as criteria for infection. In this patient population, accuracy was quite similar to that obtained with ^{99m}Tc bone imaging (63%).

Gallium-67 Imaging and Diagnostic Algorithm. Previous experience with ^{67}Ga has indicated that this agent can play a valuable role in the detection of osteomyelitis (*12,13*). Data about its contribution in diagnosing infectious spondylitis are more limited (*1–3,14,15*). Nevertheless, combined gallium and bone scan studies have shown a sensitivity of 90%, specificity of 78% and accuracy of 86% for vertebral osteomyelitis (*7*). Our findings also show that scintigraphy with ^{67}Ga is a worthwhile step in the imaging of tuberculous or nontuberculous spondylitis. In total, at 6 of 26 (23%) infected sites, scintigraphic studies prompted the detection of spondylar sepsis, whereas radiographic findings were lagging. At the remaining sites, scintigraphy correctly identified the active nature of the infectious process since, even with radiographic changes of spinal destruction, the x-rays were inconclusive in some instances as to the presence of a current or a remote and quiescent septic process. Scintigraphy with ^{67}Ga was, however, unable to differentiate between tuberculous and pyogenic spondylitis. Both entities could be found at any spinal level, be multicentric in the spine, be associated with paraspinal abscesses and also affect distant skeletal or soft-tissue sites. Also, there was no indication on ^{67}Ga scintigrams of active pulmonary tuberculosis in those individuals with tuberculous spondylitis.

From our series of patients, ^{67}Ga scanning was seen to enhance data acquired from ^{99m}Tc-MDP bone scintigraphy. Imaging with ^{67}Ga may not only detect spondylar lesions more vividly, but it also ascribes a septic origin to the less specific increased vertebral uptake seen on ^{99m}Tc-MDP bone studies. Gallium-67 examinations also document the presence of paraspinal abscesses while highlighting distant septic foci in the soft tissues or skeleton, which could be more amenable to biopsy and/or culture than the spine itself. Sequential ^{67}Ga scanning also offers the opportunity to monitor response to antibiotic therapy (*16*).

Although ^{67}Ga scintigraphy provides many answers in suspected infectious spondylitis, our overall experience is that concurrent bone imaging with ^{99m}Tc-MDP should still be included in the diagnostic scheme. This is a same-day screening test for bony lesions that also permits a rapid survey of the entire skeleton without the drawback of 48-hr delayed imaging necessary for optimal ^{67}Ga scintigraphy. Bone scanning, particularly when enhanced by SPECT (*17*), will provide better resolution than ^{67}Ga, and thus allows for more accurate anatomical localization of spinal disease sites. The high sensitivity of ^{99m}Tc-MDP for occult lesions of the spine of all types is also beneficial since a focal lesion on bone imaging that fails to accumulate ^{67}Ga will direct the clinician to other active bony processes that can be covert causes of back pain. The complementary use of ^{67}Ga and ^{99m}Tc phosphate complex scintigraphy is still needed in the investigation of certain instances of obscure back pain because it may provide a more thorough understanding of a patient's symptomatology. Certainly, in our experience, these nu-

clear studies will improve on the yield of plain film radiography in establishing the difficult diagnosis of vertebral osteomyelitis. Radiography, despite its relative insensitivity, nevertheless remains an important starting point for the integration of all diagnostic imaging procedures to achieve early recognition of the condition (Table 4).

REFERENCES

1. Swayne LC, Dorsky S, Caruana V, Kaplan IL. Septic arthritis of a lumbar facet joint: detection with bone SPECT imaging. *J Nucl Med* 1989;30: 1408–1411.
2. Bruschwein DA, Brown ML, McLeod RA. Gallium scintigraphy in the evaluation of disk-space infections: concise communication. *J Nucl Med* 1980;21:925–927.
3. Adatepe MH, Powell OM, Isaacs GH, Nichols K, Cefola R. Hematogenous pyogenic vertebral osteomyelitis: diagnostic value of radionuclide bone imaging. *J Nucl Med* 1986;27:1680–1685.
4. Van Lom KJ, Kellerhouse LE, Pathria MN, et al. Infection versus tumor in the spine: criteria for distinction with CT. *Radiology* 1988;166:851–855.
5. Swanson D, Blecker I, Gahbauer H, Caride VJ. Diagnosis of discitis by SPECT technetium-99m MDP scintigram. *Clin Nucl Med* 1987;12:210–211.
6. Price AC, Allen JH, Eggers FM, Shaff MI, James AE. Intervertebral disk-space infection: CT changes. *Radiology* 1983;149:725–729.
7. Modic MT, Feiglin DH, Piraino DW, et al. Vertebral osteomyelitis: assessment using MR. *Radiology* 1985;157:157–166.
8. Musher DM, Thorsteinsson SB, Minuth JN, Luchi RJ. Vertebral osteomyelitis. *Arch Intern Med* 1976;136:105–110.
9. Palestro CJ, Kim CK, Swyer AJ, Vallabhajosula S, Goldsmith SJ. Radionuclide diagnosis of vertebral osteomyelitis: indium-111-leukocyte and technetium-99m-methylene diphosphonate bone scintigraphy. *J Nucl Med* 1991;32:1861–1865.
10. Fontaine S, Dumas JM, Brassard R, Melanson D. Pyogenic spondylodiscitis without disc space collapse. *J Can Assoc Radiol* 1987;38:129–130.
11. Whalen JL, Brown ML, McLeod R, Fitzgerald RH. Limitations of indium leukocyte imaging for the diagnosis of spine infections. *Spine* 1991;16: 193–197.
12. Lisbona R, Rosenthall L. Observations on the sequential use of ^{99m}Tc-phosphate complex and ^{67}Ga imaging in osteomyelitis, cellulitis and septic arthritis. *Radiology* 1977;123:123–129.
13. Lisbona R, Rosenthall L. Radionuclide imaging of septic joints and their differentiation from periarticular osteomyelitis and cellulitis in pediatrics. *Clin Nucl Med* 1977;2:337–343.
14. Haase D, Martin R, Marrie T. Radionuclide imaging in pyogenic vertebral osteomyelitis. *Clin Nucl Med* 1980;12:533–537.
15. Norris S, Ehrlich MG, Keim DE, Guiterman H, McKusick KA. Early diagnosis of disc-space infection using gallium-67. *J Nucl Med* 1978;19: 384–386.
16. Alazraki N, Fierer J, Resnick D. Chronic osteomyelitis: monitoring by ^{99m}Tc-phosphate and ^{67}Ga-citrate imaging. *AJR* 1985;145:767–771.
17. Krasnow AZ, Collier BD, Hellman RS, et al. Bone SPECT 1992: clinical perspective and review. In: Freeman L, ed. *Nuclear medicine annual.* New York: Raven Press; 1992:21–68.