Utility of Bone Scanning in Disseminated Coccidioidomycosis: Case Report

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Five cases of disseminated coccidioidomycosis (DC) are presented, to illustrate the complementary nature of bone scanning and radiography in the assessment of skeletal involvement. As shown in other inflammatory and neoplastic processes, bone scanning is more sensitive than radiography in the detection of early skeletal disease, but correlation with radiographs remains a necessity.

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Coccidioidomycosis is a fungal infection caused by *Coccidioides immitis*, which has been called the most infectious fungal agent producing systemic disease (*1*). Systemic manifestations occur in 0.5% of patients with coccidioidomycosis, and 20% of these patients will have osseous lesions (*2*). The radiography of skeletal coccidioidomycoses (SC) is well documented (*1–6*), but we have found no report correlating radionuclide bone scanning with radiography in patients with SC. This report emphasizes radionuclide scanning and radiographic features in five patients with disseminated coccidioidomycosis (DC).

CASE REPORTS

Case 1. A 33-year-old white man presented with fever and pulmonary infiltrates, and was subsequently shown to have DC, manifested by skin biopsy, bone marrow, and cerebrospinal-fluid examinations, skeletal and chest radiographs, a serum complement fixation titer (SCFT) of 1:128, and a radionuclide bone scan. Therapy included amphotericin B, transfer factor, and miconazol. The skin test of coccidioidomycosis was initially nonreactive but became reactive during transfer-factor therapy. A radiographic skeletal survey revealed multiple lytic lesions with no periosteal reaction and only minimal sclerosis. These were located in the clavicles, ribs, right ischium, right scapula, right humerus, proximal ulnae and radii, proximal and distal left femur, proximal tibias, left medial and lateral malleoli, and right lateral malleolus (Fig. 1A–1D). The ^{99m}Tc-pyrophosphate (^{99m}Tc-PP$_i$) bone scan showed a diffusely mottled distribution of tracer uptake that was much less striking than the radiographs. Focal areas of increased uptake were noted in the left greater trochanter, left hip, and right ischium with diffuse mottling of the ribs and clavicles (Fig. 1E–1G). All abnormal areas on the bone scan corresponded with radiographic lesions except the left greater trochanter, which revealed no definite abnormality. The pulmonary infiltrates and skin lesions improved and the SCFT decreased to 1:8 on continuing therapy with amphotericin B and transfer factor.

Case 2. A 27-year-old Mexican–American man presented with fatigue, weight loss, cough, and dyspnea. Pleural fluid and cutaneous cyst aspirates and bronchoscopic specimens revealed DC. The SCFT was 1:4,096 and the skin test was reactive. Physical examination revealed tenderness over the distal right tibia. The ^{99m}Tc-PP$_i$ bone scan revealed increased uptake in the distal right tibia and right posterior parietal region, with resolution of the tibial lesion on follow-up bone scan 5 months later. A subsequent bone scan revealed increased uptake in the right orbital area, but corresponding radiographs revealed no abnormalities. The patient was placed

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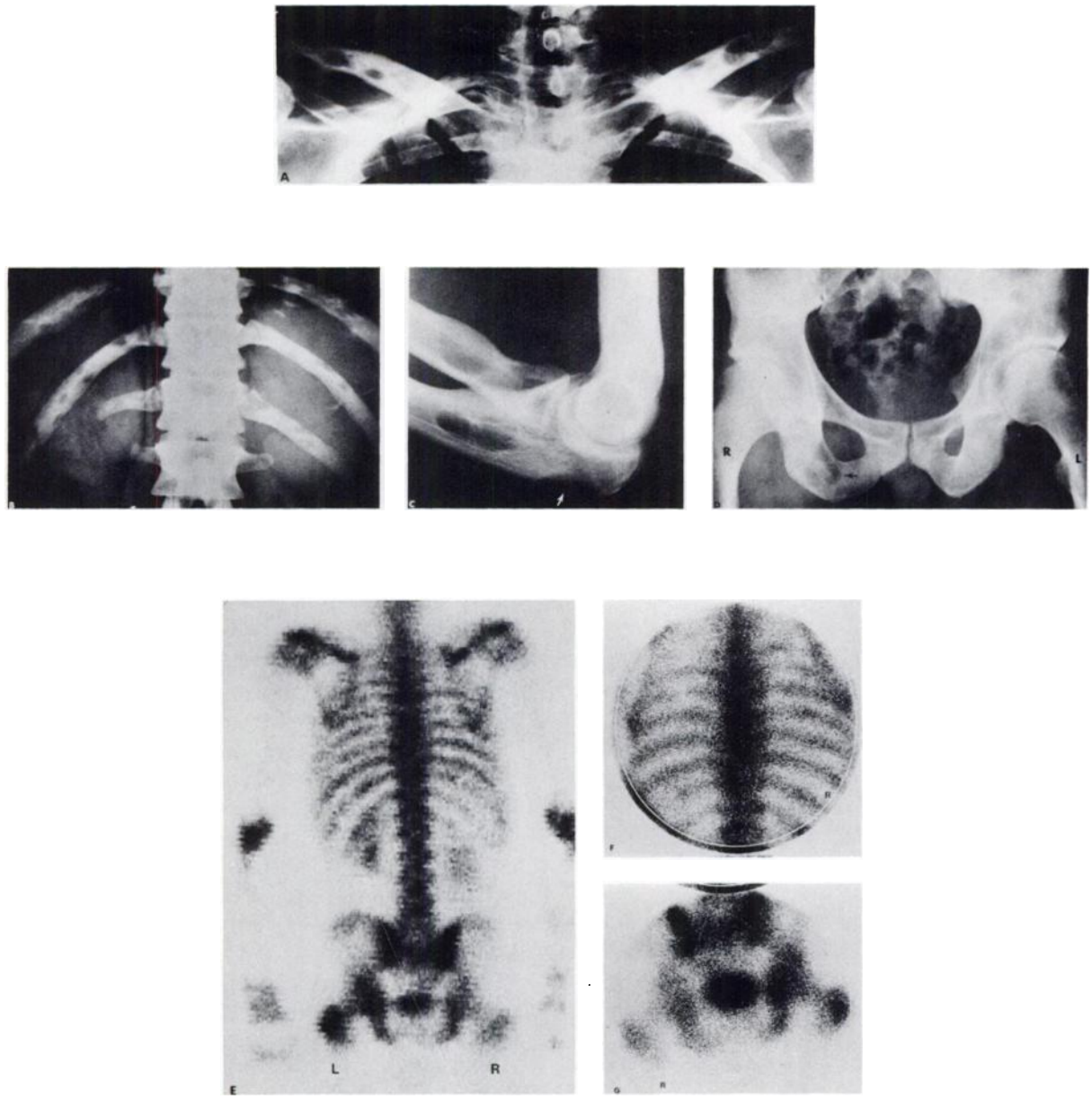

FIG. 1. Case 1. (A–D) Note multiple lytic lesions involving pelvis, radius, ulna, ribs, proximal left femur, and clavicles. Lesions are predominantly lytic, with no periosteal new-bone formation and only minimal sclerosis. Note particularly involvement of bony prominences, i.e., olecranon and ischial tuberosity (arrows). (L = left, R = right.) (E–G) Bone scan reveals several areas of increased Tc-PP_i uptake (i.e., left ischium, left trochanter, and left hip) but in general is less striking than corresponding radiographs. On close inspection it is noted that clavicles also show increased uptake and ribs have mottled appearance due to diffuse involvement.

on amphotericin B; subsequently his symptoms decreased, the pleural effusions and pulmonary infiltrates improved, and the SCFT decreased to 1:128.

Case 3. A 30-year-old black man had DC manifested by skin biopsy, right cervical-node biopsy, skeletal and chest radiographs, and radionuclide bone scan. Chest x-ray revealed hilar and paratracheal adenopathy and a right upper-lobe infiltrate. His SCFT was 1:2,048 and the skin test for coccidioidomycosis was reactive. Amphotericin B therapy was started. The initial skeletal survey showed hand lesions at the right 5th metacarpophalangeal joint and the right 2nd proximal interphalangeal joint. There were lytic lesions of the distal right 5th metacarpal and the proximal portion of the right 2nd middle phalanx, with periosteal new-bone formation. A ^{99m}Tc-PP_i bone scan revealed multiple areas of increased tracer uptake in sites that were normal on radiographic examination (Fig. 2). One of these areas, a right lower rib, subsequently became positive radiographically 4 months later. The patient's bone lesions initially progressed, but about 1 year later partial healing was noted radiographically. The paratracheal nodes and skin lesions have partially regressed and he is now asymptomatic.

Case 4. A 41-year-old white man presented ini-

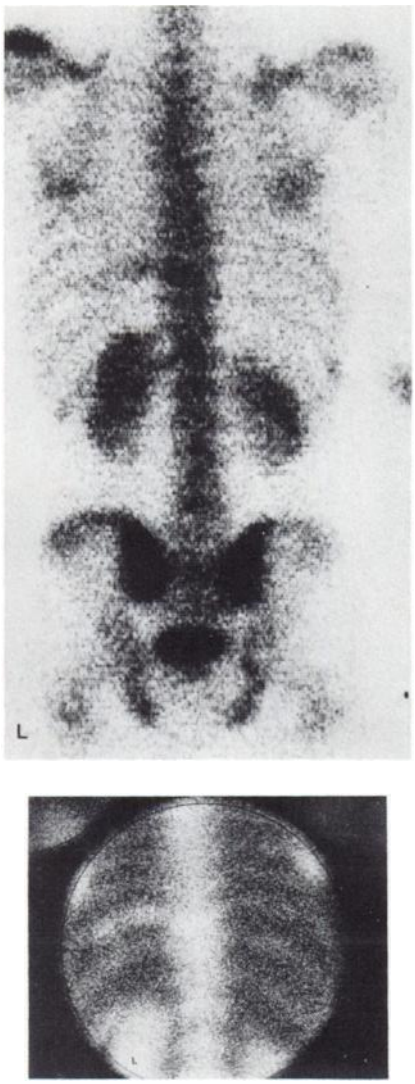

FIG. 2. Case 3. (Top and bottom.) A bone scan shows increased isotopic uptake in the left distal clavical, proximal left femur, and several ribs. A total skeletal survey revealed lesions in the right hand (not shown) but no abnormalities in the areas noted previously.

tially with arthritis of the right wrist and left 5th metatarsophalangeal joint. Subsequent right wrist synovectomy and resection of the left 5th metatarsal head revealed spherules of *C. immitis* in the synovium. The SCFT was 1:64 and the skin test for coccidioidomycosis was nonreactive. Therapy included amphotericin B and miconazole. Radiographs revealed surgical resection of the left 5th metatarsal head and base of the proximal phalanx, and multiple radiolucencies of the left carpal bones with severe destruction of the navicular bone. Technetium-99m-pyrophosphate bone scans, performed 11, 14, and 18 months after surgery, revealed increased uptake in the left 5th metatarsophalangeal joint and the left wrist (Fig. 3).

Case 5. A 61-year-old Vietnamese man arrived in the United States in May 1975 and was placed in the Vietnamese Refugee Camp at Camp Pendleton, California. In August 1976 he developed fatigue but no localizing symptoms. In March 1976 he had a slow onset of pain and swelling in the left elbow. An olecranon lesion was drained surgically and *C. immitis* was recovered. All skin tests, including that for coccidioidomycosis, were negative. Chest radiographs revealed an infiltrate in the right upper lobe, and lytic lesions in the left olecranon process and the left tibial tuberosity. A ^{99m}Tc-PP$_i$ bone scan showed increased uptake in the left tibial plateau, left ankle, and possibly the left patella. The latter two areas were normal radiographically (Fig. 4). The patient was treated with amphotericin B and experienced clinical arrest of his disease.

DISCUSSION

The radiographic features of SC, as shown in our patients, have been well described by others (*1–6*). Lesions are frequently multiple and symmetrical, with predilection for bony prominences and metaphyseal regions. They appear lytic and well delineated, with occasional sclerotic margins. Periostitis is unusual. Vertebral involvement may produce destruction of all spinal elements and lead to vertebral collapse. Relative preservation of the disk space is frequent early in the disease course.

Our observations show that skeletal radiography and scintigraphy each has its own merits and they may be complementary. The radiographs may reveal obvious osseous lesions at a time when the bone scan appears unimpressive. Although the scan in Case 1 is definitely abnormal, it is not as striking as the corresponding radiographs. The phenomenon of a

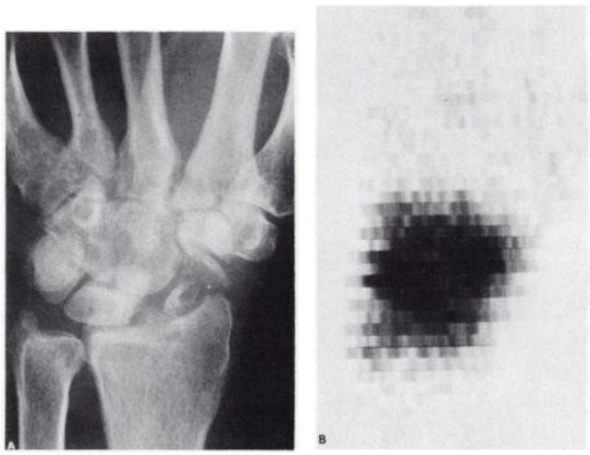

FIG. 3. Case 4. (A) Multiple radiolucencies are noted in the carpal bones, with severe destruction of the navicular bone. (B) Bone scan revealed a markedly increased tracer uptake in wrist.

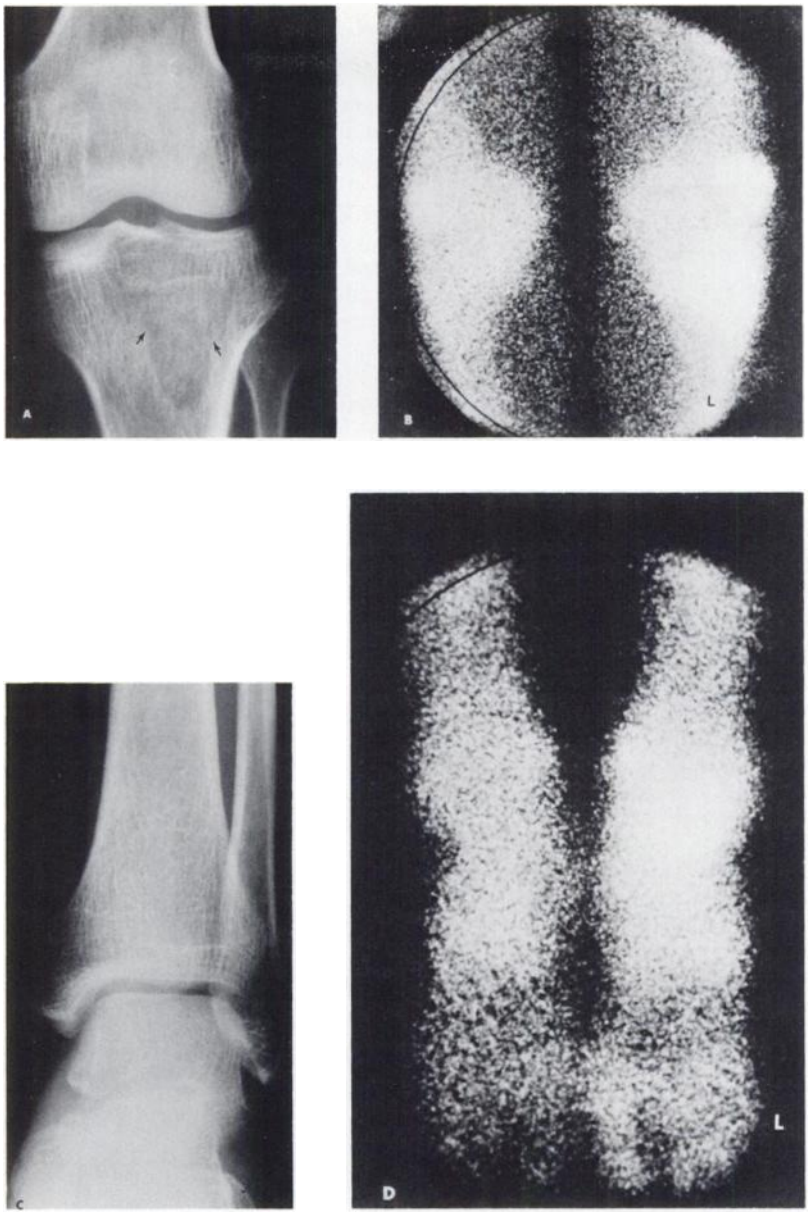

FIG. 4. Case 5. (A) A radiograph of left knee reveals a lytic defect in the proximal tibia (arrows). (B) Bone scan demonstrates increased tracer uptake in the proximal tibia and possibly left patella. (L = left.) (C) A radiograph of left ankle is normal. (D) There is increased activity in left ankle.

relatively normal bone scan in patients with diffuse disease is apparently related to a symmetrical increase of radioactive uptake in nearly all bones (*7,8*). Also, predominantly lytic lesions may fail to show increased uptake, and may even show a decreased uptake (*9,10*). More frequently, the bone scan is the more sensitive indicator, showing skeletal abnormalities at sites that appear normal on radiographs. This occurred in the second, third, and fifth patients. In the fourth patient, previous surgical intervention makes interpretation of the increased activity difficult, but the bone scan did serve to exclude other lesions.

Data are insufficient to evaluate the efficacy of bone scanning in assessing therapeutic response. In Case 2, one area became normal on a follow-up bone scan while one lesion remained unchanged and a new lesion appeared. In Case 4, no change was noted on a follow-up bone scan 18 months after the initiation of therapy. This was in spite of significant clinical improvement. Again, this must be interpreted with caution due to previous surgical intervention. In Case 5 there was an equivocal decrease in activity after six weeks of therapy.

SUMMARY

Five patients are presented, showing the radiographic and scintigraphic manifestations of skeletal

coccidioidomycosis. Diffuse skeletal involvement, detectable on radiographs, may be associated with absent or subtle abnormalities on the bone scan. More frequently the bone scan, being a very sensitive diagnostic tool, may indicate abnormalities when skeletal radiographs are normal. It is apparent that the two diagnostic tools are complementary and should be used together in the evaluation of infectious and neoplastic diseases.

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REFERENCES

1. DALINKA MK, DINNENBERG S, GREENDYKE WH, et al.: Roentgenographic features of osseous Coccidioidomycosis and differential diagnosis. *J Bone Joint Surg* 53-A: 1157–1164, 1971

2. DALINKA MK, LALLY JF, KONIVER G, et al.: Radiology of osseous and articular infections. *Crit Rev Clin Radiol Nucl Med* 7: 1–64, 1975

3. CARTER RA: Infectious granulomas of bones and joints, with special reference to Coccidioidal granuloma. *Radiology* 23: 1–16, 1934

4. BENNINGHOVEN CD, MILLER ER: Coccidioidal infection in bone. *Radiology* 38: 663–666, 1942

5. REEVES RJ, PEDERSEN R: Fungous infection of bone. *Radiology* 62: 55–59, 1954

6. DALINKA MK, GREENDYKE WH: Spinal manifestations of Coccidioidomycosis. *J Can Assoc Radiol* 22: 93–99, 1971

7. THRUPKAEW AK, HENKIN RE, QUINN JL: False-negative bone scans in disseminated metastatic disease. *Radiology* 113: 383–386, 1974

8. FRANKEL RS, JOHNSON KW, MABRY JJ, et al.: "Normal" bone radionuclide image with diffuse skeletal lymphoma. *Radiology* 111: 365–366, 1974

9. GOERGEN TG, ALAZRAKI NP, HALPERN SE, et al.: "Cold" bone lesions: A newly recognized phenomenon of bone imaging. *J Nucl Med* 15: 1120–1124, 1974

10. VIERAS F, HERZBERG DL: Focal decreased skeletal uptake secondary to metastatic disease. *Radiology* 118: 121–122, 1976