Usefulness of Gallium-67-Citrate Scans in Patients with Acute Disseminated Tuberculosis and Comparison with Chest X-rays

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Sixteen patients (4 females, 12 males; ages: 15–80 yr) were admitted to our hospital and diagnosed as having acute disseminated tuberculosis (TB). Gallium-67-citrate scans and chest x-rays were used to localize the TB. The results revealed that: (1) most patients had an underlying disease (malignancy or immunocompromise); (2) gallium lung scans demonstrated multiple patterns from a negative picture to greater than liver uptake (localized or diffuse); (3) the extrapulmonary TB focus could be clearly visualized by whole-body gallium scans; (4) most chest x-rays had a miliary pattern and few cases were negative or localized. A combination examination, including gallium scans and chest x-rays, is needed to avoid missing early diagnosis of acute disseminated tuberculosis, especially in high risk group patients.

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Diagnostic investigation of a patient suspected of having acute disseminated tuberculosis should attempt to obtain proof of tubercular infection as rapidly as possible since treatment should be initiated promptly. Positive ^{67}Ga scans could be used to increase the probability of detection of active tuberculosis in patients with negative sputum smears and thus help to justify early implementation of therapy (*1*). The chest roentgenogram is the single most important means for detecting miliary tuberculosis in the chest of a patient with acute disseminated tuberculosis (*2*). However, many inflammatory causes of discordance between the chest radiograph and ^{67}Ga scintigraphy in the thorax have been described (*3*). We recently investigated the usefulness of ^{67}Ga scans in acute disseminated tuberculosis and compared the lung scintigraphic findings with chest x-rays.

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MATERIALS AND METHODS

Materials

Sixteen patients (4 females, 12 males, age 15–80 yr) were admitted to Taichung Veterans General Hospital from September 1984 through May 1992 with a diagnosis of acute disseminated tuberculosis (Table 1). Those fulfilling one or more of the following criteria were examined in detail:

1. Culture of *M. tuberculosis* from more than one source, including sputum, urine, skin, and cerebrospinal, gastric, pleural and ascite fluid.
2. Biopsy at necropsy that demonstrated noncaseating or caseating epithelioid granulomas on histologic study in one or more organs.
3. A chest roentgenogram that revealed a miliary nodular pattern (*4*).

Technique and Interpretation of Gallium Scans

After intravenous injection of 5 mCi of ^{67}Ga-citrate (Daiichi Radioisotope Laboratories, Ltd., Tokyo, Japan), delayed 48-hr whole-body imaging was done on a large field of view camera with a triple photopeak of ^{67}Ga (93 keV, 184 keV and 296 keV with a 15% window) and a medium-energy collimator with medium resolution (Elscint APC-5). If focal lesions were found, additional spot images (oblique and/or lateral view(s)) were taken for more effective localization. On occasion, bowel preparation with laxatives or enemas was needed to eliminate the normal colonic activity of ^{67}Ga. The ^{67}Ga scan was interpreted by at least two experienced nuclear medicine physicians who had no prior knowledge of the final results. Abnormal uptake of ^{67}Ga in the lung was graded as follows: 1: less uptake than the liver; 2: uptake equal to the liver; 3: uptake greater than the liver; A: localized uptake; and B: diffuse uptake (*5*).

RESULTS

The chest x-ray was an insensitive indicator of disseminated disease, failing to detect 4 of 16 patients (25%) (Table 2). Additionally, 11 of 12 positive patients had lesions in a miliary pattern (Table 2, Figs. 1 and 2), however, only 1 of 12 positive patients showed focal changes (Table 2, Fig. 3).

Gallium-67 imaging detected extrapulmonic disease in 8 of 16 (50%) patients (Table 3, Figs. 3 and 4). The ^{67}Ga lung scans showed that there were 3 of 16 (19%) negative scans;

TABLE 1
Data of Patients with Acute Disseminated Tuberculosis

Case no.	Sex	Age	^{67}Ga lung scan	Extrapulmonary uptake	Chest x-ray	Hilar lymphadenopathy	Underlying disease
1	M	29	1B	Kidneys	Negative	Negative	No
2	F	52	2A (hila)	Knee joints	Negative	Negative	RA
3	M	77	2B	Left-spine	Miliary	Negative	Lymphoma
4	M	65	Negative	Negative	Miliary	Negative	Lymphoma
5	F	30	Negative	Left thigh	Negative	Negative	No
6	M	52	2B	Left-spine	Miliary	Negative	No
7	M	80	1B	Negative	Miliary	Negative	Esophageal CA
8	M	56	3A (BLL)	Negative	Miliary	Negative	No
9	M	73	2B	Left-spine	RUL RML	Negative	No
10	M	15	1A (right hilum)	Negative	Negative	Negative	No
11	M	61	Negative	Liver	Miliary	Negative	AML
12	M	68	1B	Negative	Miliary	Negative	No
13	M	65	3B	Negative	Miliary	Positive	Laryngeal CA
14	F	43	2B	Negative	Miliary	Negative	SLE
15	F	48	1B	Skin	Miliary	Negative	Dermatomyosistis
16	M	21	2B	Negative	Miliary	Negative	SLE

Uptake = gallium scan uptake; L = lumbar; BLL = bilateral lower lungs; BUL = bilateral upper lungs; RUL = right upper lung; RML = right middle lung; RA = rheumatoid arthritis; AML = acute myelocytic leukemia; and SLE = systemic lupus erythematous.

11 of 16 (69%) patients were either grade 1 or 2 and only 2 of 16 (12%) patients were grade 3 (Table 3, Figs. 1, 3 and 5). Additionally, 10 of the 13 positive patients showed diffuse patterns with only 3 of the 13 positive patients showing focal uptake (Table 3, Figs. 1–4).

Fifty-six percent of the patients (9 out of 16) had underlying diseases (malignancies or immunocompromised diseases) (Table 1).

DISCUSSION

The terms disseminated tuberculosis or miliary tuberculosis are commonly used. Miliary tuberculosis defines the presence of innumerable, tiny, discrete tuberculous lesions in the lungs and other organs owing to the seeding of these tissues by bloodborne tubercle bacilli. The word miliary was used originally to denote the small size of such lesions, generally less than 2 mm in diameter, or approximately the size of millet seeds (*2*). Chest radiography usually reveals a miliary pattern (*6*). Disseminated tuberculosis or miliary tuberculosis is most likely to occur in elderly, nonwhite males, often with a background of chronic disease such as alcoholism, malnutrition or diabetes. Immunologic disorders, immunosuppressive therapy and malignancy are major risk factors for disseminated tuberculosis (*2*). In our study, we observated that 9 of 16 patients were harboring a secondary underlying disease. The case fatality rate in miliary disease may be as high as 21% (*7*) and has been attributed to a delayed diagnosis and failure to initiate immediate antituberculous therapy. In fact, up to 30% of these fatalities have been associated with normal or near normal chest radiographs, contributing greatly to the lag time in the initial diagnosis of the miliary stage of the disease (*4,8*).

TABLE 2
Results of Chest X-ray in Patients with Acute Disseminated Tuberculosis

Results	Negative	Positive		Hilar
Pattern		Miliary	Focal	lymphoadenopathy
Patient no.	4	12		
		11	1	1

Gallium-67 scanning is a sensitive indicator of the presence of active tuberculosis. Abnormal patterns of ^{67}Ga uptake may precede radiographic abnormalities and the sensitivity of ^{67}Ga for the detection of active pulmonary disease is reported to be 97% (*9*). Because ^{67}Ga uptake is rarely seen in inactive tuberculosis, imaging with this agent has been reported to be superior to conventional radiography in assessing the response to chemotherapy or establishing reactivation of the disease. Successful treatment of pulmonary tuberculosis results in a marked reduction of ^{67}Ga uptake within a few months (*9*). Gallium-67 scintigraphy has also proved useful in the identification of extrapulmonary sites of tuberculosis involvement and in assessing the response to therapy. In our study, the extra pulmonary tuberculosis in 8 of 16 patients could be clearly detected by whole-body ^{67}Ga scanning.

Diffuse homogeneous pulmonary uptake of ^{67}Ga has been attributed to a number of causes. Infectious causes include bacterial pneumonia, viral pneumonitis, pneumocystic carinii, fungal infections and, as in this paper, tuberculosis. Noninfectious causes include connective tissue disease, radiation pneumonitis, drug-induced pneumonitis and inflammation following administration of lymphangiographic contrast material (*10*). Common conditions which result in a negative chest x-ray but positive ^{67}Ga lung scan include pulmonary toxicity, secondary to chemotherapeu-

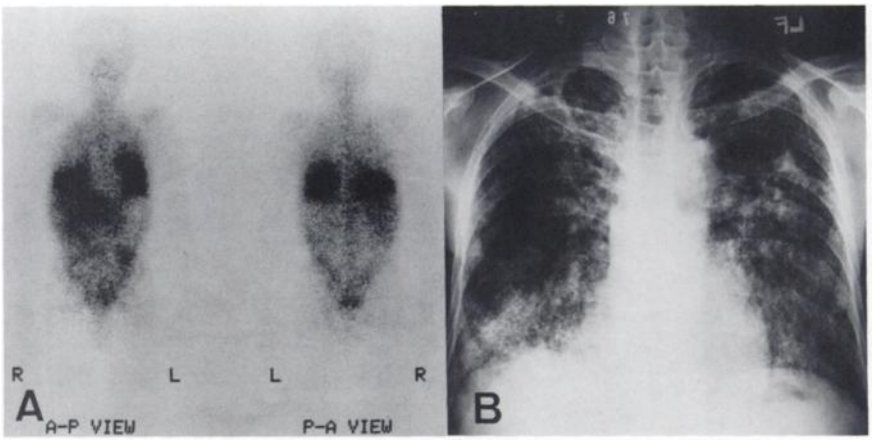

FIGURE 1. A 56-yr-old male patient. (A) The ^{67}Ga lung scan revealed intensely localized ^{67}Ga uptake in the lower portions of both lungs; however, the chest x-ray (B) demonstrated a miliary pattern lesion.

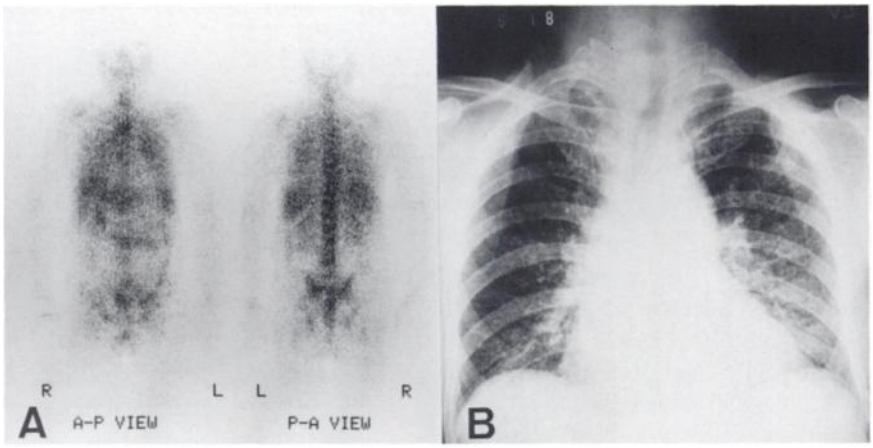

FIGURE 2. A 77-yr-old male patient. (A) The ^{67}Ga whole-body scan revealed diffused ^{67}Ga uptake in both lungs and (B) the chest x-ray demonstrated an abnormal miliary pattern.

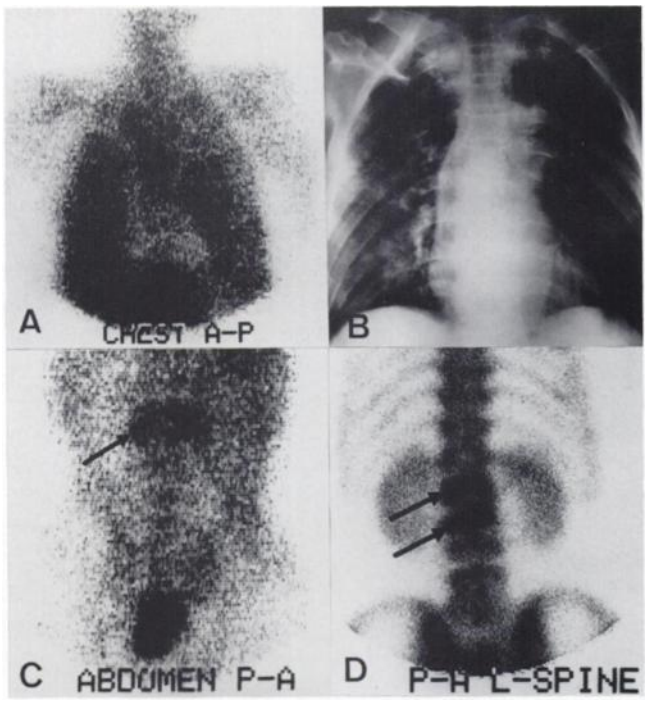

FIGURE 3. This 73-yr-old male patient had extrapulmonary TB lesions in the lumbar vertebral bodies. (A) The ^{67}Ga lung scan revealed diffused ^{67}Ga uptake in both lungs; however, the chest x-ray demonstrated localized lesions in the upper portions of both lungs (B). (C) The bone scan revealed increased MDP uptake in the lumbar spine (arrows), and (D) the ^{67}Ga scan showed congruent ^{67}Ga uptake in the same area (arrows).

tic or immunosuppressive agents, lymphangiography, pneumonconiosis, pneumocystis carinii pneumonia, subradiographic tumors and sarcoidosis (*3,11*). Those conditions which can result in a positive chest x-ray and negative ^{67}Ga lung scan include fibrosis and treated or inactive processes (*3*). Sometimes, as in Patient 4 (lymphoma), uncommon causes such as drug inference or leukopenia (chemotherapy) could result in a negative ^{67}Ga lung scan (*12,13*).

In this study, active miliary pulmonary tuberculosis is known to cause increased localized or diffuse ^{67}Ga lung accumulation (*5,10,14*) and presentation from a negative picture to a grade 3 uptake (localized or diffuse). These patterns are usually associated with an abnormal chest radiograph: most chest x-rays have a miliary pattern, but few cases were negative or localized. Because diffuse uptake of ^{67}Ga in the lungs with a normal chest x-ray has been

TABLE 3
The Results of ^{67}Ga Scans in Patients with Acute Disseminated Tuberculosis

Grade Pattern	Negative	1		2		3		Extra-pulmonary uptake
		A	B	A	B	A	B	
Patient no.	3	5		6		2		
		1	4	1	5	1	1	8

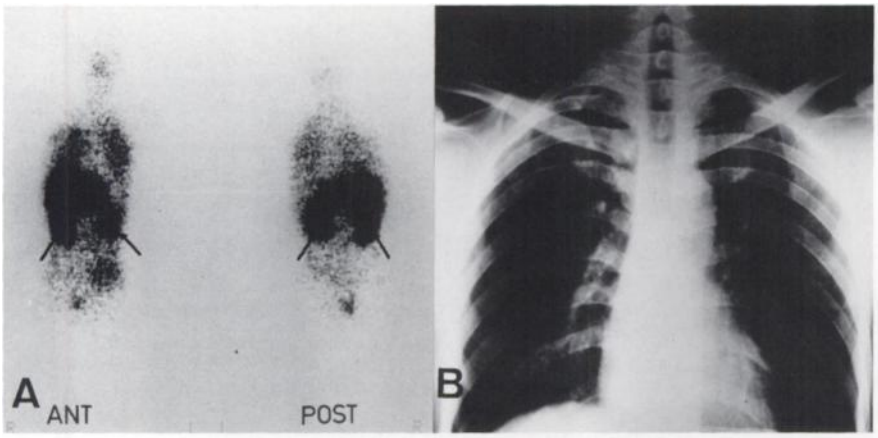

FIGURE 4. This 29-yr-old male patient had extrapulmonary TB lesions in both kidneys. (A) The whole-body ^{67}Ga scan revealed diffused ^{67}Ga uptake in both lungs and both kidneys (arrows), but the chest x-ray demonstrated no definite abnormality (B).

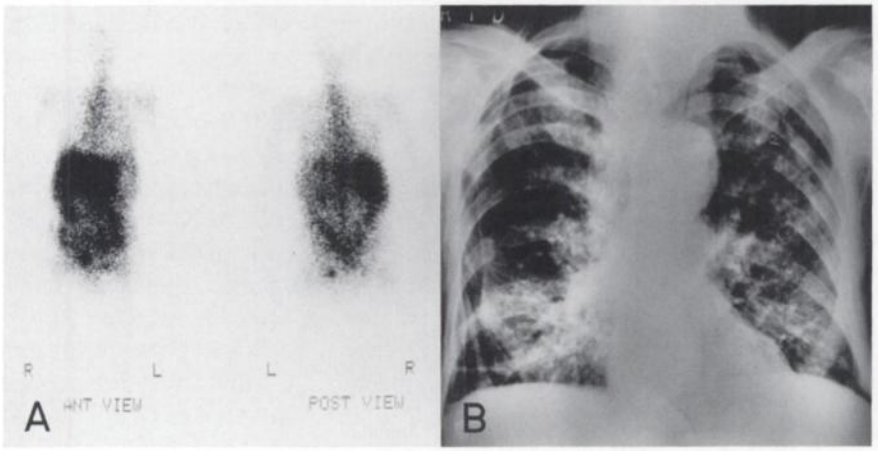

FIGURE 5. A 61-yr-old male patient. (A) The ^{67}Ga whole-body scan revealed no definite abnormality, including both lungs, but the chest x-ray demonstrated lesions in a miliary pattern (B).

reported in two patients with miliary tuberculosis (*15*), certain TB lesions may be missed with only ^{67}Ga scans or chest x-rays. We think that a combination examination, including ^{67}Ga scans and chest x-rays, is needed to avoid missing early diagnosis of acute disseminated tuberculosis, especially in high-risk patients.

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