

# Patterns of Gallium-67 Scintigraphy in Patients with Acquired Immunodeficiency Syndrome and the AIDS Related Complex

Jacob Bitran, Carlos Bekerman, Robert Weinstein, Charles Bennett, U. Ryo, and Steven Pinsky

*Departments of Medicine and Radiology, the Sections of Hematology/Oncology, Infectious Disease and Nuclear Medicine, Michael Reese Medical Center, Pritzker School of Medicine, Chicago, Illinois*

Thirty-two patients with AIDS related complex (ARC) or acquired immunodeficiency syndrome (AIDS) underwent  $^{67}\text{Ga}$  scans as part of their evaluation. Three patterns of  $^{67}\text{Ga}$  biodistribution were found: lymph node uptake alone; diffuse pulmonary uptake; normal scan. Gallium-67 scans were useful in identifying clinically occult *Pneumocystis carinii* pneumonia in seven of 15 patients with ARC who were asymptomatic and had normal chest radiographs. Gallium scans are a useful ancillary procedure in the evaluation of patients with ARC or AIDS.

J Nucl Med 28:1103-1106, 1987

The acquired immunodeficiency syndrome (AIDS) has increased dramatically in incidence since first described in 1981 (1,2). Investigators at the National Cancer Institute and the Institute Pasteur (3-5) have established a human T-cell lymphotropic retrovirus (HTLV-III) as the putative agent (5). Characteristically, patients with AIDS have lymphocytopenia with a reversal of the T lymphocyte helper to suppressor ratio, and by definition are predisposed to Kaposi's sarcoma and opportunistic infections (e.g., *Pneumocystis carinii* pneumonia (PCP) and disseminated *Mycobacterium avium-intracellulare*) (1). A larger group of patients who are infected with HTLV-III manifest less severe illnesses characterized by generalized lymphadenopathy, weight loss and fever, termed AIDS related complex (ARC); up to 20% of these patients may progress to AIDS (6).

The value of gallium-67 ( $^{67}\text{Ga}$ ) scanning in the staging and follow-up of patients with neoplasms, infections, and inflammatory conditions has been extensively reviewed (7-9); however, little data exists on the systematic use of gallium scanning in the clinical evaluation of patients with AIDS or ARC. Isolated case reports on the use of  $^{67}\text{Ga}$  scans for the early diagnosis of PCP in AIDS describe abnormal accumulation of gallium in the lungs preceding radiographic changes by

days or weeks (10). Tuazon et al. (11) and Reinder-Folmer et al. (12) correlated  $^{67}\text{Ga}$  findings with radiologic and bronchoscopic findings in patients with AIDS; however, the majority of patients in both these series had abnormal radiographs.

We herein report the basic scintigraphic patterns of  $^{67}\text{Ga}$  biodistribution that may be found in a series of patients with AIDS and ARC and the correlation of  $^{67}\text{Ga}$  scan findings with the clinical findings of these patients.

## PATIENTS AND METHODS

From January 1, 1981 to January 1, 1986, 32 patients with either AIDS or ARC seen at the Michael Reese Medical Center (MRMC) underwent  $^{67}\text{Ga}$  scanning as part of their medical evaluation. The Centers for Disease Control criteria were used to define AIDS and ARC (13). There were 29 males and three females; median age was 36 yr (range 29 to 58 yr). Of the 29 male patients, 28 were homosexual; one had hemophilia. Of the three females, one was lesbian and abused intravenous drugs; the other two women had a history of multiple blood transfusions.

All 32 patients underwent a complete history and physical (H + P), chest radiograph (C × R) and laboratory examination, which included immunoglobulin levels; skin tests for mumps, trichophyton and candida; total B&T lymphocyte counts; T lymphocyte helper ( $T_4$ )/suppressor ratio ( $T_8$ ); and T lymphocyte responses to Pokeweed mitogen and phytohemagglutinin. Since January 1, 1984, serum antibodies to HTLV-III were

Received May 2, 1986; revision accepted Jan. 30, 1987.

For reprints contact: Jacob D. Bitran, MD, Section of Hematology-Oncology, Michael Reese Med. Ctr., Lake Shore Dr. at 31st St., Chicago, IL 60616.

determined in 20 of 32 patients; 12 patients were seen prior to the widespread availability of HTLV-III antibody testing (Jan. 1, 1981 to Dec. 31, 1983). On the basis of history, physical, chest radiograph, and laboratory findings, patients were diagnosed as having either ARC or AIDS. The chest radiographs were interpreted by attending radiologists who had knowledge of the history and physical findings.

Each patient was injected intravenously with 6–8 mCi of [ $^{67}\text{Ga}$ ]citrate for imaging. The usual preparation of patients included administration of oral laxatives each day, starting on the day of radionuclide injection and continuing until imaging was completed. The  $^{67}\text{Ga}$  image was performed 48 hr or 72 hr after tracer injection with a multiplane imaging system. Simultaneous anterior and posterior images from the level of the head to below the knee were made with the patients supine. Information density of at least 400 counts/cm<sup>2</sup> was obtained in all images. The  $^{67}\text{Ga}$  scans were initially interpreted by all members (C.B., U.Y., S.P.) of the Division of Nuclear Medicine with knowledge of the patients history. Subsequently, the  $^{67}\text{Ga}$  scans were interpreted by one of us (C.B.) without knowledge of the patient's history. The scan findings were then compared with the clinical and laboratory findings.

## RESULTS

All 32 patients had lymphocytopenia with a median lymphocyte count of 900. The T<sub>4</sub>/T<sub>8</sub> ratio was well below 1.0 with a median of 0.55 (range 0.1 to 0.9). HTLV-III antibodies were found in all 20 patients tested. Patients were initially placed into the ARC or AIDS category based on the clinical and laboratory findings as described by CDC criteria (13). There were 20 patients with clinical ARC and 12 patients with clinical AIDS.

Three patterns of gallium uptake were identified: Group I consisted of 13 patients whose scans showed abnormal accumulation of  $^{67}\text{Ga}$  activity in multiple lymph node groups (e.g., cervical, axillary, and inguinal). Little to no uptake within the lungs was seen in this group (Fig. 1). Clinically, all 13 patients were thought to have ARC stage. Group II consisted of 15 patients with diffuse  $^{67}\text{Ga}$  uptake in the lungs (Fig. 2). In 14 of these 15 patients, the diffuse pulmonary uptake lead to a bronchoscopy and brushings or biopsy that showed PCP; one patient refused bronchoscopy and was treated empirically for PCP. Seven of these 15 patients had no pulmonary symptoms and were thought to have ARC (Table 1); however, the abnormal "screening" gallium scan findings lead to a diagnosis of PCP and thus placed these seven patients into AIDS. Group III consisted of four patients with no areas of abnormal accumulation of  $^{67}\text{Ga}$  (Fig. 3). These four patients were found to have AIDS and developed multiple opportunistic infections. Death occurred in all four patients within 3 mo after the "normal" gallium scan. The causes of death were *Mycobacterium avium-intracellulare* infection (one patient), Cytomegalovirus pneu-



**FIGURE 1**  
Tomographic  $^{67}\text{Ga}$  scan, selected anterior planes. The  $^{67}\text{Ga}$  scan of a patient with ARC which demonstrates abnormal accumulation of activity in multiple lymph node groups.

monia (two patients), and Cytomegalovirus encephalitis (one patient).

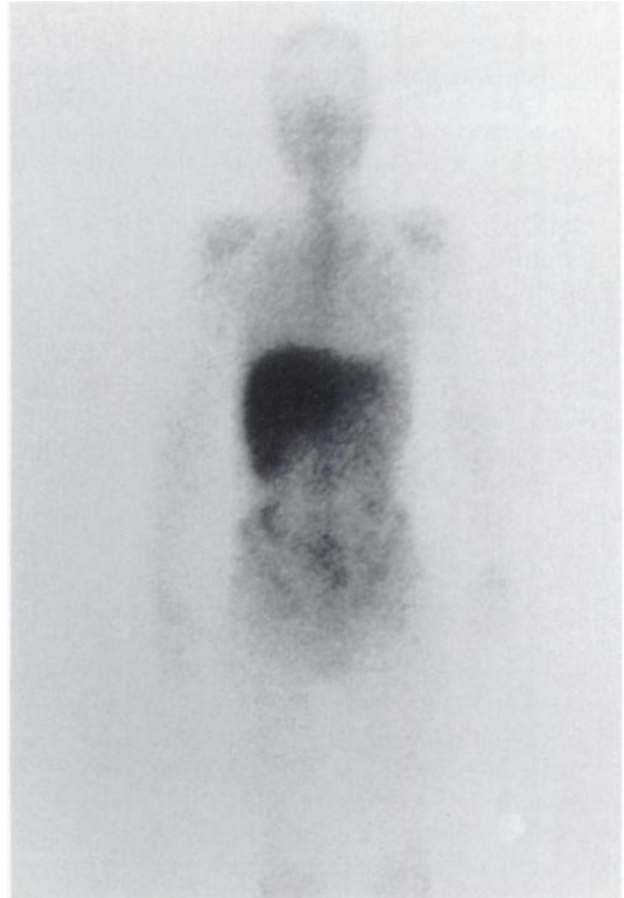
Thus, gallium scans lead to revised staging in the seven patients cited above with asymptomatic PCP (Table 1).

## DISCUSSION

The normal organ localization of  $^{67}\text{Ga}$  at 48 or 72 hr after i.v. injection and variations in its distribution related to age and sex have been reviewed in prior publications (7,8,14). However, many fundamental aspects of  $^{67}\text{Ga}$  transport, normal localization, and mechanisms of uptake in inflammatory lesions or tumors are not completely understood. After i.v. administration, the distribution of  $^{67}\text{Ga}$  depends on its migration from plasma proteins (mainly transferrin and other alpha and beta serum globulins) which act as carrier proteins for  $^{67}\text{Ga}$  to organs, tissues, or microorganisms that have a stronger affinity for the radionuclide. A change in tissue blood supply or influx of leukocytes, which are lactoferrin-rich, will result in enhanced  $^{67}\text{Ga}$  uptake.



**FIGURE 2**  
Tomographic <sup>67</sup>Ga scan, selected anterior planes. This scan is that of a patient with AIDS and *Pneumocystis carinii* pneumonia. The scan shows diffuse, intense, and bilateral lung uptake.



**FIGURE 3**  
Tomographic <sup>67</sup>Ga scan, selected anterior planes. This patient has AIDS and Cytomegalovirus encephalitis and pneumonia. The <sup>67</sup>Ga citrate scan is normal.

Gallium scans were useful in our patients with ARC or AIDS from two standpoints. First, the <sup>67</sup>Ga scan helped identify seven patients with clinically asymptomatic PCP who in addition had normal chest radiographs. Attending radiologists in the Department of Radiology interpreted these chest radiographs as normal with knowledge of the patients history and physical findings and with a heightened sense of awareness for

the presence of opportunistic infections. As shown in Table 1, seven of 20 patients (35%) who clinically were thought to have ARC were recategorized by the <sup>67</sup>Ga scan into AIDS. While the gallium scan is in no way diagnostic for PCP, the diffuse pulmonary uptake seen on scan (Fig. 2) lead to bronchoscopy and ultimately a diagnosis of, and therapy for, PCP. The mechanism of gallium uptake by the lungs in the seven patients with minimal symptoms may be related to capillary dilation or the presence of inflammatory cells. Thus, our results confirm and extend those of Tuazon et al. (11) and Reinder-Folmer et al. (12) who reported the utility of gallium scintigraphy in the diagnosis and treatment of PCP in AIDS.

The second role for gallium scan in patients with ARC or AIDS was relative to confirming the clinical diagnosis. We identified three patterns of <sup>67</sup>Ga uptake: lymph node uptake alone (Fig. 1); diffuse lung uptake (PCP), Fig. 2, normal gallium scan (Fig. 3). When gallium scan findings were used in conjunction with the clinical findings a redistribution of patients into the AIDS/ARC category occurred (Table 1). Remarkably,

**TABLE 1**  
Correlation of Initial Clinical Staging with <sup>67</sup>Ga Scan Results<sup>†</sup> Distribution of Patients

Clinical staging no. of patients	Based on [ <sup>67</sup> Ga]citrate scan patterns <sup>†</sup>		
	Group I	Group II	Group III
ARC, 20	13	7	0
AIDS, 12	0	8	4
	13	15	4

<sup>†</sup> p < 0.005 (3 × 2 contingency table).

<sup>†</sup> See Figures 1–3 for description of scan classification.

there was a 100% concordance and no inter- or intraobserver variability with respect to the interpretation of the  $^{67}\text{Ga}$  scans. The initial reviews and re-reviews lead to no changes in the  $^{67}\text{Ga}$  scan interpretation. Gallium-67 scans allow for more accurate identification of patients with either ARC or AIDS and this obviously is prognostically important.

Of the 32 patients with ARC or AIDS, four patients had normal gallium uptake, and all four patients subsequently died within 3.0 mo. An autopsy was performed in all of these patients and showed infectious processes; disseminated CMV (two patients), disseminated and mycobacterium (*M. avium-intracellulare*) (one patient) and CMV encephalitis with florid PCP (one patient). These organisms were readily identified in many of the tissue sections from lung, liver, spleen, kidney, brain, and bone marrow. Yet, the inflammatory response to these pathogens was abnormal and aberrant with virtually no granulocytes and atypical granulomas characterized by small aggregates of lymphocytes and plasma cells with few monocytes. Thus, the normal gallium scans in these patients may reflect this abnormal inflammatory response which is devoid of granulocytes and presumably gallium receptors.

In summary, three distinctive patterns of [ $^{67}\text{Ga}$ ]citrate biodistribution were present in patients with ARC or AIDS. These patterns correlated with the clinical findings of acquired immunodeficiency, i.e., ARC versus AIDS. In addition,  $^{67}\text{Ga}$  scan helped identify seven patients clinically thought to have ARC who subsequently were found to have PCP. Gallium scanning was a useful tool in the management of patients with ARC or AIDS.

## NOTES

\* (Pho/Con), Searle-Siemens Medical Systems, Iselin, NJ.

## REFERENCES

1. Fauci AS, Masur H, Gelmann EP, et al. The acquired immunodeficiency syndrome: an update. *Ann Intern Med* 1985; 102:800-813.
2. Centers for Disease Control. Kaposi's sarcoma and pneumocystis pneumonia among homosexual men. New York City and California. *MMWR* 1981; 25:308.
3. Barre-Sinoussi F, Chermann J-C, Rey F, et al. Isolation of a T-lymphotropic retrovirus from a patient at risk for acquired immune deficiency syndrome (AIDS). *Science* 1983; 220:868-871.
4. Gallo RC, Salahuddin SZ, Popovic M, et al. Frequent detection and isolation of cytopathic retroviruses (HTLV-III) from patients with AIDS and at risk for AIDS. *Science* 1984; 224:500-503.
5. Sarngadharan MG, Popovic M, Bruch L, et al. Antibodies reactive with human T-lymphotropic retroviruses (HTLV-III) in the serum of patients with AIDS. *Science* 1984; 224:506-508.
6. Francis D, Jaffe H, Fultz PN, et al. The natural history of infection with the lymphadenopathy-associated virus/human T-lymphotropic virus type III. *Ann Intern Med* 1985; 103:719-722.
7. Bekerman C, Hoffer PB, Bitran JD. The role of Ga-67 in the clinical evaluation of cancer. *Semin Nucl Med* 1984; 14:296-323.
8. Bekerman C, Hoffer PB, Bitran JD, et al. Gallium-67 citrate imaging studies of the lung. *Semin Nucl Med* 1980; 3:286-301.
9. Levenson SM, Warren RD, Richman SD, et al. Abnormal pulmonary gallium accumulation in P. carinii pneumonia. *Radiology* 1976; 119:395-398.
10. Levin M, McLeod R, Young Q, et al. Pneumocystis pneumonia: importance of gallium scan for early diagnosis and description of a new immunoperoxidase technique to demonstrate pneumocystis carinii. *Am Rev Respir Dis* 1983; 128:182-185.
11. Tuazon CU, Delaney MD, Simon GL, et al. Utility of gallium $^{67}$  scintigraphy and bronchial washings in the diagnosis and treatment of pneumocystis carinii pneumonia in patients with the acquired immune deficiency syndrome. *Am Rev Respir Dis* 1985; 132:1087-1092.
12. Reinder-Folmer SCC, Danner SA, Bakker AJ, et al. Gallium-67 lung scintigraphy in patients with acquired immune deficiency syndrome (AIDS). *Eur J Respir Dis* 1986; 68:313-318.
13. Centers for Disease Control: Revision of the case definition of acquired immunodeficiency syndrome for national reporting—United States. *Ann Intern Med* 1985; 103:402-403.
14. Bekerman C, Bitran JD, Pavel O, et al. The effects of inadvertent administration of antineoplastic agents prior to Ga-67 injection: concise communication. *J Nucl Med* 1984; 25:430-435.