Computerized Double-Tracer Subtraction Scanning with Gallium-67 Citrate in Inflammatory Diseases

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A gallium-67/technetium-99m subtraction technique was used with a variable weighting factor. That is, each image was separately set to 100%. Varying amounts of the Tc-99m images were subtracted from those of Ga-67. A total of 95 patients who had radiogallium scanning for suspected inflammatory disease were studied by the subtraction technique. Thirty of these patients had abnormal Tc-99m pyrophosphate bone scans, while 20 had abnormal radiogallium abdominal foci; 45 had defects in liver, spleen, or kidney images. The subtraction technique with variable weighting was highly successful in enhancing hot-spot visibility, and in providing information as to the anatomic location of the defect.

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Gallium-67 citrate imaging has been found useful in the detection and location of certain neoplasms as well as inflammatory lesions (*1–3*). In recent years, attempts have been made to increase the sensitivity and specificity of radiogallium scanning. Low lesion-to-background ratios have been a problem, as well as the normal physiologic uptake in certain organs such as the vertebral column, liver, and bowel. In order to improve the efficacy of Ga-67 citrate imaging, a double-tracer subtraction technique had been described by Dawson and coworkers using a dual-probe rectilinear scanner (*4*). Subsequent studies have employed either rectilinear scanners or gamma cameras with one-to-one Ga-67 and technetium-99m subtraction (*5,6*). We recently have utilized a computerized Ga-67/Tc-99m subtraction technique with variable weighting factors. The method used Ga-67 with various organ-specific technetium tracers.

Purpose of the study. The purpose was to evaluate the utility of a double-tracer subtraction technique. Three questions were asked:

1. Given an abnormal Ga-67 focus, could the subtraction technique provide more specific organ or anatomic portrayal than the standard procedure?
2. Since Ga-67 normally accumulates in osseous tissue, would concentration relative to Tc-99m in bone enhance the specificity in osteomyelitis and/or septic arthritis?
3. Could we increase the diagnostic specificity of focal hepatic, splenic, or renal lesions, discovered on conventional scanning, by means of the subtraction technique?

MATERIALS AND METHODS

A gamma camera interfaced to a computer system was used in the study. With a 20% window, the pulse-height analyzer was calibrated to accommodate the 140-keV photopeak of Tc-99m and the 184-keV

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photopeak (24% abundance) of Ga-67. A medium-energy collimator was used. Patients had received 3 mCi of Ga-67 citrate intravenously 48–72 hr previously. To reduce the count differential between the Ga-67 and Tc-99m tracers, we used one-half or less of the usual Tc-99m dose for routine organ imaging. Technetium-99m agents used were 8 mCi of pyrophosphate or diphosphonate, 1 mCi of sulfur colloid, 5 mCi of DTPA or DMSA, or 1.5 mCi of macroaggregated human albumin for bone, liver-spleen, kidney, and lung scanning. These agents were given at appropriate times before imaging, depending upon the type of study performed. Both Tc-99m and Ga-67 images were obtained, without changing the patient's position, over the area of interest based either on clinical evidence or as revealed by an abnormal conventional Ga-67 scan. Paired views in multiple projections were frequently used. Data were recorded and stored on the magnetic tape of the data system. Both images were played back into the dual 16 K, 128 × 128 matrix with a memory-to-memory subtraction feature. The Tc-99m and Ga-67 images were each expressed as 100%. Then the Tc-99m image was processed with gradually increasing weighting factors from 10 to 60%. Each of these weighted images was subtracted from the 100% Ga-67 images. That is, 10% of the radiotechnetium image was subtracted electronically from the radiogallium study, then 20%, and so on. Unprocessed and subtraction images were then photographed from a black-and-white videoscreen.

Both conventional Ga-67 images and the subtraction images were interpreted by two physicians independently. Results were classified as positive, equivocal, or negative in showing either a) excess gallium accumulation as compared with physiologic radiogallium concentration in the liver, spleen, and bone; or b) anatomic definition of an abnormal radiogallium focus, seen on the conventional gallium scan, in relation to neighboring landmarks.

Patients. The study included 95 patients, divided into three groups, who had conventional radiogallium scanning for the diagnosis of inflammatory disease. The first group included bone subtraction imaging in patients suspected of having osteomyelitis, septic arthritis, or infected prostheses and having had positive Tc-99m phosphate bone scans (30 cases). The second group of patients had subtraction imaging in an effort to define more accurately an abnormal radiogallium focus discovered on conventional radiogallium scanning for diagnosis of occult inflammatory disease (20 cases). The third group consisted of patients who were found to have focal disease of the liver, spleen, or kidney seen on Tc-99m scanning. Here subtraction imaging was performed to assess the presence or absence of radiogallium in the focal lesions (45 cases).

TABLE 1. RESULTS OF RADIOGALLIUM SUBTRACTION STUDY IN PATIENTS STUDIED FOR BONE OR JOINT DISEASE

30 patients with bone or joint abnormalities on conventional bone scan	No. of cases
Abnormal Ga-67 uptake at suspected site:	
none	18
definite	4
equivocal	8
Of 8 patients with equivocal Ga-67 accumulation:	
Subtraction technique showed excess gallium in the area	6
Subtraction technique showed no excess gallium uptake	2

TABLE 2. RESULTS OF SUBTRACTION IMAGING IN 45 CASES SUSPECTED OF HAVING INTRA-ABDOMINAL ABSCESSES

45 patients with focal defects in liver, spleen or kidney scans	No. of cases
Excess Ga-67 in lesion on conventional scan	10
No excess Ga-67 in lesion on conventional scan	35
Of the 35 patients without excess Ga-67 in the lesion:	
Subtraction imaging showed excess of Ga-67 over Tc-99m	16
Subtraction imaging did not reveal any excess of Ga-67 in area	19

RESULTS

Bone subtraction scanning. Table 1 shows the results from the 30 patients suspected of having osteomyelitis, septic arthritis, or infected hip prosthesis. Each patient had evidence of focal disease on Tc-99m bone scanning. In 18 of the patients, there was no abnormal Ga-67 accumulation on either the conventional gallium scan or on the subtraction image. On subsequent followup, none of these patients developed localized infections at the areas in question.

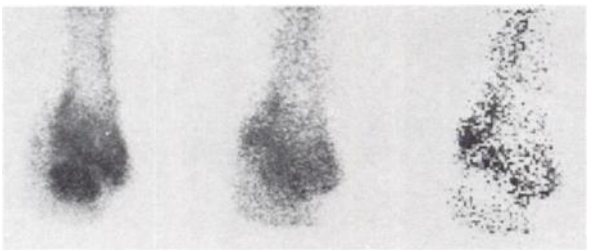

FIG. 1. Anterior views of distal left tibia in Case 1. Left: Tc-99m pyrophosphate. Center: Ga-67 citrate. Right: Subtraction image, weighting factor = 30%.

FIG. 2. Posterior radiogallium image in Case 2. There is intense focal accumulation paravertebrally on left.

In four patients there was evidence of abnormal gallium accumulation at the focal skeletal lesion on the conventional Ga-67 scan. These were all proven to have inflammatory lesions. The remaining eight cases were classified as equivocal on the initial Ga-67 scans. In this group of patients, the subtraction scan suggested excess gallium accumulation in six patients and no excess in two patients. All six of the cases that were positive on subtraction scanning were later proved to have osteomyelitis, with or without septic arthritis, on the basis of bone biopsy culture and on the clinical outcome (100% correlation).

Location of an abnormal radiogallium focus. This group consisted of 20 patients who were suspected of occult intra-abdominal abscess, and who also had an abnormal focus on a conventional Ga-67 scan. Subtraction imaging was performed after a conventional study using liver, spleen, lung, bone, or kidney imaging agents. In all 20 of these cases, we were able to locate the abnormal focus in relation to the organs (intra- or extra-organ). On surgical exploration, all of these patients were proven to have intra-abdominal abscesses. The subtraction-scan information correlated with the operative findings in each case.

Focal liver, spleen, or kidney defects. Forty-five patients with focal hepatic, splenic, or renal lesions demonstrated on the Tc-99m images were studied by the subtraction technique for the presence or absence of gallium in the focal lesions (Table 2). The results of conventional Ga-67 scanning were compared with those of the subtraction images. In ten patients, excess gallium in the area was obvious on the conventional scan. In 35 patients, no excess gallium was seen in the focal lesion on conventional Ga-67 scans. In 16 patients, however, subtraction scanning showed excess gallium in the lesions (16/35 = 46%). The positive cases were later confirmed by operation as being hepatic, splenic, or renal abscesses.

Illustrative case reports. *Case 1.* A 42-year-old man with a long-standing history of diabetes and "Charcot's joints" of the ankles presented with a spiking fever and increasing pain and swelling of both ankles (left worse than right). Clinically, acute osteomyelitis was suspected in the left ankle. A Tc-99m pyrophosphate bone scan showed diffuse uptake in the ankle region. A Ga-67 scan also showed diffuse uptake in the area. On subtraction, excess radiogallium was seen in the distal tibia (Fig. 1). This was later biopsied and the condition confirmed as acute staphylococcal osteomyelitis.

Case 2. A 21-year-old woman presented with spiking fever and pain in the left flank during a course of anticoagulant therapy for pulmonary emboli. There was clinical suspicion of an infected hematoma in the left flank. A conventional gallium scan at 48 hr postinjection showed an abnormal focus on the left side posteriorly (Fig. 2). A subtraction study was first performed with Tc-99m sulfur colloid and was subsequently repeated with Tc-99m DTPA. This showed that the focus was lying inferior and medial to the spleen, involving the superior pole of the left kidney (Fig. 3, right). The

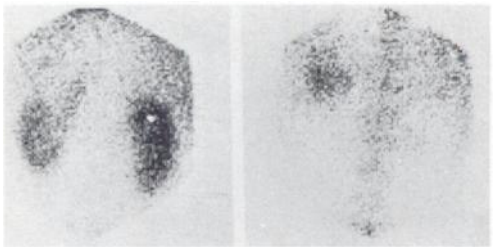

FIG. 3. Left: posterior Tc-99m DTPA study revealing defect in superior pole of left kidney. Right: Tc-99m DTPA image has been subtracted from the Ga-67 image in Fig. 2, with 30% weighting. Resulting gallium focus is accentuated.

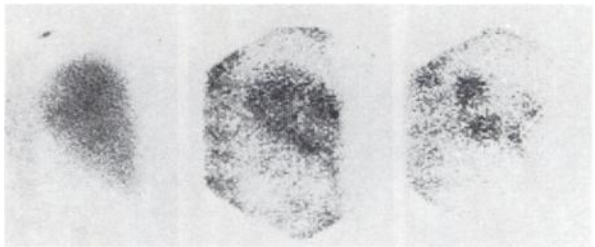

FIG. 4. Left: posterior liver scintiphoto after Tc-99m sulfur colloid. Center: radiogallium image of same region. Right: subtraction image revealing discrete hepatic areas of radiogallium accumulation.

patient was explored and a left renal abscess with a perinephric component was drained. The patient underwent a left partial nephrectomy and recovered uneventfully.

Case 3. A 52-year-old woman was admitted with a history of fever, chills, and pain in the right upper quadrant for several days. Physical examination and laboratory findings pointed toward a liver abscess. A liver scan with Tc-99m sulfur colloid showed mild nonhomogeneous uptake without clear evidence of focal defects. A conventional radiogallium scan showed liver uptake, also unevenly distributed. Subtraction imaging revealed multiple focal accumulations of radiogallium in the liver (Fig. 4). At operation, 150 cc of purulent material was drained from multiple small abscesses in the liver.

DISCUSSION

Radiogallium is commonly used for its tumor-seeking properties and for detection of inflammatory disease (*4–6*). Preliminary studies using rectilinear scanners had indicated the usefulness of Ga-67 and Tc-99m subtraction imaging in the detection of neoplastic and inflammatory lesions. The computerized Ga-67/Tc-99m subtraction technique described here enhances abnormal radiogallium foci by subtracting the interference due to tracer uptake in healthy tissues. Subtraction imaging has been found useful in reducing the normal physiologic contribution of the liver, spleen, and bones, and in enhancing the abnormal gallium foci in areas of interest. It significantly enhanced the specificity and definition of radiogallium foci relative to surrounding structures. Subtraction was helpful in the diagnosis of selected cases of both osteomyelitis and septic arthritis by clearly demonstrating excess radiogallium concentration in the bones at the sites of infection. Subtraction imaging also showed uptake of radiogallium, or its absence, in focal disease of liver, spleen, and kidney, more definitely than on conventional scans. Among the positive cases, small areas of abnormal uptake became easily identifiable and the larger ones became more clear. This modification of standard gallium scanning significantly improved the results. The useful range of subtraction was 10 to 30%. Beyond that point, statistical uncertainty became a factor and the images were less reliable.

The subtraction imaging study with variable weighting factor is also readily performed. In a busy clinical schedule, it may not be feasible to perform subtraction imaging in every patient with a normal radiogallium study. It appears, however, that two principal uses of the subtraction method are: a) when the radiogallium study is equivocal, and b) when better information is needed as to anatomic location, in order to guide further diagnostic studies or surgical exploration.

ACKNOWLEDGMENT

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