Delayed Renal Localization of Ga-67: Concise Communication

Dorothy S. Lin, Jane A. Sanders, and Bharti R. Patel

University of Mississippi Medical Center, and Veterans Administration Medical Center, Jackson, Mississippi

Five hundred Ga-67 images, requested for detection or follow-up of inflammatory or neoplastic diseases, were reviewed to evaluate the incidence of delayed renal localization and the clinical significance of different degrees of uptake. Renal uptake in 48- or 72-hr images was graded as follows: 0 = background activity; 1+ = greater than background but less than spine; 2+ = close to spine but less than liver; 3+ = same as liver; 4+ = greater than liver. On the 500 images, 996 kidneys were evaluated and among them 600 (60%) had 0 uptake and 340 (34%) had 1+. These 940 kidneys were all considered to be normal. Fifty-six (6%) had 2+ or more uptake, with possible causes for uptake being: infection 27, drug-induced renal damage ten, urinary stasis or slow excretion seven, collagen vascular disease six, renal failure four, acute tubular necrosis one (ATN), and indeterminate one. Cases of renal infection or failure tended to show more or less 4+ uptake, while drug damage, ATN, or urinary stasis tended to have 2+ uptake.

J Nucl Med 24: 894–897, 1983

Gallium-67 has been widely used for the work-up of patients with fever of unknown origin (FUO), for tumor staging, and for detection or follow-up of certain other diseases. In the first 24 hr after injection, some 12–30% of the injected dose of Ga-67 is excreted from the kidneys (*1–3*). Urinary tract uptake seen 48 hr after injection is usually considered abnormal (*4*). This investigation was undertaken in retrospect to evaluate the incidence of delayed Ga-67 renal localization and its possible causes.

MATERIALS AND METHODS

We reviewed a total of 500 consecutive Ga-67 images performed in the years of 1981 and 1982. There were 373 males and 127 females, with ages ranging from 18 mo to 78 yr.

For adults, 4–5 mCi Ga-67 citrate were given by intravenous injection and for children doses proportional to weight were used. All the images were obtained using a large-field-of-view camera equipped with high energy parallel-hole collimator and dual or triple channel pulse-height analyzer.

Renal uptake on 48- or 72-hr images was graded as follows: 0 = background activity; 1+ = greater than background but less than spine; 2+ = close to spine but less than liver; 3+ = same as liver; 4+ = greater than liver.

RESULTS

The indications for the 200 UMC images were: 50 for FUO, 49 for tumor, 101 for other diseases such as sarcoidosis, interstitial pneumonitis, tuberculosis, collagen vascular disease, etc.; the 300 VAMC images were 60 for FUO, 178 for tumor, 62 for others (Table 1).

In the 500 images, 996 kidneys were evaluated. Among them 600 (60%) had 0 uptake, 340 (34%) had 1+, and 56 (6%) had more than 2+ uptake. Different grades of renal uptake were grouped under the three main indications for the study in Table 2, and those having 0 or 1+ uptake showed proportionally the same distribution among the three groups. When correlated with patients' ages, kidneys having 0 or 1+ uptake again showed no difference in distribution in different age

Received Apr. 5, 1983; revision accepted Apr. 13, 1983.

For reprints contact: Dorothy S. Lin, MD, Nuclear Medicine Division, Dept. of Radiology, University of Mississippi Medical Center, 2500 N. State St., Jackson, MS 39216.

TABLE 1. INDICATIONS FOR THE 500 Ga-67 IMAGES

Hospital	Number of images			
	FUO	Tumor	Other	Total
UMC	50 (25%)	49 (25%)	101 (50%)	200
VAMC	60 (20%)	178 (59%)	62 (21%)	300
Total	110 (22%)	227 (45%)	163 (33%)	500

groups. Among the group whose study was indicated for tumor detection and who had recently received chemotherapy, 16% had 0 uptake while 20% had 1+.

The 56 kidneys that showed 2+ or more uptake belonged to 29 patients. The various possible causes, listed in Table 3, were: infection 27, drug-induced renal damage ten, urinary stasis or slow excretion seven, collagen vascular disease six, renal failure four, acute tubular necrosis (ATN) one, indeterminate one. The different patterns of renal uptake against the various possible causes listed in Table 4 were: bilateral diffuse 38 (68%, the leading manifestation of all causes), unilateral diffuse nine (16%, more often related to infection), focal nine (16%, majority caused by infection).

Of the 35 images, 34 had positive 2+ to 4+ renal uptake and they were correlated with other performed procedures in Table 5. The most commonly performed item, laboratory tests, had a positive rate of 61% (21/34).

DISCUSSION

The incidence of delayed Ga-67 renal localization has been reported to be 1.7% of 2000 patients, with studies performed primarily for diagnosis and staging of neoplastic disease (*5*). Another investigation yielded 6.8% in 175 patients whose studies were done mainly for detecting suspected occult inflammatory process (*2*). We obtained an incidence of 6% in 500 consecutive Ga-67 images performed for various purposes.

Of the 996 kidneys evaluated, 340 (34%) had 1+ renal uptake on the 48- or 72-hr images. The 1+ uptake was considered to be normal, since it was usually bilaterally symmetrical, GU asymptomatic and, when compared with the 600 kidneys (60%) with 0 uptake, showed similar distribution among different disease groups, age groups, and recent chemotherapy recipients. According to some previous reports, 50 μCi/kg of Ga-67 would not make normal kidneys visible after 48 hr (*2,6*). In some of our cases, the 4–5 mCi dose exceeded that range. Thus the reason for some of our normal kidneys to show faint uptake (as of 1+) could be due to the larger tracer dose we have been using. It has been discovered that dosage above the 50 μCi/kg level in small animals will cause even normal kidneys to be faintly visualized (*6*). In addition, rather faint renal gallium accumulation in the absence of renal pathology with severe hepatocellular disease has recently been reported (*7*). Among the possible explanations for the increased urinary gallium excretion discussed were: (a) that diseased liver accumulates less gallium or produces less circulating transferrin to bind gallium in the blood; and (b) that increased iron load may decrease the transferrin available for gallium binding. In our patient population, alcoholic liver disease and increased iron load due to frequent blood transfusions or sickle-cell disease are very commonly seen, and this might explain why some of our normal kidneys had 1+ uptake.

When the scans were correlated clinically and compared with other procedures, the possible cause(s) for 55 out of the 56 kidneys having 2+ or more uptake were found. Cases of renal infection or failure tended to show more or less 4+ uptake, whereas drug-induced damage, ATN, or urinary stasis tended to have 2+ uptake. In infection, half the number of kidneys showed bilateral diffuse uptake and the other half showed either unilateral diffuse or focal uptake. Among the other possible causes, bilateral diffuse uptake was also the leading finding. According to Linton et al. (*8*): intense uniform Ga-67 uptake was seen in drug-induced interstitial nephritis and

TABLE 2. RENAL Ga-67 UPTAKE GROUPED ACCORDING TO INDICATIONS FOR THE STUDY

Uptake	FUO	Tumor	Other	Total
0	111 (11%)	285 (29%)	204 (20%)	600 (60%)
1+	60 (6%)	162 (16%)	118(12%)	340 (34%)
2+ – 4+	46 (5%)	6 (0.6%)	4 (0.4%)	56 (6%)
Total	217 (22%)	453 (45.6%)	326 (32.4%)	996 (100%)

TABLE 3. VARIOUS POSSIBLE CAUSES FOR INCREASED RENAL Ga-67 UPTAKE

Possible cause	Renal uptake 2+	3+	4+	Total
Infection (possibly w/other causes)	4	8	15	27 (48%)
Drug-induced damage	6	4		10 (18%)
Urine stasis or slow excretion	7			7 (12%)
Collagen vascular disease	2	2	2	6 (11%)
Renal failure			4	4 (7%)
Acute tubular necrosis	1			1 (2%)
Indeterminate	1			1 (2%)
Total	21 (37.5%)	14 (25%)	21 (37.5%)	56 (100%)

TABLE 4. PATTERNS OF INCREASED RENAL Ga-67 UPTAKE

Possible causes	Bilateral diffuse	Unilateral diffuse	Focal	Total
Infection (possibly w/other causes)	14	5*	8	27 (48%)
Drug-induced damage	10			10 (18%)
Urine stasis or slow excretion	6	1		7 (12%)
Collagen vascular disease	4	1	1	6 (11%)
Renal failure	4			4 (7%)
Acute tubular necrosis		1*		1 (2%)
Indeterminate		1		1 (2%)
Total	38 (68%)	9 (16%)	9 (16%)	56 (100%)

* One case had only one kidney.

TABLE 5. 34 POSITIVE Ga-67 IMAGES CORRELATED WITH OTHER PROCEDURES

Examination	Positive	Negative
Blood and/or urine laboratory	21	13
IVP or retrograde pyelogram	3	6
Sonogram	2	4
TCT	1	4
Bone imaging	7	1
Histological	6	0

in minimal-change nephrotic syndrome; weaker uptake was seen in glomerulonephritis; patchy uptake in pyelonephritis; no uptake in ATN. In the diagnosis of perinephric abscesses, Hopkins et al. (*9*) suggested the combined study using a Tc-99m-labeled renal radiopharmaceutical and Ga-67, with the subtraction technique. The limits of the kidney can be defined and the site of abnormal Ga-67 localization can be assessed more accurately.

More experience is needed regarding degrees and patterns of Ga-67 renal uptake in relation to their underlying causes.

Although delayed Ga-67 renal localization is a very sensitive indicator for renal abnormality, it is, nevertheless, a very nonspecific test. A gamut of the known causes for delayed renal uptake of Ga-67 is gathered from the literature as follows:

Common.

1. Infection.

a. Acute or chronic active pyelonephritis (*2,4,5,8,10*).

b. Renal abscess (*2,3*).

c. Perirenal abscess (*3,9*).

d. Ureterosigmoidostomy (*10*).

2. Acute interstitial nephritis due to drug hypersensitivity.

a. Antibiotics—penicillin and its derivatives (*11*) (methcillin, ampicillin, oxacillin, nafcillin, carbenicillin), erythromycin (*8*), cephalosporins (*8,11*), sulfonamides (*8,11*), rifampin (*11*), pentamidine (*5*).

b. Anti-inflammatory drugs—ibuprofen (*8*), phenylbutazones (*8,11*), salts of gold (*11*), allopurinol (*8*).

c. Diuretics—thiazides (*8*), furosemide (*8,11*).

d. Analgesics, sedatives (*11*)—phenazone, phenobarbital, glofenine.

e. Antineoplastic drugs (*4*).

f. Anticonvulsant—diphenylhydantoin (*11*).

g. Anticoagulant—phenindione (*8,11*).

3. Metastatic tumor—leukemia (*1,5,10*), *lymphoma* (*1,5,10*), *malignant melanoma* (*1,5*).

4. *Urinary tract obstruction* (*2,3*).
5. *Acute renal failure* (*2*).
6. *Acute tubular necrosis* (*2*).
7. *Severe hepatocellular disease* (*7*).
8. *Collagen vascular disease* (*4*)—*polyarteritis nodosa* (*2*), *systemic lupus erythematosis* (*12*).

Uncommon.

1. *Acute or chronic allograft rejection* (*4,13*).
2. *Nephrotic syndrome* (*8*).
3. *Glomerulonephritis* (*8,12*).
4. *Renal amyloidosis* (*1,3*).
5. *Acute vasculitis* (*2,3*).
6. *Congestive heart failure* (*14*).
7. *Multiple blood transfusions—also shows decreased liver uptake* (*15*).
8. *Renal-cell carcinoma* (*16*).

Rare.

1. *Sarcoidosis* (*3*).
2. *Hepatic failure* (*4*).
3. *Hemochromatosis* (*4,10*).
4. *Wegener's granulomatosis* (*2*).

For correct interpretation of the delayed Ga-67 renal uptake, correlation with clinical history, laboratory tests, IVP, sonogram, TCT, bone imaging (*17*), and arteriography often would be helpful. But for definite diagnosis histological examination is often needed.

ACKNOWLEDGMENT

The authors thank Linda T. Prior for assistance in preparing this manuscript.

REFERENCES

1. BEKERMAN C, VYAS MI: Renal localization of ^{67}Ga-citrate in renal amyloidosis: Case reports. *J Nucl Med* 17:899-901, 1976
2. KUMAR B, COLEMAN RE: Significance of delayed ^{67}Ga localization in the kidneys. *J Nucl Med* 17:872-875, 1976
3. MENDEZ G JR, MORILLO G, ALONSO M, et al: Gallium-67 radionuclide imaging in acute pyelonephritis. *AJR* 134: 17-22, 1980
4. *Nuclear Radiology* (*Second Series*) *Syllabus*. Siegel BA, Ed. Chicago, ACR 1978, pp 496-502
5. FRANKEL RS, RICHMAN SD, LEVENSON SM, et al: Renal localization of gallium-67 citrate. *Radiology* 114:393-397, 1975
6. HURWITZ SR, KESSLER WO, ALAZRAKI NP, et al: Gallium-67 imaging to localize urinary tract infections. *Br J Radiol* 49:156-160, 1976
7. ALAZRAKI N, STERKEL B, TAYLOR A: Renal gallium accumulation in the absence of renal pathology in patients with severe hepatocellular disease. *Clin Nucl Med* 5:200-204, 1983
8. LINTON AL, CLARK WF, DRIEDGER AA, et al: Acute interstitial nephritis due to drugs. *Ann Intern Med* 93:735-741, 1980
9. HOPKINS GB, HALL RL, MENDE CW: Gallium-67 scintigraphy for the diagnosis and localization of perinephric abscesses. *J Urol* 115:126-128, 1976
10. KESSLER WO, GITTES RF, HURWITZ SR, et al: Gallium-67 scans in the diagnosis of pyelonephritis. *West J Med* 121:91-93, 1974
11. KLEINKNECHT D, KANFER A, MOREL-MAROGER L, et al: Immunologically mediated drug-induced acute renal failure. *Contrib Nephrol* 10:42-52, 1978
12. WOOD BC, SHARMA JN, GERMANN DR, et al: Gallium citrate Ga-67 imaging in noninfectious interstitial nephritis. *Arch Intern Med* 138:1665-1666, 1978
13. GEORGE EA, CODD JE, NEWTON WT, et al: ^{67}Ga citrate in renal allograft rejection. *Radiology* 117:731-733, 1975
14. HIGGINS CB, TAKETA RM, TAYLOR A, et al: Renal uptake of ^{99m}Tc-sulfur colloid. *J Nucl Med* 15:564-566, 1974
15. BLEI CL, BORN ML, ROLLO FD: Gallium bone scan in myelofibrosis: Case report. *J Nucl Med* 18:445-447, 1977
16. ANTONIADES J, HONDA T, CROLL MN, et al: Gallium 67 scanning in patients with renal cell carcinoma. *J Urol* 109: 564-566, 1973
17. LIN DS, SANDERS JA, FLOWERS WM JR: Increased renal uptake of [^{99m}Tc]methylene diphosphonate. *Int J Nucl Med Biol* 9:201-207, 1982