The Spectrum of Gallium-67 Renal Activity in Patients with No Evidence of Renal Disease

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Thirty-seven gallium-67 images were reviewed retrospectively to determine relative renal gallium activity (RGA) in patients with no evidence of renal disease. Twenty-four patients were classified as having no evidence of renal disease (NRD). RGA was identified in 50.0% (12/24) of patients in the NRD group. We conclude that the presence of RGA neither suggests nor rules out renal disease. Altered nonrenal biological factors (such as saturation of iron-binding capacity) may decrease soft-tissue gallium accumulation while activity in the kidney remains unchanged. The latter provides renal images with better signal-to-noise ratio. Current imaging equipment may allow renal visualization in these patients.

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Gallium-67 citrate has been widely used for the evaluation of inflammatory diseases of the kidneys. It is often claimed that renal gallium activity (RGA) beyond 24 hr after injection suggests an inflammatory process such as infection (*1*), interstitial nephritis (*2,3*), or abscess (*4,5*). Previous reports have stated that ". . .the kidneys normally do not appear on the 48–72-hr scan" (*6*). This finding has been supported by others (*1,7*). Hauser and Sherman stated that this criterion may be too strict and that minimal activity may be seen in the kidneys at 48 hr or later (*8,9*). The purpose of this report was to determine the spectrum of RGA in patients with no evidence of renal disease.

MATERIALS AND METHODS

A retrospective review of Ga-67 scintigrams performed between March and October of 1981 was done. All subjects in our study were inpatients. They were included in the study if the hospitalization records were available for review and if a urinalysis, BUN, and creatinine were obtained during the hospital stay. Thirty-seven patients met these specifications. Eleven were studied in search of an infectious focus. The other patients were mainly evaluated for either sarcoidosis or neoplasia (see Tables 1–3).

All adult patients received 3–5 mCi (111 to 185 MBq) of Ga-67 citrate intravenously; children received 50 μCi/kg (1.85 MBq/kg). A bowel preparation kit was used if not contraindicated. All images were obtained on the same gamma camera. One million counts per view (posterior) were obtained using 20% windows on the 93-, 184-, and 296-keV photopeaks. When liver/spleen studies were available, these were helpful in the assessment of the right kidney. The time from injection to imaging was recorded. Three nuclear medicine physicians interpreted the scintigrams for renal gallium activity (RGA) in each kidney using the grading system in Table 4 (Fig. 1). All kidneys were graded at either 48 or 72 hr, or both. The distribution of activity was also characterized as diffuse or focal. If a disagreement existed regarding grade, a consensus was obtained. The patient records were reviewed for (a) evidence of renal disease; (b) chemotherapy, other drugs; (c) radiotherapy; or (d) blood transfusions.

Regarding the presence or absence of renal disease, the following criteria were used:

(1) No evidence of renal disease (NRD). This group

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TABLE 1. KIDNEYS WITH NO DISEASE

No. Case	Diagnosis	Chemotherapy irradiation, etc.	Renal gallium Activity grades (see Table 4) 48 hr (left/right)	72 hr (left/right)
1	Sarcoid	None	0/0	0/0
2	Sarcoid	None		0/0
3	Hodgkin's	None	0/0	0/0
4	Hodgkin's	None	0/0	
5	Sarcoid	None	0/0	
6	Febrile seizures	None	0/0	
7	Hodgkin's	None	0/0	0/0
8	Sarcoid	Prednisone	0/0	
9	Hodgkin's	MVPP/SCDB*	0/0	0/0
10	Cathartic abuse colitis	None	0/0	0/0
11	Abdominal pain, cause unknown	None	0/0	
12	Abdominal pain	None	ID/ID§	ID/ID
13	Viral syndrome	None	1/1	
14	Lymphoma	None	1/0	
15	Pelvic AVM	None	0/ID	0/ID
16	Mood disorder	None		2/ID
17	Hodgkin's	None	2/2	2/2
18	Eosinophilia	None	2/2	
19	Hodgkin's	None	2/0	2/0
20	Hodgkin's Wound abscess	Ampicillin Gentamicin	1/1	2/1
21	Liver hemangioma	None	1/1	2/2
22	Lymphoma	None	1/1	2/2
23	Lung carcinoma	Radiation†		1/2
24	Hodgkin's	None	2/3	2/3
25	Wilms' tumor (right kidney)	Radiation†	ID	ID
26	Leukemia	Multiple drugs Multiple RBCs Transfusion	4/4	4/4

* MVPP = methotrexate vincristine, procarbazine, prednisone.
* SCDB = streptozotocin, cyclophosphamide, doxorubicin, BCNU.
† Radiation port did not include kidneys.
§ Indeterminate.

TABLE 2. KIDNEYS WHERE THE PRESENCE OR ABSENCE OF DISEASE IS UNCERTAIN (PRD)

No. Case	Diagnosis	Chemotherapy irradiation, etc.	Renal gallium activity grades 48 hr (left/right)	72 hr (left/right)
27	Sarcoid	None	0/0	
28	Pelvic abscess	gentamicin		1/0
29	Pneumonia	cephapirin/gentamicin	ID/ID	
30	Small bowel obstruction	None	1/1	1/1
31	Sterile pyuria	None	1/0	1/0
32	UTI and right thigh abscess	nitrofurantoin		2/2

TABLE 3. KIDNEYS WITH DEFINITE DISEASE

No. Case	Diagnosis	Chemotherapy irradiation, etc.	Renal gallium activity grades 48 hr (left/right)	72 hr (left/right)
33	Left pyelonephritis	Gentamicin	3*/0	4*/0
34	Leukemia	Cisplatin	4/4	
		Amphotericin		
35	Rheumatoid arthritis	Gold	3/3	
	Nephrotic syndrome	Penicillamine		
36	Benign prostatic hypertrophy	Gentamicin	2*/1	2*/1
	Urosepsis			
37	Pyelonephritis	Cisplatin	2*/1	
	Ovarian cancer	Melphalan		

* Focal activity.

consisted of subjects with a normal urinalysis (no casts, no WBC-RBC/hpf, no bacteria, no protein, normal pH and specific gravity). In addition, these patients also had normal BUN (<20 mg/dl) and creatinine (<1.4 mg/dl).

(2) Definite renal disease (DRD), defined by significant abnormalities in any of the above tests (hematuria >10 RBC/hpf, pyuria >10 WBC/hpf, casts, 3+ to 4+ protein, BUN >25 mg%, and creatinine >1.8 mg%). Some of these patients had additional abnormal data from IVP, ultrasonogram, or urine culture.

(3) Probable renal disease (PRD). This group did not fulfill the criteria for either of the above categories, and was not analyzed.

RESULTS

Thirty-seven cases were reviewed. Twenty-six patients were classified as having no evidence of renal disease (NRD), six as probable renal disease (PRD), and five as definite renal disease (DRD). The clinical diagnosis, therapy, and grade of renal activity are listed in Table 1-3. The average age was 36.6 yr (range 13 mo to 69 yr).

TABLE 4. KIDNEY GRADING SYSTEM

0	No renal activity.
1+	Slightly increased activity relative to background.
2+	Definite increased activity with well-defined outline, but activity is less than in liver.
3+	Same as above, but activity is equal to liver.
4+	Activity greater than liver.
ID*	Grade cannot be assessed, due to bowel activity.

* ID = Indeterminate

The average age in each category was: 0 grade, 31.2 yr; 1+ grade, 46.5 yr; 2+ grade, 35.5 yr; 3+ grade, 32.6 yr; 4+ grade, 32.0 yr. There were 22 males and 15 females.

The 26 patients in the NRD group form the basis of this report. If a subject had asymmetric activity, we classified him according to the kidney with greater activity. In two patients the degree of RGA could not be determined, due to bowel activity. RGA was identified in 50.0% (12/24) of patients in the NRD group. The degree of RGA was 2+ or less in 83% (10/12) of those with positive kidneys.

The NRD patients were divided into two categories:

Category 1-Patients with neoplasia, exposure to chemotherapy, radiotherapy (where radiation port did not include kidneys), or multiple blood transfusions.

Category 2-Kidneys of patients without neoplasia and no exposure to the above.

Only 27% (3/11) in Category 2 had RGA, whereas 69% (9/13) in Category 1 had RGA (see Table 5).

The patients in the DRD group are shown in Table 3. RGA was 2+ or higher in all five. In addition, three of the five had either focal and/or asymmetric RGA.

Thirteen patients in the NRD group were imaged at both 48 and 72 hr. RGA did not change in 77% (10/13), and increased one grade level in 23% (3/13). Most NRD patients had diffuse symmetric activity or only minimal asymmetry of one grade or less between kidneys. Patient 19, however, had 2+ RGA on the left and no obvious activity in the right kidney.

DISCUSSION

Previous literature has stated that any RGA at 48 hr or beyond is suggestive of renal disease (*1*,*6*,*7*), but more

FIG. 1. Examples of grades of renal gallium activity. (Left) Grade 0; Quiescent sarcoidosis after treatment with prednisone (male, age 32). (Near left) Grade 1: Viral syndrome (female, age 43). (Center) Grade 2: Poorly differentiated lymphoma, not on chemotherapy at time of study (male, age 39). (Near right) Grade 3: Rheumatoid arthritis and nephrotic syndrome secondary to gold and penicillamine (male, age 56). (Right) Grade 4: Pyelonephritis, left kidney (male, age 64).

recent literature argued that this criterion may be too strict (*8,9*). Our series showed that RGA was present in 50.0% of patients with no obvious renal disease. The degree of RGA, however, was 2+ or less in most patients (83%).

The above findings suggest that the presence of RGA beyond 24 hr does not always indicate, though it does not exclude, renal disease. Table 5 suggests that neoplasia, exposure to chemo- or radiotherapy, or multiple blood transfusions may increase the likelihood of renal visualization beyond 24 hr. The percentage difference between positive patients in Categories 1 and 2, however, was not statistically significant ($p > 0.05$) with this small number of patients. Renal biopsies were not done, so the absolute exclusion of renal disease in some patients cannot be assured. It is difficult to imagine a nonpathologic process in the kidneys that could cause the asymmetry seen in Patient 19. It is not likely, however, that the RGA seen in the NRD group represents silent renal disease in every patient.

The visualization of the kidneys in the patients with no obvious renal disease may be secondary to one or more factors: Increased and prolonged RGA appears to be associated with alterations in gallium-binding serum proteins. Chemotherapy and radiation therapy have been reported to decrease Ga-67 activity in many parenchymal organs and soft tissues with the exception of the kidney, where it remains the same (*11–13*). Accordingly, liver and background activity may be decreased, giving images a more favorable kidney-to-background ratio. Recently, Engelstad (*15*) reported increased renal activity and decreased liver activity in patients after multiple blood transfusions (see Fig. 2). Total or partial saturation of iron-binding proteins is the most likely explanation for renal visualization in these patients. Radiation and/or chemotherapy decreases the capacity of the serum to bind gallium (*11*). A similar pattern with possible identical mechanism has also been reported with primary hemochromatosis (*16*). The information presented in Table 5 is compatible with this hypothesis.

TABLE 5. PATIENTS IN THE NRD GROUP

Grade	Patients
Category 1*	
0	4
1+	1
2+	6
3+	1
4+	1
ID	1
Total	14
Category 2	
0	8
1+	1
2+	2
3+	0
4+	0
ID	1
Total	12

* See text.

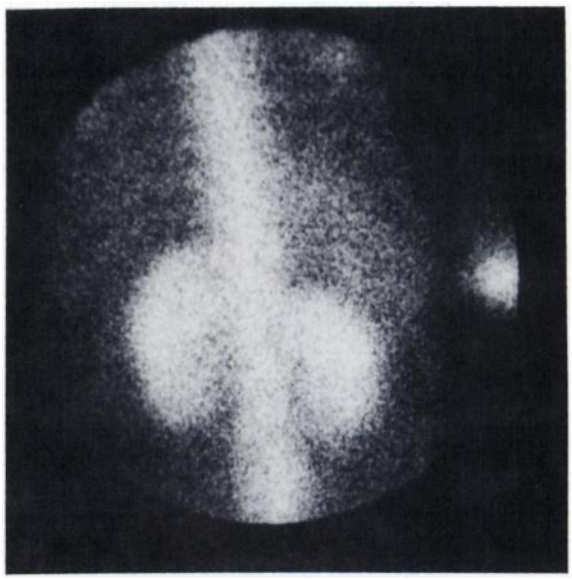

FIG 2. Symmetric diffuse Grade 4 RGA. This 39-yr-old male had leukemia complicated by upper gastrointestinal bleeding that required 23 units of packed red blood cells. Although BUN, creatinine, and urinalysis were normal, diffuse leukemic infiltration of the kidneys is possible.

TABLE 6. RENAL GALLIUM SERIES PERFORMED WITH RECTILINEAR SCANNERS

Author	Percentage of positive scans
Kumar et al. (*10*)	6.8% (12/175)
Frankel et al. (*7*)	1.7% (34/2000)
RENAL GALLIUM SERIES PERFORMED WITH GAMMA CAMERAS USING MORE THAN ONE PHOTOPEAK	
Lin et al. (*19*)	39.7% (396/966) kidneys)

Nelson et al. (*17*) did organ assays of Ga-67 activity in patients with neoplasia who died after injection with this radiotracer. They reported that as high as 4% of the dose may be in the kidneys after 24 hr. They also noted increased whole-body retention of Ga-67 in a patient with a large tumor burden. This patient had a high RGA assay in spite of no renal histological abnormalities and no functional impairment.

Modern imaging equipment may allow renal visualization in some NRD patients. Hoffer et al. (*18*) objectively documented the superiority of a gamma camera over a rectilinear scanner in the evaluation of normal and abnormal sites in a gallium scan. Most of the renal gallium literature is based on scans obtained with rectilinear scanners.

More recent studies have been performed with gamma cameras. The percentage of kidneys visualized is higher when a gamma camera with dual or triple window is used. Table 6 shows the percentage of positive studies in the available, reasonably large studies of renal gallium. Hurwitz et al. (*4*) and Linton et al. (*2*) found an even higher percentage of positive renal gallium studies (64% and 62%, respectively) when using a gamma camera, but the populations studied had a high probability of renal disease.

The mechanism for the increasing or unchanging RGA from 48 to 72 hr in the NRD group is undetermined. Further studies are needed to confirm this observation.

In assessing the RGA we often found liver/spleen scintigrams to be of value. A photon-deficient renal fossa on the gallium study, similar to that on the liver scintigram, allows more confidence in ascribing a grade "0" in the right kidney. When no renal fossa is visualized on the gallium scintigram despite a prominent fossa on the liver image, this suggests RGA of at least Grade 3+.

CONCLUSION

Thirty-seven patients were evaluated for RGA, and this was correlated with the presence or absence of renal disease. Renal gallium activity was observed in 12/24 (50.0%) of patients with normal BUN, creatinine, and urinalysis. Two patients in the NRD group may have subclinical renal disease (Patients 19 and 26). The visualization of the kidneys may be secondary to altered nonrenal biological factors related to either therapy or the primary disease. Modern gamma cameras with triple-peak capability are probably the main reason for renal visualization in these patients. Renal visualization in patients with no obvious renal disease is usually 2+ or less, but exceptions probably occur.

We suggest the following guidelines in the interpretation of kidneys on gallium images:

(1) Renal disease is suggested when RGA is greater than Grade 2, focal and/or asymmetric with greater than one grade difference between kidneys.

(2) Nonrenal biological factors must be considered before renal disease is diagnosed.

(3) Renal disease is not suggested (nor excluded) by either Grade 1 or 2, diffuse, symmetric, or minimally asymmetric RGA.

(4) The distinction between Grades 1 and 2 and between Grades 3 and 4 is sometimes subtle. It is more practical to use the liver for reference, and decide whether RGA is less than, equal to, or greater than, liver activity.

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