Serial Ga-67 Citrate Imaging in Children with Neoplastic Disease: Concise Communication

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To investigate the role of Ga-67 imaging in children with neoplastic disease, 83 Ga-67 scans, obtained in 46 children with neoplastic disease, were retrospectively analyzed. The series included 19 children who had two to five serial Ga-67 scans while undergoing therapy over periods as long as 4 yr. Three patterns were identified in the children who had serial Ga-67 imaging: a) twelve children with tumors that were initially gallium-avid had normal scans after chemotherapy and/or radiotherapy; b) four children had persistently positive Ga-67 scans while being treated; and c) three children with gallium-avid tumors developed a normal scan after therapy, but later had a gallium-avid recurrence. All 12 children in the first group were alive and clinically disease-free after a mean followup time of 38 mo. Six of the seven children with persistently gallium-avid tumors or gallium-avid recurrent tumors died during a mean followup time of 15.5 mo. The results of this small series suggest that further investigation is warranted to determine whether the results of serial Ga-67 imaging have any prognostic significance in children with neoplastic disease.

J Nucl Med 20: 210–214, 1979

The utility of Ga-67 imaging for the detection of neoplastic lesions has been studied much more extensively in adults (*1-4*) than in children (*5-9*). Recent studies suggest that Ga-67 imaging may be useful for the evaluation of children with neoplastic disease, especially those with lymphomas or soft-tissue sarcomas (*8-9*). However, Lepanto et al. (*6*) found a true-positive rate of only 37% (17/46) for Ga-67 in a site-by-site correlation study of pathology and scans in children with neoplastic disease, and stated that clinical management of their patients was never altered by the Ga-67 scan. They concluded, therefore, that the Ga-67 imaging did not benefit children with neoplastic disease.

We have had the opportunity to perform Ga-67 scans in 46 children with neoplastic disease, and have obtained two to five serial studies in 19 of these children who were undergoing therapy. These studies have been reviewed to investigate the role of serial Ga-67 imaging in children with neoplastic disease.

METHODS

Forty-six children (50% male, average age 9.7 yr, range 1-18) with surgically or biopsy-proven neoplastic disease were referred for Ga-67 imaging. Their diagnoses are shown in Table 1. A total of 83 Ga-67-citrate scans were performed on these children over a period of 7 yr. Nineteen of the children

Received Sept. 15, 1978; revision accepted Oct. 19, 1978.

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TABLE 1. TOTAL STUDY POPULATION*

Diagnosis	No	Studies	Positive
Hodgkin's lymphoma	14	20	10
Non-Hodgkin's lymphoma	10	24	10
Rhabdomyosarcoma	4	8	4
Teratoma	4	8	4
Wilms' tumor	4	4	1
Hepatoblastoma	3	8	3
Neuroblastoma	3	6	3
Retinoblastoma	2	2	1
Melanoma	1	2	2
Leukemia	1	1	1
Total	46	83	39

*Includes pretreatment and posttreatment scans.

(53% male, average age 9.2 yr, range 1-18) had two to five serial Ga-67 scans over followup periods ranging from 1 to 48 mo.

Each patient received an i.v. injection of Ga-67 citrate (40 μCi/kg) and head-to-foot rectilinear scans were performed with a dual-probe 5-in. scanner at 48 and 72 hr postinjection. A medium-energy collimator was used, and a count density of at least 250 ct/cm^2 was obtained. A window spanning the 184- and 296-keV photon peaks was used and images were displayed at 5:1 minification. In selected patients, additional 200,000-count gamma-camera spot views were obtained using a medium-energy parallel-hole collimator.

The data in this series were analyzed retrospectively. The original Ga-67 interpretations were used, since it was these readings that affected the clinical course of the patients. All positive Ga-67 scans were confirmed by surgery, biopsy, or other diagnostic tests (e.g., ultrasound, computed body tomography). Patients were assumed to be disease-free, though without conclusive proof, when they had a normal Ga-67 scan, a normal chest radiograph, normal serum chemistry, no palpable organomegaly or adenopathy, and were otherwise clinically disease-free. These patients were usually not further evaluated.

RESULTS

A total of 83 Ga-67 scans were ordered in 46 children. Thirty-nine of the scans (47%) showed a gallium-avid lesion (Table 1). Tissue confirmation showed that all but one of these sites (a spleen in a child with lymphoma) represented neoplastic disease. Hodgkin's disease or non-Hodgkin's lymphoma accounted for 44 of the 83 scans (53%). Although a positive scan in this group was a reliable indicator of disease, Ga-67 failed to detect splenic (n=4) or liver (n=1) involvement in four children with gallium-avid lesions outside the abdomen. Experience with various nonlymphomatous tumors was limited, but patients with rhabdomyosarcoma (n=4), teratoma (n=4), and hepatoblastoma (n=3) all had gallium-avid lesions before therapy. The most intense Ga-67 accumulation in the series was seen in the patients with hepatoblastoma.

Nineteen patients with a gallium-avid primary tumor had two to five serial Ga-67 studies over a 1-mo to 4-yr interval. Twelve patients showed loss of Ga-67 avidity and no evidence of metastases after therapy (Table 2). Thirty-five Ga-67 studies were obtained in these children, and the average interval for followup of Ga-67 imaging was 26.5 mo. Half the children in this group had their initial followup scan within 6 mo, five had it within 1-2 yr, and one patient was restudied 27 mo after his initial scan. At this writing, after a mean clinical followup time of 38 mo (range 18-149 mo), these children are clinically free of disease. An example of the changes seen in this group is shown by a child with neuroblastoma (Fig. 1).

TABLE 2. SERIAL Ga-67 IMAGING (GROUP 1. ABNORMAL→NORMAL)

Diagnosis	No	Studies	Mean Ga-67 Followup (mo)
Hodgkin's lymphoma	4	8	38
Non-Hodgkin's lymphoma	5	17	33
Hepatoblastoma	2	7	25
Neuroblastoma	1	3	10
Total	12	35	$\bar{x}$ = 26.5

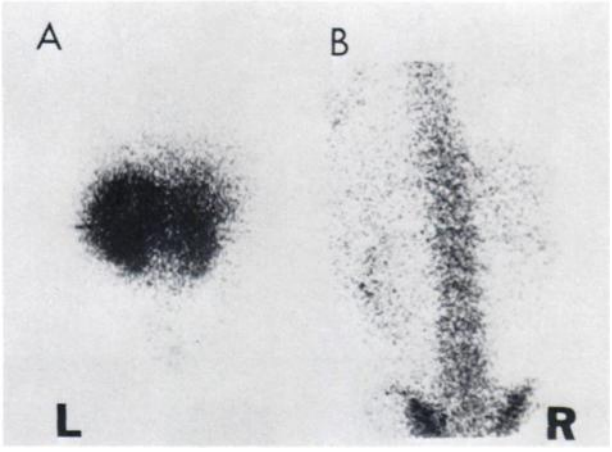

FIG. 1. This 10-year-old girl had a large gallium-avid neuroblastoma (A). Eight months later (B), after partial surgical resection and chemotherapy, the abdomen reveals no abnormal Ga-67 accumulation. She remains clinically disease-free 11 mo after scan (B).

Four patients showed persistently positive Ga-67 scans, even though they were receiving chemotherapy and radiotherapy (Table 3 and Fig. 2). The patient with teratoma was not restudied until 2 yr after his initial presentation. At that time he showed increased Ga-67 activity at the site of his original lesion and in metastatic foci; he also had clinical evidence of relapse, and died 2 mo later. The patient with treatment-resistant Hodgkin's disease was still alive but had developed widespread disease and appeared to be terminal.

Three other patients initially had gallium-avid tumors and showed loss of Ga-67 accumulation after chemotherapy or radiotherapy (Table 4). When these children were restudied later, however, they had evidence of distant gallium-avid metastases. They were receiving chemotherapy at the time of these studies. Figure 3 shows the sequence of studies in a 5-year-old boy who presented initially with a soft-tissue rhabdomyosarcoma. The lesion was partially resected and the patient received chemotherapy. He did well for over a year, but then developed nonspecific CNS symptoms, including drowsiness and headache. A Ga-67 scan revealed increased activity in the parieto-occipital area. The lesion was also visualized by computed transmission tomography and confirmed as metastatic rhabdomyosarcoma by open biopsy. This child died 4 mo after discovery of the cranial lesion. The other two children in this group died within 6 mo of the time when their recurrent gallium-avid lesions were discovered.

TABLE 3. SERIAL Ga-67 IMAGING (GROUP 2. ABNORMAL→ABNORMAL)

Diagnosis	No.	Studies	Ga-67 Followup (mo)
Teratoma	1*	2	26
Melanoma	1*	2	2
Neuroblastoma	1*	2	4
Hodgkin's lymphoma	1	3	26
Total	4	9	$\bar{x} = 14.5$

*Died

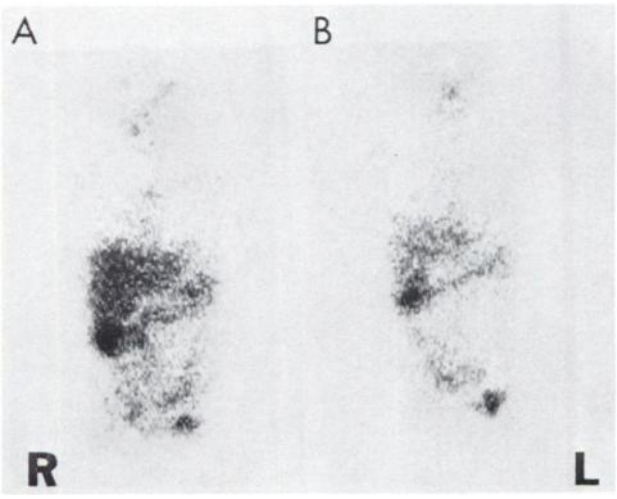

FIG. 2. This 15-year-old girl had a gallium-avid malignant melanoma in the left inguinal and right subhepatic regions (A). These foci remained visible two months later despite chemotherapy (B). The child died 6 wk later.

TABLE 4. SERIAL Ga-67 IMAGING (GROUP 3. ABNORMAL→NORMAL→ABNORMAL)

Diagnosis	No.	Studies	Ga-67 Followup (mo)
Non-Hodgkin's lymphoma	1*	3	10
Rhabdomyosarcoma	1*	4	14
Teratoma	1*	5	15
Total	3	12	$\bar{x} = 13$

*Died

DISCUSSION

Gallium-67 citrate was first advocated for tumor imaging in 1969 by Edwards and Hayes (*10*). Since that time its utility in detecting a variety of neoplasms in adult patients has been reported. Cancer is not as common in children as in adults, but it is the second leading cause of death in the pediatric age group (*11*). Early detection and staging of tumors is especially important, since certain childhood neoplastic diseases (e.g., lymphoma, leukemia) often respond favorably to chemotherapy and/or radiotherapy. Accordingly, the ability of Ga-67 citrate imaging to aid in the staging of neoplastic disease has been investigated. Lepanto et al. (*6*) found a low true-positive rate (37%) in a site-by-site correlation study in children with neoplasms and suggested that Ga-67 imaging was not useful for staging. The results reported by Bekerman et al. (*8*) were more encouraging. They detected 87% (27/31) of sites involved with lymphoreticular neoplasms. Their analysis included nodes in the mediastinum, abdomen and periphery, as well as deposits in the liver and spleen. They had one false-negative study in four patients with splenic lymphoma and reported similar results for soft-tissue sarcomas. The current series did not have site-by-site correlation in many patients, but did record false-negative Ga-67 scans in four patients with splenic lymphoma and in one with hepatic lymphoma.

Lepanto et al. (*6*) concluded that Ga-67 citrate imaging had no value in children with neoplastic disease, since the results of Ga-67 scans did not

alter patient management. Their study, like other pediatric series about Ga-67 imaging, investigated scans obtained at one point in time, i.e., it was a cross-sectional rather than a longitudinal study. The current experience with serial imaging provides a different basis for determining the impact of Ga-67 imaging on patient management. The evidence suggests that serial imaging will detect recurrence or metastasis of a tumor that was initially gallium-avid, even if the patient is receiving chemotherapy or radiotherapy at the time of imaging. This is important, since experimental animal data (*12*) suggest that some forms of radiotherapy and chemotherapy may transiently elevate serum iron, saturate the iron-carrying proteins (which also transport Ga-67), and result in decreased tumor uptake.

The findings in children who initially responded to therapy and later developed recurrent gallium-avid foci of disease (Group 3) are of interest. Edeling, in his most recent paper (*9*), reports an additional three children who showed this pattern. He states that serial Ga-67 imaging was performed in 14 children, but he does not provide details concerning the correlation between their images and clinical course. He does, however, report a large series of children (n=58) with treated neoplastic disease, and shows that 29 had confirmed true-positive Ga-67 images. Thus the available data suggests that Ga-67 images obtained in children on therapy will demonstrate disease if the original tumor was gallium-avid. The fact that Ga-67 scans provide a whole-body survey to locate these tumor deposits and direct other diagnostic imaging procedures or biopsy attempts increases their utility in this group of children.

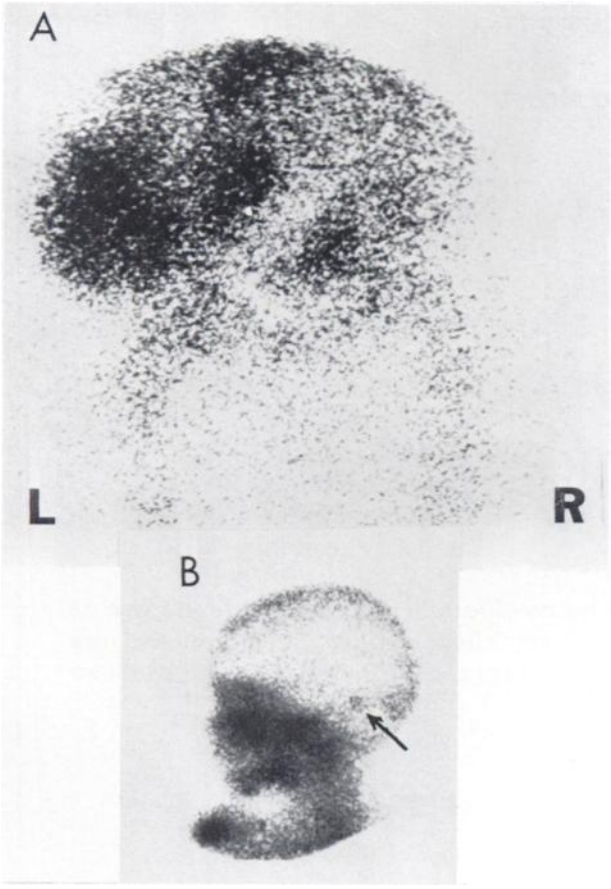

FIG. 3. This 4½-year-old boy had a gallium-avid rhabdomyosarcoma on his left buttock (A). The lesion was resected and the child received chemotherapy. A year later, while the child was on chemotherapy, a gallium-avid, biopsy-proven metastasis occurred in the parieto-occipital region of the brain (B, arrow). He died 4 mo later.

The recent data of Bidani et al. (*13*) suggest that Ga-67 imaging may have prognostic significance in children with neuroblastoma. They studied ten children with untreated neuroblastoma; six showed Ga-67 uptake in their lesions and four had gallium-negative tumors. Age of onset, tumor staging, size, cell types, and therapeutic history were similar. The only difference in the two groups was survival (average survival = 15 mo in the gallium-avid group; 49 mo in the gallium-negative group). We have serial images in only two children with neuroblastoma (Tables 2 and 3), so we cannot comment directly about this disease. In the current study, however, six of seven children with persistent or recurrent gallium-avid tumors died, whereas all 12 whose tumors became gallium-negative after therapy are clinically disease-free. These findings suggest that the potential of Ga-67 imaging as a prognostic indicator in children with neoplastic disease should be investigated by a controlled prospective study.

On the basis of our experiences with serial imaging, we now use Ga-67 initially in the pretreatment stage of disease to determine whether the primary tumor is gallium-avid. If the primary lesion is gallium-avid, serial Ga-67 images are obtained after therapy. The first scan is usually obtained within 1 to 2 mo after therapy begins, and the frequency of later scans is based on the child's response to initial therapy. Long-term followup scans are usually obtained only when there is a change in the patient's clinical course. If the repeat scan shows an area of increased Ga-67 activity, other diagnostic tests (e.g., ultrasound, computed tomography, or biopsy) are used to verify the lesion and appropriate alterations in therapy are made. When Ga-67 imaging is used in this way, we have found it a useful adjunct to the management of children with neoplastic disease.

ACKNOWLEDGMENT

This work was supported in part by USPHS Grant No. GM-10548.

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