Pediatric Solid Tumors: Evaluation by Gallium-67 SPECT Studies

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A retrospective review of 37 children with a variety of solid tumors who underwent 60 ^{67}Ga single-photon emission computed tomographic (SPECT) studies was performed. These studies were correlated with clinical and radiological findings and, where possible, histopathologic confirmation. In all studies, SPECT gave better definition and better anatomic localization of disease sites than obtained with planar views. SPECT detected more lesions in the head and neck (planar 16, SPECT 19), chest (planar 39, SPECT 45), and abdomen (planar 22, SPECT 24). In six of 20 patients scanned following chemotherapy, SPECT was useful in demonstrating that tracer accumulation in a normally located and shaped thymus indicated uptake resulting from thymic regeneration rather than tumor recurrence. It is concluded that ^{67}Ga SPECT studies are very useful in the pediatric population, where perhaps because of their small size, interpretation of standard planar views may be difficult.

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Gallium-67 (^{67}Ga) scintigraphy is well established in the management of patients with lymphoma (*1*). It has also been shown to have a definite role in the management of pediatric solid tumors (*2*). Single photon emission computed tomography (SPECT) provides better anatomic localization by improved three-dimensional visualization and better lesion definition by improved lesion contrast (*3*). The addition of SPECT to ^{67}Ga scintigraphy in adults has been shown to increase the sensitivity of this investigation (*4–6*). It was thus decided to review the ^{67}Ga studies in 37 children with a variety of solid tumors in whom 60 SPECT examinations had been undertaken.

MATERIALS AND METHODS

Thirty-seven children with a variety of solid tumors were enrolled in the study. There were 12 children with Hodgkin's disease, 12 with non-Hodgkins lymphoma, five with rhabdomyosarcoma, two with hepatoblastoma, two with soft-tissue sarcoma, and one each with chondrosarcoma, Ewing's sarcoma, thymic carcinoma, and malignant histiocytosis. There were 21 males and 16 females, with an age range at diagnosis of 1–15 yr (mean 8 yr). All studies were performed on a large field-of-view gamma camera that had SPECT capability (Starcam 400 AC; General Electric, Milwaukee, WI), 24 and 48 hr following the i.v. injection of [^{67}Ga]citrate. The minimum dose administered was 80 MBq and was scaled to body weight up to a maximum of 240 MBq.

Anterior and posterior whole-body studies were performed 24 and 48 hr postinjection, using a count density of 400,000 counts over the chest. A medium-energy collimator was used and triple pulse-height analysis carried out with 20% windows centered over the 93, 184, and 296 keV photon peaks. SPECT studies were performed at 48 hr over clinically relevant regions of the body or at sites of possible abnormality seen on the initial 24-hr whole-body studies. A further planar image was obtained at 48 hr over the part of the body undergoing the SPECT study. The SPECT studies were acquired on a 64 × 64 matrix collecting 64 projections in a 360° elliptical orbit at a rate of 30–40 sec per projection. Following uniformity correction, 6 mm transaxial, coronal, and sagittal tomograms were reconstructed using backprojection with a Ramp-Hanning filter.

SPECT and planar ^{67}Ga studies were interpreted together by two observers on separate occasions. The results of the planar and SPECT ^{67}Ga studies were correlated with the clinical findings, radiological studies (chest x-ray, chest CT, abdominal CT, and/or ultrasound) and, where possible, histopathologic confirmation. In all instances in which there was a discrepancy between the ^{67}Ga and radiologic findings, both the isotope studies and x-ray investigations were reviewed together.

RESULTS

Sixty SPECT examinations were performed on 37 children undergoing ^{67}Ga evaluation for staging of a variety of solid tumors. In only one child, a 1-yr-old girl with pelvic rhabdomyosarcoma, was the known tumor not gallium avid. In all studies, SPECT gave better definition and better anatomic localization of disease sites, when compared with the planar studies (Table 1). SPECT detected more lesions in the head and neck (planar 16, SPECT 19) (Fig. 1), in the chest

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TABLE 1
Planar Versus SPECT Lesion Detection

	Head and neck	Chest	Abdomen	Limbs
Lesions detected on planar study	16	39	22	2
Sensitivity (planar)	84%	83%	88%	100%
Specificity (planar)	100%	100%	100%	100%
Lesions detected on SPECT study	19	45	24	2
Sensitivity (SPECT)	100%	96%	96%	100%
Specificity (SPECT)	100%	100%	100%	100%

(planar 39, SPECT 45) (Fig. 2) and in the abdomen (planar 22, SPECT 24), but the same number of lesions as planar in the limbs.

Five patients had more extensive disease demonstrated on the gallium studies than assessed clinically and radiologically. In three patients, the gallium study demonstrated previously undetected lesions in the chest and in two patients further foci were demonstrated in the abdomen. All of these five patients had clinical and/or radiological features of widespread disease, which was biopsy proven at a gallium-avid site different to the additional ^{67}Ga study abnormality.

In only one patient, more lesions were detected radiologically than on the gallium study. This occurred in a patient with two lung field metastases detected on chest CT. The diameters of these two lung field metastases were ≤5 mm and these small sizes explain why these lesions were not detectable on the gallium study. In three patients in whom there were equivocal abnormalities on the abdominal CT, ^{67}Ga SPECT studies were useful in excluding abdominal disease.

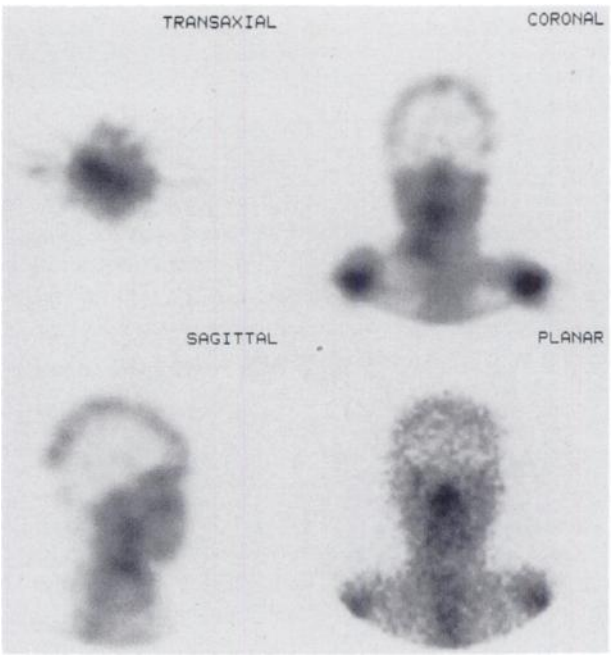

FIGURE 1
A 7-yr-old boy presented with right cervical lymphadenopathy, which was biopsy proven non-Hodgkins lymphoma. The planar study is normal. The SPECT study, in particular the coronal slice, demonstrates the presence of disease in the right cervical region and in Waldeyer's ring on the right, which was later confirmed on indirect laryngoscopy.

Normal thymic uptake was demonstrated on the SPECT study only in one of 24 patients studied prior to chemotherapy. Twenty patients had scans performed following chemotherapy; six of these had uptake in the thymus resulting from thymic regeneration. This was confirmed by biopsy in one patient and in the others by clinical follow-up and x-ray evaluation, with no evidence of recurrent disease. The age range for these six children who had thymic regeneration demonstrated on the post-therapy gallium study was 4–17 yr with a mean of 9.5 yr. The SPECT study was very useful in these patients as it confirmed uptake in a bilobed distribution in the anterior mediastinum, confirming that the gallium was localized in a normal thymus and not at a site of tumor recurrence (Fig. 3). One patient presented with thymic carcinoma and the gallium study demonstrated avid tracer uptake in an abnormally enlarged and abnormally shaped thymus indicating active disease at this site, rather than physiological thymic uptake (Fig. 4). With SPECT, these patterns were readily distinguishable from disease in mediastinal or hilar regions (Fig. 5). Comparison of the transaxial slices in Figures 4 and 5 reveals the advantages of SPECT imaging in localizing mediastinal masses. In Figure 4, the uptake is obviously confined to the anterior mediastinum whereas in Figure 5, the transaxial slices clearly demonstrate the abnormal uptake to be localized in the pulmonary hilar regions.

DISCUSSION

Cancer in childhood is a leading cause of mortality. Accurate staging and early detection of recurrent disease are essential for cure and adequate control of the disease. The usefulness of ^{67}Ga studies in the management of both adult and pediatric patients is established (*1*,*2*). However, our findings indicate that the addition of SPECT results in greater lesion detection in the head, neck, chest and abdomen as well as better assessment of the extent and location of involvement, when compared with the planar studies. Because of the ability of SPECT to separate different foci of abnormal uptake and to display images in coronal, sagittal and transaxial planes, lesions are better delineated and localized. This is important in both the initial evaluation and post-therapy follow-up of children as SPECT will enable a higher likelihood of detecting residual disease after treatment if it is well delineated on the baseline staging study.

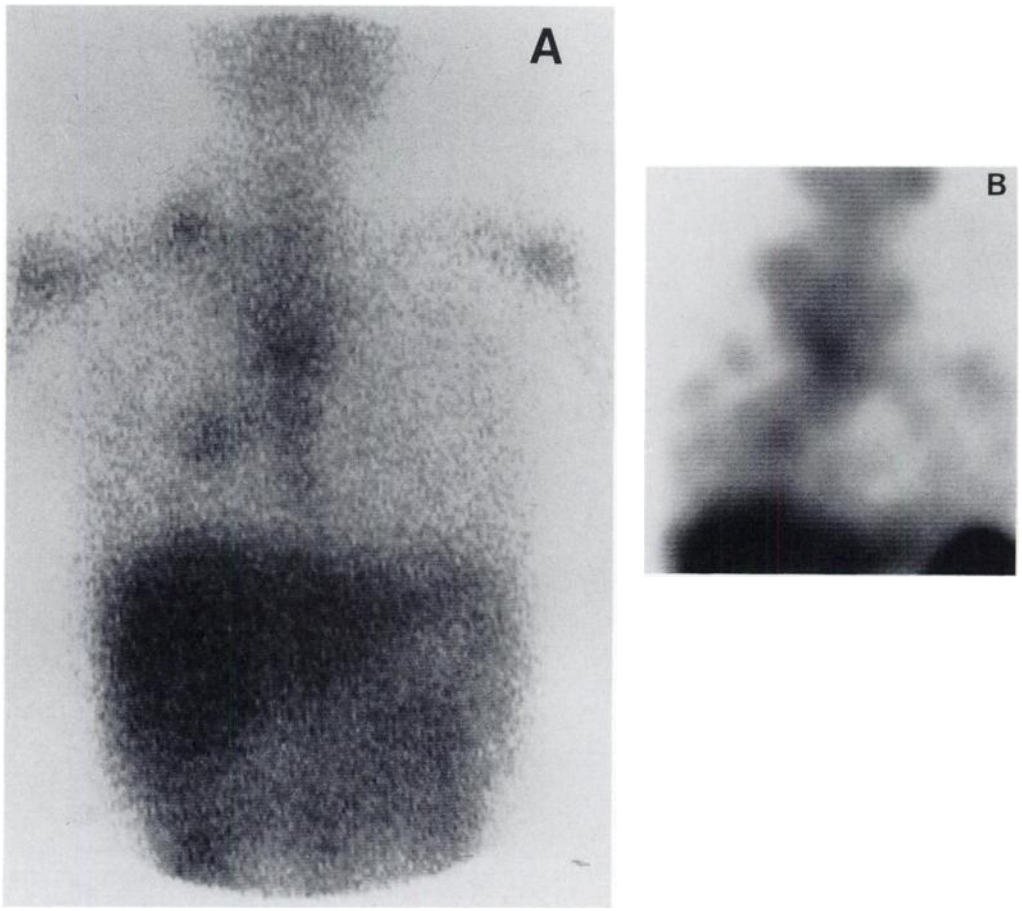

FIGURE 2
A-yr-old girl presented with right supraclavicular lymphadenopathy which was biopsy proven histiocytic lymphoma. The planar study (A) demonstrated previously undetected disease in the right pulmonary hilum. The coronal slices of the SPECT study (B) revealed active disease, not seen on the planar study, involving the right infraclavicular and right paratracheal lymph nodes contiguously between the supraclavicular and pulmonary hilar nodes on the right.

SPECT was found to be particularly valuable in identifying the site of lesions detected in the chest on the planar study, because of the proximity of the anatomical structures in which gallium uptake can occur both normally and in disease. In particular, this was critical in identifying thymic uptake.

In our experience, ^{67}Ga uptake in the thymus frequently occurs following chemotherapy. In this study six of 20 children scanned following chemotherapy had ^{67}Ga positive thymic uptake, which SPECT demonstrated to be tracer present in a normally located and shaped thymus. This is explained by physiologic thymic regeneration following chemotherapy, one of the causes of the 'rebound phenomenon' described by Cohen et al. (*7*). This was biopsy proven in one patient and confirmed on clinical and radiologic follow-up in the others. We disagree with Tumeh et al. (*4*), who stated that physiologic thymic regeneration does not accumulate gallium. Their postulate, that the emergence of thymic uptake following chemotherapy indicates tumor recurrence rather than thymic regeneration, is not in keeping with our findings or the findings of others (*8*, *9*). Donahue et al. (*8*) found increased thymic gallium localization due to biopsy-proven thymic regeneration and not tumor involvement in two children at an inactive stage following chemotherapy for a known malignancy. Hibi et al. (*9*) reported seven patients with strongly positive thymic uptake which occurred 2–12 mo after the initiation of therapy and which was nonmalignant on clinical follow-up, with no evidence of tumor progression at the thymus.

In three patients, abdominal CT was equivocal in its findings as to the presence or absence of significant lymphadenopathy. The ^{67}Ga SPECT study was useful in excluding active disease at the site of the equivocal CT findings. This confirms the complimentary nature of these two investigations. CT gives excellent anatomic definition and is able to demonstrate lymph nodes clearly. Gallium-67 studies provide functional information and can determine whether lymphadenopathy shown on CT imaging is due to active disease or residual fibrotic change. In addition, gallium studies may iden-

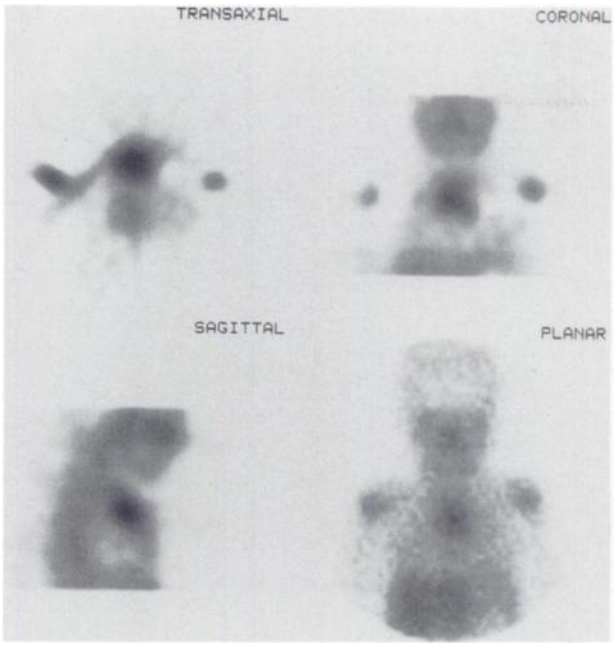

FIGURE 3
A 3-yr-old boy had presented with Hodgkin's disease involving the left cervical chain. The follow-up ^{67}Ga study performed 7 mo after the commencement of chemotherapy demonstrated no active disease in the neck but uptake in the chest. The SPECT study confirmed uptake in a bilobed distribution in the anterior mediastinum confirming that the gallium was localized in a normal thymus, thus indicating thymic regeneration and not tumor recurrence.

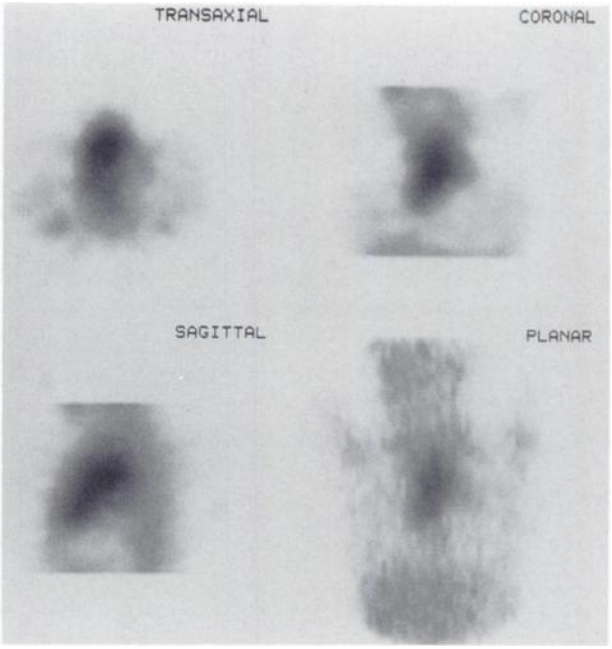

FIGURE 4
A 12-yr-old girl presented with a persistent cough and a chest x-ray revealed a mediastinal mass. The gallium study demonstrated avid tracer uptake in an abnormally enlarged and abnormally shaped thymus indicating tumor involvement at this site, rather than physiological thymic uptake. Histopathology confirmed the presence of thymic carcinoma.

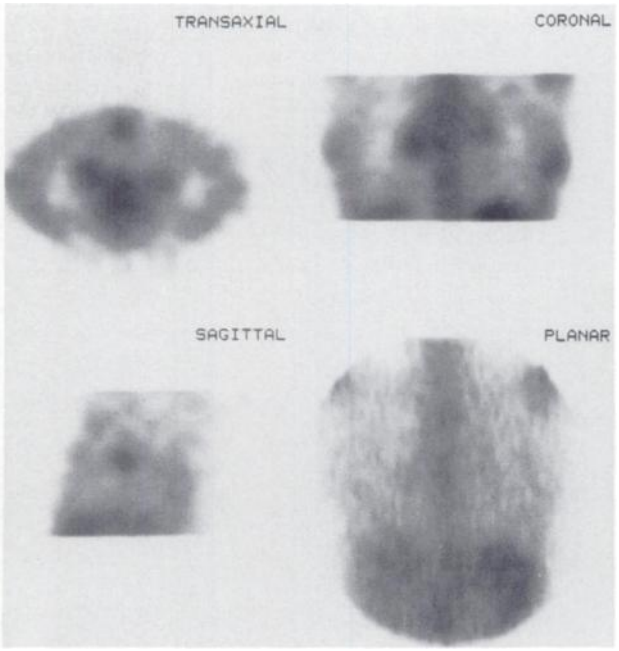

FIGURE 5
A 14-yr-old boy presented with relapse of known Hodgkin's disease, confirmed by a positive bone marrow examination. The planar study demonstrates faint bilateral mediastinal uptake. The SPECT study localizes the uptake to disease in pulmonary hilar lymph nodes.

tify disease involvement in nodes not demonstrably enlarged by alternative imaging modalities (*4*).

CONCLUSION

Gallium-67 SPECT studies, by achieving greater lesion contrast and improved delineation of site, are very useful in the pediatric population, in which, perhaps because of their small size, interpretation of standard planar views may be difficult.

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