^{67}Ga-CITRATE FOR SCANNING EXPERIMENTAL STAPHYLOCOCCAL ABSCESSES

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Two types of rat staphylococcal abscesses concentrated ^{67}Ga sufficiently to permit imaging by rectilinear scanning. Gallium-67 used for the detection of numerous tumors has clear potential as a new, non-invasive tool for the localization of deep abscesses. While ^{67}Ga would be of little value in the differentiation of abscess from tumor, it should prove most helpful in confirming a clinical impression of deep abscess and in formulating a therapeutic approach.

Localization of suspected deep abscesses remains a difficult clinical problem. Conventional diagnostic roentgenologic approaches are frequently nonproductive and more effective noninvasive techniques are needed. In 1969 ^{67}Ga concentration by certain tumor types was reported by Edwards and Hayes (*1*), and subsequent reports have described concentration of the isotope by inflammatory processes (*2–5*). Because of the potential importance of these interesting clinical findings, it was considered desirable to explore, in an experimental prospective study, the conditions for scanning deep abscesses in animals.

MATERIALS AND METHODS

Preparation of bacteria. A coagulase positive *Staphylococcus aureus* strain isolated from a patient was inoculated into 100 ml of Trypticase Soy broth (Difco) and incubated overnight at 37°C. The bacteria were harvested by centrifuging at 10,000 rpm for 15 min at 5°C. The bacterial pellets were washed with 10 ml normal saline, centrifuged as before, and suspended in 10 ml normal saline. The final concentration of the bacterial suspension averaged 1×10^{10} colony forming units per milliliter.

Rat retroperitoneal abscesses. Seven groups of male Sprague-Dawley rats weighing approximately 250 gm were anesthetized with ether, shaved over the left lumbar region, and injected with 7×10^9 *Staphylococcus aureus* (approximately 1.0 ml) deeply into the paraspinous muscles (Day 0). The area of injection was marked with a single cutaneous 4-0 silk suture. The method resulted in a 54% incidence of detectable paraspinal abscesses with retroperitoneal extension at the time of sacrifice: 3, 6, 9, 12, 15, 24, and 30 days after injection of bacteria. Most of the 3-day and 30-day animals did not have abscesses; therefore the subsequent discussion refers only to the remaining five groups (see Table 1 for the number of rats with abscesses in each group). The ^{67}Ga was given 72 hr before sacrifice. Samples of blood, femoral muscle, kidney, liver, abscess wall, and abscess contents, were obtained at necropsy for analysis of ^{67}Ga content. In addition, 24- and 72-hr scans were obtained in an eighth group of rats with 15-day abscesses.

Rat subcutaneous abscesses. Three male Lewis-Wistar rats averaging 375 gm were anesthetized, shaved over the right thigh and injected subcutaneously with 7×10^9 *Staphylococcus aureus* and 60 mg Talc, USP, in a total volume of 0.6 ml. Gallium-67 was injected on Day 5; scans were obtained on Day 8 before the animals were sacrificed.

Tissue uptake and scanning. One hundred μCi/kg of sterile, carrier-free ^{67}Ga (Diagnostic Isotopes, Upper Saddle River, N.J.) with 7 mg/kg of sodium citrate was administered intravenously. Preliminary experiments suggested a slightly higher concentration of ^{67}Ga in the abscess wall at 72 hr (six rats) compared with the 24-hr (eight rats) uptake (0.93 ± 0.22 vs 0.81 ± 0.21; not statistically significant: $p > 0.3$). Scans were performed 24 and 72 hr after administration of the isotope using an Ohio-Nuclear

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scanner with a 5-in. crystal and an 85-hole collimator. The animals were sacrificed after the second scan, and the tissue uptake of ^{67}Ga was measured in an automatic well counter. All results were expressed as percent of the administered dose per gram of tissue, normalized to a 1-kg animal.

RESULTS

Rat retroperitoneal abscesses. Abscesses varying in size from 1 cm in diam to 2 × 3 × 4 cm were produced in the 6-, 9-, 12-, 15-, and 24-day groups. These lesions were firm, retroperitoneal masses often surrounding the kidney but not involving renal parenchyma. Characteristically, the abscess wall measured 0.5–2.0 mm in thickness; the abscess content varied from green liquid in the 6-day abscess to firm rubbery material in the older lesions. Cultures and gram stain of the contents of 25 of the 33 abscesses were done: 24 yielded *Staphylococcus aureus*; one grew a Proteus species. The mean ^{67}Ga uptake by the various tissues is given in Table 1. Uptake of the isotope by the abscess wall increases with the age of the abscess to a maximum at 15 days. This uptake is statistically significantly different from the uptake at all other time periods (ANOVA; Scheffe Multiple Comparison Test, 95% confidence level). The uptake by kidney, abscess contents, liver, and femoral muscle remains relatively constant with no consistent statistically significant differences observed. The increasing ratio of abscess wall uptake to kidney and liver uptake is shown in Fig. 1.

Abscesses were obtained in four of the rats in the eighth group. These 15-day abscesses could not be reliably discerned on the 24-hr scan because of the high activity of the bowel but were clearly delineated on the 72-hr scan (Figs. 2, 3). These should be compared to the scan of a normal rat (Fig. 4). The tissue uptakes of ^{67}Ga in these four rats were comparable to those of the main group (see Table 1):

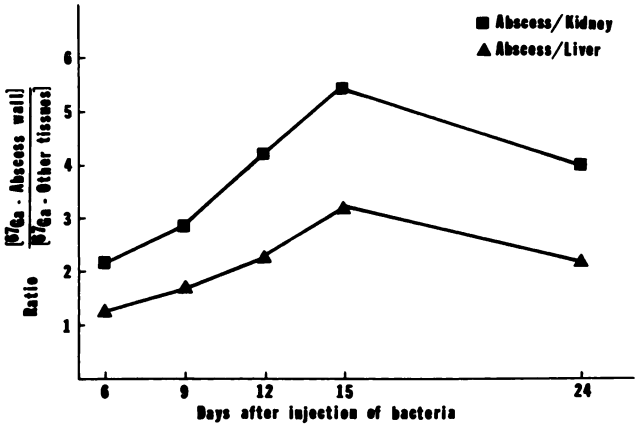

FIG. 1. Retroperitoneal abscesses: ratio of ^{67}Ga uptake by abscess wall to uptake by kidney and liver.

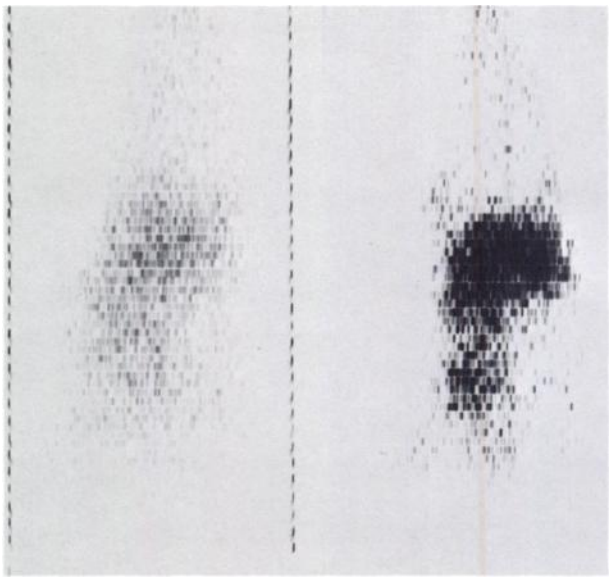

FIG. 2. Rat A. Retroperitoneal abscess: 24- and 72-hr whole-body posterior scans with ^{67}Ga citrate.

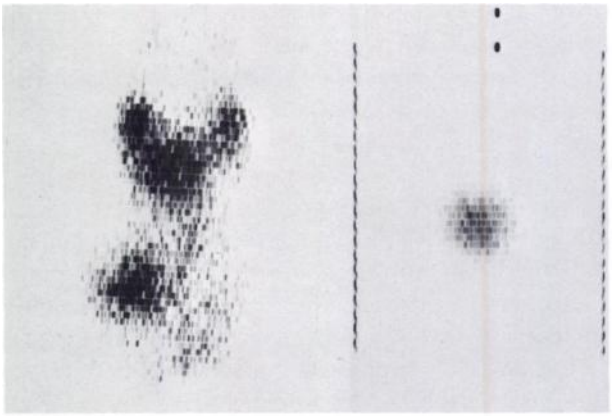

FIG. 3. Rat B. Retroperitoneal abscess: 72-hr ^{67}Ga-citrate anterior scans; whole-body and excised abscess.

abscess wall, 0.92 ± 0.23; abscess contents, 0.10 ± 0.03; femoral muscle, 0.02 ± 0.004; kidney, 0.18 ± 0.01; and liver, 0.35 ± 0.05.

Rat subcutaneous abscesses. Seventy-two hour scans (Fig. 5) showed increased uptake over the abscess site in all three animals. Unlike the retroperitoneal abscesses, these lesions were extensive collections of green purulent material extending into the underlying muscle without discrete walls. Necrotic appearing muscle tissue surrounding the pus had increased ^{67}Ga uptake (1.81 ± 0.41) compared with that of the purulent material (0.21 ± 0.04), kidneys (0.26 ± 0.01), liver (0.47 ± 0.15), or nearby normal appearing muscle (0.01 ± 0.006).

DISCUSSION

Examples of ^{67}Ga uptake by infectious processes have been noted coincidentally in several tumor up-

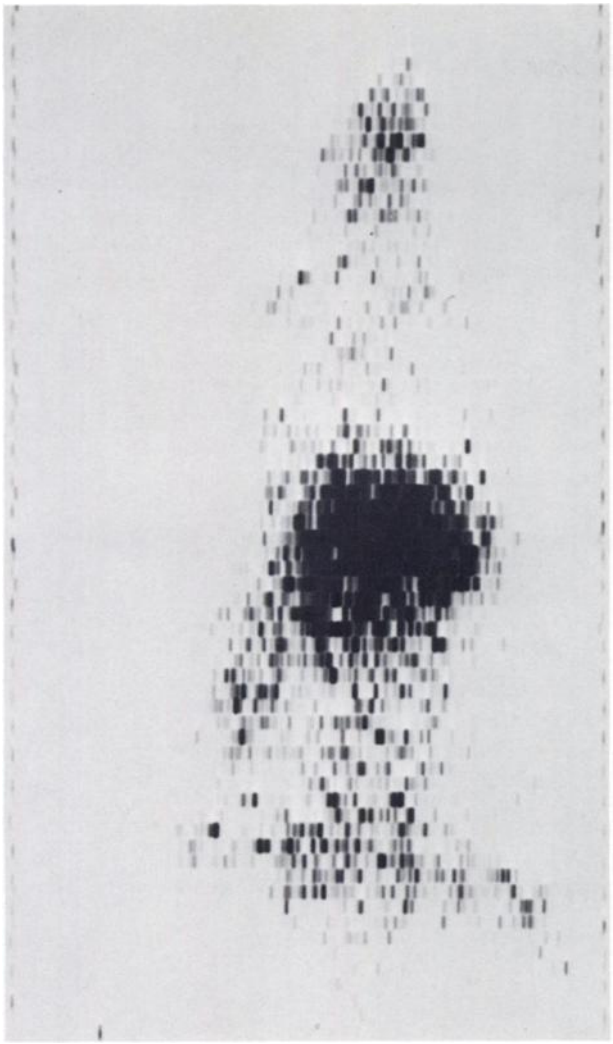

FIG. 4. Rat C. 72-hr posterior whole-body scan with ^{67}Ga-citrate. No abscess.

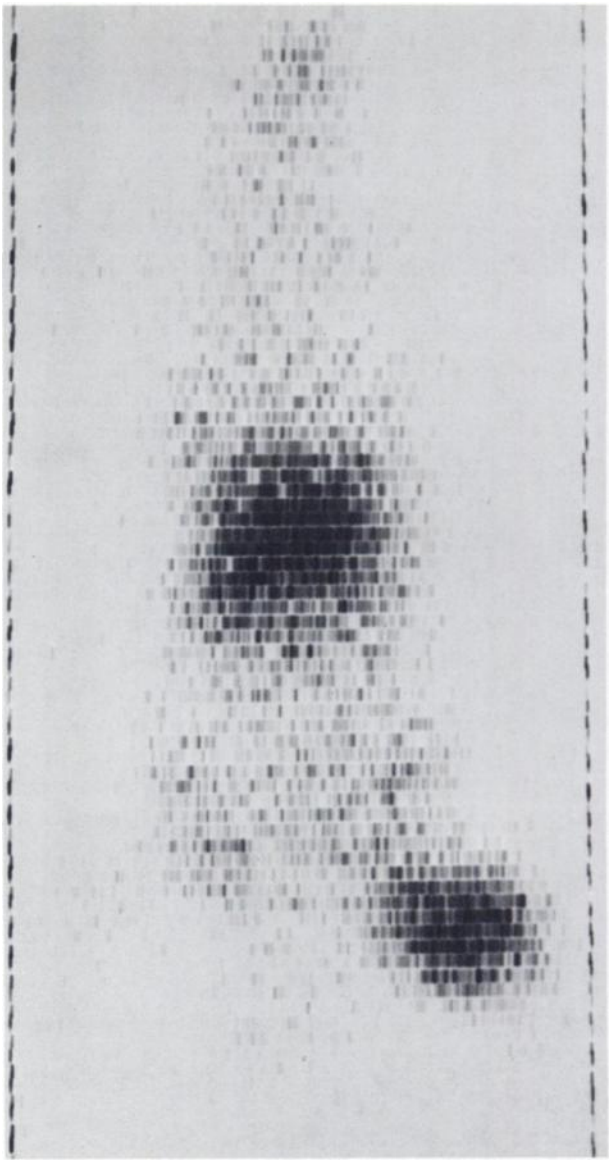

FIG. 5. Rat D. Subcutaneous abscess: 72-hr posterior whole-body scan with ^{67}Ga-citrate.

take studies: lung abscess, breast abscess, hepatic abscess, pneumonitis, osteomyelitis, pulmonary tuberculosis, chronic pulmonary disease (*2–5*). These reports offered a potential tool for the localization of suspected deep abscesses and prompted the present study in animals. Our data indicate that well-formed staphylococcal abscesses concentrate the isotope sufficiently to permit delineation on whole-body scans. Assuming a 3:1 ratio of abscess wall uptake to liver and kidney uptake is needed for the production of diagnostic scans, satisfactory scans should be obtainable by the ninth day and for some time

TABLE 1. TISSUE UPTAKE OF ^{67}Ga

Days $\bar{p}$ injection of bacteria	Percent administered dose/gm tissue (% ±s.d.)*				
	6 (n = 8)	9 (n = 8)	12 (n = 6)	15 (n = 7)	24 (n = 4)
Abscess wall	0.40 ± 0.11	0.58 ± 0.18	0.70 ± 0.25	0.92 ± 0.20	0.70 ± 0.25
Abscess contents	0.22 ± 0.11	0.20 ± 0.06	0.20 ± 0.06	0.15 ± 0.04	0.14 ± 0.08
Femoral muscle	0.03 ± 0.01	0.03 ± 0.01	0.03 ± 0.01	0.03 ± 0.005	0.02 ± 0.005
Kidney	0.19 ± 0.03	0.21 ± 0.03	0.16 ± 0.01	0.17 ± 0.02	0.18 ± 0.02
Liver	0.32 ± 0.06	0.36 ± 0.04	0.32 ± 0.05	0.29 ± 0.05	0.33 ± 0.07

* Normalized ot 1.0-kg body weight.

thereafter. Scans of hepatic abscesses or abscesses contiguous to the liver may still present technical problems. A clinical situation in which this scanning method would be very helpful is postoperative abscess formation (abdominal or gynecologic surgery). This diagnosis is usually suspected in the second postoperative week at which time an abscess, assuming its formation dates from surgery, would be expected to concentrate ^{67}Ga.

The mechanism for ^{67}Ga uptake has not been elucidated for either tumors or inflammatory processes. It has been postulated that the lower pH of some tumor tissue (due to increased anaerobic glycolysis) allows greater dissociation of the gallium-citrate molecule, resulting in the formation of stable gallium-proteinate complexes (*6*). A similar mechanism could be invoked for abscesses where the pH decreases with the increasing age of the abscess. In staphylococcal abscesses there may be a second, complementary mechanism: the lymphatic effluent from the abscess area has been shown to decrease after initial infection (*7*), permitting further retention of gallium-proteinate complexes. The concentration of gallium does not appear to be related to binding by specific proteins such as fibrinogen or gamma globulin (*2*). The possibility of transport of the isotope to the abscess site by polymorphonuclear neutrophils has been suggested (*4*) but not clearly demonstrated.

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