Indium-111-Labeled Leukocyte Scintigraphy in Hemodialysis Access-Site Infection

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Bacterial sepsis, a significant complication of chronic hemodialysis, is generally the result of infection at the vascular access site. We retrospectively reviewed the utility of indium-111- (^{111}In) labeled autologous leukocyte scintigraphy in 26 patients (30 scans) with synthetic vascular grafts, on chronic hemodialysis, in whom hemodialysis access site infection was a diagnostic consideration. Leukocyte scintigraphy correctly identified all fifteen access-site infections; there was one false-positive study, for an overall sensitivity and specificity of 100% and 93%, respectively. Of particular significance is the fact that in nine (60%) of the fifteen access-site infections, physical examination was normal. Our data indicate that ^{111}In-labeled leukocyte scintigraphy is a useful procedure for the diagnosis of hemodialysis access-site infection, and it is especially valuable when physical examination of the access site is normal.

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Infection is a serious complication for patients with end-stage renal disease receiving hemodialysis. Factors making this patient population especially susceptible to infection include reduced immune competency, and the presence of a vascular access site. It is estimated that ~75% of the episodes of bacteremia that occur in these patients originate at the hemodialysis access site. Complications include septic emboli, endocarditis, and meningitis (*1,2*). Despite its superficial location, physical examination of the access site has been reported to be normal in up to one-third of infections (*1*).

Indium-111- (^{111}In) labeled autologous leukocyte imaging is an accepted method for localization of infection in general and has been reported as sensitive for the diagnosis of vascular graft infections (*3–14*). We undertook this retrospective study to evaluate the role of leukocyte imaging in the diagnosis of hemodialysis access-site infection.

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MATERIALS AND METHODS

Patient Population

Twenty-six patients, 10 males and 16 females 28–84 yr old (mean = 42 yr) in whom hemodialysis access-site infection was a diagnostic consideration, were examined with ^{111}In-labeled leukocyte scintigraphy. Each patient had a single upper extremity polytetrafluoroethylene (PTFE) graft for hemodialysis. All 26 patients underwent labeled leukocyte imaging as part of an initial diagnostic evaluation. Four patients, whose access sites were infected at the time of the original imaging, were reimaged following a course of medical therapy. A total of 30 scintigrams were performed on the 26 access sites. For purposes of analysis, these data were treated as 30 scintigrams performed on 30 access sites.

Results of leukocyte counts, blood cultures, and physical examination of the access site within 48 hr of the radionuclide study were noted. Data on the duration of symptoms and the administration of antibiotics also were recorded. To minimize false-positive studies secondary to hematoma formation, patients were not dialyzed during the 24 hr duration of the radionuclide procedure.

An access site was considered infected if percutaneous or intraoperative cultures grew out organisms or if frank pus was present. An access site was considered infection free if percutaneous or intraoperative cultures were reported as no growth, and smears revealed no white cells (pus). In the absence of microbiologic confirmation, the site was considered infection free based upon the patient's clinical course.

Scintigraphy

Autologous mixed leukocyte labeling with ^{111}In oxine was performed according to the method of Thakur et al. (*3*). Scintigraphy was performed 24 hr after reinjection of ~18.5 MBq (500 μCi) labeled leukocytes. Whole-body imaging was performed on one of two large field of view gamma cameras, equipped with a medium-energy parallel-hole collimator. Energy discrimination was provided by dual 20% windows centered over the 174 and 247 keV photopeaks of ^{111}In. A 6-min static image of each access site was also obtained.

Radiotracer uptake at the hemodialysis access site was graded as:

0: equal to surrounding soft-tissue activity.
1: slightly greater than surrounding soft-tissue activity.
2: moderately greater than surrounding soft-tissue activity.
3: markedly greater than surrounding soft-tissue activity.

Labeled leukocyte activity of grade 1 or greater was also characterized as focal or diffuse.

RESULTS

Fifteen of the thirty access sites were infected, all microbiologically confirmed; of the fifteen access sites classified as infection free, absence of infection was microbiologically confirmed at eight sites; the remaining seven sites were classified as infection free based upon clinical outcome. All patients with infected access sites were on antibiotic therapy at the time of leukocyte imaging, and ten patients had been ill for at least three weeks at the time of scintigraphy. Physical examination was positive for infection in 6 of the 15 infected access sites and negative in the other nine.

Sixteen access sites demonstrated leukocyte accumulation of at least grade 1. This activity was focal in 13 cases, and diffuse in 3. Fifteen of these sixteen siteswere infected. The focal uptake pattern was seen in localized access site infection, while the diffuse pattern was identified in extensive infection of both the PTFE graft as well as its subcutaneous "tunnel" (Fig. 1). One infection-free access site demonstrated focal accumulation: a thrombosed PTFE graft (Table 1).

Four infected access sites were restudied after 10–14 days of additional antibiotic therapy. In three of the repeat studies, leukocyte activity at the access site was grade 0, and the infection was considered resolved clinically in all three instances (Fig. 2). In the fourth case, repeat leukocyte imaging was virtually unchanged from the initial study (Fig. 3); the PTFE graft was removed and operative confirmation of infection was obtained.

Fourteen access sites demonstrated grade 0 leukocyte

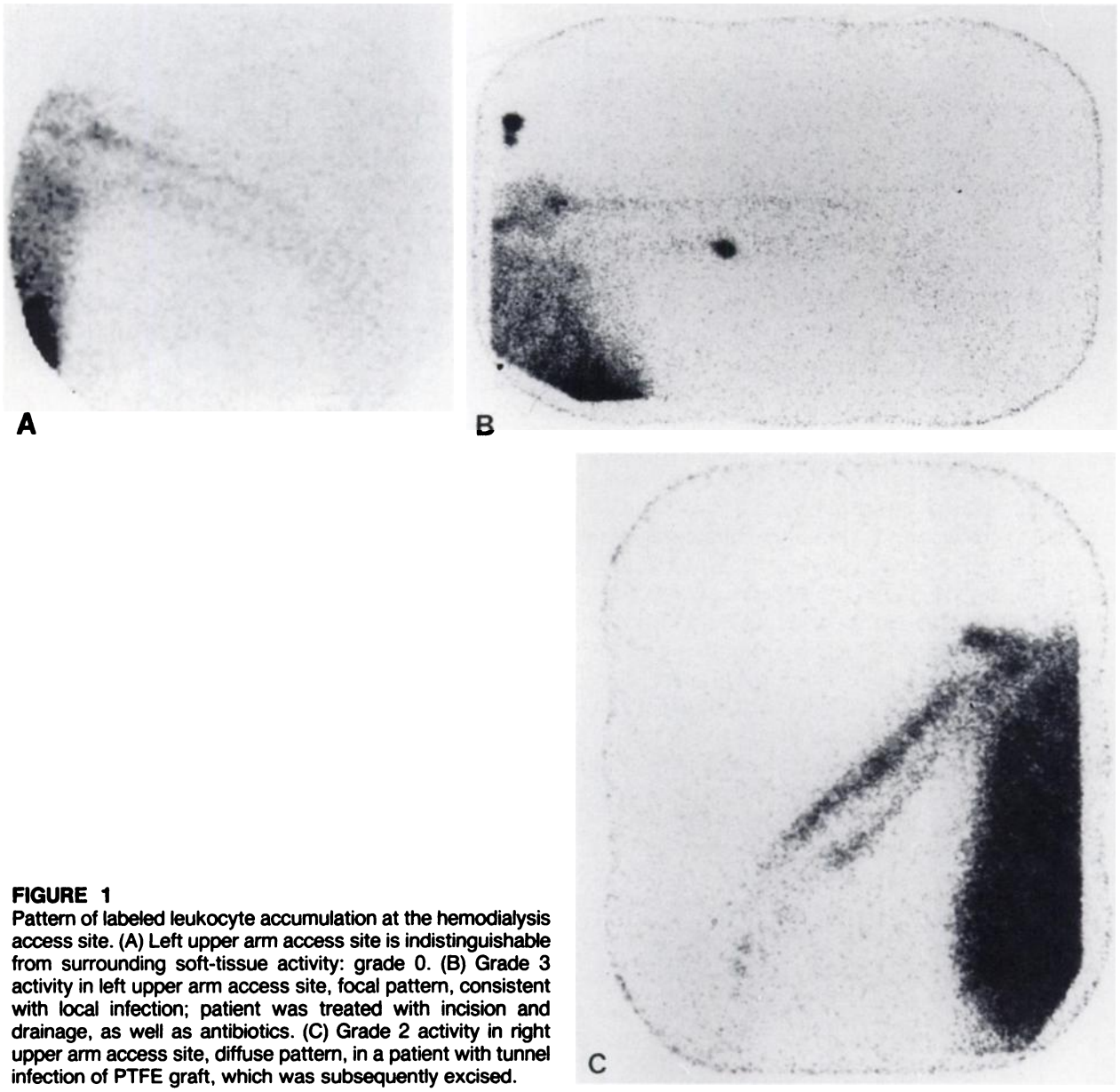

FIGURE 1
Pattern of labeled leukocyte accumulation at the hemodialysis access site. (A) Left upper arm access site is indistinguishable from surrounding soft-tissue activity: grade 0. (B) Grade 3 activity in left upper arm access site, focal pattern, consistent with local infection; patient was treated with incision and drainage, as well as antibiotics. (C) Grade 2 activity in right upper arm access site, diffuse pattern, in a patient with tunnel infection of PTFE graft, which was subsequently excised.

TABLE 1
Positive Leukocyte Images (n = 16)

Patient No.	Age	Sex	Duration of illness	Leukocyte count (mm^3)	Blood culture	Physical exam	Graft infection
1	60	F	11 wk	8700	Pseudomonas	(−)	Yes
2	64	F	2 wk	9500	Pseudomonas Klebsiella	(−)	Yes
3	66	F	5 wk	16000	*S. Aureus*	(−)	Yes
4	37	F	2 wk	6700	Pseudomonas	(+)	Yes
4*	37	F	4 wk	6100	Pseudomonas	(+)	Yes
5	35	F	2 wk	12500	*S. Aureus*	(+)	Yes
6	50	F	4 wk	4200	*S. Aureus*	(−)	Yes
7	58	F	2 wk	7600	Streptococcus	(+)	Yes
8	28	M	4 wk	11000	Negative	(+)	No
9	41	M	3 wk	5700	*S. Aureus*	(−)	Yes
10	50	F	4 wk	6000	*S. Aureus*	(−)	Yes
11	60	M	1 wk	12000	*S. Aureus*	(−)	Yes
12	60	M	4 wk	2000	*S. Aureus*	(+)	Yes
13	35	F	1 wk	5300	*S. Aureus*	(−)	Yes
14	39	F	3 wk	7000	*S. Aureus*	(−)	Yes
15	84	M	4 wk	8500	*S. Aureus*	(+)	Yes

* Repeat scintigraphy performed after 2 wk of additional antibiotic treatment.

activity and all were infection free (Table 2). A comparison of white cell counts, blood cultures, physical examination, and leukocyte imaging is presented in Table 3. The overall sensitivity of leukocyte imaging was 100%, the specificity 93%, and the accuracy 97% (29–30 studies).

DISCUSSION

The advent of extracorporeal hemodialysis in 1943 provided a means whereby patients with end-stage renal disease could be sustained for long periods of time. The introduction of the external arteriovenous shunt, and of the endogenous fistula permitted convenient, and routine, access to the circulation. The synthetic vascular prosthesis offers another means of access to the circulation; this is particularly valuable in those patients who have exhausted peripheral venous sites. Unfortunately, like any implanted foreign material, such prostheses are subject to infection, which may not only jeopardize the function of the graft, but may also result in serious systemic sequelae for the patient. It has been estimated that ~75% of all bacteremic episodes in patients on chronic hemodialysis originate at the hemodialysis access site. Complications include endocarditis, septic emboli, and meningitis (*1,2*); prompt diagnosis and institution of appropriate therapy is necessary.

The diagnosis of hemodialysis access-site infection can be an arduous task. While an elevated leukocyte count and bacteremia may indicate the presence of infection, they do not localize its source. Despite its superficial location, physical examination of the access site is unreliable. Erythema, warmth, and induration, are frequently present in the normal hemodialysis access site. Purulent discharge, fluctuance, and severe tenderness are considered diagnostic of access-site infection, yet these findings are absent in up to one-third of these infections, and even when present may not accurately reflect the extent of infection. The early diagnosis of this condition can, therefore, be a major challenge.

Indium-111-labeled leukocyte imaging is an accepted method of diagnosing foci of infection in the general population (*3–7*) and several reports attest to its utility in vascular graft infections (*8–14*). The hemodialysis access-site graft, however, is unique among vascular grafts in that it serves as a port of entry to the circulation. As such, it is repeatedly (up to several times weekly) subject to puncture, and the potential for introduction of infection is enhanced, a fact borne out by the observation that while the overall incidence of vascular graft infection is ~2%, the incidence of hemodialysis access-site infection ranges from 10% to 20% (*2,9,15*). In addition to an increased incidence of infection, repeated puncture of the access site may result in local inflammatory changes and hematoma formation, both of which could conceivably have an adverse affect on the specificity of leukocyte imaging. This was not the case in our series, however, where the specificity was 93%. Two other factors may also adversely affect the specificity of leukocyte imaging in vascular graft infection: graft thrombosis and recent (<1 wk) graft placement (*9,13,16,17*). There were a total of five thrombosed, infection-free grafts in the 30 PTFE grafts studied: there was one false-positive leukocyte image among the five. None of the grafts imaged had been implanted <2 wk prior to imaging; consequently the possibility of a false-positive result secondary to recent graft placement could not be assessed in this series.

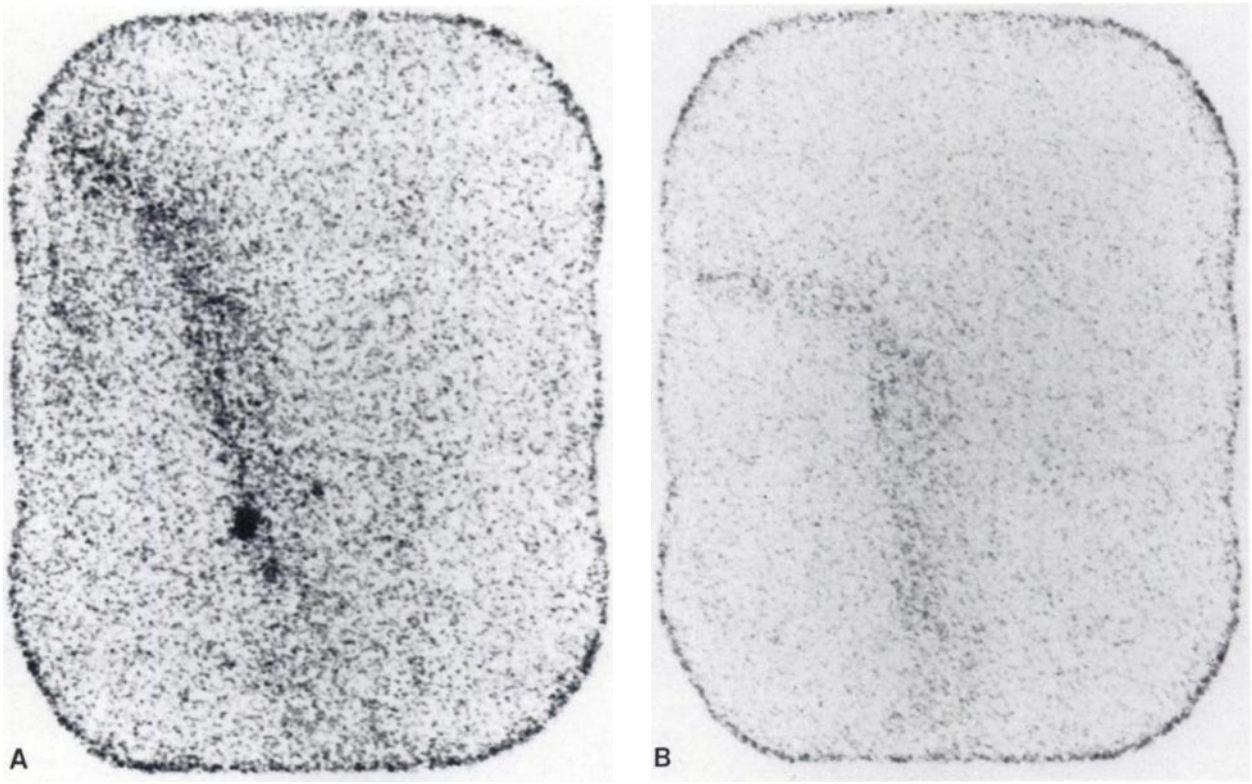

FIGURE 2
A 66-yr-old female had been ill for 5 wk. Leukocyte count was 16000 mm^3, blood cultures were positive for *S. Aureus;* physical examination of the access site was negative for infection. (A) Leukocyte image of left forearm access site reveals grade 2 activity. (B) Repeat leukocyte imaging performed after ten days of additional antibiotic therapy, demonstrates grade 0 activity at the access site. Blood cultures were negative and leukocyte count was normal at this time. Final diagnosis was resolved access-site infection.

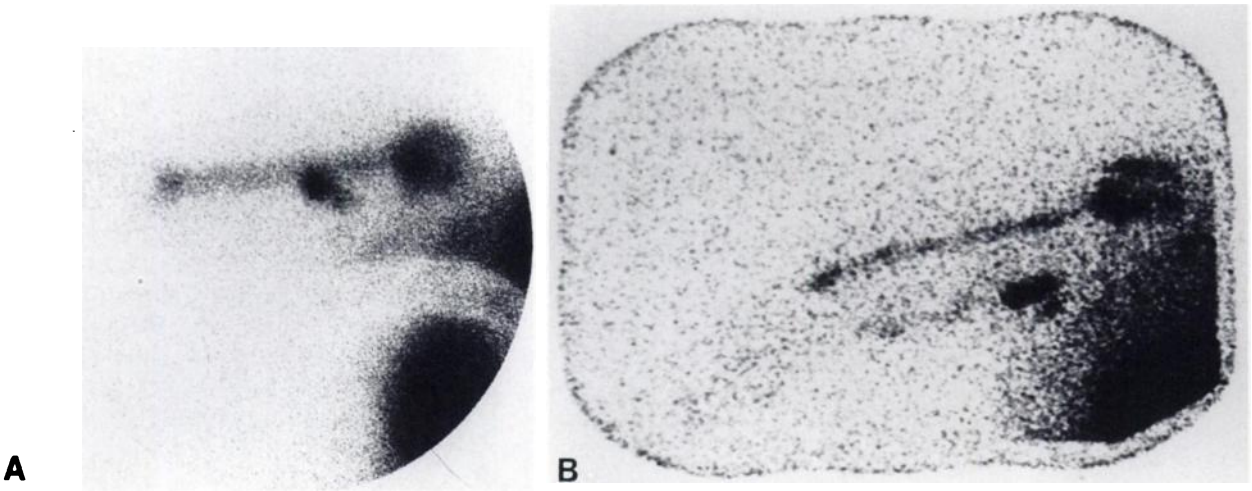

FIGURE 3
A 37-yr-old female had been ill for 2 wk. (A) Grade 3 activity is present at the access site. Leukocyte count at this time was 6700 mm^3; blood culture were positive for pseudomonas. Physical examination of the access site was consistent with infection. (B) Leukocyte imaging was repeated 2 wk later, following additional antibiotic therapy. Blood cultures and physical examination were both still positive; leukocyte count was 6100 mm^3. Abnormal activity at the access site persists, essentially unchanged from (A). An infected graft was surgically removed.

TABLE 2
Indium-111-Leukocyte Activity at Hemodialysis Access Site (n = 30)

	Leukocyte Activity				
Infection	0	1	2	3	Totals
(+)	0	4	7	4	15
(−)	14	0	1	0	15
Total	14	4	8	4	30

Antibiotic therapy and chronicity of infection have been implicated as causes of false-negative results in leukocyte imaging (*18–20*). All patients with access-site infection were on antibiotics at the time of scintigraphy; ten patients had been ill for at least three weeks prior to imaging. Neither of these factors affected the sensitivity of the procedure (100%) in this series.

Because patients with hemodialysis access sites may have infection unrelated to their access site, the specificity of labeled leukocyte imaging is important. All of the patients in our study were clinically suspected of having an access-site infection and, therefore, the true specificity of the test could not be ascertained. However, the accuracy of labeled leukocyte imaging was 97% in this series, while the accuracy of physical examination, the principal noninvasive method of diagnosing access-site infection was 67%. Indium-111-labeled leukocyte imaging was clearly superior to physical examination in our patient population.

Extragraft sites of infection were identified in two patients; osteomyelitis and a soft-tissue abscess; because of the low frequency of false-positive results at the hemodialysis access site, the demonstration of extragraft sites of leukocyte accumulation provided important information in the search for the true source of infection in our patient population.

The extent of infection in a hemodialysis access site governs, to some degree, patient management. While localized infection may resolve with incision and drainage together with antibiotic therapy, extensive infection (tunnel infection) generally requires graft excision (*15*). In our series, the pattern of labeled leukocyte uptake in the access site correlated with the extent of the infection: focal with localized infection and diffuse with extensive tunnel infection. Thus, this radionuclide procedure may help to separate those individuals in whom local treatment may suffice from those in whom graft excision may be needed.

TABLE 3
Comparison of Diagnostic Modalities for Hemodialysis Access Site Infection (n = 30)

	Leukocyte count*	Blood culture	Physical exam	Leukocyte imaging
Sensitivity	27%	100%	40%	100%
Specificity	67%	67%	93%	93%
Accuracy	47%	83%	67%	97%

*Considered positive for infection when leukocyte count was at least 11,000 mm^3.

Four patients underwent repeat leukocyte imaging after a course of medical therapy; the follow-up images confirmed the presence or absence of infection in each case, suggesting that this procedure may provide a reliable, objective method of evaluating patient response to therapy.

Finally, though physical examination and leukocyte imaging were equally specific for access-site infection, (93%), the radionuclide study was considerably more sensitive (100% versus 40%). The higher incidence of false-negative physical examinations in our series in comparison to what has been previously published, (60% versus 33%) probably reflects a bias in patient referrals; i.e., patients imaged were more frequently those in whom the source of infection was not clinically obvious.

In conclusion, our data indicate that ^{111}In-labeled leukocyte imaging is an accurate method of diagnosing hemodialysis access-site infection; any leukocyte accumulation above background at the access site, regardless of the intensity of this accumulation, is indicative of infection. The sensitivity of the procedure is not affected by antibiotic treatment or duration of symptoms. Leukocyte imaging also may provide a simple, reliable method of monitoring patient response to therapy.

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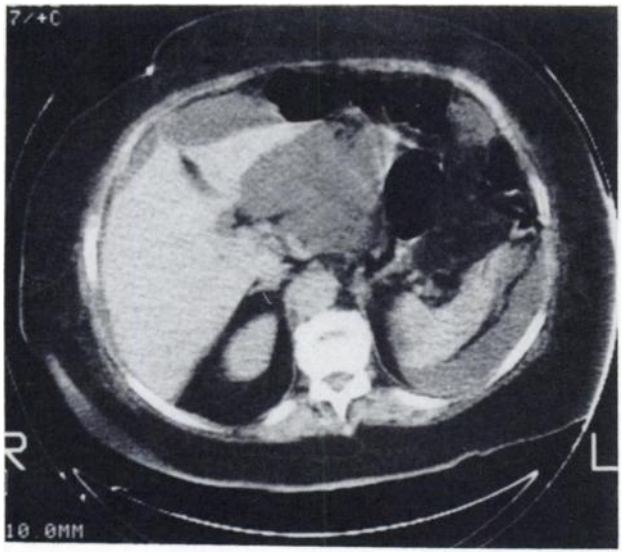
FIRST IMPRESSIONS



PURPOSE:
Postcholecystectomy evaluation of bile duct patency. The interesting sequential images presented here demonstrate a biliary leak. Following the first impression that the scan was abnormal, consideration of the changing pattern of the radiotracer distribution led to the final diagnosis of a biliary leak. In this case, the CT scan supported the diagnosis, which was confirmed at autopsy.

TRACER:
[^{99m}Tc]DISIDA

ROUTE OF ADMINISTRATION:
Intravenous injection

TIME AFTER INJECTION:
5, 15, and 30 minutes

INSTRUMENTATION:
Gamma Camera ("Picker")

CONTRIBUTORS:
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