
Comparison of Technetium-99m-HM-PAO Leukocytes with Indium-111-Oxine Leukocytes for Localizing Intraabdominal Sepsis

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Technetium-99m-HM-PAO (^{99m}Tc]HM-PAO) leukocyte and indium-111-oxine (^{111}In -oxine) leukocyte scanning were carried out simultaneously in 41 patients at 4 hr and 24 hr after reinjection to determine whether the 4-hr ^{99m}Tc scan could replace the 24-hr ^{111}In scan for detecting intraabdominal sepsis. Abdominal infection was confirmed in 12 cases. The 4-hr ^{99m}Tc -leukocyte scan, the 4-hr ^{111}In -leukocyte scan, and the 24-hr ^{111}In -leukocyte scan yielded a sensitivity of 100%, 67%, and 100%, respectively, and a specificity of 62%, 90%, and 86%, respectively. The 24-hr ^{99m}Tc -leukocyte scan also produced a sensitivity of 100%, but it was falsely positive in all 29 cases without infection due to physiologic bowel uptake. False-positive 4-hr ^{99m}Tc -leukocyte scans were also produced by physiologic bowel uptake in seven cases all of whom had true-negative 4-hr and 24-hr ^{111}In -leukocyte scans. Because of the high incidence of false-positive 4-hr [^{99m}Tc]HM-PAO leukocyte scans, it was concluded that they could not replace 24-hr ^{111}In -leukocyte scans for detecting intraabdominal sepsis, and that serial ^{99m}Tc leukocyte scans starting earlier than 4 hr after reinjection must be evaluated.

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Ultrasound, computed x-ray tomography and indium-111 (^{111}In) leukocyte scanning all have an established role in the detection of intraabdominal sepsis (1,2). Indium-111-leukocyte scans are the technique of choice in the absence of localizing signs (1-3), or immediately after surgery when there are technical difficulties for the other imaging techniques, or when it is necessary to clarify whether a fluid collection is purulent (4). The technique of labeling leukocytes with technetium-99m- (^{99m}Tc) hexamethylpropylene amine oxime (HM-PAO) has been developed as an alternative method of localizing inflammation and infection (5). Compared to ^{111}In -leukocytes, this method has the ad-

vantages of convenience, better imaging characteristics, and lower patient radiation dose associated with ^{99m}Tc (6), as well as selective labeling of granulocytes (5,7). Potential disadvantages of [^{99m}Tc]HM-PAO leukocytes for the detection of abdominal infection are physiologic uptake in the bowel, gall bladder, kidney and bladder (5,8-10), with the variable magnitude and anatomical distribution of bowel uptake likely to provide the greatest impediment.

Surgical management of acute abdominal infection requires an accurate localization to be made as quickly as possible. However, the routine choice of imaging time must be late enough to allow for the expected range in the rate of leukocyte migration to acute and chronic abdominal abscesses. Four hours is the latest time during normal working hours when a ^{99m}Tc -leukocyte scan can be carried out on the same day as reinjection, and is the earliest time at which positive uptake in intraabdominal sepsis has been reported (5,10). Physiologic bowel uptake is not always present at this time, and has been described as faint and only in the proximal colon (8-10). The earliest time for a scan on the following day is at least 20 hr after reinjection when physiologic bowel uptake of ^{99m}Tc is generally to be expected.

A comparison has been made between [^{99m}Tc]HM-PAO leukocyte and ^{111}In -leukocyte scanning carried out simultaneously in each of a series of patients to determine if the 4-hr ^{99m}Tc scan could replace the 24-hr ^{111}In scan for localizing intraabdominal sepsis. Indium-111-leukocyte scans at 4 hr were included since 4 hr and 24 hr are the routine imaging times used at this hospital with this technique. Technetium-99m scans at 24 hr also were carried out to confirm the general appearance of physiologic bowel uptake by this time, and to determine if they could assist in the distinction between uptake in bowel and uptake in intraabdominal sepsis.

MATERIALS AND METHODS

Patient Population

Forty-one consecutive patients (22 males, 19 females, age range 19-85 yr, mean 53 yr) were investigated for suspected intraabdominal sepsis.

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Cell Separation and Labeling

A mixed leukocyte suspension was labeled with [^{99m}Tc]HM-PAO by a method similar to that recommended by the manufacturer (Amersham International plc, UK). Briefly, 51 ml of venous blood was withdrawn into a syringe containing 9 ml of acid citrate dextrose, 45 ml of the solution was then sedimented for 60 min in 5 ml Hespan (Dupont, N. Billerica, MA), and the remainder was centrifuged at 2000 g for 10 min to obtain cell-free plasma (CFP1). The leukocyte-rich plasma from the sedimented solution was centrifuged at 150 g for 5 min, the cell pellet was resuspended in 1 ml of CFP1, and the supernatant centrifuged at 2000 g for 10 min to form cell-free plasma (CFP2). The cell suspension was incubated with [^{99m}Tc]HM-PAO (2 ml, 400 MBq) at room temperature. After 10 min, CFP2 (5 ml) was added to the suspension which was then centrifuged at 150 g for 5 min. The cell pellet was resuspended in 5 ml of CFP1, and the cell-bound and supernatant activities were measured before the cell suspension was reinjected into the patient. Mean values of labeling efficiency (11) and reinjected ^{99m}Tc activity were 47% (s.d. ± 14%) and 160 MBq (s.d. ± 56 MBq), respectively.

Indium-111-oxine mixed leukocytes were prepared from a blood sample (60 ml anticoagulated with 500 IU preservative-free heparin) taken immediately after the above sample was collected. The labeling procedure (11) was modified to reduce the possibility of cell damage by shortening the ¹¹¹In incubation time from 15 min to 10 min (12), and by resuspending the cells in a plasma-saline solution (rather than saline) at each stage after labeling. The ¹¹¹In labeling was carried out at the same time as that for [^{99m}Tc]HM-PAO leukocytes, and the ¹¹¹In leukocytes were reinjected immediately after the latter. Mean values of labeling efficiency and reinjected ¹¹¹In activity were 78% (s.d. ± 13%) and 13 MBq (s.d. ± 3 MBq), respectively.

Image Acquisition

Technetium-99m images and ¹¹¹In images were recorded at 4 hr and 24 hr after reinjection, using an International General Electric 400T gamma camera (Milwaukee, WI), 20 percent energy windows, and a medium-energy collimator. Separate 20 percent windows were used for the 173 keV and 247 keV gamma rays emitted by ¹¹¹In. Evaluation of the 4-hr ^{99m}Tc image was the main purpose of this study, and it was estimated that not more than 10% of its total counts would be due to scattered radiation from ¹¹¹In.

Image Evaluation

Each ^{99m}Tc and ¹¹¹In image was viewed by two experienced observers and reported as positive on the criteria that there was abnormal uptake within the abdomen other than the liver, spleen, bone marrow, kidneys, and bladder.

Confirmation of Diagnosis

Surgical and bacterial evidence was used to confirm or exclude infection in 16 cases, and a combination of clinical, hematologic and radiologic evidence, and long-term follow-up was used in the remaining 25 cases.

RESULTS

Of the 41 patients studied, infection was confirmed in 12 cases (Table 1). The site of infection was localized

TABLE 1
Results of 4-hr and 24-hr [^{99m}Tc]HM-PAO Leukocyte and ¹¹¹In-leukocyte Scans

| | ^{99m} Tc-leukocytes | | ¹¹¹ In-leukocytes | |
|----------------------------|------------------------------|--------|------------------------------|--------|
| | 4 hr | 24 hr | 4 hr | 24 hr |
| True-positive [*] | 12 | 12 | 8 | 12 |
| (Sensitivity) | (100%) | (100%) | (67%) | (100%) |
| True-negative [†] | 18 | 0 | 26 | 25 |
| (Specificity) | (62%) | (0%) | (90%) | (86%) |

^{*} No. of patients with infection: 12.

[†] No. of patients without infection: 29.

in the 4-hr ^{99m}Tc scan, the 24-hr ^{99m}Tc scan, and the 24-hr ¹¹¹In scan of each case, but the 4-hr ¹¹¹In scan was correctly positive in only eight cases (Fig. 1). Physiologic bowel uptake occurred in addition to abscess uptake in one 4-hr ^{99m}Tc scan (over the proximal colon), and in eight of the 24-hr ^{99m}Tc scans as shown in Figure 1B (over either the proximal colon or the proximal and distal colon). The single case of cholecystitis produced the only gall bladder uptake of ^{99m}Tc at 4 hr seen in the entire study, and in this patient, gall bladder activity also was observed in the 24-hr ^{99m}Tc scan, the 4-hr ¹¹¹In scan, and the 24-hr ¹¹¹In scan. In the only patient with infection who also had inflammatory bowel disease, abscesses were confirmed at surgery around the colostomy site. The 4-hr ^{99m}Tc and ¹¹¹In scans showed intense diffuse uptake, which included abscesses and inflamed bowel, but the 24-hr ^{99m}Tc and ¹¹¹In scans showed focal uptake over the sites of infection, which could be resolved from the diffuse bowel activity.

In the 29 cases where infection was excluded, there were eleven 4-hr ^{99m}Tc scans, three 4-hr ¹¹¹In scans, and four 24-hr ¹¹¹In scans reported as abnormal (Table 1). All of the 24-hr ^{99m}Tc scans showed false-positive abdominal uptake. Gall bladder uptake was not seen in any of the 4-hr ^{99m}Tc scans and in just one of the 24-hr ^{99m}Tc scans of patients without infection. Each of the four patients with a false-positive 24-hr ¹¹¹In scan also had a false-positive 4-hr and 24-hr ^{99m}Tc scan, and three had a false-positive 4-hr ¹¹¹In scan. Of these four patients, inflammatory bowel disease was the cause of the abdominal uptake in two cases: one patient had intense diffuse uptake throughout the large bowel in all images except for the 4-hr ¹¹¹In scan where activity was absent over the descending colon, and the second patient with a partial colectomy showed localized uptake in each scan over the rectal stump inflamed with ulcerative colitis. The cause of the false-positive uptake in the third patient was unclear; all images except the 4-hr ¹¹¹In scan showed intense diffuse activity over the proximal colon, but other investigations including a laparotomy were normal. The fourth patient had diffuse uptake over the same anatomical site (right lower ab-

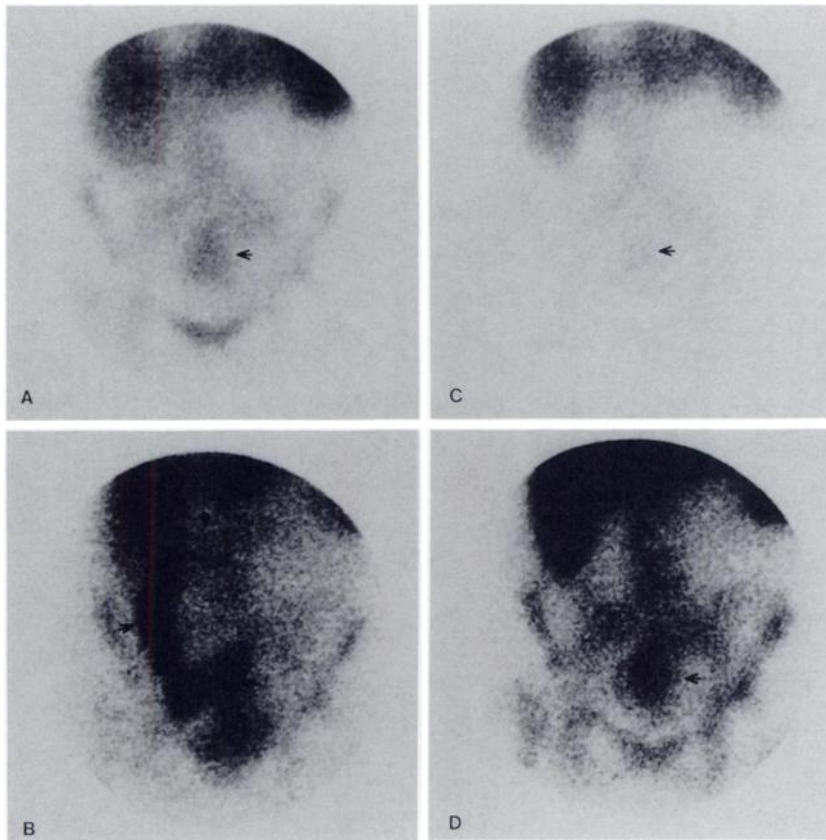


FIGURE 1

Anterior abdominal images of a patient showing abnormal uptake (arrows) over a mid-line pelvic abscess in the ^{99m}Tc]HM-PAO leukocyte scan at 4 hr (A) and at 24 hr (B), and in the ^{111}In leukocyte scan at 4 hr (C) and at 24 hr (D). At 4 hr, the abscess uptake was more intense in the ^{99m}Tc -leukocyte scan (A) than in the ^{111}In -leukocyte scan (C). At 24 hr, there was additional abnormal diffuse uptake over the ascending and transverse colon (arrows) in the ^{99m}Tc -leukocyte scan (B).

domen) in each scan, which was attributed to noninfective inflammation caused by peritoneal dialysis, and the patient's pyrexia was confirmed microbiologically to be due to lung infection.

All the remaining seven patients with false-positive 4-hr and 24-hr ^{99m}Tc scans had true-negative 4-hr and 24-hr ^{111}In scans, and the abdominal ^{99m}Tc activity was attributed to physiologic bowel uptake at both times (Fig. 2). Abnormal ^{99m}Tc uptake was generally over the proximal colon at 4 hr, and in four of these cases this activity was judged to be sufficiently localized at this time to resemble that of an abdominal abscess (Fig. 2A). In these seven cases of physiologic bowel uptake, the ^{99m}Tc activity had spread distally by 24 hr (Fig. 2B), to form a similar distribution to the additional bowel uptake found in the true-positive cases (i.e., in the proximal colon or the proximal and distal colon).

DISCUSSION

The main disadvantage of ^{111}In -leukocytes for the management of intraabdominal sepsis is the delay of 24 hr between reinjection and reporting. Chelates such as tropolone (13) and 2-mercaptopyridine-N-oxide (14), which permit cell labeling in plasma, reduce the change of cell damage, and pure granulocytes labeled in plasma have shown faster transit through the pulmonary vasculature than other cell preparations (15).

However, clinical evaluations have not demonstrated a significant improvement in diagnostic accuracy (16–18), and they contrast with the high sensitivity at 4 hr found in this study with ^{99m}Tc -leukocytes.

Unlike the bowel, physiologic uptake in the bladder and kidneys could be recognized in all ^{99m}Tc -leukocyte scans, and was not therefore counted as abnormal activity. While the more intense bladder activity did not hinder the detection of lower abdominal abscesses in the cases studied, it could make the identification of infection in this area more difficult. Physiologic bladder and kidney uptake was absent in all ^{111}In leukocyte scans.

False-positive physiologic bowel uptake must be identified when surgical intervention is being considered. It was a major limitation to the use of gallium-67-citrate for detecting intraabdominal sepsis (19), and seriously hindered the correct interpretation of ^{99m}Tc -leukocyte scans in this study. A true-positive case (of an abdominal abscess without enteric communication) could not always be distinguished from a false-positive case (due to physiologic bowel uptake) by comparing the ^{99m}Tc uptake at 4 hr with that at 24 hr. Either case could produce the same localized distribution at 4 hr and the same change in this distribution by 24 hr to include part or most of the large bowel (compare Fig. 1A-B images with Fig. 2A-B). Moreover, this pattern of uptake can be produced by either inflammatory bowel

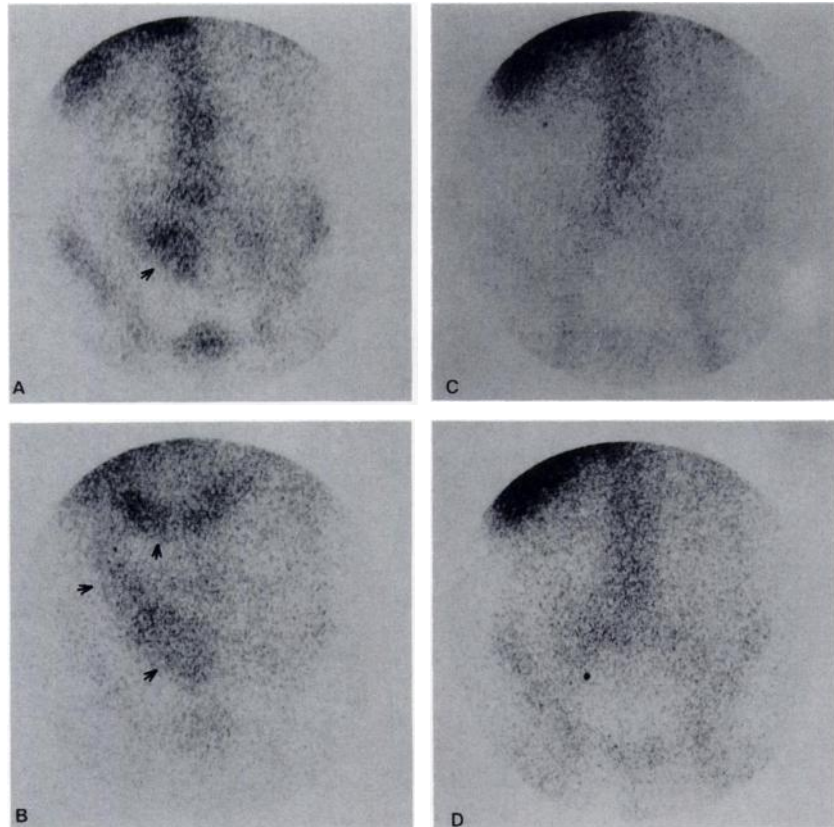


FIGURE 2

Anterior abdominal images of a patient in whom intraabdominal sepsis was excluded. However, the [^{99m}Tc]HM-PAO leukocyte scan showed a localized area of abnormal activity (arrow) just right of the pelvic mid-line due to physiologic bowel uptake at 4 hr (A), with more diffuse abnormal activity in addition over the ascending and transverse colon (arrows) due to physiologic bowel uptake at 24 hr (B). The 4-hr (C) and 24-hr (D) ^{111}In -leukocyte scans were normal (the dot in the 24-hr image was an artifact).

disease (9,10) or by an abscess with enteric communication (3). There were insufficient cases of inflammatory bowel disease to verify that it could be separated from physiologic bowel uptake on the basis of uptake intensity (10). However, one case showed that an abscess could be resolved from co-existent inflammatory bowel disease in both the 24-hr ^{99m}Tc and ^{111}In -leukocyte scans, but not in either of the corresponding 4-hr scans.

It has been reported that physiologic bowel uptake of ^{99m}Tc may arise from biliary excretion (10,20). The much lower incidence of this uptake in 4-hr ^{99m}Tc -leukocyte scans of infected cases compared to noninfected cases suggests that intraabdominal sepsis may reduce this source of ^{99m}Tc excretion.

CONCLUSIONS

The sensitivity of the 4-hr [^{99m}Tc]HM-PAO leukocyte scan was as high as the 24-hr ^{111}In -leukocyte scan, and the absence of uptake in the former allowed abdominal infection to be excluded. Nevertheless, the 4-hr ^{99m}Tc scan could not replace the 24-hr ^{111}In scan for the localization of intraabdominal sepsis because of its poor specificity. The sensitivity and specificity of serial ^{99m}Tc -leukocyte scans starting earlier than 4 hr after reinjection must be evaluated to determine whether they could provide a method for localizing intraabdominal sepsis. Until the results are known, ^{111}In -leukocyte scanning

should remain the standard cell labeling technique for investigating intraabdominal sepsis.

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