

DETECTION OF INFLAMMATORY LESIONS WITH ^{99m}Tc HMPAO LABELLED LEUKOCYTES

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ABSTRACT

This study was undertaken to evaluate the usefulness of ^{99m}Tc HMPAO leukocyte imaging in the detection of inflammatory lesions. A group of 35 patients with suspected infection or inflammatory lesions was studied. Leukocytes from 45 millilitres of blood from each patient were labelled with ^{99m}Tc HMPAO. The mean labelling efficiency was 44%. After dynamic image, the static images were taken at 30-60 minute, 4 and 24 hour after injection of labelled leukocytes. Most of the positive scans were best seen at 4 hour and lasted till 24 hour. The overall sensitivity, specificity and accuracy was 92%, 95% and 94% respectively.

It is concluded that ^{99m}Tc HMPAO leukocytod imaging is a very helpful diagnostic investigation for infection or inflammatory lesions.

Key Words : Leukocyte imaging, Inflammatory lesion, Radionuclide imaging

INTRODUCTION

Gallium-67 (^{67}Ga) citrate has been used routinely in the detection of inflammation (1-4). Since 1976 ^{111}In labelled leukocytes scans have been shown to be useful in the detection of infections and inflammatory lesions (5-10). ^{99m}Tc -hexamethylpropylene-amineoxime (HMPAO) has been reported as an alternative agent to ^{111}In oxime for labelling leukocytes (11). ^{99m}Tc HMPAO labelled leukocytes has many advantages over ^{111}In oxime with respect to radiation dose to the patient, image quality, acquisition time, availability and expense, therefore ^{99m}Tc HMPAO has become the preferred agent for labelling leukocytes for imaging of various inflammatory conditions (12-14).

This work reports our clinical experience with the use of ^{99m}Tc HMPAO to label leukocytes in patients suspected of having various inflammatory conditions.

MATERIALS AND METHODS

Patients

The study included 35 patients, 18 males and 17 females, with an age range from 11 to 77 years (mean age 40.4 yr). Of these, 6 had suspected intraabdominal sepsis, 10 suspected brain abscess, 3 suspected bone infection, 3 suspected polycystic kidneys, 10 had fever of unknown origin and one each had suspected inflammatory bowel disease, splenic abscess and cellulitis of leg. The final diagnosis was confirmed with surgery in 14 patients, histologic and/or microbiologic findings in 12, endoscopy in one and autopsy in one. The diagnosis was based on computed tomography and/or ultrasonography and clinical findings in 4 patients. Final diagnosis was not achieved in 3 patients with fever of unknown origin.

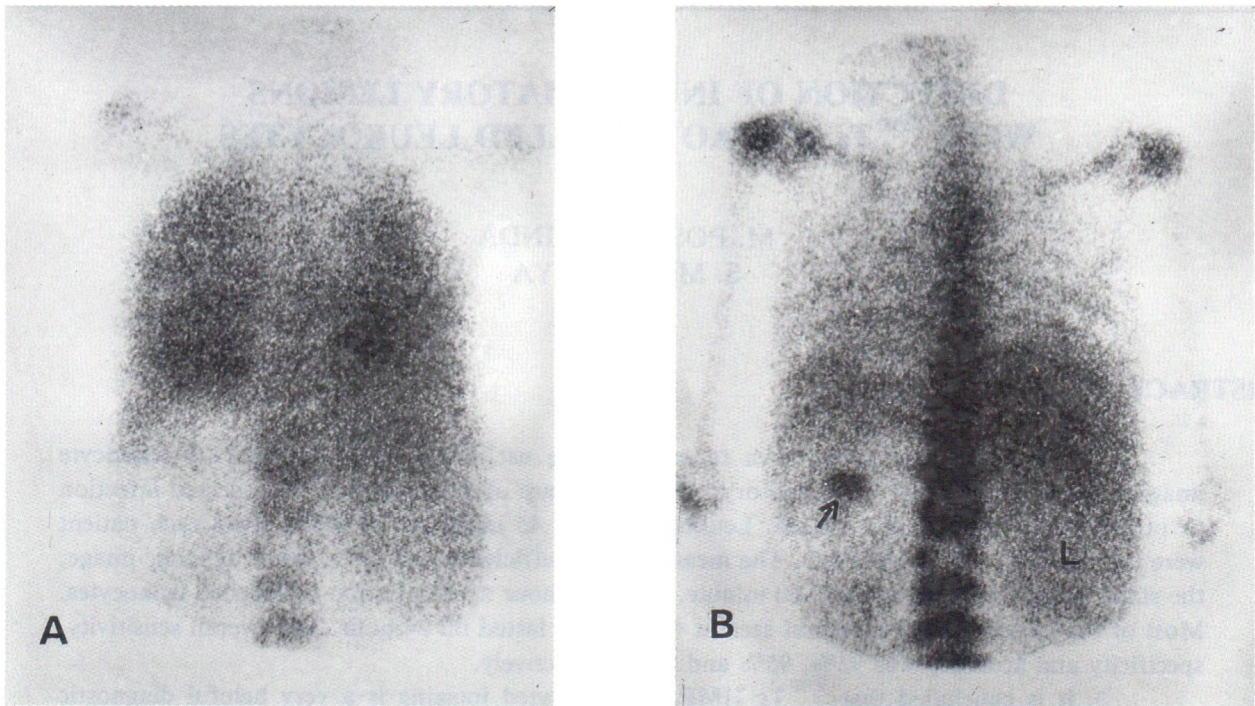


Fig 1 Abnormal uptake of ^{99m}Tc HMPAO labelled leukocytes at splenic bed (arrow) in a patient with abdominal sepsis post splenectomy, (A) 1 hour and (B) 4 hours after injection of labelled leukocytes. Both images are posterior view. L = liver

White blood cell labelling with ^{99m}Tc HMPAO

Fourty five ml of venous blood was collected from patient into 8 ml of acid citrate dextrose (ACD) solution. Mixed leukocytes were separated and labelled with ^{99m}Tc HMPAO according to method described by Costa et al. (13). After reconstitution, ^{99m}Tc HMPAO leukocytes was injected intravenously to the patient with the average activity of 300 MBq (8.1 mCi).

An intravenous blood sample was taken about 45 minutes after injection for the calculation of labelled leukocyte recovery. The cell labelling efficiency was $42.8 \pm 15.7\%$ (Mean \pm S.D).

Imaging protocol

Patients underwent planar imaging at 30-60 min, 4-6 h and 18-24 h after injection. Initial dynamic acquisition of 20×60 seconds frames, 64×64 matrix resolution, immediately post injection were carried out whenever appropriated at the suspected site. A Phillip's gamma camera was used in the initial period of study, then the IGE 400 AC/STARCAM system was used instead. A low energy, general purpose collimator was employed and 500 k counts per image

were recorded in the ^{99m}Tc energy window (140 KeV with 20% window).

RESULTS

The results of studies are shown in Table 1. All patients with true positive findings in inflammatory or infectious disease showed intense activity in the affected sites at 4 hour or even earlier with further increased or persisted activity at 24 hour image. Three of 6 patients with suspected intra-abdominal abscess were true positive, 2 of these, the diagnosis were confirmed at surgery while the other patient with suspected abdominal sepsis after splenectomy was subsequently improved after antibiotic therapy (Fig. 1). The remaining 3 patients were true negative (one hematoma, one recurrent cancer of distal ureter, one loculated ascites). Two of the 3 patients with suspected infected polycystic kidneys demonstrated multiple hot rim lesions in both kidneys which were better seen at 24 hour images (Fig. 2). The other patient with false negative scan demonstrated only multiple big cold lesions in enlarged liver while ultrasound revealed multiple cysts in the liver and the kidneys. But this patient had received antibiotic treatment one week before ^{99m}Tc HMPAO leukocytes imaging.

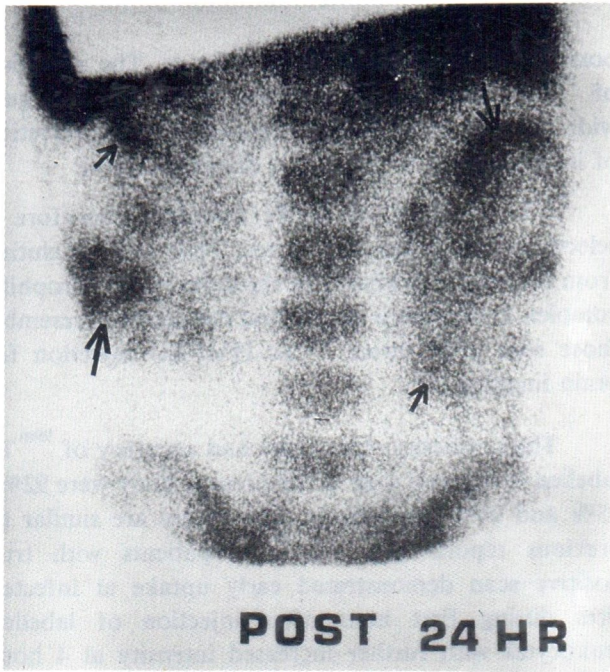


Fig 2 Posterior view of 24 hour image of a patient with polycystic renal disease shows multiple areas of abnormal uptake in both enlarged polycystic kidneys (arrows). Ultrasound and CT scan did not reveal a source of infection.

In the suspected brain abscess group, 2 patients had abnormal uptake at 4 hours and 24 hours images and were proved later to be brain abscesses (Fig. 3). One patient in this group yielded false positive scan, this patient showed a big focal uptake at left thalamus region at 1 hour image but was virtually disappeared at 4 hour and 24 hour images, germinoma of left thalamus was found at surgery (Fig. 4). The remaining 7 patients were subsequently proved to have brain tumours in 6 patients and meningitis in one patient.

In bone infection group, 2 patients with suspected infected hip prostheses had positive images (Fig. 5) and the diagnosis was confirmed at surgery in both patients. The remaining patient with negative scan was finally proved to have no infection of lumbar spine.

Of the 10 patients with fever of unknown origin, 7 patients were true negative with ^{99m}Tc leukocytes scan. Final diagnosis was not achieved in the remaining 3 patients.

One of each patient with ulcerative colitis and splenic abscess was correctly diagnosed with ^{99m}Tc HMPAO leukocytes imaging. The ulcerative colitis was better diagnosed by 4 hour image (Fig. 6) while the splenic abscess was better diagnosed by 4 hour and 24 hour images (Fig. 7). One patient with suspected cellulitis of leg who had negative scan was finally diagnosed to have cardiomyopathy.

The overall sensitivity, specificity and accuracy of labelled leukocyte imaging was 92%, 95% and 94% respectively.

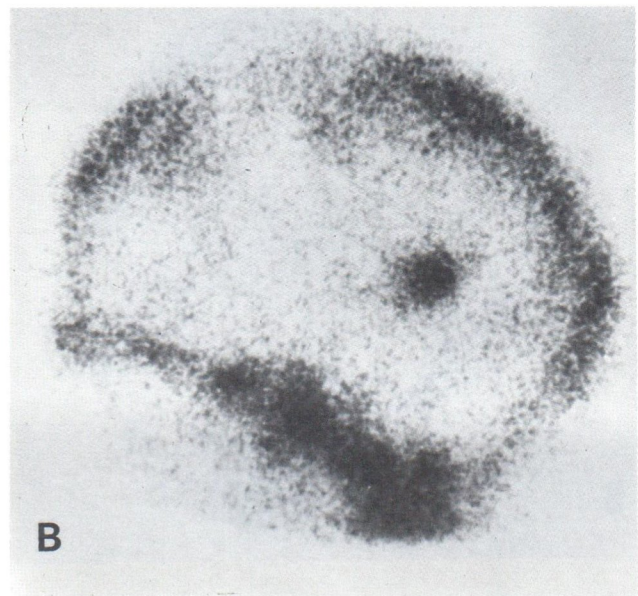
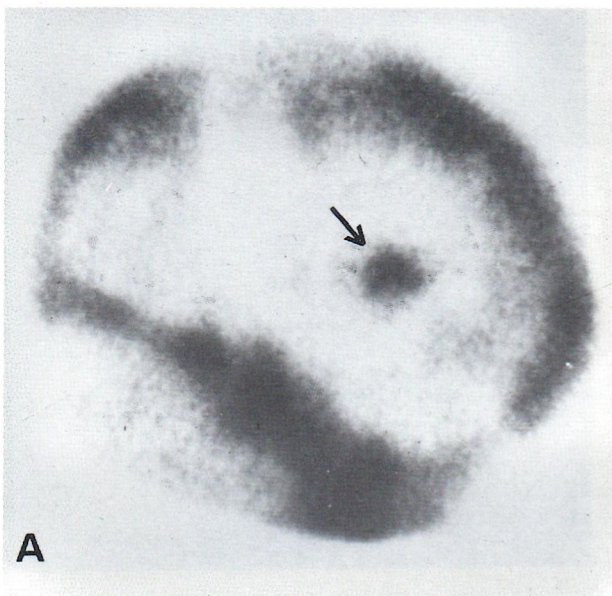


Fig 3 Left lateral view of brain show a focal abnormal activity at temporal lobe region (arrow), (A) 4 hours and (B) 24 hours after injection. Brain abscess was found at surgery in this patient.

DISCUSSION

^{67}Ga citrate has been used in the determination of abscesses but it is difficult to differentiate the uptake of ^{67}Ga in infection from uptake in a tumour, therefore it lacks specificity. ^{111}In labelling of leukocytes has been proved to be more useful in detection of infection and inflammatory lesions (8-10). Apart from some undesirable properties of ^{111}In , its use is not

possible for developing country like us. The invention of $^{99\text{m}}\text{Tc}$ HMPAO in labelling leukocytes has gain wide interests in study of its reliability in the detection of inflammatory or infectious diseases (11-14).

$^{99\text{m}}\text{Tc}$ HMPAO is highly lipophilic therefore it selectively labels the leukocytes. Free activity eluting from the cells is probably in the form of a hydrophilic complex, thus there is no cerebral radioactivity resemble those seen after direct $^{99\text{m}}\text{Tc}$ HMPAO injection for brain imaging (12).

The sensitivity, specificity and accuracy of $^{99\text{m}}\text{Tc}$ labelled leukocytes scan in the present study were 92%, 95% and 94% respectively. The values are similar to previous reports (12, 14). Most patients with true positive scan demonstrated early uptake at infected sites during first hour after injection of labelled leukocytes with further increased intensity at 4 hour image and persisted or even further increased intensity at 24 hour image. One patient with infected polycystic kidney had negative scan at 1 hour image but was positive at 4 hour and 24 hour. The patient with splenic abscess demonstrated a big cold lesion in early image with decreased in size of the lesion in the late images which indicated increase accumulation of labelled leukocytes with time around the lesion. Hence three phase scan provided better diagnostic validity as shown in this and other studies (10).

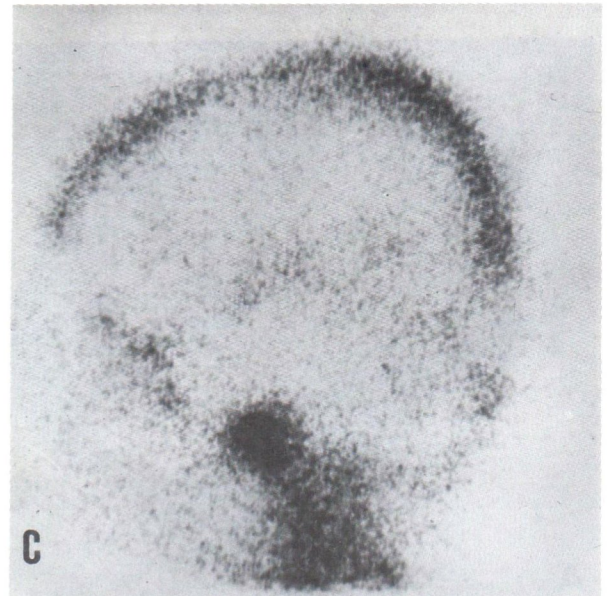
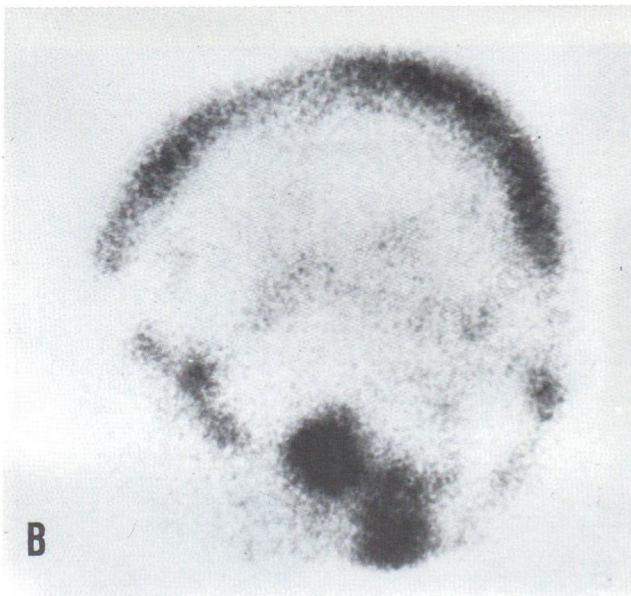
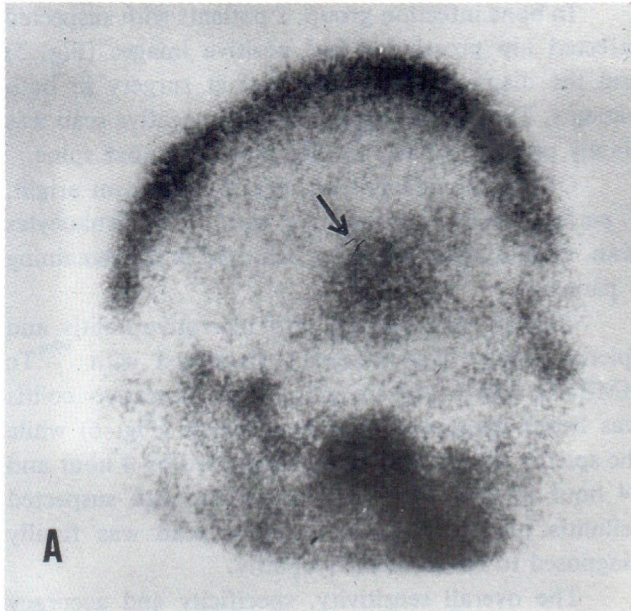


Fig 4 Left lateral view of brain in a patient shows a big abnormal uptake at temporal region (arrow) at 1 hour after injection (A), the activity was virtually faded away at 4 hour (B) and 24 hours (C). Germinoma of left thalamus was found at surgery.

Our findings agree with other reports that patients with suspected inflammation in the abdominal region should be imaged during the first 4 hour after administration of ^{99m}Tc leukocytes to avoid false positive findings resulted from nonspecific bowel activity which was always at least weakly visualized at 18-24 hour and in some patients in the 6 hour image (10, 12, 14).

The only one false positive finding found in this study was in a patient with brain tumour. However the intense activity at the lesion was seen only at 1 hour image which may represent high vascularity at the lesion. Thus the late image at 4 hour and 24 hour are more specific to diagnose brain abscess. However positive findings of ^{111}In -leukocytes scan in some malignancies have been reported (15, 16).

The only one false negative finding in this study was found in a patient with suspected polycystic kidney, but this patient had on antibiotic therapy one week prior to the study. It is possible that the infective process had already subsided. CT and Ultrasonography, although highly sensitive in diagnosis of polycystic renal disease, are not able to specifically indicate the presence of infection while labelled leukocyte imaging are highly sensitive and specific for the detection of infection as demonstrated in this study and other studies (17, 18).

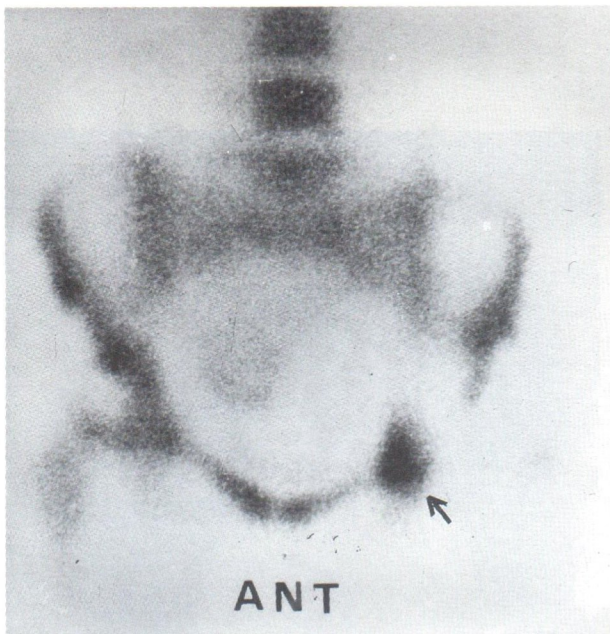


Fig 5 Anterior pelvis of a patient with infected prosthetic hip joint shows marked abnormal uptake (arrow) at 4 hour image.

It has been reported that labelled leukocyte imaging as well as immunoscintigraphy (IS) using antigranulocyte monoclonal antibodies are sensitive and accurate imaging modality for detection of infected joint prostheses (14, 19, 20). Our results were also good in patients with infected prosthetic hip. However it is necessary to correlate the finding of labelled leukocyte imaging or IS with ^{99m}Tc MDP bone imaging in the detection of periprosthetic infection (19, 20).

All 7 patients with fever of unknown origin were true negative with ^{99m}Tc leukocytes. It has been shown previously that there is very low frequency of detectable infection in these patients (21).

In conclusion, our results with ^{99m}Tc HMPAO labelled leukocytes imaging exhibit the usefulness of this technique in the diagnosis or exclusion of various infectious and inflammatory processes. Although most of the lesions were better demonstrated at 4 hour after injection of labelled leukocytes, 1 hour and 24 hour images are also recommended for better sensitivity and specificity in the diagnosis. The readily available ^{99m}Tc and HMPAO kits are more suitable in developing countries than ^{111}In for labelling leukocytes.



Fig 6 Anterior abdomen of a patient with ulcerative colitis at 4 hours after injection shows abnormal accumulation of ^{99m}Tc HMPAO labelled leukocytes in the entire colon.

Table 1 RESULTS OF STUDIES WITH Tc-99m LABELLED LEUKOCYTES

INITIAL DIAGNOSIS	TP	FP	TN	FN	NO DIAGNOSIS
INTRA-ABDOMINAL ABSCESS (n=6)	3	—	3	—	
INFECTED POLYCYSTIC KIDNEYS (n=3)	2	—	—	1	
BRAIN ABSCESS (n=10)	2	1	7	—	
BONE INFECTION (n=3)	2	—	1	—	
ULCERATIVE COLITIS (n=1)	1	—	—	—	
SPLENIC ABSCESS (n=1)	1	—	—	—	
CELLULITIS (n=1)	—	—	1	—	
FEVER OF UNKNOWN ORIGIN (n=10)	—	—	7	—	3
TOTAL (n=35)	11	1	19	1	3

TP = True positive
TN = True negative

FP = False positive
FN = False negative

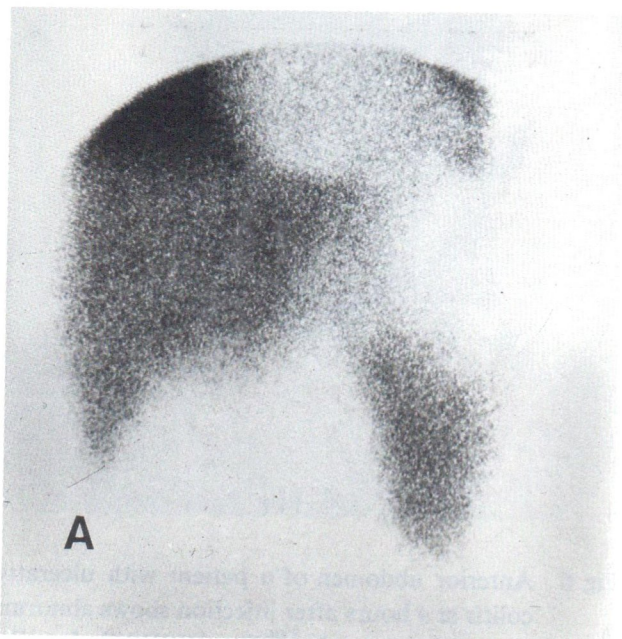


Fig 7 A

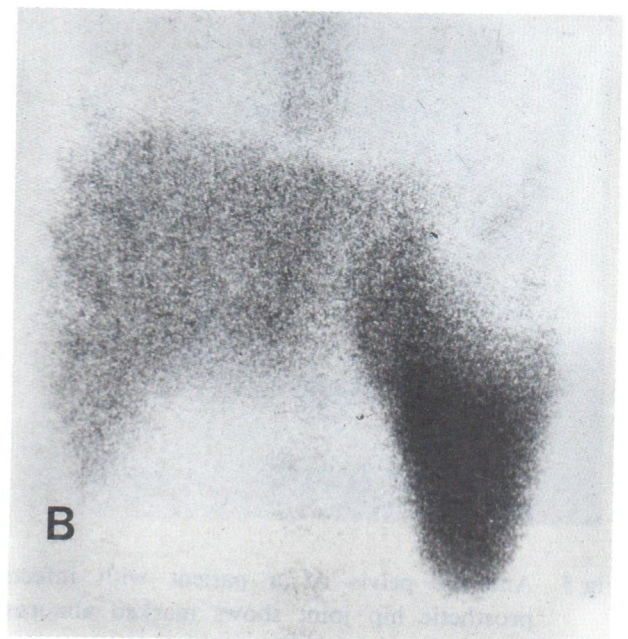


Fig 7 B

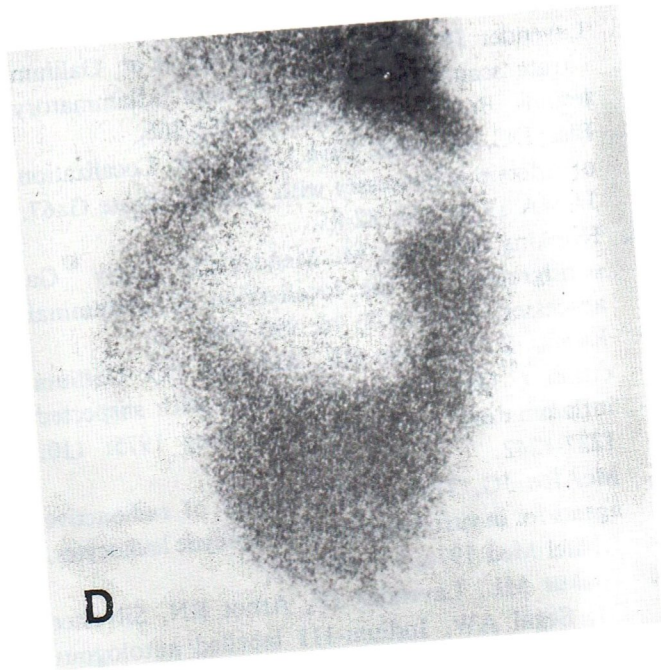
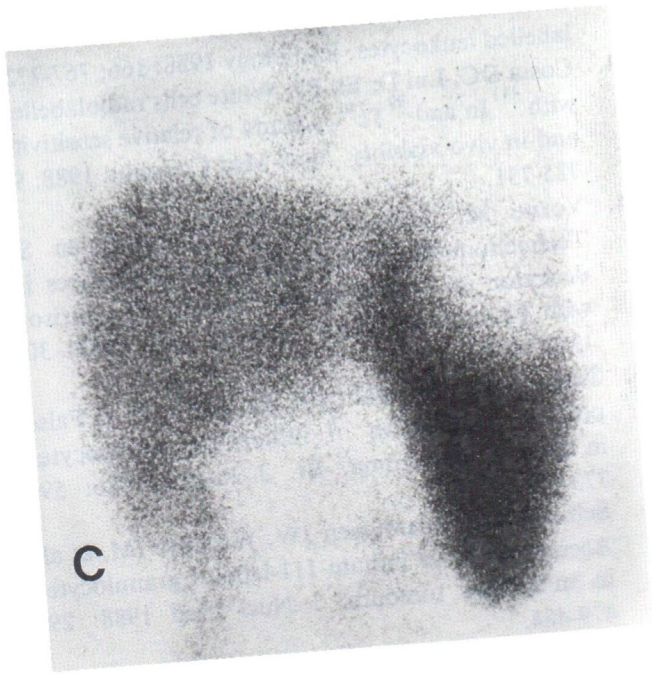


Fig 7 C

Fig 7 D

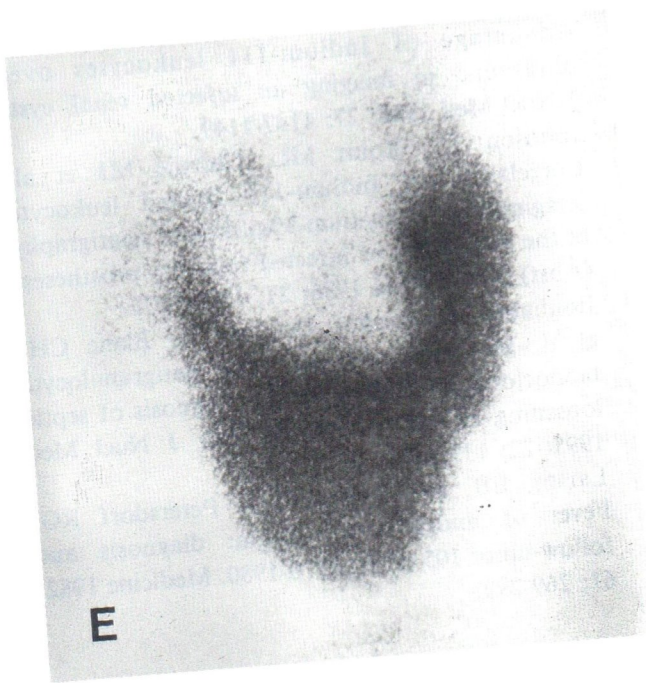


Fig 7 E

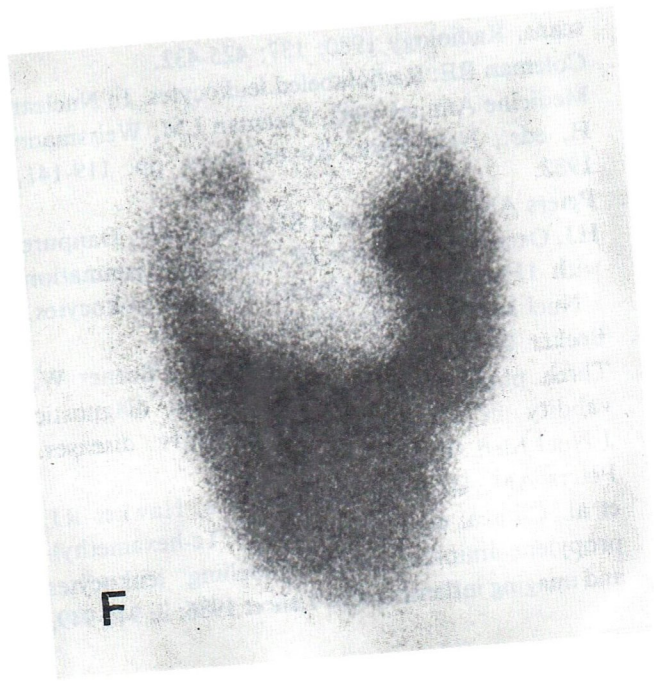


Fig 7 F

Fig 7 Anterior (upper row) and left lateral (lower row) views of abdomen in a patient with splenic abscess show a big cold lesion in enlarged spleen at 1 hour image (A and D), the focal defect is decreased in size with time according to increased accumulation of labelled leukocytes around the lesion as shown in 4 hour images (B and E) and 24 hour images (C and F).

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