Diagnosis of Prosthetic Vascular Graft Infection by Technetium-99m-HMPAO-Labeled Leukocytes

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The purpose of this study was to determine the usefulness of ^{99m}Tc-HMPAO-labeled leukocyte scans in the diagnosis of prosthetic vascular graft infection. **Methods:** We performed 75 scans in 61 patients with vascular grafts. Thirty-six patients were evaluated for suspected infection and 25 were control patients. Scintigraphic images were performed at 5 min, 30 min, 3 hr and, occasionally, 24 hr. Persistent increased uptake at 3 hr along the suspected area of the graft was considered evidence of graft infection. **Results:** All 20 infected grafts were detected with ^{99m}Tc-HMPAO leukocyte scan. The sensitivity and specificity of the scan in the detection of infected graft were 100%. We also detected two pelvic abscesses, two infected fistulae, two soft-tissue infections, three cases of ischemic colitis, one acute diverticulitis, one infected hematoma, one septic arthritis and one noninfected hematoma. One patient with a superficial groin infection had a negative scan. The eight pseudoaneurysms did not show scintigraphic evidence of graft infection. Correlative CT studies were performed in 12 cases. **Conclusion:** Technetium-99m-HMPAO-labeled leukocyte scan is an accurate and valuable diagnostic method for evaluation of suspected prosthetic vascular graft infection.

Key Words: vascular graft infection; technetium-99m-HMPAO leukocyte scan

J Nucl Med 1994; 35:1303–1307

Vascular graft infection (VGI) is one of the most serious complications in reconstructive vascular surgery. Although its incidence is not high, with an average of 2%–2.5% (*1*), the importance of vascular graft infection lies in its high morbidity-mortality rate (*2–3*). Infection may become evident soon after graft placement but, more commonly, it is not seen until weeks or months later. Diagnosis of prosthetic vascular graft infection can be difficult given that the symptoms are usually nonspecific, and their detection by conventional radiographic methods, such as computed tomography (CT) or ultrasound (US), is often difficult (*1*). The aim of this paper is to evaluate the diagnostic usefulness of ^{99m}Tc-HMPAO leukocyte scans in the diagnosis of vascular graft infection.

METHODS AND MATERIALS

We obtained 75 scans with ^{99m}Tc-HMPAO-labeled mixed leukocytes in 61 patients, 59 male and 2 female (range, 16 to 84 yr; average, 65) with prosthetic vascular graft. The implantation of the graft was due to abdominal aortic aneurysm in the case of 15 patients, occlusive atherosclerotic disease in 44 patients, trombosed popliteal aneurysm in one patient and vascular trauma in one patient.

Out of the 69 grafts studied, the most frequent type was the aorto-bifemoral graft, present in 48 patients. Others include: axilo-bifemoral graft present in five patients; ilio-femoral present in five; femoro-popliteal present in four; femoro-femoral present in two; axilo-femoral present in two; aorto-femoral present in one; ilio-popliteal present in one; and femoro-tibial present in one.

Fifty scans were performed in 36 patients because of clinical and/or radiological suspicion of vascular graft infection. Eight of these patients presented pseudoaneurysm at the level of distal aorto-bifemoral graft anastomosis. The other 25 patients were considered control patients. The interval between surgery and imaging ranged between 7 days and 13 yr. During the early postoperative period (1 mo), a total of 23 scans were obtained, with an additional 52 obtained during the subsequent period.

Mixed leukocytes were labeled with ^{99m}Tc-HMPAO according to Peter's method (*4*). After injection of 145–185 MBq of ^{99m}Tc-HMPAO-labeled leukocytes, we obtained a dynamic study and scintigraphic images at 5 min, 30 min, 3 hr and, occasionally, 24 hr. A whole-body scan was performed at 3 hr to detect possible inflammation sites other than vascular grafts.

With the aim of avoiding physiological intestinal activity arising from biliary excretion that can appear in late images, all patients were systematically fasted from the time of reinjection of labeled leukocytes until late images were obtained at 3-hr postinjection.

Persistent increased uptake at 3 hr along the expected area of the graft was considered evidence of vascular graft infection on the leukocyte scan. Lack of infection in scan-negative patients was confirmed by clinical follow-up of the patients. The diagnosis of infected graft was confirmed by culture in all cases.

Correlative CT studies were performed in 12 patients with suspicion of vascular graft infection. The presence of perigraft fluid and/or gas collection was considered evidence of graft infec-

Received Oct. 6, 1993; revision accepted Mar. 1, 1994.

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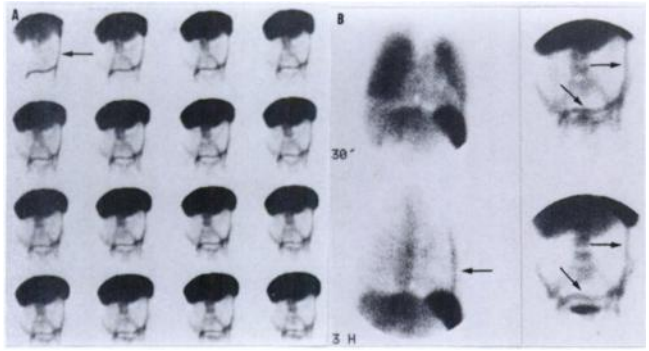

FIGURE 1. Infected left axilo-bifemoral graft (*S. aureus*). Dynamic study (A) and static images (B). Early and persistent uptake of labeled leukocytes (arrows).

tion on CT. The interval between the performing of the HMPAO scan and the CT was never greater than 7 days.

RESULTS

Prosthetic vascular graft infection was present in a total of 20 patients. In the culture, staphylococcus aureus was found in ten cases, corinebacterium was found in three; pseudomonas aeruginosa was found in two; staphylococcus epidermidis was found in one; staphylococcus aureus and enterococcus durans were found in one; enterobacter and corynebacterium were found in one; enterobacter and actinobacter were found in one; and E. coli and klebsiella pneumoniae were found in one.

All 20 cases of infected graft were detected on ^{99m}Tc-HMPAO-labeled leukocyte scans (Fig. 1). No other grafts, including those studied for suspected graft infection but were considered to be sterile (n = 30) and the control group (n = 25), presented persistent uptake of labeled leukocytes. On the basis of these results, the sensitivity and specificity of ^{99m}Tc-HMPAO leukocyte scans in the diagnosis of vascular graft infection was 100%.

All cases of vascular graft infection presented an intense, early and persistent uptake of labeled leukocytes. At 3 hr, no noninfected anatomic graft was visualized. Some superficial extra-anatomic grafts were weakly detected at 3 hr, resulting in the necessity to perform late images (24 hr). Neither the location of the graft nor the time which had passed since surgery caused any change in the results. Eight vascular graft infections were detected by scan during the early postoperative period and 12 in the subsequent period. At the time of the scan, all vascular graft infection patients were subject to antibiotic therapy.

We also detected extragraft migration of labeled leukocytes in two pelvic abscesses, two infected cutaneous fistulae, three ischemic colitis (Fig. 2), two soft tissue infections, one acute diverticulitis of the sigmoid colon (Fig. 3), one infected hematoma and one septic arthritis. One superficial groin infection presented a negative scan. A noninfected hematoma located in the thigh and at some distance from the graft, presented leukocyte uptake. The three cases of ischemic colitis were present in patients (age 65 or over) who were suffering from occlusive atherosclerotic disease. Two of these conditions were localized at the level of sigmoid and descending colon, while the third was localized in the transverse colon. The diagnosis was confirmed by colonoscopy in all cases.

The eight pseudoaneurysms present in our study presented a characteristic scintigraphical appearance (Fig. 4). In the ^{99m}Tc-HMPAO-labeled leukocyte scan, pseudoaneurysms were always visualized as a "hot spot" in the dynamic study, which is easily detected in 5-min and 30-min images, whereas significant uptake of labeled leukocytes is never seen in 3-hr scans.

CT was also performed in 12 patients with vascular graft infection suspicion. All six cases of vascular graft infection in this subgroup were detected by ^{99m}Tc-HMPAO leukocyte scan, whereas CT was positive in only four (Fig. 5). Pelvic abscess and acute diverticulitis were detected by both methods. No false-positive results were found on CT.

DISCUSSION

Prosthetic vascular graft infection is the cause of a high morbidity and mortality rate in patients who undergo vascular reconstructive surgery. The leading pathogen agent found in vascular graft infection is S. aureus, followed by S. epidermidis, S. faecali and E. coli (*1,2*). Its clinical presentation is nonspecific, making it very important to have methods of diagnosis available which carry out early diagnosis and localization—CT and US have been widely used to this end (*5–7*). During the last few years, MRI has also been employed to detect vascular graft infection (*8–9*).

In 1980, Causey et al. (*10*) were first to study vascular graft infection using ^{67}Ga-citrate. According to the results presented in the various works, the sensitivity of the ^{67}Ga scan ranged between 70%–100%, and its specificity was between 94%–100% (*6,10,11*).

In 1981, Sterick and Fawcet (*12*) were first to use ^{111}In-labeled leukocyte scan in the detection of vascular graft infection, and since then, ^{111}In-labeled leukocyte scans

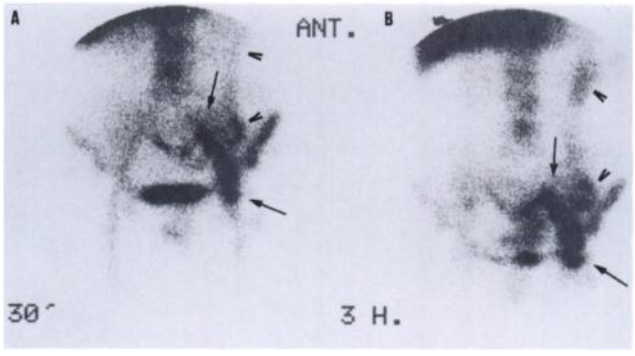

FIGURE 2. Infected aorto-bifemoral graft (*S. aureus*) and ischemic colitis. Static images performed at 30 min (A) and 3 hr (B). Early and intense uptake of ^{99m}Tc-HMPAO-labeled leukocytes is evident along right ilio-femoral limb of the graft (arrows). Less intense and delayed uptake is evident in descending and sigmoid colon due to ischemic colitis (arrows head).

have been widely used in the diagnosis of this type of pathology (*13–19*). Since the publication of the work carried out by Peters et al. in 1986 (*4*), ^{99m}Tc-HMPAO has become widely used for leukocyte labeling. Paakinen et al. (*20*) were first to study a case of vascular graft infection using ^{99m}Tc-HMPAO leukocyte scan, which was also used by Vorne et al. (*21*), who obtained a sensitivity and specificity of 100% and 96%, respectively, in a sample of 27 patients with vascular grafts.

During the last 4 yr, we have obtained a total of 75 ^{99m}Tc-HMPAO leukocyte scans from patients with prosthetic vascular graft, 50 with suspected vascular graft infection and 25 control subjects. Twenty of the grafts were infected. The sensitivity and specificity which we obtained in the detection of the vascular graft infection was 100%, similar to that reported by Vorne et al. (*21*), Bruner et al. (*15*), Williamson et al. (*16*) and Becker et al. (*18*). Dynamic study and early images were performed to obtain correct location of the graft (*22*). Although all the vascular graft infections in our study presented weak uptake of labeled leukocytes at 30 min, it should be noted that leukocyte migration at the site of the infected graft always increased significantly in the delayed images.

In the group of patients with positive scans and vascular graft infections, the vascular graft was removed and a new graft placed in ten cases, and the other ten were treated with antibiotic therapy. Five patients died during the follow-up period. Lack of infection in scan-negative patients was confirmed by clinical follow-up of the patients.

Even though there have been few reports on vascular graft infection detected using ^{99m}Tc-HMPAO leukocyte scans, it seems that the false-positive results obtained are lower than those obtained when using ^{111}In-leukocyte scans (*23*). Vorne et al. (*21,24*) obtained a single false-positive result in a patient studied only some 3 days after the implantation of the vascular graft, which was certainly caused by postsurgery perigraft inflammatory reaction. In our series, we did not obtain any false-positive results. A

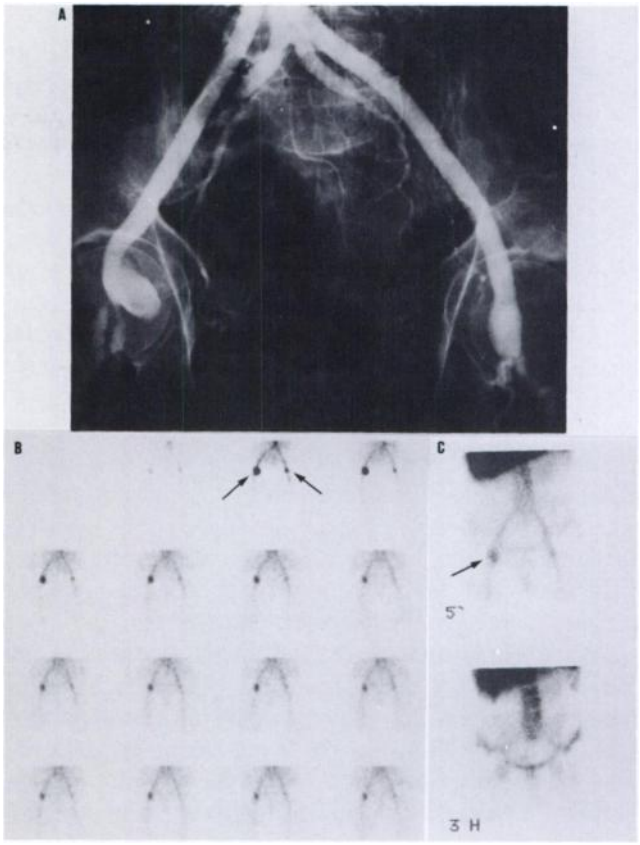

FIGURE 4. Noninfected bilateral pseudoaneurysms. (A) Angiography with contrast material revealed bilateral pseudoaneurysm with a large pseudoaneurysm of the right femoral artery. Labeled leukocyte scans (B) and (C): dynamic study and static images. Pseudoaneurysms are visualized like a hot spot in the dynamic study (arrows). In the static images, a large right pseudoaneurysm is easily detected on the 5-min image (arrow), whereas significant uptake of labeled leukocytes is not seen on the 3-hr image.

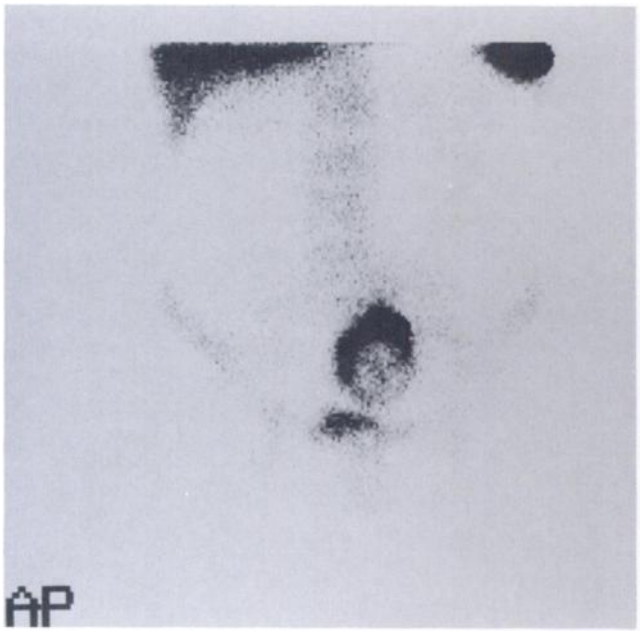

FIGURE 3. Acute diverticulitis of the sigmoid colon detected on anterior abdominal leukocyte scan.

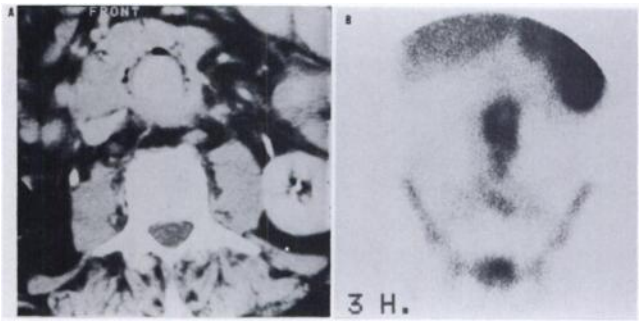

FIGURE 5. Infected aorto-bifemoral graft and abdominal aortic perigraft abscess (*E. coli* and kebsiella pneumoniae). (A) CT shows soft-tissue density mass and small gas pockets in the graft bed. (B) Technetium-99m-HMPAO leukocyte scan demonstrates increased uptake in the region of the aortic graft.

total of 23 patients were explored in the early postoperative period, two in the first 7 days, and there were no cases of pathological uptake. Other reported causes of false-positive results using ^{111}In have been: (1) the formation of intraprosthetic trombosis (*25*) (2) noninfected pseudoaneurysm (*26*) (3) hematomas (*27*) and (4) lymphocele (*28*).

In our study, the eight patients with pseudoaneurysms did not show scintigraphic evidence of graft infection. Usually pseudoaneurysms are considered a potential cause of false-positive results in labeled leukocyte scintigraphy (*26*). The most likely explanation for these false-positive results is the labeling of "contaminating" platelets and red cells (*29*). In the ^{99m}Tc-HMPAO leukocyte scan, pseudoaneurysms are always visualized as a hot spot in the dynamic study, which is easily detected in very early (5 min) and early (30 min) images, whereas significant uptake of labeled leukocytes is never seen in delayed (3 hr) scans. In the HMPAO scan, the contamination of platelets and red cells is less (*30*) and if we suspect pseudoaneurysm, we perform a dynamic study and images at 5 min.

Although we have not obtained any false-positive results in the evaluation of the graft area, one patient with noninfected post-traumatic hematoma in the thigh presented uptake of labeled leukocytes. The hematoma was drained and its aseptic nature was confirmed. The extra-graft location of this hematoma did not invalidate the correct evaluation of the graft area.

The usefulness of scans using labeled leukocytes in the detection of extra-graft pathology are well documented (*16,21*). Williamson et al. (*16*) found that in five patients with fever, the scan was normal with respect to the graft, but positive in other areas (two colitis, one infected catheter wound, one subhepatic abscess and one infected amputation stump). Vorne et al. (*21*) found extra-graft uptake in two infected wounds, one perforated colon, one soft-tissue infection and one pulmonary infiltration. In our study, the scan revealed two pelvic abscesses, two infected fistulas, three ischemic colitis, two soft-tissue infections, one acute diverticulitis of the sigmoid colon, one infected hematoma and one septic arthritis. In one patient with superficial groin infection the scan was normal. Thus, we consider that in all the scans performed in patients with suspected vascular graft infection, it is necessary to carry out a whole-body study, at least in delayed images.

CT has proved to be a useful diagnostic method in the detection of vascular graft infection (*5,31*). Johnson et al. (*6*) consider a CT for vascular graft infection to be positive if one of the following findings is present: (1) thickened graft wall or increased perigraft soft tissue, (2) perigraft fluid, (3) anastomotic pseudoaneurysm, (4) graft occlusion (excluding intentional surgical occlusion) or (5) gas collection in the graft bed. On the basis of these criteria, the sensitivity of CT in the detection of vascular graft infection is higher than 90%, but the number of false-positive results is high, which gives rise to a low specificity of 70%–75% (*5,6,31*). If we wish to increase the level of specificity we must consider only the presence of perigraft fluid and gas collection in the graft bed (*5,32*) as suggestive of graft infection. There are few comparative studies on the usefulness of CT and leukocyte scans in the detection of vascular graft infection. Mark et al. (*33*) obtained better results with CT, especially in the valuation of the retroperitoneal extension of groin infections, with similar results in the evaluation of groin infections. Williamson et al. (*16*), in a series of 30 explorations using general criteria in CT evaluation, obtained a sensitivity of 75% with CT, and a sensitivity of 100% with ^{111}In-leukocyte scans. When applying more specific CT criteria, the CT sensitivity fell to 37%. They concluded that leukocyte scans are the preferred diagnostic method of choice in the evaluation of patients with suspected vascular graft infection. Becker et al. (*18*) and Berridge et al. (*17*) reached similar conclusions. Cerqueira et al. (*34*) consider that explorations with labeled leukocytes give CT a better specificity and the possibility of performing whole-body studies. Six of the 12 grafts evaluated by CT in our series were infected. The CT was only positive in four, with a pelvic abscess and an acute diverticulitis also being detected. The ^{99m}Tc-HMPAO leukocyte scan correctly evaluated all of these studies.

The use of ^{111}In-labeled human polyclonal immunoglobulin G (HIG) in the detection of vascular graft infection has recently been proposed (*35*). The reported series are limited and it is therefore premature to confirm its usefulness.

CONCLUSION

Technetium-99m-HMPAO-labeled leukocyte scans are currently the diagnostic method of choice in the evaluation of suspected prosthetic vascular graft infection. In our study, no false-positive scans were obtained in the evaluation of vascular grafts. CT has a limited specificity for vascular graft infection and only provided a diagnosis if perigraft fluid and/or gas collection in the graft bed was present. With respect to scans performed with ^{67}Ga or ^{111}In, ^{99m}Tc-HMPAO has the advantage of being more easily available, offering a better quality of image, obtaining the results more quickly and, probably, reducing the number of false positive results.

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