Chronic Prosthetic Vascular Graft Infection Visualized with Technetium-99m-Hexamethylpropyleneamine Oxime-Labeled Leukocytes

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Technetium-99m-HMPAO labeled leukocytes demonstrated chronic femoro-femoral prosthetic vascular graft infection several times during an 18-mo period in a 77-yr-old man. The intensity and distribution of the uptake in the graft were fluctuating in different imaging occasions possibly indicating the strength and location of the infection. Gallium-67-citrate imaging showed negative results twice. The reason for negative ^{67}Ga results remained obscure. The infected graft was removed and the patient did well 5 mo postoperatively.

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Infection occurring in an artificial prosthetic vascular graft is one of the most serious complications in vascular surgery (*1*). The reported frequency of prosthetic vascular graft infections after vascular surgery is low, about 2%–6% (*1*). The mortality rates range from 25% to 75% with the incidence of morbidity, particularly limb loss, ranging from 22% to 75% (*1,2*). Thus, early and accurate detection of occult graft infection is important so that therapy may be started. However, the diagnosis of graft infection is difficult. The symptoms of infection are nonspecific and indolent (*1,2*) and detection can be difficult with conventional radiographic methods. Imaging with ^{111}In or ^{99m}Tc-labeled leukocytes (*2–4*) and ^{67}Ga-citrate (*5,6*) have proved to be valuable tools for diagnosis of prosthetic graft infection.

We report one case of chronic vascular graft infection that was visualized repeatedly with ^{99m}Tc-hexamethylpropyleneamine oxime (HMPAO)-labeled leukocytes, but was negative in ^{67}Ga imaging.

Case Report

A 77-yr-old man was admitted to the hospital in May 1988 for pulsating tumor in the left groin. Left aorto-femoral and femoro-femoral synthetic vascular grafts had been placed 6 yr earlier for aortoiliac atherosclerotic occlusive disease. A pseudoaneurysm in the left lateral part of the femoro-femoral graft was noted and removed at surgery. No signs of graft infection were seen in operation. He had mild fever postoperatively, and three days after the operation ^{99m}Tc-WBC scan revealed graft infection in the femoro-femoral prosthesis (Fig. 1A). The leukocyte labeling method and imaging procedure have been described earlier (*7*). Erythrocyte sedimentation rate (ESR) and white blood cell (WBC) count were normal. Serum C-reactive protein (CRP) was mildly elevated (36 mg/l, normal <10 mg/l) 3 days after the operation, but it was at a normal level 6 days later. Serous drainage from the wound in the left inquinal region was seen, but culture of the drainage was negative twice. He was treated with cefuroxime and mecilliname antibiotics and discharged from the hospital at eleventh postoperative day in good condition, except for slight serous drainage from the wound region. One month later the patient did well and no clinical symptoms of infection were present. However, ^{99m}Tc-WBC imaging showed somewhat greater uptake in the femoro-femoral prosthesis. Oral penicillin therapy was started.

Thereafter, the patient was in good condition and remained clinically symptomless. However, in September 1988, ^{99m}Tc-WBC imaging revealed still abnormal uptake in the prosthesis. ESR, WBC count, and CRP were at normal levels. Gallium-67-citrate scintigraphy was negative (Fig. 2A). Technetium-99m-HMPAO-labeled platelet imaging with the method previously reported (*8*) showed focal uptake in the femoro-femoral graft and beginning occlusion of the graft was suggested (Fig. 3). However, the patient did well. Eight months later in May 1989 doppler ultrasonography showed still normal flow in the prosthesis. In June 1989, he developed symptoms of occlusion of the femoro-femoral graft and pain and swelling in the left groin. Some days later fistulation with purulent drainage was seen. Technetium-99m-WBC imaging showed patchy accumulation in the graft (Fig. 1B). ESR, WBC count, and CRP were normal. Drainage culture grew staphylococcus species (non-aureus) three times. The patient was treated with cefalexin and dicloxacillin antibiotics. Purulent drainage from the fistula continued and fistulography in August 1989 revealed a pus cavity around the femoro-femoral graft. Transient mild increases in CRP and ESR levels were seen in September 1989, but the patient did well clinically. Antibiotic therapy was changed for trimethoprimsulphadiazim

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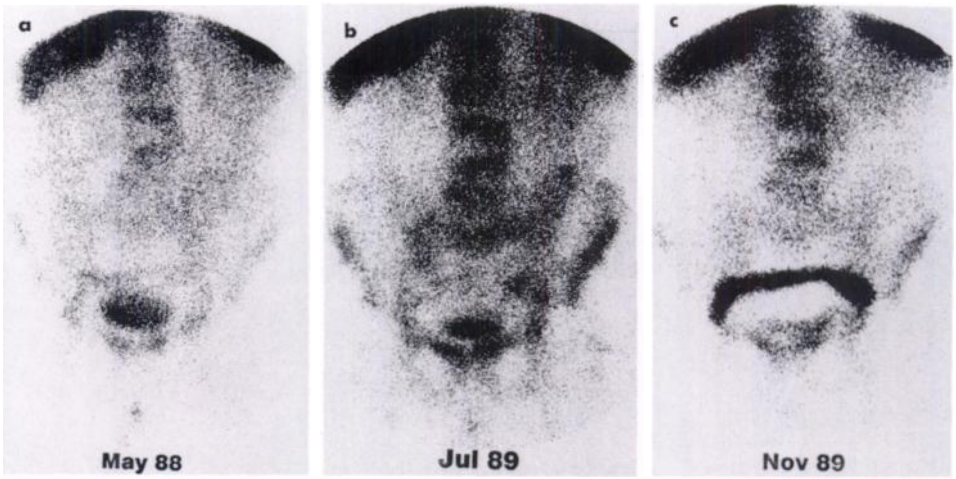

FIGURE 1. Anterior ^{99m}Tc-WBC images of the pelvis 4 hr postinjection in (a) May 1988, (b) July 1989, and (c) November 1989. Note the changes in the distribution and intensity of the uptake.

combination. The fistula continuously excreted pus. In November 1989, ^{99m}Tc-WBC scan showed strongly increased uptake around the femoro-femoral graft (Fig. 1C). The intensity of uptake was about 2.5 times as high as that in the first ^{99m}Tc-WBC imaging. No abnormal accumulation of ^{67}Ga was seen (Fig. 2B). CRP and WBC values were normal, and ESR was mildly increased (30 mm/hr). A new fistula close to the old fistula was opened. The fistula drainage culture grew *peptostreptococcus anaerobicus* bacteria.

In December 1989, the infected femoro-femoral graft was removed at surgery and a new iliaco-femoral bypass using autologous vein was placed. Abundant pus was seen around the infected graft. Bacterial culture grew peptostreptococcus species. Before the operation, the patient was given ^{99m}Tc-WBC and samples of removed graft and nearby tissue obtained at surgery were imaged with a computer-connected gamma camera and studied histologically. Histology revealed signs of acute, subacute, and chronic inflammation. The uptake of radiolabel was greatest in samples containing graft material. The percentage of granulocytes in differential count also was greater in samples from the graft than in samples taken outside the graft.

The patient had mild fever postoperatively. There was a transient increase in CRP values up to 190 mg/l. Both fistula and thigh wound cultures grew *enterobacter cloacae.* He was treated with cephalexin, tinidazole, and erythromycin antibiotics. At 2 wk postoperatively, the wound was healed, the new bypass was open, no signs of infection were present, and the patient was discharged from the hospital. Five months later he was still in good condition.

DISCUSSION

This case clearly demonstrates the difficulties in diagnosing vascular graft infection. This is in agreement with many previous reports (*1–4*). Clinically, the patient did well. Laboratory findings for infection were at normal levels or were only slightly elevated during most of the observation period, and the signs of graft infection were minimal until the fistulation of the left groin. The best diagnostic method was ^{99m}Tc-WBC imaging. Infection was clearly visualized on leukocyte imaging. The intensity and distribution of uptake, however, were fluctuating, possibly demonstrating the strength and location of the infection. It seems possible to follow-up the stage of vascular graft infection by quantitative imaging. The greatest uptake was seen before removal of the infected prosthesis, representing

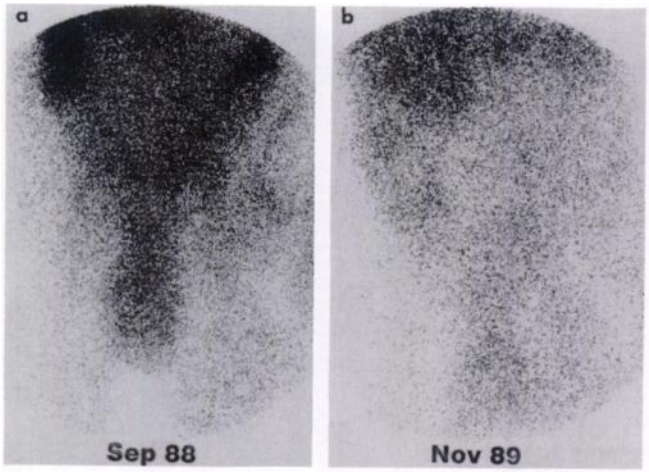

FIGURE 2. No significant uptake of ^{67}Ga in the graft in (a) September 1988 and (b) November 1989.

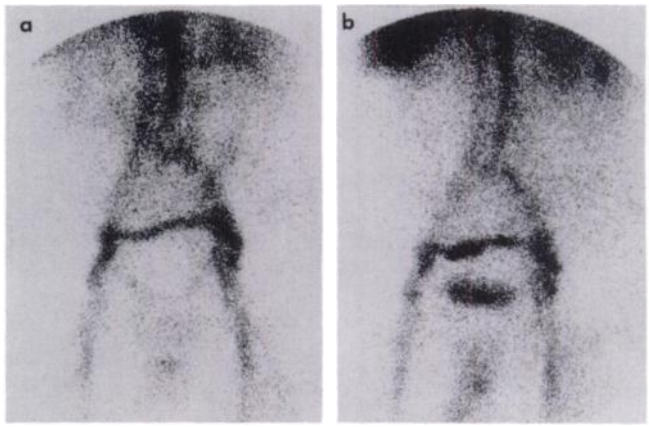

FIGURE 3. Anterior ^{99m}Tc-platelet images of the pelvis (a) 0.5 hr and (b) 4 hr postinjection. There is focal uptake in the graft at 4 hr.

more than a two-fold comparison with the initial imaging. At that time, the fistula was continuously excreting pus and ESR also was increased, suggesting aggravation of the infection. One may suppose that platelet contamination could cause significant uptake in leukocyte imaging. Specimens of labeled cells were evaluated both by an automated hematologic analyzer and microscopy. Only minimal contamination of platelets was noted, indicating that ^{99m}Tc uptake was caused by labeled leukocytes.

Gallium-67 imaging was negative twice. This is an unexpected finding because ^{67}Ga scintigraphy has been shown to demonstrate graft infections quite well in earlier reports (*4–6*). Gallium-67 and ^{99m}Tc-WBC imaging gave almost equal results in a recent study (*4*). This case was clinically chronic infection. Gallium-67 has been better than ^{111}In-labeled leukocytes in detection of some chronic infections (*9,10*). Histology of the removed graft and nearby tissue revealed signs of chronic, subacute, and acute inflammation as well as foreign body reaction. Bacterial culture showed infection. Abdominal nonspecific background uptake was not the reason for the negative ^{67}Ga finding. Adequate blood supply is essential in ^{67}Ga accumulation in inflammatory lesions (*11*). The pus cavity around the graft may have decreased blood supply near the graft, thus preventing transferrin-bound ^{67}Ga from reaching the infection site. The transferrin level was not measured and it remains unclear whether a defect in the ^{67}Ga transport system could have been present.

Focal uptake of ^{99m}Tc-labeled platelets in the infected graft was seen 9 mo before the occlusion of the graft. This is in agreement with reports demonstrating that ^{111}In-labeled platelets can be used in the follow-up of prosthetic graft occlusion (*12*). Because of image quality and radiation dose, ^{99m}Tc-labeled platelets could be better in this respect.

Wound cultures after the first operation were negative perhaps due to antibiotic therapy. After fistulation about 1 yr postoperatively, the fistula drainage culture grew several different species of bacteria at different occasions as well as during antibiotic therapy. Although the samples were not taken from the perigraft region, it seems probable that the species of bacteria can be changed in chronic vascular graft infection.

In conclusion, ^{99m}Tc-WBC was the best method in diagnosing chronic vascular graft infection. Quantitative imaging may be helpful in the follow-up of disease. Negative results in ^{67}Ga imaging cannot exclude graft infection.

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EDITORIAL

Chronic Prosthetic Vascular Graft Infection Visualization with Gallium-67

Vorne et al. chronicle the 18-mo saga of a chronically infected femoral-femoral crossover graft that was periodically treated with antibiotics after numerous diagnostic ^{99m}Tc-leucocyte (WBC) and ^{67}Ga scans. It raises some issues regarding the evaluation and treatment of prosthetic vascular graft infections.

Although relatively rare, comprising approximately 2% of arterial reconstructions, graft infections remain a major cause of mortality and significant morbidity in this patient population. The nightmare of the vascular surgeon, this problem poses several dilemmas. The clinical presentation can be quite insidious, delaying the diagnosis and often life-saving treatment. This is particularly true of aortic or retroperitoneal grafts that reside a distance from the skin surface and therefore do not often present with distinct clinical findings unless a bowel fistula occurs. Most peripheral prosthetic graft infections, especially those that involve the groin, are more readily detected because of clinical

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