인공슬관절 전치환술 환자에서 ^{99m}Tc-HMPAO-백혈구 스캔을 이용한 인공관절 감염의 진단

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^{99m}Tc-HMPAO-labelled Leucocyte Scintigraphy in the Diagnosis of Infection after Total Knee Replacement Arthroplasty

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Abstract

Purpose: This study was performed to evaluate the usefulness of ^{99m}Tc-HMPAO-labelled leucocyte scintigraphy for diagnosing prosthetic infection after total knee replacement arthroplasty without the aid of following bone marrow scintigraphy. **Materials and Methods:** The study subjects were 25 prostheses of 17 patients (one man and 16 women, mean age: 65 years) who had total knee replacement arthroplasty. After injection of ^{99m}Tc-HMPAO-labelled leucocyte, the whole body planar and knee SPECT images were obtained in all patients. The subjects were classified into three groups according to clinical suspicion of prosthetic infection: Group A (n=11) with high suspicion of infection; Group B (n=6) with equivocal suspicion of infection, and Group C (n=8) with asymptomatic contralateral prostheses. Final diagnosis of infection was based on surgical, histological and bacteriological data and clinical follow-up. **Results:** Infection was confirmed in 13 prostheses (11 in Group A and 2 in Group B). All prostheses in Group A were true positive. There were two true positives, one false positive and three true negatives in Group B, and six true negatives and two false positives in Group C. Overall sensitivity, specificity, and accuracy for diagnosis of the infected knee prosthesis were 100%, 75% and 88%, respectively. **Conclusion:** ^{99m}Tc-HMPAO-labelled leucocyte scintigraphy is a sensitive method for the diagnosis of infected knee prosthesis. However, false positive uptakes even in asymptomatic prosthesis suggest that bone marrow scintigraphy may be needed to achieve improved specificity. **(Korean J Nucl Med 1999;33:413-21)**

Key Words: Knee, Prosthesis, Inflammation, ^{99m}Tc-HMPAO leucocyte, Radionuclide imaging

Received Jun. 12, 1999; revision accepted Aug. 6, 1999.
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Introduction

Although prosthetic infection is relatively rare after total knee replacement arthroplasty (TKRA),

it is one of the most serious postoperative complications requiring revision arthroplasty.[1,2] Therefore, differentiation of infection from non-infectious complication is important in the management of patients with TKRA.

Scintigraphy with ^{111}In or ^{99m}Tc-HMPAO-labelled leucocyte has been reported as the most accurate diagnostic method for bone infection of the extremities after surgery.[3,4] In the literature review, ^{111}In-labelled leucocyte is more commonly used than ^{99m}Tc-HMPAO-labelled leucocyte, and the report of the diagnostic usefulness of ^{99m}Tc HMPAO-WBC scan after total knee replacement surgery is limited. However, the routine use of ^{111}In-labelled leucocyte scan is limited by high cost, relatively poor image quality and poor availability, especially in Korea. ^{99m}Tc has more advantages than ^{111}In as a radionuclide for gamma camera imaging. ^{99m}Tc is inexpensive and widely available. It has better physical properties including higher radioactivity dose administration, shorter half life, lower irradiation dose and more favorable decay scheme for gamma cameras. These characteristics permit a high counting rate, high quality image and the acquisition of SPECT.[9-13]

We performed this study to evaluate the diagnostic usefulness of ^{99m}Tc-HMPAO-labelled leucocyte scintigraphy in patients with clinical suspicion of prosthetic infection after TKRA.

Materials and Methods

1. Subjects

Between June 1995 and August 1998, ^{99m}Tc-HMPAO leucocyte scintigraphy was performed for 20 patients with clinical suspicion of the infected prostheses after TKRA. After excluding 3 patients who lacked adequate clinical follow up data to confirm the scintigraphic findings, 25 prostheses of 17 patients (16 women, 1 man; age range 36-81 year; mean 65 year) were included as study subjects. Nine patients had undergone unilateral arthroplasty and eight patients had undergone bilateral arthroplasty including asymptomatic contralateral prosthesis. The median interval between TKRA and scintigraphy was 9 month (range: 9 weeks to 12 year). The median duration of clinical symptoms was 5 month (range: 3 weeks to 4 year). All but one patients received antibiotic therapy before scintigraphy.

The prostheses were classified into three groups according to the clinical and laboratory findings: Group A (n=11) with strong suspicion of the infected knee prosthesis because of clinical (local hyperthermia, pain, or pustulent discharge) and laboratory signs (elevated CRP or ESR) of infection, Group B (n=6) with equivocal for infection because of pain and limited range of motion with or without elevated ESR or CRP, and Group C (n=8) with asymptomatic contralateral prosthesis.

2. ^{99m}Tc-HMPAO-labelled leucocyte scintigraphy

The labelling technique we used for ^{99m}Tc-HMPAO (Ceretec®, Amersham Inc, London, UK) mixed leukocyte was as described by Lee et al.[14] The average labelling efficiency was 88% (72-97%).

In all patients, the anterior and posterior whole body images were obtained at 4-6 hours after intravenous administration of 1220±240 MBq of ^{99m}Tc-HMPAO-labelled leucocyte using a large field of view dual heads gamma camera (Biad XLT 24, Trionix Research Laboratory, Twinsburg, OH, USA) equipped with a low energy high resolution collimator. Subsequently, SPECT of the knee joints were performed with triple heads SPECT cammera (Triad XLT 20, Trionix Research Laboratory, Twinsburg, OH, USA) equipped with an ultrahigh resolution parallel hole collimator.

Three tomographic images were reconstructed after filtered back projection using a hamming filter.

3. Analysis

The scintigraphic images including both planar and SPECT images were visually analyzed by two nuclear physicians (D.H.M. and J.S.K.) blinded to the diagnosis and clinical information, except for the site of prosthesis. The SPECT images were independently reviewed in transverse, coronal, and sagittal planes using an interactive digital image display system which allowed adjustment of image display parameters. When disagreement occurred, a consensus reading was obtained by discussion.

The degree of increased activity on ^{99m}Tc-HMPAO leucocyte scintigraphy was graded in comparison with normal contralateral soft tissue and distal femoral bone marrow activity as follows: grade 0=no increased activity in periprosthetic area or activity similar to contralateral soft tissue; grade I=minimal increase, definitely less than normal marrow, grade II=definite increase, equivalent to or slightly less than normal marrow, subdivided into diffuse (IIa), focal (IIb) or combined (IIa+b); grade III=definite increase, greater than normal marrow. The scintigraphy with significantly increased periprosthetic activity (grade II and III) was interpreted as positive for infection.

Final diagnosis of infection was based on surgical, histological and bacteriological data and clinical follow-up. In patients who underwent surgery, knee prostheses were considered as infected if infective organisms were identified on intraoperative cultures, if frank purulence was present at surgery, or if histologic evidence of inflammation (polymorphonuclear leucocytes or lymphocytes) was present. Knee prostheses were classified as non-infected status if operative smears, culture, or histology demonstrated no leucocytes and no organisms. In the absence of surgical intervention, final diagnoses were based on clinical course with a minimum follow-up of 1 year after imaging.

Results

In final diagnosis, total 13 prosthetic joints were infected, including all 11 prostheses of Group A and two prostheses of Group B. The diagnosis of prosthetic infection was confirmed by surgery (n=12) or by favorable clinical and laboratory response to antimicrobial therapy (n=1). The most common microorganism was Staphylococcus aureus (n=6), followed by Enterobacter (n=2) and Pseudomonas (n=2). Multiple organisms were identified in four patients (Table 1). Of six prostheses in Group B, three were surgically confirmed as aseptic loosening, two by surgery and one by clinical and radiographic findings. There were no infection or loosening of the knee prosthesis in remaining one prosthesis of Group B and all eight prostheses of Group C.

Of the 13 prostheses with infection, six showed evenly increased periprosthetic uptake around both femoral and tibial components in ^{99m}Tc-HMPAO labelled leucocyte scintigraphy (Fig. 1), four showed more prominent uptake around tibial component, and the remaining three showed more prominent uptake around femoral component. The periprosthetic uptake of grade IIa+b around knee prosthesis was most common (7/13, 54%) pattern of planar image in infected knee prostheses (Table 1). SPECT image showed diffuse and focal uptake pattern in all of cases with abnormal periprosthetic uptake and provided more information of three dimensional distribution of increased uptake around prostheses (Fig. 1).

Of the 12 prostheses without infection, one of Group B and two of Group C showed increased periprosthetic uptake and were falsely interpreted

Table 1. Summary of Patient Data Who underwent ^{99m}Tc-HMPAO-labelled Leucocyte Scintigraphy for the Diagnosis of Prosthetic Infection

No. of Prosthesis	Interval*	Groups†	Grade of Uptake‡	Scan Result	Culture
1	2 mo	A	IIa	TP	S. aureus
2	6 mo	A	IIa+b	TP	S. aureus, Enterococcus
3	8 mo	A	IIa+b	TP	S. aureus, S. epidermis
4	8 mo	A	IIa+b	TP	S. aureus, Enterococcus
5	18 mo	A	III	TP	no growth
6	3 yr	A	IIa	TP	no growth
7	11 yr	A	IIa+b	TP	S. aureus, Pseudomonas
8	6 mo	A	IIa+b	TP	S. aureus
9	6 mo	A	III	TP	E. coli
10	6 mo	A	IIa+b	TP	no growth
11	9 mo	A	IIb	TP	Pseudomonas
12	12 yrs	B	IIa	FP	no growth
13	6 yrs	B	I	TN	no growth
14	4 yrs	B	IIa+b	TP	no growth
15	11 yrs	B	0	TN	no growth
16	3 mo	B	0	TN	not done
17	3 mo	B	IIa	TP	no growth
18	6 yrs	C	IIa+b	FP	not done
19	8 mo	C	0	TN	not done
20	4 yrs	C	0	TN	not done
21	3 yrs	C	0	TN	not done
22	6 mo	C	0	TN	not done
23	6 mo	C	0	TN	not done
24	9 mo	C	0	TN	not done
25	6 mo	C	IIa+b	FP	not done

* Interval between TKRA and scintigraphy.

† Groups: A, high clinical suspicion of prosthetic infection; B, equivocal clinical suspicion of prosthetic infection; C, asymptomatic contralateral prosthesis.

‡ Grade: 0=no increased activity or similar to contralateral site; I=minimal increase, much less than normal marrow, II=definite increase, equivalent to or slightly less than normal marrow, subdivided into diffuse (IIa), focal (IIb) or combined (IIa+b); III=definite increase, greater than normal marrow.

as infected. One of Group B was confirmed as aseptic loosening by surgery (Fig. 2). The cause of periprosthetic uptake in those two prostheses of Group C was uncertain.

The scintigraphy showed true positives in all of Group A. In Group B, there were two true positives, one false positive and three true negatives. In asymptomatic contralateral prostheses (Group C), two were false positive and the rest were true negative. Overall sensitivity, specificity, and accuracy of planar image for prosthetic infection were 100% (13/13), 75% (9/12), and 88% (22/25), respectively. In patients with the suspected prosthetic infection (Group A and B), the sensitivity, specificity and accuracy of planar images were 100% (13/13), 75% (3/4), and 94% (16/17), res

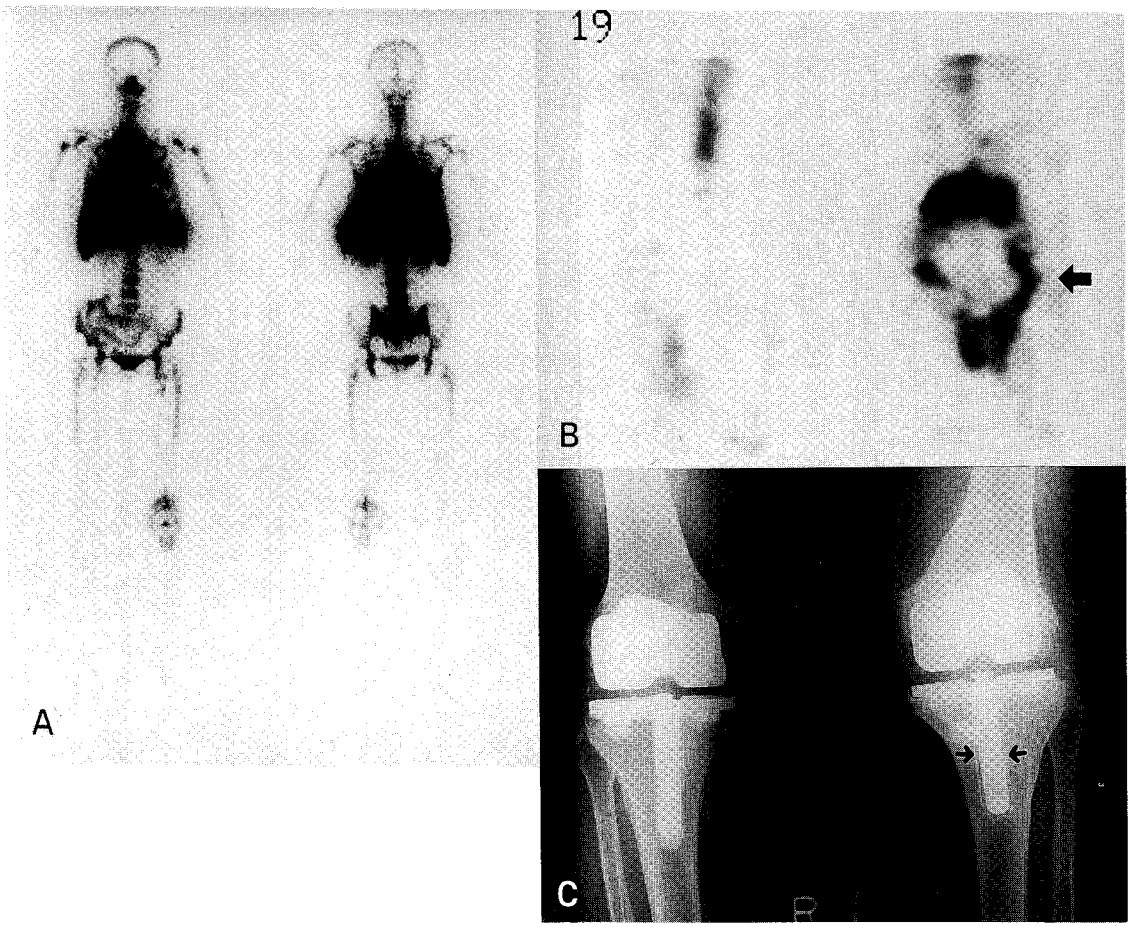

Fig. 1. ^{99m}Tc-HMPAO leucocyte scintiscan of a 67-year old woman with left knee pain. She had undergone bilateral total knee replacement arthroplasty 4 years before. (A) The anterior and posterior whole body planar images show diffuse and focal increased uptake (grade IIa+b) around femoral and tibial components of the left knee prosthesis. Note that there is no abnormal uptake (grade 0) in the asymptomatic right knee prosthesis. (B) Coronal SPECT image reveals increased periprosthetic uptake and precise distribution of focal inflammatory foci (arrow). (C) Simple radiograph of both knees shows bone resorption (arrows) at the bone-implant interface of the tibial component of the left knee prosthesis suggesting loosening. Infection of the left knee prosthesis was confirmed by histology of the operative specimen.

pectively. The accuracy of SPECT image was not different from that of planar image.

Discussion

Complications of TKRA include patellofemoral arthritis (11%), heterotopic bone formation (10%), loosening (7%), deformity (4%), fracture (3%) and infection (2%).[1,15]

Infection of the orthopedic implant can be evaluated on the basis of clinical, radiographic and laboratory evaluations. However, the diagnosis and precise localization of infection site are often difficult. MR imaging has been reported as a very useful method for bone infection (sensitivity 95%, specificity 88%),[8] but, in patients with orthopedic implants, it is inadequate to diagnose the infection around implants due to metallic artifacts.

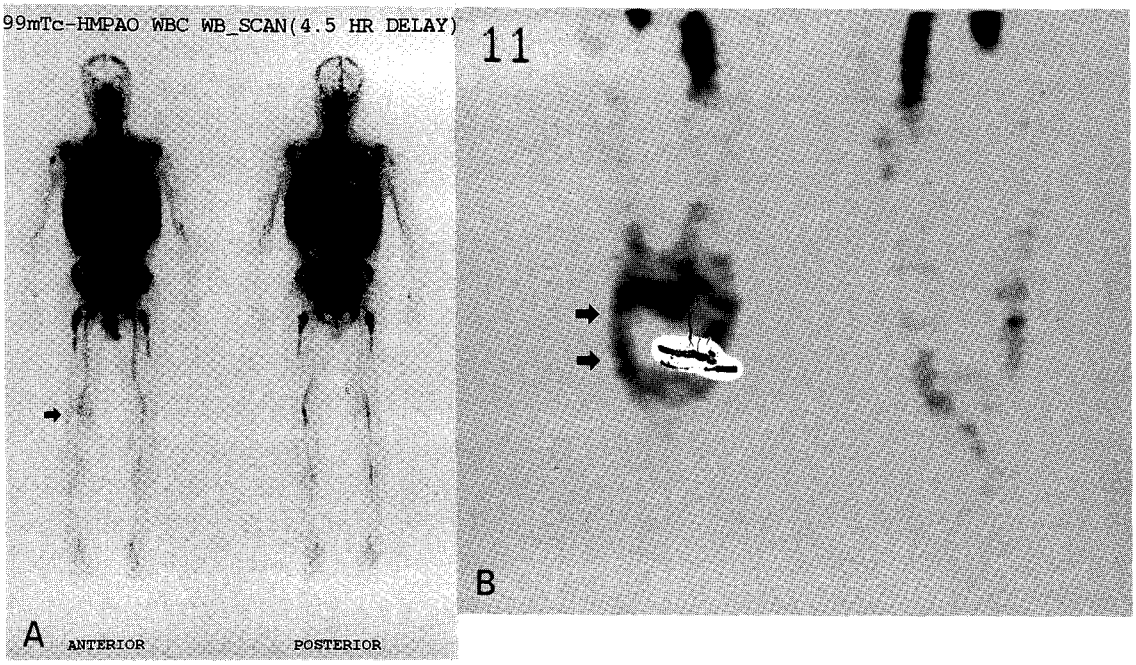

Fig. 2. ^{99m}Tc-HMPAO leukocyte scintiscan of a 54-year-old man with right knee pain and swelling. He had undergone right total knee replacement arthroplasty 12 years before. (A) The anterior and posterior whole body planar images show mild and diffuse uptake (grade IIa) around the femoral component of the knee prosthesis (arrow). (B) Periprosthetic uptake is better clarified on coronal SPECT image than planar image (arrows). Aseptic loosening was confirmed by surgery.

Nuclear imaging has long been recognized as an effective method for the detection of skeletal infection including infected orthopedic implant. However, in the evaluation for the complications of knee prosthesis, bone scan is limited because persistently increased periprosthetic uptake can be seen for several years after prosthetic implantation and similar pattern of uptake is shown in both infection and aseptic loosening.[6,16] Recently, to improve the accuracy of radionuclide-aided diagnosis for the prosthetic infection, various dual-tracer modalities, including bone and gallium scan, labelled leucocyte and bone scan, and labelled leucocyte and sulfur colloid scan combinations, have been studied.[3-9] It has been noted that the combined ^{111}In-labelled leucocyte and ^{99m}Tc-bone marrow scans were the most accurate methods.[6,8] ^{111}In-labelled leucocyte scans have been widely used for the diagnosis of bone infection, but the disadvantages of ^{111}In as a radionuclide are well known.[9-13]

Labelling of leucocyte with ^{99m}Tc-HMPAO has two distinct advantages over ^{111}In: First, ^{99m}Tc-HMPAO is easily produced from a kit and it is widely available, while ^{111}In is not readily available. Second, owing to its relatively short half life, ^{99m}Tc can be injected in about 40 times higher radioactive dose than ^{111}In, which allows the acquisition of SPECT and a more precise localization of radioactive foci of labelled leucocyte accumulation, compared with ^{111}In-labelled leucocyte.

Our results suggest that the scintigraphy using ^{99m}Tc-HMPAO labelled leucocyte is more convenient than ^{111}In-labelled leucocyte as well as highly sensitive and accurate for diagnosing pro-

sthetic infection. The sensitivity were 100% in highly suspicious group (Group A) and in equivocal group (Group B). In the study using ^{99m}Tc-HMPAO labelled leucocyte by Esper et al, including 13 cases of knee prostheses, there were seven true positives, five true negatives, one false negative (sensitivity 87%, specificity 100%, accuracy 92%).[10] Their results showed relatively lower sensitivity and higher specificity than ours. These differences might have been resulted from followings: Labelling efficiency of their study was lower than ours; It was not known whether antibiotic therapy was done before the scintigraphy in their study; SPECT image was not performed, although the gold standard for diagnosing infection and scintigraphic criteria for prosthetic infection were similar.

A large number of studies reported that antibiotic therapy before the scintigraphy, chronicity of infection and low labelling efficiency were the main causes of false negatives. Deviller et al reported that two of the three false negatives were seen in patients taking antibiotics at the time of ^{99m}Tc-HMPAO-labelled leucocyte scintigraphy.[17] But, Datz and Thorne reported a large series showing no significant difference in the detection of infection sites in patients with or without antibiotic therapy.[18] In our study, there was no false negative and all but one patients received no antibiotic therapy before scintigraphy.

The duration of the infection could also influence the sensitivity of scintigraphy. In the study by Vorne et al, ^{99m}Tc-HMPAO-labelled leucocyte scintigraphy showed false negatives in two out of three patients with chronic osteomyelitis (above 2 weeks), while it was truly positive in all of the six patients with acute osteomyelitis (below 2 weeks).[19] A reduced sensitivity in case of chronic osteomyelitis was also seen with ^{111}In-labelled leukocyte. Schauwecker et al reported a sensitivity of 100% in patients with acute osteomyelitis, but only 60% in patients with chronic osteomyelitis.[4] This phenomenon could be explained by the fact that the lesion is well perfused and infiltrated mostly by polymorphonuclear cells in acute phase, while in the chronic phase, it is poorly perfused and infiltrated mostly by lymphocytes and monocytes, and they used pure leucocytes for labelling. Other studies using ^{99m}Tc-HMPAO-labelled mixed leucocytes did not find any significant difference between acute and chronic infection.[17,18] In our study using mixed leucocytes, most patients with infected knee prostheses were subacute or chronic stage (3 week to 4 year) and there were no false negatives.

Poor labelling efficiency may also be responsible for the false negative results. In the study of Esper et al, one of the false negatives showed a poor labelling efficiency, of which the poorest was 28%.[10] In our study, labelling efficiencies were very high (mean 88%, minimum 72%).

In our study, one of 17 prostheses with clinical suspicion of infection and two of eight contralateral asymptomatic prostheses showed false positive result. False positive result can be seen in patients with a change in the normal distribution of bone marrow. Active marrow in adults is normally present in the axial skeleton, humeral heads, and proximal femur, but not in knee joint area, although there is individual variation. However, some authors reported that false-positive patterns of ^{111}In-labelled leucocyte uptake can result from postsurgical alterations of bone marrow activity in the non-functioning bone marrow spaces adjacent to knee prostheses.[3,5,6] Palestro et al reported that periprosthetic activity was present in 50% of the uninfected knee prostheses.[6] They also reported that the specificity and accuracy of the combined ^{111}In-labelled leucocyte and sulfur colloid imaging in assessment of knee prosthesis infection were

higher than those of ^{111}In-labelled leucocyte scan alone (specificity 100% vs 75%, accuray 95% vs 78%). Therefore, if the bone marrow scintigraphy using ^{99m}Tc-sulfur colloid is followed after ^{99m}Tc-HMPAO labeled leucocyte uptake, false positive may be reduced and the specificity for diagnosing prosthetic infection can be improved.

Moragas et al reported that increased uptake in infected knee prostheses was always diffuse.[9] In this study, we expected that aseptic condition such as aseptic loosening shows focal periprosthetic uptake and infected condition shows more diffuse periprosthetic uptake. So, we divided periprosthetic uptake of grade II into IIa, IIb, and IIa+b, to identify differential uptake patterns for septic and aseptic conditions. However, focal uptake patterns (grade IIb or IIa+b) were not seen in three cases confirmed as aseptic loosening and diffuse uptake combined with focal hot spots (grade IIa+b) was the most common findings in infected knee prostheses. In three cases, the focal hot spots within the diffuse uptake were confirmed as prominent dirty granulation tissue or purulent collection at surgery.

This study has several limitations. First, number of cases with equivocal suspicion of prosthetic infection and number of true negatives in patients with suspected prosthetic infection are small, Second, the bone marrow scan was not performed. Further studies are needed with large number of cases and the value of additional bone marrow scintigraphy combined with ^{99m}Tc-HMPAO-labelled leucocyte scintigraphy for diagnosis of the prosthetic infection should be evaluated.

In conclusion, ^{99m}Tc-HMPAO-labelled leucocyte scintigraphy is a sensitive method for diagnosis of the infected knee prosthesis. To improve the specificity for diagnosing prosthetic infection, however, the bone marrow scintigraphy would be followed after ^{99m}Tc-HMPAO labeled leucocyte scintigraphy.

요 약

목적: 이 연구는 인공슬관절 전치환술을 받은 환자들에서 인공관절의 감염을 진단하는데 ^{99m}Tc-HMPAO 표지 백혈구 스캔의 진단적 유용성을 평가하고자 하였다. **대상 및 방법**: 인공슬관절 전치환술 후 감염이 의심되어 ^{99m}Tc-HMPAO 표지 백혈구 스캔 검사를 받은 20예 중 최종진단이 확실한 17명의 25예의 인골슬관절을 대상으로 하였다. 대상 환자는 남자가 1명, 여자가 16명으로, 평균연령은 65세였다. 모든 환자에서 ^{99m}Tc-HMPAO 표지 백혈구를 이용한 전신 평면영상과 슬관절 SPECT를 얻었다. 대상군은 임상적으로 감염이 의심되는 정도에 따라 3군으로 나누었다. 감염이 강하게 의심되었던 인공슬관절군 (A군: 11예), 감염 여부를 감별하기 어려웠던 인공슬관절군 (B군: 6예), 무증상의 반대측 인공슬관절군 (C군: 8예)으로 분류하였다. 최종진단은 수술, 조직소견, 균 배양 및 임상적 추적검사로 결정하였다. **결과**: A군 인골관절 11예 모두와 B군의 6예중 2예, 총 13예가 감염으로 확진되었다. ^{99m}Tc-HMPAO 표지 백혈구 스캔은 A군 11예 모두에서 진양성을 보였고, B군에서는 진양성 2예, 위양성 1예, 진음성 3예를 보였으며, C군에서는 위양성 2예와 진음성 6예를 보였다. 전체적으로 인공슬관절의 감염을 진단하는 데 있어서 그 예민도, 특이도, 및 정확도는 각각 100%, 75%, 88%이었다. **결론**: 인공슬관절 감염의 진단에 있어 ^{99m}Tc-HMPAO 표지 백혈구 스캔은 매우 예민한 방법이었다. 그러나, 상대적으로 낮은 진단적 특이도를 높이기 위하여 추가적인 골수 스캔이 인공슬관절 감염이 의심되는 환자의 진단에 필요하리라 생각된다.

References

1) Lovelock JE, Griffiths HJ, Silverstein AM, Anson PS. Complications of total knee replacement. *AJR* 1984;142:985-91.
2) Simmons TD, Stern SH. Diagnosis and management of the knee infected total knee arthroplasty.

Am J Knee Surg 1996;9:99-106.

3) Seabold JE, Nepola JV, Marsh JL, Hawes DR, Justin EP, Ponto JA, et al. Postoperative bone marrow alterations: Potential pitfalls in the diagnosis of osteomyelitis with In-111-labelled leukocyte scintigraphy. *Radiology* 1991;180:741-7.
4) Schauwecker DS, Park H-M, Mock BH. Evaluation of complicating osteomyelitis with Tc-99m MDP, In-111 and Ga-67. *J Nucl Med* 1984; 25:849-53.
5) King AD, Peters AM, Stuttle AWJ, Lavender JP. Imaging of bone infection with labelled white blood cells: role of contemporaneous bone marrow imaging. *Eur J Nucl Med* 1990;17:148-51.
6) Palestro CJ, Swyer AJ, Kim CK, Goldsmith SJ. Infected knee prostheses: Diagnosis with In-111 leukocyte, Tc-99m sulfur colloid and Tc-99m MDP imaging. *Radiology* 1991;179:645-8.
7) Magnuson JE, Brown ML, Hauser MF, Berqusit TH, Fitzgerald RH, Klee GG. In-111-labeled leukocyte scintigraphy in suspected orthopedic prosthesis infection: comparison with other imaging modalities. *Radiology* 1988;168:235-9.
8) Schauwecker DS. The scintigraphic diagnosis of osteomyelitis. *AJR* 1992;158:9-18.
9) Moragas M, Lomena F, Herranz R, Garcia C, Piera A, Muxi P, et al. ^{99m}Tc-HMPAO leucocyte scintigraphy in the diagnosis of bone infection. *Nucl Med Commun* 1991;12:417-27.
10) Esper EL, Dacquet V, Paillard J, Bascoulergue G, Tahon MM, Fonroget J. ^{99m}Tc-HMPAO-labelled leucocyte scintigraphy in suspected chronic osteomyelitis related to an orthopaedic device: Clinical usefulness. *Nucl Med Commun* 1992; 13:799-805.
11) Ramos DL, Martin-Comin J, Bajen MT, Roca M, Ricart Y, Castell M, et al. Simultaneous administration of ^{99m}Tc-HMPAO-labelled autologous leucocytes and ^{111}In-labelled non-specific polyclonal human immunoglobulin G in bone and joint infections. *Nucl Med Commun* 1996;17: 749-57.
12) Chik KK, Magee MA, Bruce WJ, Higgs RJ, Thomas MG, Allman KC, et al. Tc-99m stannous colloid-labelled leukocyte scintigraphy in the evaluation of the painful arthroplasty. *Clin Nuc Med* 1996;21:838-43.
13) Lantto T, Kaukonen JP, Kokkola A, Laitinen R, Vorne M. Tc-99m HMPAO labeled leukocytes superior to bone scan in the detection of osteomyelitis in children. *Clin Nuc Med* 1991;17:7-17.
14) Lee DS, Shin HS, K Ahn, Chung JK, Lee MC, Choi KW, et al. ^{99m}Tc-HMPAO labelled WBC scan in experimental abscess by labelling autologous leucocytes with in-house-synthesized HMPAO. *Korean J Nucl Med* 1991;25(2):252-8.
15) Cameron HU, Hunter GA. Failure in total knee arthroplasty: Mechanism, revisions and results. *Clin Orthop* 1982;170:141-7.
16) Schneider R, Soudry M. Radiographic and scintigraphic evaluation of total knee arthroplasty. *Clin Orthop* 1985;205:108-20.
17) Devillers A, Moisan A, Jean S, Arvieux C, Bourquet P. Tc-99m HMPAO leucocyte scintigraphy for the diagnosis of bone and joint infections: A retrospective study in 116 patients. *Eur J Nucl Med* 1995;22:302-7.
18) Datz FL, Thorne DA. Effect of antibiotic therapy on sensitivity of In-111-labelled leukocyte scans. *J Nucl Med* 1986;27:1849-53.
19) Vorne M, Soini I, Lantto T, Paakkinen S. Technetium-99m HMPAO-labelled leukocytes in the detection of inflammatory lesions: Comparison with gallium-67 citrate. *J Nucl Med* 1989; 30:1332-6.