Comparison of Radionuclide Bone and Gallium Scans in the Therapeutic Evaluation of Bone Lymphoma

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= 국문 초록 =

골임파종의 치료효과판정을 위한 핵의학적 골스캔과 갈륨스캔의 비교

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문태용[1,2] · 황인태[1] · 김의신[2]

완전 치유되었던 골임파종 환자에서 치료효과를 판정하기위해 치료후 ^{99m}Tc-MDP 스캔과 ^{67}Ga 스캔으로 추적검사한 35례를 후향적으로 분석하였다.

^{99m}Tc-MDP 스캔은 35례중 29례에서 치료중, 33례에서 치료후 추적검사하였고, ^{67}Ga 스캔은 16례중 13례에서 치료중, 15례에서 치료후 추적검사를 하였다. 핵의학적검사의 병적섭취농도의 분류는 4단계로 나누었는데 ^{99m}Tc-MDP 스캔의 경우 정상 천장골관절 섭취농도와 같은 병변의 섭취농도를 3으로, ^{67}Ga 스캔의 경우 정상간의 섭취농도와 같은 병변의 섭취농도를 3으로 기준하였다.

치료중과 치료후 치료효과를 나타내는 소견은 ^{99m}Tc-MDP 스캔의 경우 각각 66.0 %(19/29), 72.7 %(24/33)였으며 ^{67}Ga 스캔의 경우 각각 84.6 %(11/13), 86.7 %(13/15)였다. 치료전, 치료중, 치료후의 병변 섭취농도는 ^{99m}Tc-MDP 스캔의 경우 각각 3.06, 2.34, 1.75였으며, ^{67}Ga 스캔의 경우 각각 3.22, 1.42, 1.30이었다.

따라서 골임파종에서 치료효과를 판정하는 추적검사로는 ^{67}Ga 스캔이 ^{99m}Tc-MDP 골 스캔보다 더 예민한 결과를 나타내었다.

= **Abstract** =

Objective: We retrospectively analysed ^{99m}Tc-MDP bone and ^{67}Ga scans to evaluate therapeutic response of bone lymphoma among patients with complete remission.

Subjects and Methods: We reviewed 35 cases with an increased uptake finding ^{99m}Tc-MDP bone scans and 16 ^{67}Ga scans that were follow-up studies during and after therapy. The ^{99m}Tc-MDP bone and ^{67}Ga scans were graded visually from 1 to 4 in which grade 3 means same uptake density as that of normal sacroiliac articulation in bone scan and normal liver in ^{67}Ga scan, respectively.

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Results: The improvement findings during and after therapy were found in 66.0% (19/29) and 72.7% (24/33) with ^{99m}Tc-MDP bone scan, 84.6% (11/13) and 86.7% (13/15) with ^{67}Ga scan, respectively. The mean grades of the uptake density in ^{99m}Tc-MDP bone scan were 3.06 before, 2.34 during, 1.75 after therapy. Those in the ^{67}Ga scan were 3.22 before, 1.42 during 1.30 after therapy.

Conclusion: ^{67}Ga scans appeared more sensitive than bone scans in evaluating therapeutic response of bone lymphoma.

Key Words: Radionuclide Scan, Bone Disease, Lymphoma

INTRODUCTION

To evaluate the effect of therapy and also tumor recurrence, it is important to know the functional status of the tumor since morphologic information is not sufficient. Perfusion, metabolism and receptor distribution in the tumor bed may be necessary parameters in determining a therapeutic strategy and monitoring the effects of therapy. In recent years, the contrast enhanced CT scan, Gd-DTPA enhanced magnetic resonance imaging(MRI) and spectroscopy(MRS), and some nuclear medicine studies including PET have been utilized. Complete remissions can be achieved in some patients with bone lymphoma by combination chemotherapy and localized radiotherapy[1]. The length of time to reach complete remission by plain X-ray film and computed tomography is very difficult since lymphomas infiltrate bone marrow[2]. Biopsies are invasive and can hardly be used routinely. ^{99m}Tc-MDP bone scintigram may be useful for the detection of skeletal involvement of some significant lesions[3]. Although the ^{67}Ga scintigram has been used to evaluate treated lymphoma[4], it is limited for evaluation of skeletal lymphoma because of its poor sensitivity and resolution[3]. MRI may be able to detect bone lymphoma not detected by biopsy, thereby leading to more accurate staging and more appropriate therapy[5]. However, MRI and nuclear bone scan findings also appear limited for the evaluation of therapeutic response due to their low specificities. We retrospectively analyzed our data to evaluate the role of ^{99m}Tc-MDP bone and ^{67}Ga scan to define the therapeutic response of bone lymphoma.

MATERIALS AND METHODS

We retrospectively reviewed 35 cases with an increased uptake finding of ^{99m}Tc-MDP bone scans and 16 ^{67}Ga scans that were obtained during and after chemotherapy and/or localized radiotherapy. There were 35 patients who were alive with clinically free of disease in 1.5-6.8 years. They were 29 diffuse large cell lymphomas, 3 lymphoblastic lymphomas, 2 differentiated small lymphocytic lymphomas and 1 follicular small cleaved cell lymphoma diagnosed by biopsies obtained from bone lesions. The mean age of the patients was 42.9 years (range, 19 to 71 years), 20 were male and 15 female. All patients were treated by various chemotherapy regimens for an average of 9 months (range, 1 to 66 months). 16 of them also received localized radiotherapy during or after completion of chemotherapy. Bone lymphomas with skeletal lesions were found in the femur (n=9), pelvis (n=7), humerus (n=6), tibia (n=4), spine (n=3), scapula (n=2), rib (n=2), clavicle (n=1) and foot (n=1). ^{99m}Tc-MDP bone scans were obtained using a gamma camera 2-3 hr after injection of ^{99m}Tc-MDP. Adult patients received 25mCi(925 MBq) and patients younger than 18years old

Table 1. Grades according to Uptake Density of ^{99m}Tc-MDP Bone and ^{67}Ga Scans

Grades	^{99m}Tc-MDP bone	^{67}Ga scans
1	= normal bone	= normal bone
2	> normal bone and < normal SIA	> normal bone and < normal liver
3	= normal SIA	= normal liver
4	> normal SIA	> normal liver

SIA: sacroiliac articulation

Table 2. The Cases of Follow-up ^{99m}Tc-MDP and ^{67}Ga Scans

Cases	^{99m}Tc-MDP		^{67}Ga scan	
	(+)	(−)	(+)	(−)
Pretherapeutic cases	35	5	16	4
F.U. during Therapy	29		13	
F.U. after Therapy	33		15	

F.U.: Follow Up

Table 3. Incidences of Improving Bone and Gallium Scan Findings During and After Therapy of Bone Lymphomas

Examinations	Bone Scan	Gallium Scan
	Cases(%)	Cases(%)
During Therapy	19/29(66.0)	11/13(84.6)
After Therapy	24/33(72.7)	13/15(86.7)

received 0.2 mCi/kg(11.1 MBq/kg). ^{67}Ga scintigrams were obtained at 48–72hr after intravenous administration of 8–10 mCi(11.1–37 ×107 Bq) of ^{67}Ga citrate. Whole body and spot images of ^{99m}Tc-MDP bone and ^{67}Ga scans were obtained, and abnormalities were graded visually as grade 1 to 4 by comparing lesion to non-lesion activity densities(Table 1) During and after adjuvant chemotherapy, all patients had routine clinical evaluations, blood work, primary skeletal MRI, abdominal and pelvic CT scans and a chest radiograph every 4 or 6 months for the first 3 years, twice every year for the following 2 years, and then every year. Additional studies, including biopsy, were done if suggested by clinical examination. Successful therapy with chemotherapy

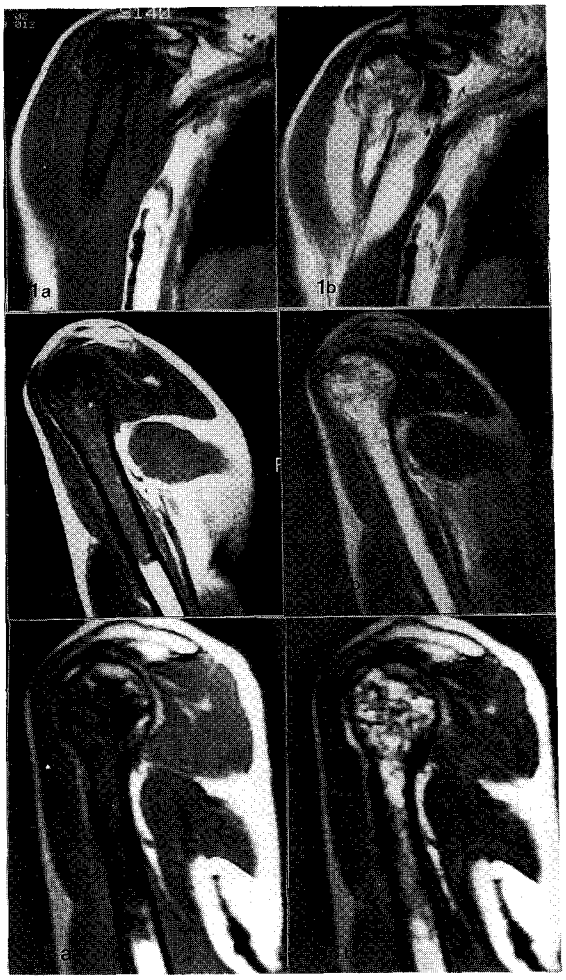

Fig. 1. 1a and 1b were the T1 and T2 weighted MR images prior to the therapy, which the patient had bone lymphoma in the right humerus. There were abnormal findings involving bone marrow and surrounding soft tissue. 2a and 2b were those during the therapy, 3a and 3b were those after completion of the therapy. There were abnormally changed findings representing decreased size of soft tissue tumor, fat replacement and fibrosis.

and/or localized radiotherapy was based on the reduction or disappearance of pain and/or swelling that were no longer clinically evident after 1.5 years following therapy.

RESULTS

Of 40 pretherapeutic bone scans and 20 ^{67}Ga

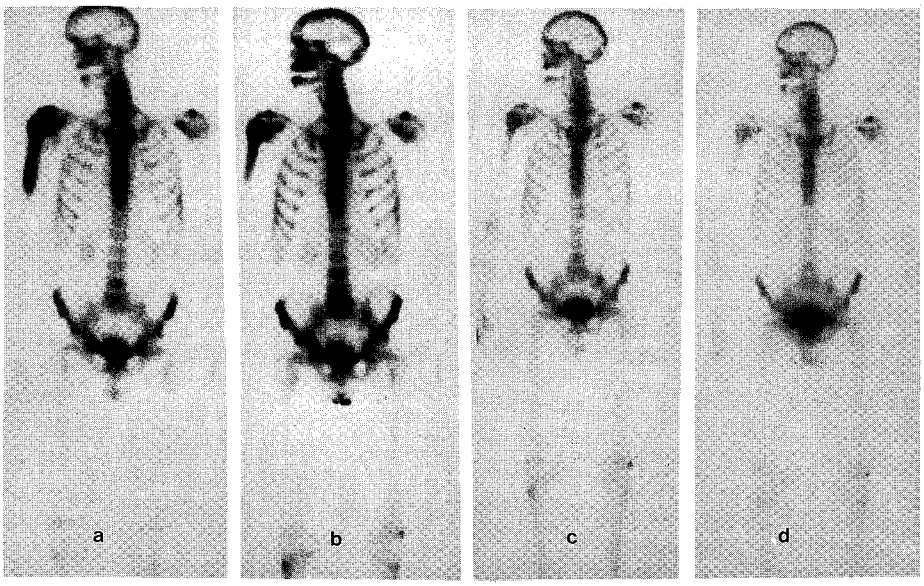

Fig. 2. (a) was the bone scan prior to the therapy, theat showed increased bony tracer uptake pattern(G4) in the right humeral lymphoma. (b) and (c) were those during the therapy, that showed the uptake densities of G3 and G2. (d) was that after completion of the therapy, which showed that of G1.

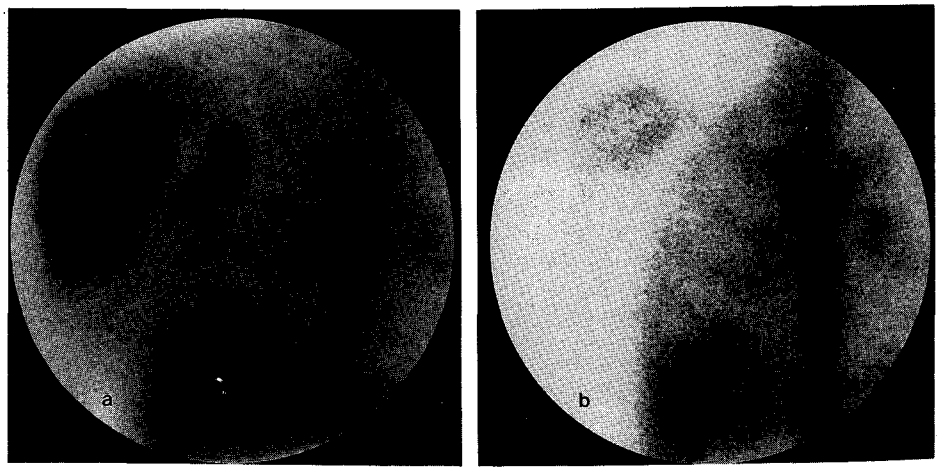

Fig. 3. (a) was the gallium scan prior to the therapy, which showed markedly increased gallium uptake density(G4) in the right humerus. (b) was that during the therapy, which showed no abnormal uptake pattern to G1.

scans in lymphoma patients with complete remission, the incidences of abnormal findings with increased uptake pattern were 87.5% (35/40) with ^{99m}Tc-MDP bone scan and 80% (16/20) with ^{67}Ga scan before therapy(Table 2). The mean time of the follow-up bone scan during therapy was 5.1 months(range, 2 to 11 months) in 35 cases and that of the ^{67}Ga scan 4.5 months(range, 3 to 9 months) in 16 cases. The mean time of the follow-up bone scan

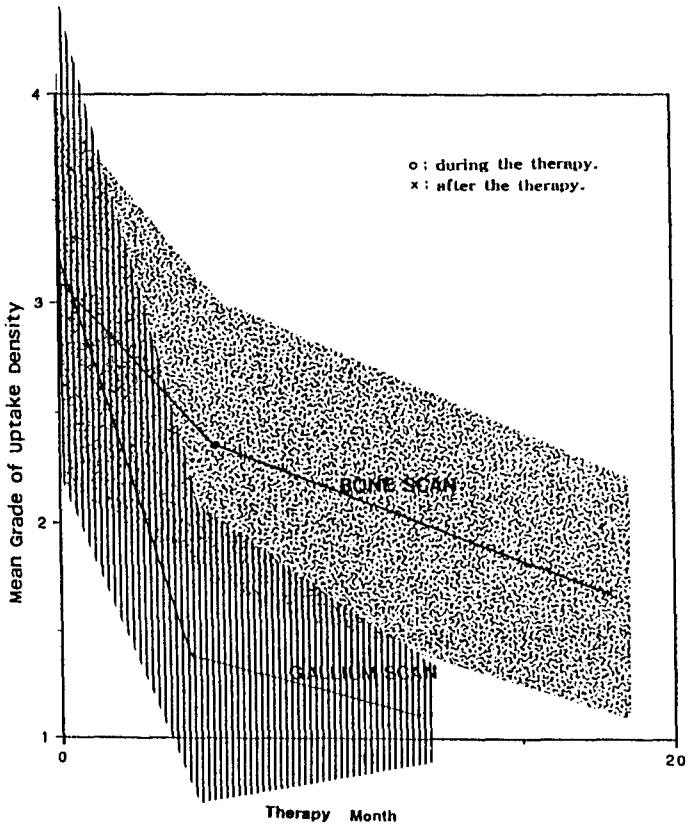

Fig. 4. The follow-up gallium scan for evaluating therapeutic response of bone lymphoma revealed more sensitive change than those of the bone scans.

Table 4. Mean Grades of ^{99m}Tc-MDP and ^{67}Ga Scan Abnormalities Before, During and After Therapy

Treatments	Bone Scans		Gallium Scans	
	Cases	Mean Grades(ρ)	Cases	Mean Grades(ρ)
Before	35	3.06(0.84)	16	3.22(1.06)
During	29	2.34(0.68)	13	1.42(0.74)
After	33	1.75(0.66)	15	1.30(0.28)

GS: Grades.
(ρ): standard deviation

after therapy was 17.8 months(range 5 to 84 months) and that of the ^{67}Ga scan 11.5 months(range 5 to 24 months). The incidences of improved findings during therapy in cases with successful therapeutic response of bone lymphoma were 66.0% (19/29) with the bone scan and 84.6%(11/13) with the ^{67}Ga scan. Those after complete therapy were 72.7%(24/33) with the bone scan and 86.7%(13/15) with the ^{67}Ga scan(Table 3). The representative case is illustrated in Fig. 1-3. The mean grades of the bone scan with successful therapeutic response were 3.06(n=36) before therapy, 2.34(n=29) during therapy, 1.75(n=33) after therapy(Fig. 2). And those of the ^{67}Ga scan were 3.22(n=16) before therapy, 1.42(n=13) during therapy and 1.30(n=15) after therapy(Fig. 4)(Table 4).

DISCUSSION

Primary bone lymphoma is stage I disease

and secondary bone lymphoma is stage IV disease according to classification. The definitive diagnosis of recurrent bone lymphoma is diffi cult to make by using imaging criteria alone since a wide variety of primary and secondary neoplasms or inflammatory processes may have similar radiological findings. Therefore it has been based on aspirate smears and bone marrow biopsies. However, the bone biopsies can not be repeatedly performed to evaluate therapeutic response after chemotherapy and/or radiotherapy. The evaluation of therapeutic response is very important in consideration of bone marrow transplant before it becomes too late. If bone lymphomas do not respond, the patient generally requires additional and/or other therapy, while dramatic therapeutic response simply needs clinical observation or curettage for symptomatic tumor necrosis. A bone scan is a sensitive(but nonspecific) imaging technique for the detection of bone lesions, but the positive findings with increased radiotracer accumulation simply reflect the pattern of bone response to a local insult. The gallium scan is an useful imaging technique to detect certain active lymphomas, but it is not sensitive to detect a small residual bone lymphoma. Plain X-ray and CT scan are not reliable to evaluate early posttherapeutic changes in the bone marrow. Suspicious lesions before and following therapy may be detected by CT or MRI. However, the Dana-Farber Cancer Institute series suggest that neither the CT scan appearance of the mass nor the magnitude of change during therapy could exclude the possibility of residual tumor[4]. In general, the size of the residual mass correlated with a higher likelihood of residual cancer but residual mass may not be residual lymphoma[2,6]. A residual mass that contains only necrotic-fibrotic tissue can resolve in time and thus an incomplete remission may never show recurrence. However, it is important to identify patients whose residual masses have a high likelihood of relapse, especially in large cell non-Hodgkin's lymphoma where the issue of residual masses is much less clear[7,8]. An accurate estimate of residual viable tumor would facilitate the use of appropriate therapy. MRI reflects the varying tissue characteristics of the T1 and T2 relaxation times. MRI has been successfully used as and adjunct to standard marrow biopsies in determining marrow involvement of tumor[9].

All imaging modalities show a significant limitation in evaluation of therapeutic response or differential diagnosis of residual or recurrent bone lymphoma from post-therapeutic changes. MRI or bone scan was not better than ^{67}Ga scan in that regard because ^{99m}Tc-MDP bone scan reflect persistent increasing actvity due to increased bony turnover. Both bone and ^{67}Ga scans appear to be helpful in examining whole bony structures and/or soft tissue abnormalities. In summary, although the bone scan was more sensitive in detecting of bone lymphoma ^{67}Ga scans appeared more sensitive than bone scans in evaluating therapeutic response of bone lymphoma.

REFERENCES

1) Klimo P, Connors JM: *MACOP-B chemotherapy for the treatment of diffuse large-cell lymphoma. Ann J Med 102:596-602, 1985*
2) Canellos GP: *Residual mass in lymphoma may not be residual disease. J Clin Oncol 6:931-933, 1988*
3) Orzel JA, Sawaf NW, Richardson ML: *Lymphoma of the skeleton: Scintigraphic Evaluation. AJR 150:1095-1099, 1988*
4) Keplan WD, Jochelson MS, Herman TS, Nadler LM, Stomper PC, Takvorian T, Andersen JW and Canellos GP: *Gallium-67 imaging: A predictor of residual tumor viability and clinical outcome in patients with diffuse large-cell lymphoma. J Clin Oncol 8:1966-1970, 1990*

5) Hoane BR, Shields AF, Porter BA, Shulman HM: *Detection of lymphomatous bone marrow involvement with magnetic resonance imaging. Blood 78:728-738, 1991*

6) Shipp MA, Harringyon DP, Klatt MM: *Identification of major prognostic subgroups of patients with large cell lymphoma treated with m-BACOD or M-BACOD. Ann Intern Med 104: 757-765, 1986*

7) Stewart FM, Williamson BR, Innes DJ, Hess CE: *Residual tumor masses following treatment for advanced histiocytic lymphoma; Diagnostic and therapeutic implications. Cancer 55:620-623, 1985*

8) Lewis E, Bernardino ME, Salvador PG, Cabanillas FF, Barnes PA, Thomas JL: *Post-therapy CT detected mass in lymphoma patients: Is it viable tissue? J Comput Assist Tomogr 6: 792-795, 1982*

9) Olson DO, Shields AF, Scheurich CJ, Porter BA, Moss AA: *Magnetic resonance imaging of the bone marrow in patients with leukemia, anaplastic anemia, and lymphoma. Invest Radiol 21: 540, 1986*

10) Moon TY, Kim EE, Legaspi JR, Park JM, Kim YC, Chung JK, Kim BS, Lee SK, Kim KI: *Efficacy of MRI for therapeutic evaluation of bone lymphoma. J Korean Radiol Soc 31:157-163, 1994*