Case Report

혈관내 B 대세포 림프종 환자에서 발견된 ^{99m}Tc-MIBI의 미만성 골수 섭취

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Diffuse Bone Marrow Uptake of ^{99m}Tc-MIBI in A Case of Intravascular Large B-cell Lymphoma

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Intravascular large B-cell lymphoma (IVLBCL) is a subtype of diffuse large cell lymphoma, characterized by proliferation of lymphoid cells in the intravascular space of various organs without causing a mass effect. Although ^{18}F-FDG PET is a powerful imaging tool in lymphoma, the usefulness of ^{18}F-FDG PET in the assessment of IVLBCL is still controversial. ^{99m}Tc-MIBI, a tumor imaging radiopharmaceutical with a different mechanism from that of ^{18}F-FDG, has been reported to be also effective in lymphoma. However, there is nearly no report on the efficacy of ^{99m}Tc-MIBI in the assessment of IVLBCL. We present one case of IVLBCL that showed ^{99m}Tc-MIBI accumulation in the involved bone marrow as an incidental finding, which was discrepant from that of ^{18}F-FDG PET. (Nucl Med Mol Imaging 2009;43(4):352-356)

Key Words: Intravascular large B-cell lymphoma, ^{99m}Tc-MIBI, ^{18}F-FDG PET

Introduction

Intravascular large B-cell lymphoma (IVLBCL) is a rare and aggressive subtype of diffuse large cell lymphoma, characterized by proliferation of large lymphoid cells in the intravascular space of various organs.[1-3] Because IVLBCL usually do not form a mass, it is difficult to diagnose and to assess involvement of a specific organ by imaging tools like CT.[4-5] This is similar in case of ^{18}F-FDG PET. Although ^{18}F-FDG PET has been used as a powerful functional imaging tool in the assessment of various lymphoma, its diagnostic performance in IVLBCL is still controversial. While some researchers reported the efficacy of ^{18}F-FDG PET for the diagnosis of IVLBCL when lymphoma is clinically suspected,[6-9] others reported more controversial results on the efficacy.[10-13]

^{99m}Tc-MIBI is a lipophilic cationic radiopharmaceutical, mostly used in the study for myocardial perfusion. In addition, ^{99m}Tc-MIBI is a good radiopharmaceutical for tumor imaging as it is accumulated in mitochondria-rich tumor cells. Also in lymphoma, uptake of ^{99m}Tc-MIBI has been reported in several types of pathology.[14-16] In this report, we present a case of IVLBCL that showed uptake of ^{99m}Tc-MIBI in the involved bone marrow, as a discrepant result from that of ^{18}F-FDG PET.

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Case Report

A 41-year-old female patient visited our hospital for suspicious hidden malignancy. The patient initially had abdominal pain, general weakness and poor oral intake. Tenderness was over RUQ area. Otherwise, no abnormal

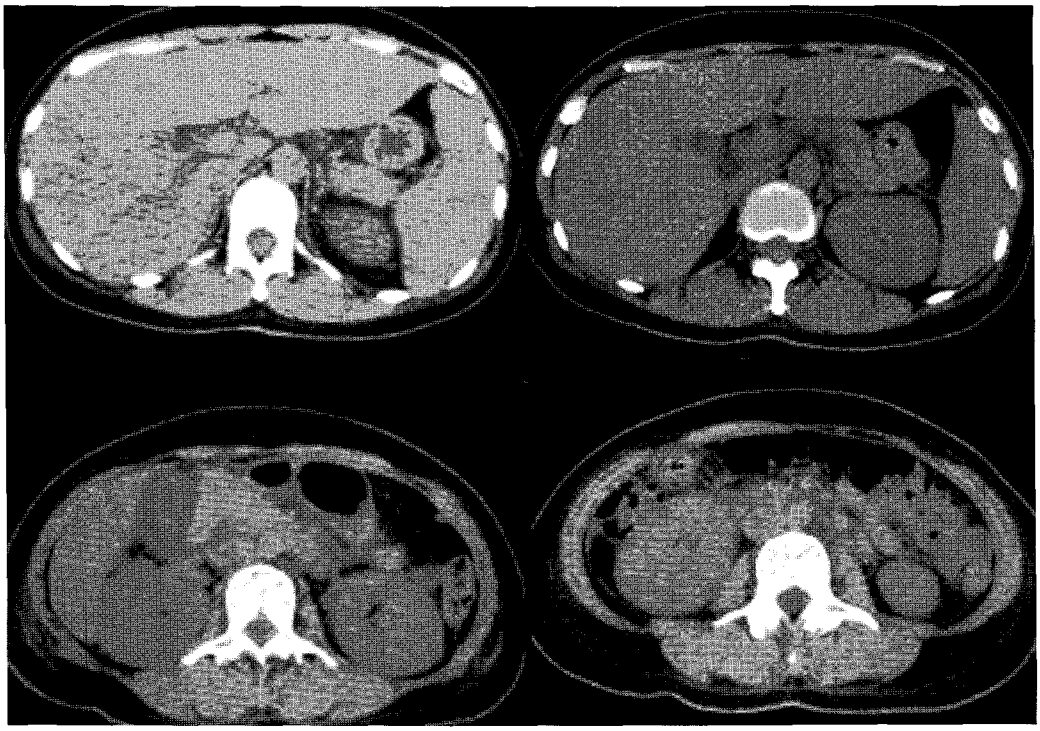

Figure 1. Non-contrast abdominal CT showed hepatosplenomegaly, diffuse periportal edema, gall bladder wall edema and enlargement of both kidneys.

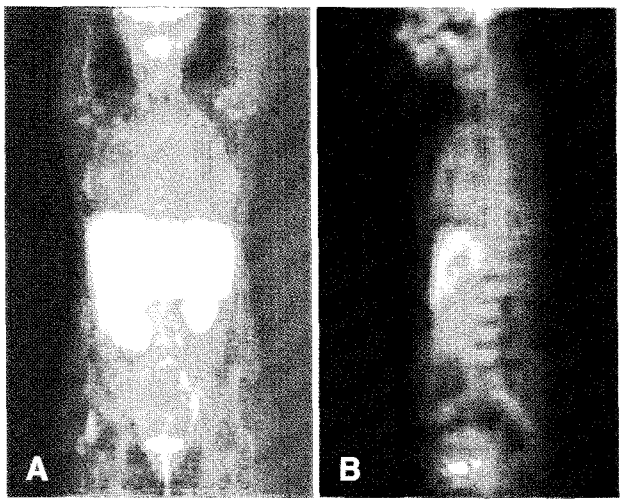

Figure 2. MIP images (A) of ^{18}F-FDG PET/CT showed hepatomegaly and diffuse increased ^{18}F-FDG uptake in the spleen and renal parenchyma. No significant focal hypermetabolic lesion suggesting malignancy was detected in the scan-covered area. Sagittal image (B) showed no significant abnormal hypermetabolic lesion suggesting malignancy.

finding was found in physical examination. Laboratory tests showed hypercalcemia (Ca 19.0 mg/dL, P 3.8 mg/dL), mild azotemia (BUN 31 mg/dL, Cr 2.4 mg/dL), abnormal liver function (AST 108 U/L, ALT 68 U/L, negative viral markers) and especially, high serum lactate dehydrogenase (LDH 2355 IU/L). Sodium, potassium and chloride levels were 132 mEq/L, 4.1 mEq/L and 94 mEq/L, respectably. The C-reactive protein (CRP) level was 1.5 mg/dL. Complete blood count (CBC) was within normal limit. On imaging studies including abdominal ultrasonography and CT, hepatosplenomegaly, diffuse periportal edema, edema of gall bladder wall, enlargement of both kidneys, moderate amount of ascites, and small amount of pleural effusion were observed (Fig. 1). However, there was no specific mass lesion detected. Also on ^{18}F-FDG PET/CT, mildly increased FDG uptake in the spleen and renal parenchyma was found, without a specific focal lesion (Fig. 2).

For evaluation of hypercalcemia, parathyroid scan using ^{99m}Tc-MIBI was performed. In addition to typical protocol of ^{99m}Tc-MIBI parathyroid scan, whole body scan was acquired just after delayed ^{99m}Tc-MIBI parathyroid scan. On ^{99m}Tc-MIBI scan, abnormal uptake was observed in the axial skeleton or the bone marrow (Fig. 3). Afterwards, bone scan using ^{99m}Tc-MDP was

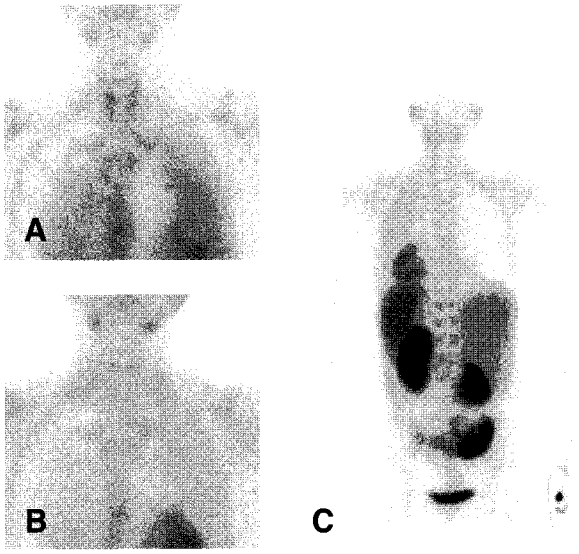

Figure 3. ^{99m}Tc-MIBI scan (A) of neck and chest at 15 minutes after injection showed abnormally increased uptake in the lung and the skeleton of spine and sternum, which suggested uptake in the bone marrow. At 150 minutes after injection, uptake in the lung was nearly disappeared while the bone marrow uptake persisted (B). Posterior view of whole body scan (C) also showed diffuse increased uptake in the bone marrow. Intense uptakes in the both kidneys were also demonstrated.

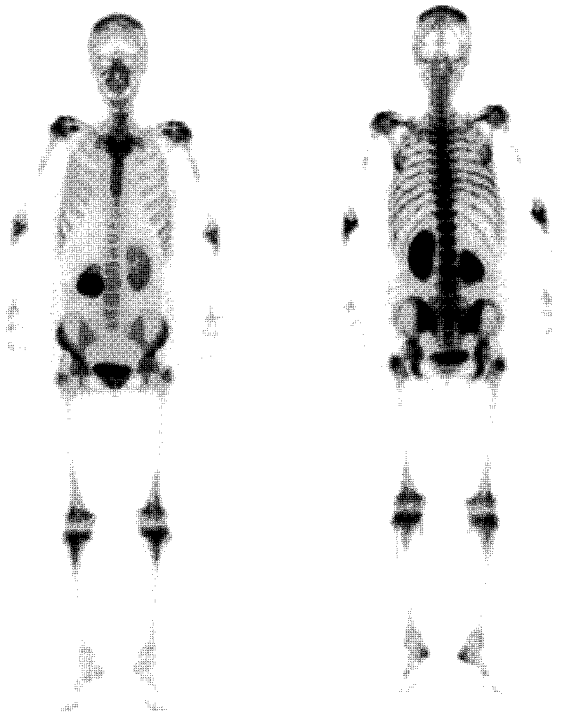

Figure 4. ^{99m}Tc-MDP bone scan showed a diffuse increased uptake in the axial skeleton and periarticular area of long bones, which suggested expansion of the bone marrow or infiltration of the bone marrow by malignant cells.

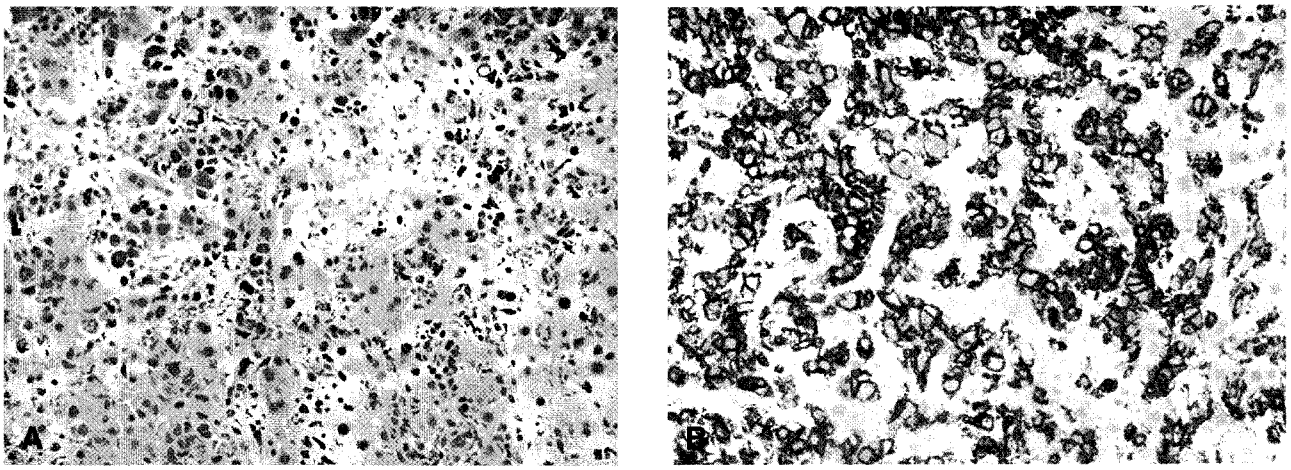

Figure 5. H & E stain (×400, A) showed sinusoidal infiltration of the bone marrow by abnormal large lymphoid cells. Immunostain (×400, B) showed numerous positive cells for L26 (CD20). The patient was confirmed as IVLBCL.

performed for bone lesions, and diffuse increased uptake was observed in the axial skeleton and periarticular area of long bones, which suggested diffuse marrow expansion or infiltration by malignant cells (Fig. 4).

Bone marrow biopsy was performed and normocellular marrow (cellularity 30-50%) with intra-sinusoidal malignant cells was revealed. On immunohistochemical staining, CD3, L26, Ki-67, bcl-2, and bcl-6 were positive, while CD10 was negative (Fig. 5). Cytology studies of pleural effusion and cerebrospinal fluid were negative for malignant cells. Finally, the patient was diagnosed as IVLBCL of stage IV_B.

Discussion

IVLBCL is a rare and aggressive disease with poor prognosis. It was initially coined as 'angioendotheliomatosis proliferans systematisata', and as is expressed in this term, IVLBCL is limited to the intravascular space and usually does not form any mass lesion or extravascular disease.[3-5]

The presentation type of IVLBCL is classified into Asian and European variants. The Asian variant usually involves the kidney and the bone marrow, and often manifests hemophagocytic syndrome characterized by pancytopenia, hepatosplenomegaly, and other symptoms related with bone marrow involvement. The other European variant usually involves the central nervous system and skin, and often manifests neurological symptoms and skin lesions such as erythematous tender plaques, panniculitis, and telangiectasis.[17,18] The Asian variant like the presented case requires biopsy of involved organs to be confirmed. Although an imaging study may be a clue for the diagnosis of malignancy and a guide to select an organ for biopsy, most of anatomical imaging studies fail to detect a lesion in case of IVLBCL, as there is no specific mass lesion.

^{18}F-FDG PET is a powerful imaging tool for assessment of patients with Hodgkin and non-Hodgkin's lymphoma (NHL). However, there is a controversy on the efficacy of ^{18}F-FDG PET in IVLBCL. While some studies have reported that ^{18}F-FDG PET is useful for the diagnosis of IVLBCL when this type of lymphoma is clinically suspected,[6-9] another study argued that usefulness of ^{18}F-FDG PET in the initial or posttherapeutic assessment is limited, probably due to small tumor cell number per volume.[13] Also in this case, ^{18}F-FDG PET/CT showed only hepatosplenomegaly and mildly increased diffuse FDG uptake in the spleen and renal parenchyma without abnormal hypermetabolism, even in the bone marrow. In contrast, ^{99m}Tc-MIBI scan that was performed for the evaluation of hypercalcemia incidentally showed diffuse uptake in the axial skeleton, which suggested uptake in malignant cells involving the bone marrow. ^{99m}Tc-MDP bone scan also showed diffuse increased uptake in axial skeleton and periarticular long bones, corresponding to the results of bone marrow biopsy.

^{99m}Tc-MIBI is a well-known radiopharmaceutical for tumor imaging, with a different mechanism from that of ^{18}F-FDG by accumulating in mitochondria-rich tumor cells. In addition, the uptake of ^{99m}Tc-MIBI has a correlation with expression of Pgp-170, a product of the multidrug resistant gene-1 (MDR-1).[19,20] As a result, diagnostic accuracy of ^{99m}Tc-MIBI scan has been reported to be around 85% in lymphoma.[15,16] The presented case of IVLBCL showed discrepant findings of the bone marrow between ^{99m}Tc-MIBI scan and ^{18}F-FDG PET, and ^{99m}Tc-MIBI showed the lymphoma involvement of the bone marrow. This case suggests the need of further studies on ^{99m}Tc-MIBI as a potential complementary radiopharmaceutical to ^{18}F-FDG in tumor imaging, especially in case of IVLBCL.

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