Case Study

Superior Clinical Impact of FDG-PET Compared to MRI for the Follow-up of a Patient with Sacral Lymphoma

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The assessment of residual tumors after treatment of malignant lymphoma (ML) is often difficult. Here we report a case of non-Hodgkin’s lymphoma with a huge sacral tumor. After chemotherapy and following radiation therapy, a residual mass was detected on magnetic resonance imaging (MRI). However, a hypermetabolic lesion in the sacrum disappeared on 18F-fluorodeoxyglucose positron emission tomography (18F-FDG-PET) and clinically the patient was considered to achieve complete remission. Seven months after the completion of radiation therapy, a new tumor-like lesion in the sacrum developed on MRI, but hypermetabolic lesions were not detected on 18F-FDG-PET. Recurrence of lymphoma was denied by open biopsy of the lesion. 18F-FDG-PET has been of widespread use not only for staging but for post-treatment assessment of ML. Although MRI is a standard imaging tool for the assessment of bone involvement of ML, there have been few reports documenting the results of comparative studies on the usefulness of 18F-FDG-PET and MRI for the evaluation of residual mass in bone involvement of ML. The present case suggests that 18F-FDG-PET is superior to MRI not only in the evaluation of a residual mass but in the judgment of recurrence after treatment of such patients. [J Clin Exp Hematopathol 49(2): 109-115, 2009]

Keywords: malignant lymphoma, bone involvement, residual tumor, recurrence, 18F-fluorodeoxyglucose positron emission tomography (FDG-PET/CT)

INTRODUCTION

Malignant lymphoma (ML) involving bone can be separated into primary lymphoma of bone (PLB) and secondary lesions. PLB is defined as either development in a single skeletal site, with/without regional lymph node involvement or multiple bone lesions with no visceral or lymph node involvement. Patients with other visceral sites or multiple lymph nodes at multiple sites, in addition to a bone tumor, are excluded from PLB. In both of the groups, it is not easy to evaluate the viability of residual bone disease after treatment on magnetic resonance imaging (MRI) alone, although it is a standard imaging tool for the assessment of bone involvement of ML. The clinical usefulness of 18F-fluorodeoxyglucose positron emission tomography (18F-FDG-PET) for bone lymphoma has not been fully confirmed for the above purpose.

We describe here the results of a comparative study of the usefulness between MRI and 18F-FDG-PET for the evaluation of viability of residual mass and for the judgment of recurrence of bone lymphoma.

CASE REPORT

A 66-year-old Japanese woman noticed numbness on the left hip in the middle of March 2004. It gradually deteriorated and the pain appeared in the middle of May 2004. Soon thereafter she visited her neighboring hospital and was admitted. A solid mass replacing a greater part of the sacrum was detected on MRI. Because she developed urinary and bowel disturbance soon after admission, emergency laminectomy of SI-4 with biopsy of the mass was performed. The biopsy section revealed diffuse proliferation of medium-sized to large lymphoid cells with round or oval-shaped nuclei and one or more nucleoli (Fig. 1A, 1B). These lymphoid cells were positive for CD20, Bcl-2 and Bcl-6, but were negative for CD45R0. Invasion of the surrounding muscular tissue was detected in several places. The patient was diagnosed as having diffuse large B-cell lymphoma (DLBCL). A single left supraclavicular lymphadenopathy was found and it was removed surgically. The biopsy specimen of the lymph node was occupied by follicular structure which was composed of centrocytes with an immunophenotype similar to that of the
sacral mass (Fig. 1C, 1D). Centroblasts were rarely seen. The lesion was diagnosed as follicular lymphoma (FL) and was classified as grade 1.

The patient was referred to our hospital in July 2004. Though the patient had numbness from the left hip to the left lower limb, severe sacral pain, and gait disturbance, her general state was good. White blood cell count was 6,200/μL (neutrophils 55%, lymphocytes 32%, eosinophils 4%, basophils 1% and monocytes 8%). Hemoglobin concentration was 12.3 g/dL and platelet count was 27.8 × 10^4/μL. Lactate dehydrogenase level was within normal range but soluble interleukin-2 receptor (sIL-2R) was elevated to 2,020 U/mL (normal range 220-530). A computed tomography (CT) scan showed no mediastinal lymphadenopathy, but confirmed some axillary and paraaortic lymphadenopathy around the lower abdominal aorta and the left iliac artery with a maximum diameter of 1 cm and 3 cm, respectively. MRI demonstrated that the mass replaced a greater part of the sacrum and the mass invaded into the spinal canal (Fig. 2A, 2B). The mass showed an isointense signal compared with the surrounding muscle on both T1- and T2- weighted images (WI) and was enhanced with gadolinium-diethylenetriamine pentaacetic acid (Gd-DTPA). Combined PET/CT showed hypermetabolic lesions in the sacrum, in the left lower paraaortic to the left parailiac artery region, and in both axillary regions, all of which were confirmed on conventional CT or MRI, and furthermore in the left supraclavicular region (Fig. 3A). However, there was no palpable lymphadenopathy. Standardized uptake value (SUV) of the sacral lesion was 7.9. Fluorescence in situ hybridization analysis of the biopsy samples of both the sacral mass and the left supraclavicular lymph node revealed immunoglobulin heavy chain-bc-l/f-2 fusion signals. From these results, sacral lymphoma which was diagnosed as DLBCL was supposed to be transformed from FL. The likelihood of this case being PLB was not high because of the definition of PLB by the WHO classification.1 In

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Fig. 1. Biopsy samples of the sacral mass (1A, 1B) and left supraclavicular lymph node (1C, 1D). (1A) Ill-defined nest-like growth of lymphoma cells is seen in the soft tissue. (1B) The proliferating cells are medium-sized to large with round or oval-shaped nuclei and one or more nucleoli. A cell in mitosis is seen. (1C) The normal nodal architecture is effaced by nodular growth of lymphoid cells. Reactive germinal centers are not apparent in the two nodules. (1D) Nodules are composed of monotonous proliferation of centrocytes with virtual absence of centroblasts. Two large nuclei in the upper center are probably of follicular dendritic cells. Hematoxylin & eosin stain; (1A) × 20, (1B) × 100, (1C) × 10, (1D) × 100.
contrast, the possibility that the present case was primary nodal FL invading the sacrum as a secondary lesion could not be excluded. However, we supposed that this case was PLB of the sacrum with involvement of the regional as well as multiple lymph nodes at multiple sites because the sacral lesion was bulky whereas other nodal lesions were relatively small in size. The patient was evaluated as having clinical stage IV disease according to the Ann Arbor classification.

After the first cycle of combined chemotherapy with pirarubicin hydrochloride, cyclophosphamide, vincristine and prednisolone (THP-COP), the sacral mass decreased in size on MRI and her clinical symptoms considerably improved. The levels of sIL-2R decreased to 794 U/mL. After the second cycle of chemotherapy, to which Rituximab was added (R-THP-COP), additional decrease in the size of the sacral mass was seen on MRI. Paraaortic lymphadenopathy also regressed on abdominal echo. However, the sacral mass revealed no remarkable additional reductions in size in spite of subsequent 3 cycles of R-THP-COP. At that time, the hypermetabolic lesion of the sacral mass and swollen lymph node in the distant area disappeared, and only a weak hypermetabolic lesion (SUV 3.9) was recognized on PET/CT. MRI one month after the event demonstrated an additional new lesion in the upper left segment of the sacrum showing signal similar to that of the mass in the right segment (Fig. 5C, 5D). These new lesions were enhanced with Gd-DTPA. Furthermore, previous residual mass still remained, but sIL-2R was not elevated. At the open biopsy of the mass in the left segment of the sacrum, the lesion looked like normal bone and it was histopathologically confirmed to be connective tissue without lymphoma cells. Thereafter, the symptoms of of the above chemotherapy, all of the hypermetabolic lesions disappeared on PET/CT in the middle of March 2005 (Fig. 3B). At the same time, the residual sacral mass revealed no additional decrease in size and the degree of enhancement on MRI. Local radiation of 40 Gy to the sacrum with the involved field was then performed, but the sacral mass revealed no remarkable change in size and the degree of enhancement on MRI (Fig. 4A, 4B). The patient was free from any symptoms and was discharged from the hospital at the beginning of May 2005. Thereafter the patient was doing well and followed at our hospital as an outpatient.

In the middle of December 2005, the patient developed right sacral pain. A new tumor-like lesion in the upper right segment of the sacrum (S1-2) was found on MRI, which showed isointense signal on T1-WI and hyperintense signal on T2-WI (Fig. 5A, 5B). In contrast, only a very weak hypermetabolic lesion (SUV 3.9) was recognized on PET/CT. MRI one month after the event demonstrated an additional new lesion in the upper left segment of the sacrum showing signal similar to that of the mass in the right segment (Fig. 5C, 5D). These new lesions were enhanced with Gd-DTPA. Furthermore, previous residual mass still remained, but sIL-2R was not elevated. At the open biopsy of the mass in the left segment of the sacrum, the lesion looked like normal bone and it was histopathologically confirmed to be connective tissue without lymphoma cells. Thereafter, the symptoms of.
Fig. 3. (3A) Anterior and lateral views of 18F-fluorodeoxyglucose positron emission tomography (PET) on admission show hypermetabolic lesions in the sacrum, in the left lower paraaortic to the left parailiac artery region, in both axillary regions, and in the left supraclavicular region. (3B) Anterior view of PET after the completion of chemoradiotherapy in March 2005 shows no hypermetabolic lesions. Hypermetabolic lesions in thyroid gland are supposed to be due to chronic thyroiditis.

Fig. 4. Axial (4A) and sagittal (4B) views of T1-WI of the sacrum after radiation therapy demonstrate a residual mass with the same intensity as before (arrows).
Fig. 5. Axial views of MRI of the sacrum 7 months after the completion of radiation therapy demonstrate a new tumor-like lesion in the upper right segment of the sacrum (arrows). The lesion shows isointense signal on T1-WI (5A) and hyperintense signal on T2-WI (5B). Axial views of MRI of the sacrum, 1 month after the new tumor-like lesion developed, demonstrate another tumor-like lesion in the left segment of the sacrum (arrows). This new lesion also shows isointense signal on T1-WI (5C) and hyperintense signal on T2-WI (5D).

Fig. 6. Axial (6A) and sagittal (6B) views on T1-WI of the sacrum 6 months after the second biopsy confirms the disappearance of the two tumor-like lesions detected in January 2006. These lesions are replaced by normal bone tissue.
the patient gradually improved, the new sacral tumor-like lesions disappeared, and replacement by the normal bone was found on MRI in July 2006 (Fig. 6A, 6B). Furthermore, previous residual mass decreased in both size and enhancement effect. The patient is doing well without any sign of recurrence at the time of the last follow up in December 2008.

**DISCUSSION**

For the evaluation of treatment effect of ML involving bone, MRI is generally considered as a standard imaging tool. However, it is not easy to differentiate viable lesions from treatment-related changes, such as tumor necrosis and fibrosis by this method. In the present case, the sacral mass revealed considerable decrease in size after the first two cycles of chemotherapy, but an abnormal signal lesion on MRI remained, with the same intensity as that seen at the onset, even after completion of chemoradiotherapy. These features were quite similar to those reported by Mengiardi et al. who summarized MRI characteristics of PLB during and after successful treatment. In their report, signal intensities of PLB at the initial presentation (isointense on T1-WI and hyperintense on T2-WI) unchanged through the follow-up period. Although MRI showed a rapid decrease in tumor volume during the first 3 months of chemotherapy, minor signal abnormalities without clinical relevance may persist for up to 2 years.

The present case revealed two huge tumor-like lesions on MRI in the different sites of the sacrum 7 months after the completion of radiation therapy (RT). These new lesions showed isointense signal on T1-WI and hyperintense signal on T2-WI. Although signal intensity of PLB on MRI is variable especially on T2-WI, a pattern of isointense signal on T1-WI and hyperintense signal on T2-WI, also seen in our patient after chemoradiotherapy, has been most frequently reported. Therefore, recurrence of lymphoma was strongly suspected from the findings of MRI in the present case. On the other hand, recurrence was not suggestive from the findings of PET/CT and, finally, lymphoma cells were not detected in the biopsy sample and recurrence was ruled out. New abnormal signal lesions on MRI mimicking bone lymphoma in the present case were supposed to be the process of the restructuring of the bone after chemoradiotherapy. Furthermore, a persistent abnormal signal lesion in the initial sacral mass on MRI was supposed to be inviable from the clinical course. The patient was supposed to achieve complete remission after the completion of chemotherapy when the hypermetabolic lesions first disappeared on PET/CT in March 2005. It is therefore considered that PET/CT is superior to MRI for the follow-up study of our patient.

There have been many reports describing the clinical usefulness of PET for the staging and follow-up of ML. It has been reported to improve diagnostic accuracy in ML compared to PET or CT alone, and PET is essential for the post-treatment assessment of DLBCL. As mentioned above, PET has been acknowledged as an excellent imaging tool for the management of ML. However, there have been only a few reports suggesting superior clinical usefulness of PET to MRI in the assessment of bone involvement of ML. Recently, diffusion-weighted MRI (DWI) has been spreading for the purpose of distinguishing malignancies from benign lesions in various body regions other than central nervous system such as the cervical lymph node and nasal cavity. In bone tumors, apparent diffusion coefficient value on DWI has been reported to be useful for monitoring the therapeutic response of primary bone sarcomas. However, the usefulness of DWI has not been confirmed in the evaluation of bone lymphoma. It is therefore concluded by the observation of the present case that the use of PET in addition to MRI is important for the follow-up study of bone involvement of ML at the present.

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