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Case Report

A Case of Focal Bone Marrow Reconversion Mimicking Bone Metastasis: The Value of ^{111}Indium Chloride

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We present a case of a 66-year-old man with esophageal carcinoma. ^{18}Fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) for evaluating distant metastasis and staging revealed ^{18}F-FDG uptake in the third lumbar vertebra and other vertebrae. Magnetic resonance imaging could not differentiate bone metastases from benign bone lesions. We considered the possibility of bone marrow reconversion. ^{111}Indium chloride (^{111}In-Cl_3) scintigraphy with single-photon emission computed tomography/computed tomography (SPECT/CT) revealed erythroid bone marrow components in the bone lesions. The diagnosis of bone marrow reconversion was pathologically confirmed by a bone biopsy of the third lumbar vertebra. The patient underwent esophagectomy and has remained disease-free in the 2 years since. To the best of our knowledge, this is the first report to describe the usefulness of ^{111}In-Cl_3 with SPECT/CT for the diagnosis of bone marrow reconversion.

Key words: ^{111}Indium chloride scintigraphy, SPECT/CT, bone marrow reconversion, ^{18}F-FDG PET/CT, bone metastasis

18 Fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) has become an acceptable and established diagnostic tool for both cancer diagnosis and staging. Benign bone lesions such as bone marrow reconversion are sometimes confused with bone metastasis on ^{18}F-FDG PET/CT and magnetic resonance imaging (MRI) [1, 2]. We report a case of bone marrow reconversion that mimicked bone metastasis in a patient with esophageal carcinoma, and demonstrate that ^{111}Indium chloride (^{111}In-Cl_3) with single-photon emission computed tomography/CT can contribute to the diagnosis of bone marrow reconversion.

To the best of our knowledge, this is the first report to describe the usefulness of ^{111}In-Cl_3 with SPECT/CT for the diagnosis of bone marrow reconversion.

Case Report

A 66-year-old man (height 154 cm, body weight 62.9 kg) with a history of heavy smoking and alcohol-induced cirrhosis was referred to our hospital for treatment of esophageal squamous cell carcinoma. He had no clinical symptoms such as abdominal pain or lumbago. His blood pressure was 134/71 mmHg, pulse was 89 beats/min and oxygen saturation on room air

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was 99%. The results of his physical examination were normal. The results of laboratory examinations, including white blood cell count, platelet count, and levels of hemoglobin, C-reactive protein, alkaline phosphatase, and lactate dehydrogenase were within the normal ranges. Levels of tumor markers, including squamous cell carcinoma antigen and carcinoembryonic antigen, were within normal limits. The patient's serum carbohydrate antigen 19-9 level was slightly elevated (69.8 U/mL). Upper gastrointestinal endoscopy and biopsy showed two 35-mm type 0-IIc moderately differentiated squamous cell carcinoma lesions in the upper third of the esophagus.

A CT scan showed no obvious distant metastases but revealed slightly enlarged lymph nodes in the recurrent laryngeal nerve regions on both sides. ^{18}F-FDG PET/CT for the evaluation of distant metastasis and staging showed accumulations of ^{18}F-FDG in the main tumors and no significant accumulation of ^{18}F-FDG in the mediastinal lymph nodes, but there was ^{18}F-FDG uptake in the third lumbar (L3) vertebra (maximum standardized uptake value [SUVmax]: 4.12) and subtle uptake in the other vertebrae (arrowhead) (Fig. 1).

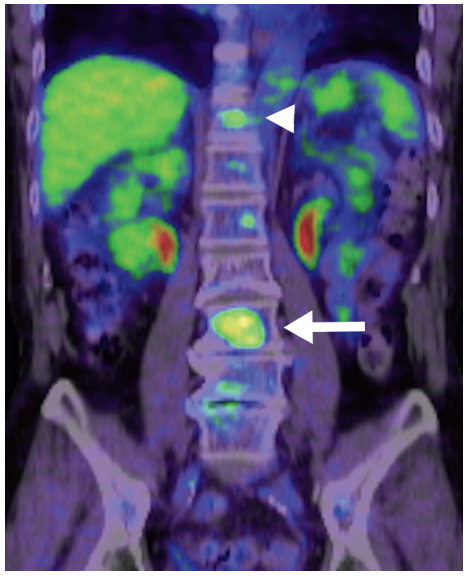

Fig. 1 ^{18}Fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT) findings. A sagittal reconstructed ^{18}F-FDG PET/CT image showing high uptake in the third lumbar (L3) vertebral body (arrow) and subtle uptake in the other vertebrae (arrowhead). The maximum standardized uptake value (SUVmax) of the L3 vertebra was 4.12.

On the CT images obtained by an integrated ^{18}F-FDG PET/CT scanner, this uptake corresponded with a slightly high-attenuation bone lesion with preserved bone trabeculae (not shown). MRI of the spine showed a hyperintense bone lesion on short tau inversion recovery (STIR) images and a hypointense lesion on T1-and T2-weighted images of the L3 vertebra (Fig. 2, arrows). Fat-saturated T1-weighted images after gadolinium administration showed diffuse enhancement of the L3 vertebral lesion. Focal bone lesions with similar MR signal features were detected in the other lumbar vertebrae (Fig. 2, arrowheads). Normal fatty marrow was seen in the background of the spine. We considered the possibility of bone marrow reconversion of the L3 vertebra. For further evaluation, ^{111}In-Cl_3 scintigraphy with SPECT/CT was performed 48 h after intravenous injection of 74 MBq of ^{111}In-Cl_3 using a dual-head camera (GE Discovery NM/CT 670, GE Healthcare, Waukesha, WI, USA). Planar and SPECT/CT scintigraphy showed an abnormal increase in tracer uptake in the L3 vertebra (arrows) and subtle uptake in the other vertebrae (arrowhead) (Fig. 3). The ^{111}In-Cl_3 uptake pattern detected by SPECT/CT was similar to the ^{18}F-FDG uptake pattern corresponding to the bone lesions on MRI. On the basis of these imaging features, bone marrow reconversion was strongly suspected. However, to confirm bone marrow reconversion, a CT-guided bone biopsy with a 13-gauge bone biopsy needle was taken from the L3 vertebral lesion. Histological examination did not reveal any cancer cells, but did show hypercellular bone marrow (Fig. 4). The patient underwent esophagectomy. Histological examination from the resected specimen showed that moderately differentiated squamous cell carcinoma had invaded the submucosal layer (the middle third) with mild venous invasion, but detected no lymphatic invasion or lymph node metastasis. The patient has been regularly followed up and remains disease-free 2 years after surgery.

Discussion

At birth, hematopoietic (red) bone marrow is present throughout the entire skeleton, but then starts to convert to fatty (yellow) bone marrow [3]. This maturation process typically progresses from the peripheral to the central skeleton and is usually completed by the age of 25 years, although its speed depends on

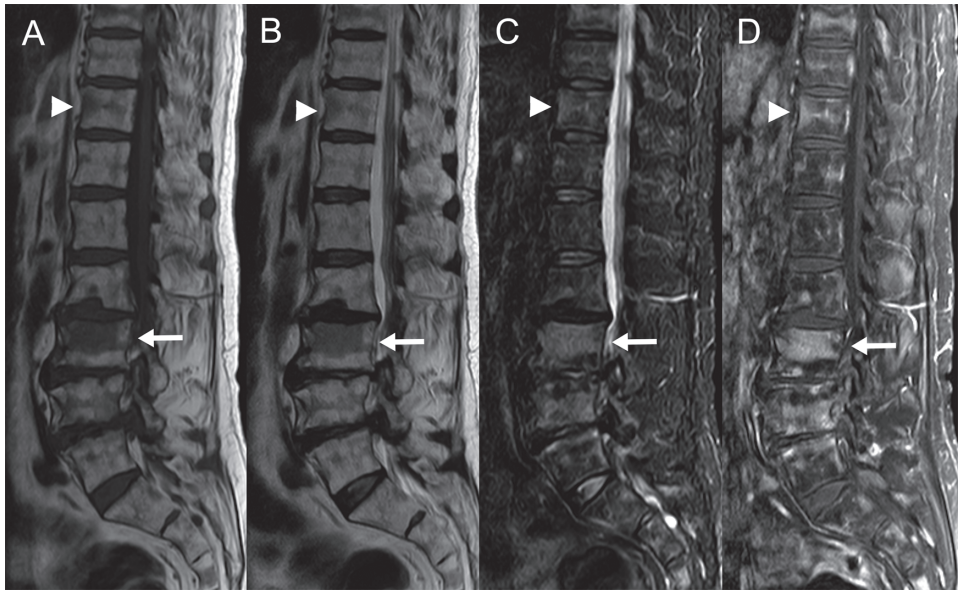

Fig. 2 Magnetic resonance imaging (MRI) findings. Sagittal T1-weighted (**A**) and T2-weighted (**B**) spin-echo MR images of the thoracolumbar spine showing a focal hypointense lesion in the L3 vertebral body (arrows). Sagittal short tau inversion recovery (STIR) image (**C**) and fat-saturated T1-weighted image after gadolinium administration (**D**) showing a hyperintense lesion with contrast enhancement in the L3 vertebral body (arrows). Patchy focal bone lesions with similar signal features to the L3 bone lesion were detected in the other lumbar vertebrae (arrowheads).

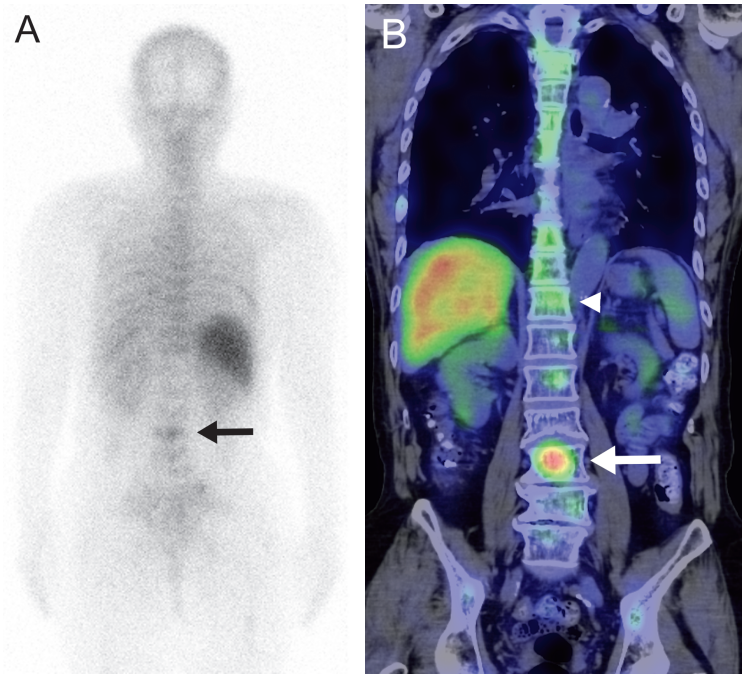

Fig. 3 ^{111}Indium chloride ($^{111}In-Cl_3$) scintigraphy with single-photon emission computed tomography/computed tomography (SPECT/CT) findings. The posterior planar (**A**) and SPECT/CT (**B** coronal) scintigraphy images showing abnormal increase in tracer uptake in the L3 vertebra (arrows) and subtle uptake in the other vertebrae (arrowhead). The $^{111}In-Cl_3$ uptake pattern detected by SPECT/CT was similar to the $^{18}F-FDG$ uptake pattern corresponding to the bone lesions on MRI.

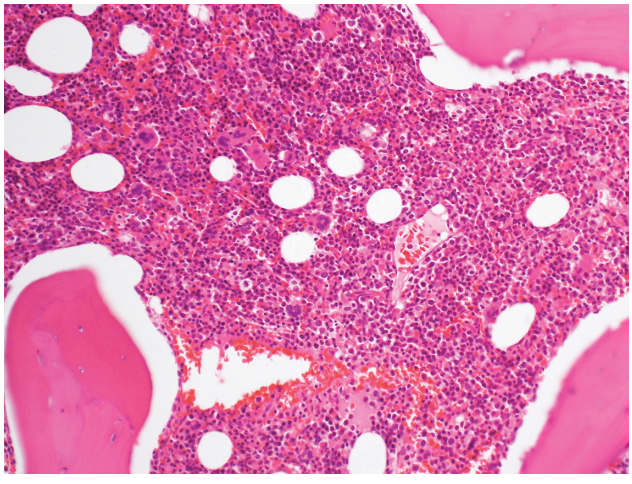

Fig. 4 Pathological findings. Bone biopsy specimen of the L3 vertebral lesion showed hypercellular bone marrow with a reduced proportion of adipocytes. No neoplastic cells were seen (hematoxylin and eosin staining).

an individual's sex and underlying medical conditions. Red marrow consists of 40% water, 40% fat, and 20% protein, whereas yellow marrow consists of 15% water, 80% fat, and 5% protein [4]. In normal adult marrow, yellow marrow may reconvert to the marrow under conditions that cause a need for increased hematopoiesis. This reconversion may have several causes, including stress, obesity, middle age (in women), heavy smoking, long-distance running, high-altitude living, obstructive sleep apnea syndrome, chronic anemia, and administration of hematopoietic growth factors [3, 4]. The reconversion process proceeds in the reverse pattern of the original red-to-yellow conversion. It may occur diffusely, or focal areas of the red marrow may appear in a background of the yellow marrow [2, 3]. In our patient, a smoking history may have contributed to the progression of bone marrow reconversion.

Several imaging modalities, such as bone scintigraphy, CT, MRI, and ^{18}F-FDG PET/CT, are used to evaluate bone lesions. Currently, MRI and ^{18}F-FDG PET/CT have been playing important roles in the detection and evaluation of bone metastases. However, bone marrow reconversion is sometimes misdiagnosed as bone metastasis because of its high cellularity, although in some cases non-neoplastic bone lesions can be easily differentiated from neoplastic lesions on MR images such as in-phase and out-of-phase gradient-echo MR imaging [5]. Reconverted bone marrow may show a masslike pattern with high cellularity and MR signal characteristics of hypercellular hematopoietic marrow, and those of tumor infiltration or highly cellular neoplastic bone marrow can be similar [2, 6]. Like MRI, ^{18}F-FDG PET/CT may give false-positive results for bone metastasis [1]. A previous report evaluating imaging features of hyperplastic hematopoietic bone marrow and bone metastasis showed that if the SUVmax of a bone lesion was more than 3.6 on ^{18}F-FDG PET/CT, the lesion could be considered metastatic [7]. In our case, the multiple bone lesions detected on ^{18}F-FDG PET/CT and MRI were similar to tumor infiltrations caused by bone metastases, and we could not rule out the possibility of malignancy.

^{111}In-Cl_3 scintigraphy with SPECT/CT could be an additional diagnostic tool for focal bone marrow reconversion. ^{111}In-Cl_3 scintigraphy is a noninvasive method for evaluating the anatomic extent of the erythropoietic element. Iron radionuclides are ideal physiologically but are unsuitable for erythroid bone marrow scintigraphy because of their high-energy radiation. ^{111}In-Cl_3 has been used clinically as a reliable alternative tracer in bone marrow scintigraphy because of its transportation in the plasma by transferrin and its suitable energy characteristics [8]. After intravenous injection, ^{111}In-Cl_3 is rapidly coupled to serum transferrin and eliminated from the plasma with a half-life of 5 h. Approximately 30% of the administered tracer is found in the bone marrow, 20% in the liver, 7% in the kidneys, and 1% in the spleen. The remaining activity is distributed throughout the body fluids without any specific tissue accumulation [9]. In previous reports, planar scintigraphy with ^{111}In-Cl_3 was usually used to predict the clinical severity of diffuse bone marrow diseases such as myelofibrosis, aplastic anemia, and myelodysplastic syndrome, particularly to detect the disappearance of a physiologically active bone marrow [8-10]. Planar scintigraphy alone is not sufficient to evaluate and diagnose focal bone lesions. A new hybrid imaging system, SPECT/CT, has advantages over planar imaging because it provides a more precise localization of lesions with focal tracer uptake and improves clinical diagnostic confidence. In our case, ^{111}In-Cl_3 accumulation detected by SPECT/CT conformed remarkably to the images of FDG-PET/CT and MRI, thus contributing to the correct diagnosis.

We encountered a case of bone marrow reconversion that mimicked bone metastasis in a patient with

esophageal carcinoma. The bone marrow reconversion was ultimately diagnosed using a biopsy specimen. ^{111}In-Cl_3 scintigraphy with SPECT/CT can contribute to the diagnosis of bone marrow reconversion.

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