Letter to the Editor

Bone marrow reconversion mimicking pelvis metastases in a patient with rectal cancer: a pitfall on magnetic resonance images

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Introduction

The bone marrow is one of the largest organs in the body. There are two main types of bone marrow in human body: red and yellow bone marrow in the human body. Their proportions are determined by the overall distribution of fat and water, which ultimately determines the magnetic resonance imaging (MRI) signal intensity. At birth, red bone marrow (40% fat, 40% water and 20% protein) is present throughout the entire skeleton. It gradually converts into yellow bone marrow (80% fat, 15% water and 5% protein) (1). The conversion begins in the extremities and progresses toward the axial skeleton, and it can always be completed by approximately 25 years of age (1-3).

When the existing hematopoietic marrow cannot meet the demand for hematopoiesis, the body shifts marrow distribution with replacement of yellow marrow by red marrow, which is called bone marrow reconversion (BMR) (4). However, the occurrence of BMR can be misleading, and its interpretation of imaging can be challenging. Regarding the patients with malignancies, it is occasionally difficult to differentiate BMR from bone metastasis, raising the risk of delayed or missed diagnoses. BMR located in some vertebrae of patients with malignant tumor mimicking bone metastases has been reported by sporadic literatures (5-8). However, little literature reports BMR located in the pelvis. Herein, we report a case of BMR in a patient with rectal cancer which was misdiagnosed as bone metastases by a radiologist using original pelvic MRI.

Case presentation

A 45-year-old woman (height 150 cm, body weight 40 kg) was referred to our hospital for treatment of bloody stools, which lasted for about 3 months. In addition, she had a 2-year history of constipation, and roughly a 2-year history of grade 2 anemia (Hb: 60–90 g/L). A digital rectal examination (DRE) revealed a tumor about 6 cm from the anus, which was firm, immobile and it occupied 2/3 of the intestinal tract lumen. Meanwhile, laboratory examination revealed anemia (Hb: 80 g/L).

The patient subsequently underwent a pelvic MRI on April 1st, 2017. The pelvic MR images demonstrated a primary tumor located on upper rectum and penetrated the surface of the visceral peritoneum with an inhomogeneous hypointense signal on T1-weighted images and inhomogeneous hyperintense signal on T2- and diffusion-weighted images. Multiple enlarged lymph nodes were identified on the pelvic region (regional) and the peritoneal region (nonregional) with hypointense signals on T1-weighted images, and hyperintense signals on T2- and diffusion-weighted images. Diffuse abnormal signals were noticed in the sacrum and bilateral ilia with hypointense signals on T1- and T2-weighted images, hyperintense signals on diffusion-weighted images, and diffuse mild enhancement on fat-saturated T1-weighted images (*Figure 1*). Based on the MRI features of this patient, the radiologist diagnosed the patient as rectal cancer with multiple bone metastases of the sacrum and bilateral ilia,

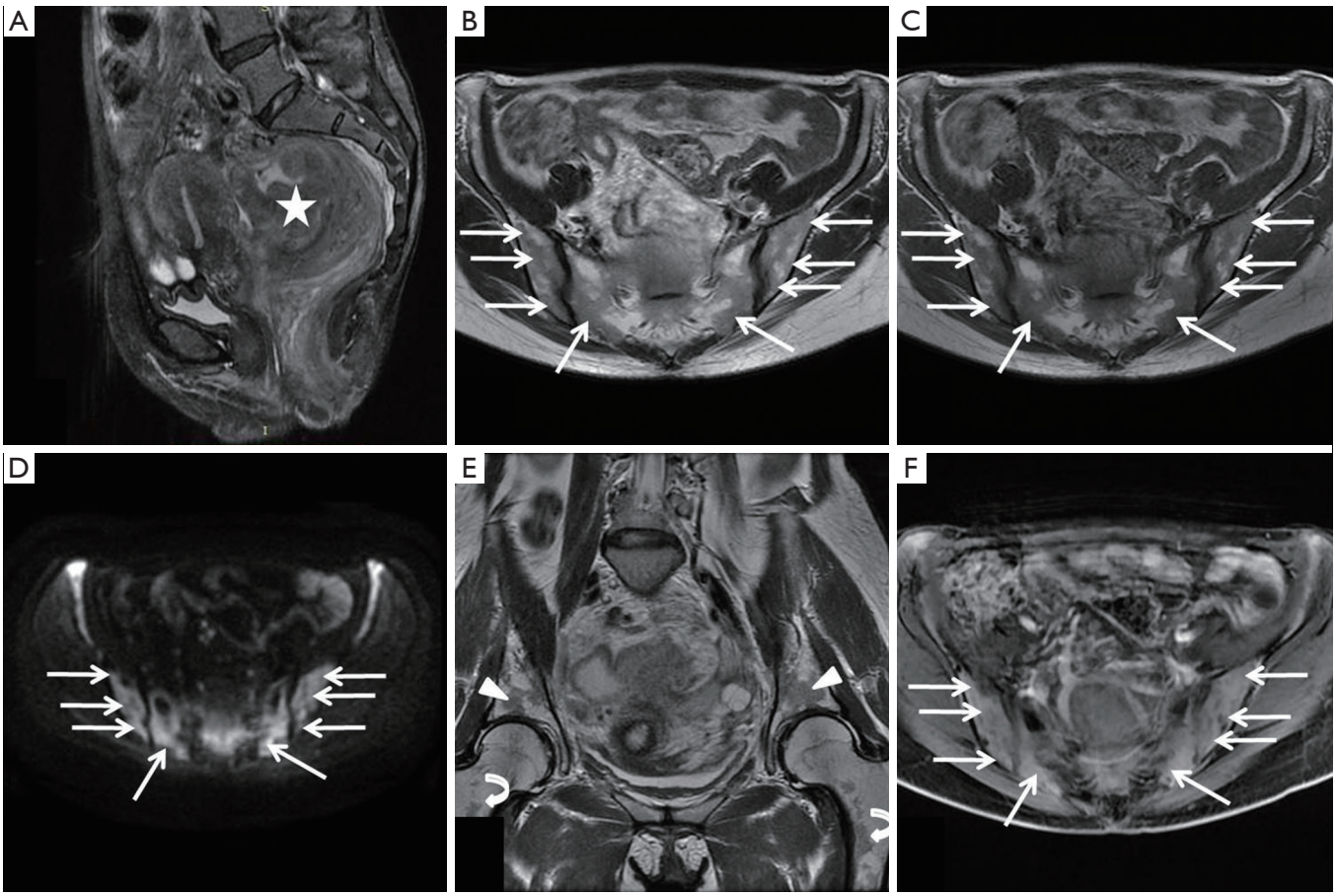

Figure 1 Pelvic MR images for a 45-year-old female patient with rectal cancer. (A) Sagittal T2-weighted MR image with fat saturation reveals a large primary tumour with slight heterogeneous hypointensity in the upper rectum (star); (B) axial T1-weighted MR image reveals diffuse multiple hypointensity lesions in the sacrum bone and bilateral ilium bone (arrows); (C) axial T2-weighted MR image reveals diffuse multiple hypointensity lesions in the sacrum bone and bilateral ilium bone (arrows); (D) axial diffusion-weighted MR image reveals diffuse hyperintensity lesions in the sacrum and bilateral ilia (arrows); (E) coronal T2-weighted MR image reveals multiple patchy hypointensity lesions in the bilateral iliac fossa bone (arrowheads) and upper femur (curved arrow); (F) axial contrast T1-weighted MR image reveals the lesions in the T1-weighted and T2-weighted images diffuse being enhanced in the sacrum bone and bilateral ilia (arrows).

staged as T4N2M1.

Consequently, colonoscopy examination was performed which indicated that the tumor was located about 6 cm away from the anus. Pathological examination of the tissue showed evidence of rectal adenocarcinoma. For further evaluation, whole body bone scintigraphy with ^{99}mTc-methylene diphosphonate (^{99}mTc-MDP) was performed on April 6th, and revealed abnormal radiotracer uptake in the pelvis, especially in sacroiliac joint, which suggested metastatic disease (*Figure 2*). In addition, ^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography/computed tomography (^{18}F-FDG PET/CT) was performed on April 11th, and revealed obvious ^{18}F-FDG uptake in the primary tumor with maximum standardized uptake value (SUVmax) of 14.69, while there were slight diffuse ^{18}F-FDG uptakes in the vertebras, sternum, sacrum, ilium, and femurs with a SUVmax of 2.816 (*Figure 3*). The ^{18}F-FDG PET/CT findings: (I) diffuse distribution in the vertebral body, sternum, sacrum, ilium and femurs; (II) slightly high uptake with lower SUVmax, contributed to the diagnosis of BMR. Ultimately, the diagnosis of BMR was histopathologically confirmed by a bone marrow biopsy of the ilium, which was performed on April 12th and revealed erythroid hyperplasia rather than

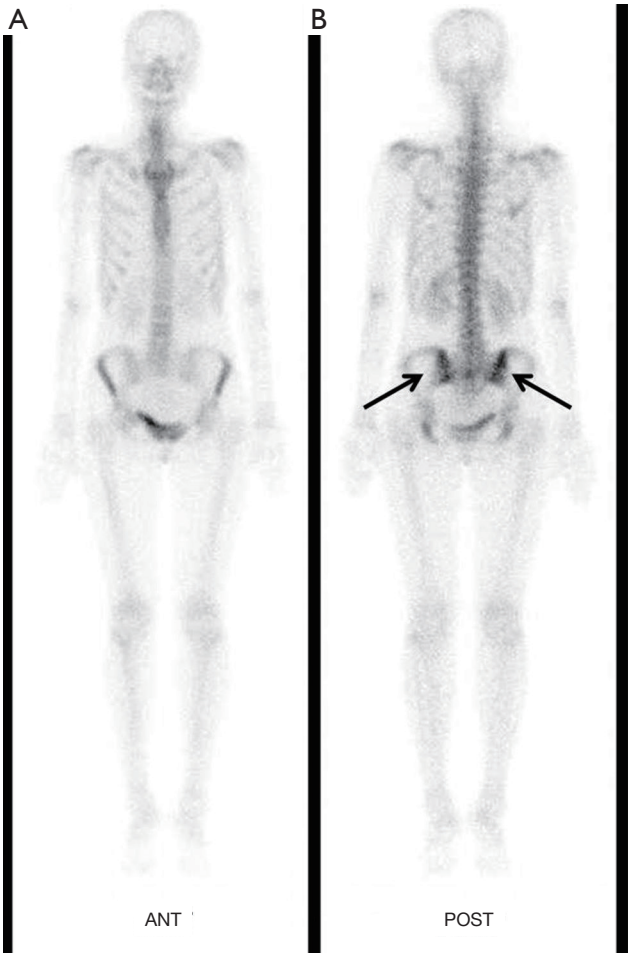

Figure 2 Whole body bone scintigraphy with ^{99}mTc-methylene diphosphonate (^{99}mTc-MDP) for the patient. Anterior (A) and posterior (B) image of bone scintigraphy reveals abnormal radiotracer uptake in the pelvis, especially in the sacroiliac joints (arrows), suspicious of bone metastases.

bone marrow metastasis.

Discussion

Generally, in a healthy person, the bone marrow undergoes conversion from hematopoietically active red marrow to hematopoietically inactive yellow marrow in a very orderly and predictable pattern (9). This conversion is from distal to proximal, from the appendicular to the axial skeleton and from the diaphyses of the long bones toward the metaphyses (9). Increased demand for hematopoiesis prompts reconversion from fatty marrow to active red marrow, and the reconversion process occurs in the exact reverse order: centripetally from the axial to the appendicular skeleton (2). BMR can be a consequence of both non-medical conditions (e.g., heavy smoking and intense oxygen-bearing sports) and medical conditions (e.g., obesity and related respiratory disorders, diabetes, chronic conditions related to anemia, treated with hematopoietic growth factors) (4). In our case, since the primary tumor in the upper rectum was relatively large, and the patient had a 2-year history of constipation and severe anemia, we deemed that rectal cancer had developed over the past 2 years. In addition, during the 2-year history of anemia, the patient did not receive medical treatment for anemia and she just took food supplements. In this report, we described the rectal cancer patient with pelvic MRI features mimicking pelvis metastases due to BMR, which was attributed to chronic anemia.

MRI is the most sensitive imaging modality that evaluates the bone marrow. The signal intensity depends on the relative amount of protein, water, fat, and cells within the marrow (10). Yellow marrow appears hyperintense on T1-weighted images, because it is composed of fatty elements, and it shows intermediate response to high signal intensity on T2-weighted images. It saturates similarly to subcutaneous fat on T2-weighted sequences with fat saturation and on STIR sequences. Red marrow demonstrates low/intermediate signal intensity on T1-weighted images, and it shows intermediate signal intensity on T2-weighted images, which can result in difficulty in distinguishing between red marrow and yellow marrow; it displays mild high signal intensity on STIR images.

Although MRI is an excellent noninvasive modality for evaluating bone marrow and detecting marrow lesions, it causes a dilemma when differentiating physiological marrow reconversion from suspicious pathologies. In patients with malignancies, it is occasionally difficult to differentiate BMR from bone metastasis. Sporadic literatures reported BMR located in vertebrae (5-8). For example, Okuda *et al.* reported the MRI of a patient with esophageal adenocarcinoma showed patchy signal changes in the thoracic vertebral body, which mimicked bone metastases on MR (5). Tanaka reported the MRI of a patient with esophageal carcinoma showed patchy signal changes in the lumbar vertebral body, which mimicked bone metastases (6). Yu and colleagues reported the MRI of a patient with prostate cancer showed patchy signal changes in the lumbar vertebral body, which mimicked bone metastases (7). In addition, several literatures reported BMR induced by granulocyte-colony stimulating factor (G-CSF) located in the lower extremities mimicking bone metastases on MRI (11,12). However, there

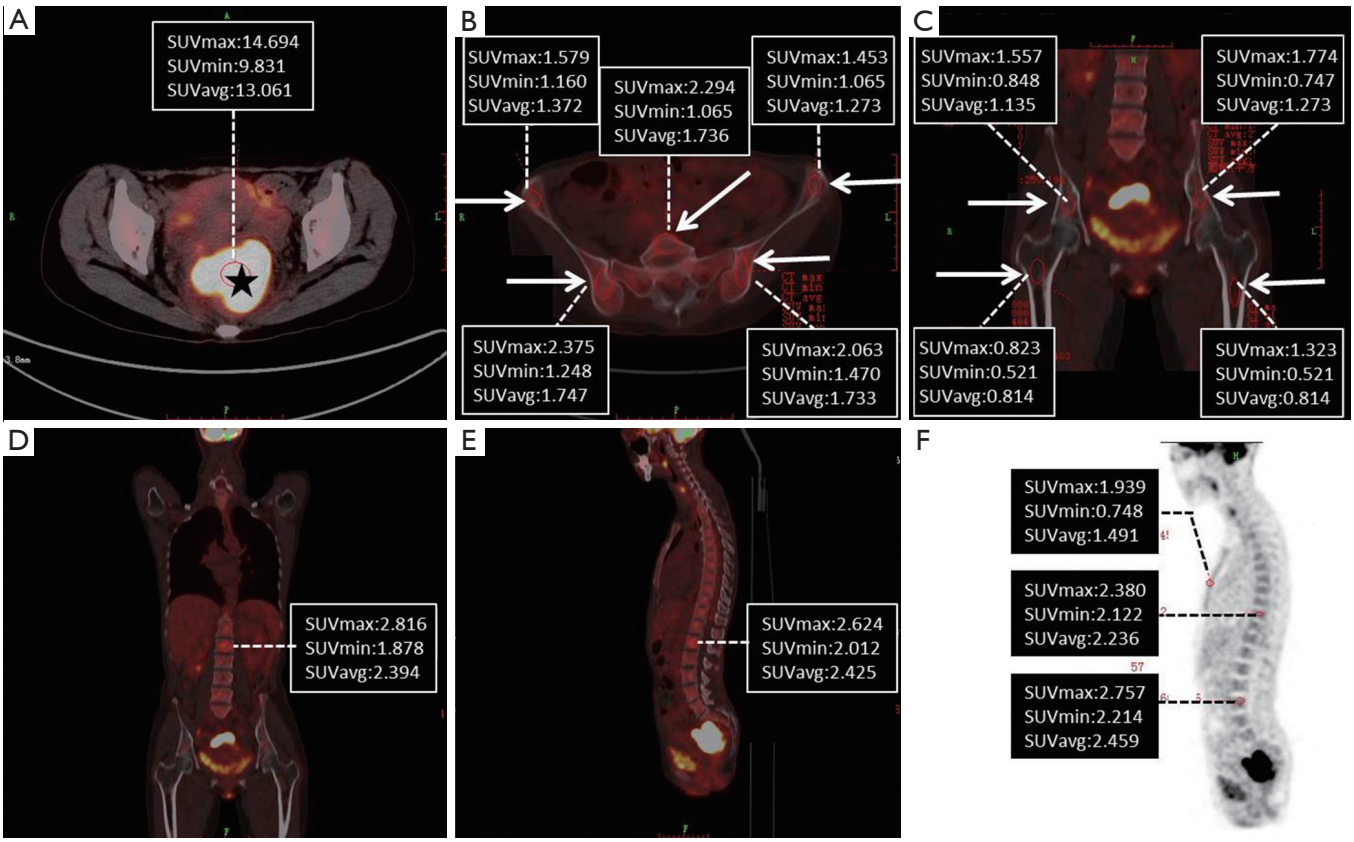

Figure 3 ^{18}F-FDG PET/CT fusion images for a 45-year-old female patient with rectal cancer. (A) Axial ^{18}F-FDG PET/CT fusion image demonstrates a primary tumour with high uptake with a SUVmax of 14.694 in the rectum (star); (B) axial ^{18}F-FDG PET/CT fusion image reveals multiple patchy slight uptake in the sacrum and bilateral ilia (arrows) with a SUVmax lower than 2.4; (C) coronal ^{18}F-FDG PET/CT fusion image reveals multiple patchy slight uptakes in the bilateral ilia and femurs (arrows) with a SUVmax lower than 1.8; (D) coronal ^{18}F-FDG PET/CT fusion image reveals multiple patchy slight uptakes in the vertebras; (E) sagittal ^{18}F-FDG PET/CT fusion image reveals multiple patchy slight uptakes in vertebras; (F) sagittal ^{18}F-FDG PET image reveals diffused slight uptakes in the vertebrae and sternum with a SUVmax lower than 2.8.

has been little literature reporting the BMR was diffusely located in pelvis. In our case, the MR images demonstrated a diffuse abnormal signal in the sacrum and bilateral ilia with hypointense signals on T1- and T2-weighted images, hyperintense signals on diffusion-weighted images and diffuse mild enhancement on fat-saturated T1-weighted images. It is often difficult to distinguish bone metastasis and BMR with conventional MRI. The MRI chemical shift technique assesses fatty infiltration, which suggests yellow bone marrow, and distinguishes between BMR and bone metastasis (5). However, MRI chemical shift techniques, for instance, the proton density fat fraction (PDFF) technique, is commonly used for hepatic MRI rather than pelvic MRI for clinical purposes.

A bone scan or bone scintigraphy can help diagnose the whole body. Bone scintigraphy is generally used clinically to evaluate a number of bone conditions, including cancer of the bone or metastasis, locate bone inflammation or fractures, as well as bone infections (13). The most common radiopharmaceutical for bone scintigraphy is ^{99}mTc with MDP, which adsorbs onto the crystalline hydroxyapatite mineral of the bone (13). In our case, the whole-body bone scintigraphy with ^{99}mTc-MDP revealed suspicious bone metastases in the pelvis. Therefore, whole body bone scintigraphy with ^{99}mTc-MDP could not differentiate the BMR from bone metastases. It is reported that imaging of ^{111}In-Cl_3 scintigraphy is effective when differentiating BMR from bone metastases (5,8). ^{111}In-Cl_3 scintigraphy is a

noninvasive technique to evaluate the anatomic extent of the erythropoietic element, because of its transportation in the plasma by transferrin and its suitable energy characteristics (5). However, ^{111}In-Cl_3 scintigraphy is not commonly used clinically, especially in developing countries.

PET/CT scanning, with the tracer ^{18}F-FDG, called ^{18}F-FDG PET/CT, is widely used in clinical oncology for diagnosis, staging, and monitoring of the treatment of cancers. However, several literatures have reported BMR that was confused with metastasis when using ^{18}F-FDG PET/CT (6,8). Meanwhile, a previous report evaluating imaging findings 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 as metastatic (14). In our case, the SUVmax of the vertebrae, sternum and pelvis were all lower than 3.6. Meanwhile, the symmetric distribution pattern of slight high uptakes in the vertebras, sternum, sacrum, ilia and femurs contributed to the correct diagnosis of BMR. In addition, the uptake of ^{18}F-FDG by tissues reveals the degree of glucose uptake, rather than the Hb level. Therefore, in our case, the anemia condition may not directly affect the SUVmax of the tissues.

In summary, we encountered a rectal cancer patient with BMR due to chronic anemia, and the pelvic MRI demonstrated bone marrow signal changes were related to reconversion from fatty to hematopoietic marrow, mimicking pelvic bone metastasis. Combined with the features of bone scintigraphy, we also could not rule out the possibility of pelvic metastasis. In our case, its ^{18}F-FDG PET/CT features were: (I) slight high uptake with lower than SUVmax of 3.6; (II) diffused distribution in the vertebras, sternum, sacrum, ilium and femurs. These features highly contributed to the diagnosis of BMR rather than bone metastasis. Therefore, radiologists and oncologists should be aware of the possible appearance of BMR mimicking bone metastasis on pelvic MR images to avoid misinterpretation and excessive treatment.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Informed Consent: Written informed consent was obtained from the patient for publication of this manuscript and any accompanying images.

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