Clinical Case Report

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Bone marrow necrosis secondary to metastatic adenocarcinoma revealed by ^{18}F-FDG PET/CT

A clinical case report

Ping Dong, MD, Rong Tian, MD, Lin Li, MD, Minggang Su, MD*

Abstract

Rationale: Bone marrow necrosis (BMN) is a rare malignancy-associated hematologic disorder characterized by necrosis of myeloid and stromal marrow elements with preservation of cortical bone.

Patient concerns: A 43-year-old female complaining of dizziness and vaginal bleeding for more than 2 months was presented to our department.

Diagnosis: Due to the laboratory test results, radiographic findings, especially ^{18}F-fluoro-2-deoxy-D-glucose (^{18}F-FDG) positron emission tomography/computed tomography (PET/CT) which revealed that bone marrow was characterized by diffuse ^{18}F-FDG uptake with extensive central photopenia, and pathologic results, she was diagnosed with metastatic adenocarcinoma accompanied with BMN. And the cancer most likely originated from reproductive system or breast.

Interventions: There was no effective interventions for her before knowing the accurate origin of adenocarcinoma.

Outcomes: Two weeks later, unfortunately, she died.

Lessons: ^{18}F-FDG PET/CT is a useful diagnostic modality in patients with BMN. Malignant tumor should always be considered in patients with extensive BMN, even in young people.

Abbreviations: ^{18}F-FDG = ^{18}F-fluoro-2-deoxy-D-glucose, BMN = bone marrow necrosis, CA-125 = cancer antigen 125, CA15–3 = carbohydrate antigen 15–3, CA19–9 = carbohydrate antigen 19–9, CA72–4 = carbohydrate antigen 72–4, CDX2 = caudal-type homeodomain transcription factor 2, CEA = carcino-embryonic antigen, CK7 = cytokeratin 7, CK20 = cytokeratin 20, CT = computed tomography, CUP = carcinoma of unknown primary, DIC = diffuse intravascular coagulation, MPO = myeloperoxidase, MRI = magnetic resonance imaging, NSE = neurone-specific enolase, PET/CT = positron emission tomography/computed tomography, SUV = standardized uptake value, TNF = tumor necrosis factor, TTF-1 = thyroid-transforming factor-1.

Keywords: ^{18}F-FDG PET/CT, bone marrow necrosis, metastatic adenocarcinoma

1. Introduction

Bone marrow necrosis (BMN) is disruption of the normal marrow architecture and necrosis of medullary stroma and myeloid tissue of the hematopoietic bone marrow.[1,2] BMN is most closely linked to malignancy (90%), among which hematological malignancy accounts for the most (60%).[2,3]^{18}F-fluoro-2-deoxy-D-glucose (^{18}F-FDG) positron emission tomography/computed tomography (PET/CT) is an useful diagnostic modality in patients with carcinoma of unknown primary (CUP).[4] Although presentation of BMN on ^{18}F-FDG PET/CT has been previously reported, a case characterized by diffuse bone marrow ^{18}F-FDG uptake with extensive central photopenia on ^{18}F-FDG PET/CT was very rare.[5,6]

2. Case report

A 43-year-old female was presented to our hospital, complaining of dizziness and vaginal bleeding for more than 2 months. Full blood count revealed anemia (red blood cell 2.24×10^{12}/L [4.3–5.8×10^{12}/L], hemoglobin 63 g/L [130–175 g/L]), and thrombocytopenia (platelet 14×10^{9}/L [100–300×10^{9}/L]). Coagulation studies showed increased D-dimer (38 mg/L [<0.55 mg/L]). Her blood biochemical studies revealed increased total bilirubin (56.3 μmol/L [5.0–28 μmol/L]), alanine aminotransferase (78 IU/L [<50 IU/L]), aspartate aminotransferase (55 IU/L [<40 IU/L]), alkaline phosphatase (1081 IU/L [140–420 IU/L]), glutamyl endopeptidase (207 IU/L [<60 IU/L]), lactate dehydrogenase (1787 IU/L [150–370 IU/L]), and hydroxybutyrate dehydrogenase (1202 IU/L [72–370 IU/L]), and decreased concentration of sodium (127.5 mmol/L [137–147 mmol/L]) and chloridion (87.2 mmol/L [99–110 mmol/L]). Hepatitis markers were negative. Her serum tumor markers including carcino-embryonic antigen (CEA), carbohydrate antigen 15–3 (CA15–3), carbohydrate antigen 19–9 (CA19–9), cancer antigen 125 (CA-125), carbohydrate antigen 72–4 (CA72–4), and neurone-specific enolase (NSE) were elevated 2 to 31-folds.

The brain magnetic resonance imaging (MRI), chest computed tomography (CT), pelvic ultrasonography, and histology post diagnostic dilation and curettage did not reveal clinical significant

Editor: Nagabhushan Seshadri.

The authors declare that there is no conflicts of interest.

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Medicine (2017) 96:49(e9067)

Received: 22 February 2017 / Received in final form: 10 November 2017 / Accepted: 13 November 2017

http://dx.doi.org/10.1097/MD.0000000000009067

findings. But extensive lymphadenopathies, sclerotic bone lesions (white arrow) on abdominal CT (Fig. 1A and B), and also diffuse foci on whole body bone scintigraphy (Fig. 1C and D) indicated metastatic disease from an unknown primary. ^{18}F-FDG PET/CT scanning was done to search for unknown primary tumor. The patient was administered ^{18}F-FDG (275 MBq, 5 MBq/kg body weight) and imaged for 2.5 minutes per bed after 1 hour ^{18}F-FDG injection on a Gemini 16 PET/CT scanner (Philips Healthcare, Netherlands). We used the body weight method for standardized uptake value (SUV) normalization. PET images revealed multiple lymphadenopathies (SUVmax 5.9; Fig. 1E) in bilateral neck, mediastinum, mesostenium, and retroperitoneum, and a left adrenal mass (SUVmax 5.0; Fig. 1E and F). Most importantly and interestingly, we found that the bone marrow was characterized by diffuse ^{18}F-FDG uptake (SUVmax 4.5) with extensive central photopenia (black arrow), especially in the vertebrae and proximal limbs. This phenomenon suggested metastases with central necrosis (Fig. 1E and G). There were just a few sclerotic lesions on CT component (Fig. 1H). ^{18}F-FDG PET/CT was unable to find out the primary cancer. Bone marrow biopsy from iliac crest revealed areas of coagulation necrosis (white arrow), phagocytic reaction, and scattered alien epithelial cells (black arrow) (Fig. 2A and B). Immumohistochemical staining showed positive for CEA (Fig. 2C) and cytokeratin 7 (CK7) (Fig. 2D) markers, and negative for myeloperoxidase (MPO), cytokeratin 20 (CK20), caudal-type homeodomain transcription factor 2 (CDX2), and thyroid-transforming factor-1 (TTF-1). The pathologic results were compatible with metastatic adenocarcinoma infiltration accompanied with BMN. The cancer most likely originated from reproductive system or breast. Two weeks later, she died of tumor.

This case report was approved by the Ethics Committee of West China Hospital of Sichuan University, Chengdu, China, and the written informed consent was obtained.

3. Discussion

Bone marrow necrosis is a rare but ominous finding in various malignancies, which is the most common underlying disorder of BMN, accounting for 90%, including leukemia, lymphoma, and metastatic carcinoma.[2,7,8] It is also associated with some benign diseases like infections, sickle-cell anemia, hyperparathyroidism, anorexia, antiphospholipids, hemolytic uraemic syndromes, and diffuse intravascular coagulation (DIC).[2,9–11] BMN due to certain pharmaceutical agents such as imatinib, rituximab, and fludarabine have also been reported.[5,12–15] The mechanism of BMN involves various pathologic conditions, such as microcirculation failure, inflammatory and tumor cell infiltration in bone marrow, side-effect of chemotherapy and radiotherapy, aberrant cytokine, especially tumor necrosis factor (TNF), and so on.[2,16–21] Although the mechanism leading to BMN with certain pharmaceutical agents therapy is not yet clear, the increased rate of prothrombotic cellular material release and increased rate of apoptosis have been believed to be responsible.[22] In our case, the mechanism of BMN may be tumor cell involvement in marrow microvasculature and aberrant cytokine production, such as TNF.

Without specific clinical symptoms, necrotic cells and intact cortical bone are the pathological findings for BMN.[2,17,23] However, the initial consideration of this disease usually comes from various imaging modalities. MRI has been the mainstay for diagnosis of bone marrow disease. The typical MRI appearance of BMN is characteristically diffuse, geographic pattern of signal abnormality with central area of variable signal intensity surrounded by a distinct peripheral enhancing rim.[24] To the best of our knowledge, studies using PET modality to evaluate this disease is relatively uncommon. Since the combination of PET and CT, ^{18}F-FDG PET/CT has emerged as a promising new imaging modality which reflects both morphological and glucose metabolic features of malignant disease.[25] Several studies have already reported the utility of PET/CT for bone marrow assessment detecting any alteration in malignant.[4,5] But bone marrow ^{18}F-FDG uptake in these cases was limited. The notable feature in our case was the characteristic ^{18}F-FDG PET/CT findings of diffuse bone marrow ^{18}F-FDG uptake with extensive central photopenia. These findings were confirmed by bone marrow biopsy, which may alter treatment options. Therefore, BMN was thought to be secondary to metastatic adenocarcinoma. So for, there is no report

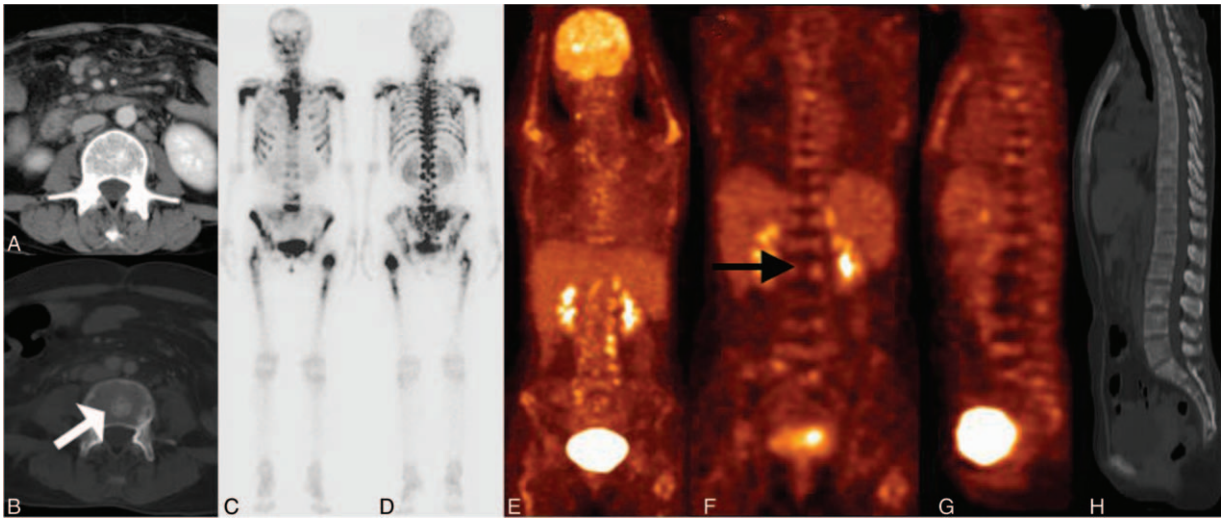

Figure 1. (A–D) Multiple lymphadenopathies, sclerotic bone lesions (white arrow) on abdominal CT, and also diffuse osteoblastic foci on whole body bone scintigraphy. (E, F) ^{18}F-FDG PET/CT revealing multiple lymphadenopathies (SUVmax 5.9) in bilateral neck, mediastinum, mesostenium, and retroperitoneum, and a left adrenal mass (SUVmax 5.0). (E, G) Bone marrow with diffuse ^{18}F-FDG uptake and extensive central photopenia (black arrow) (SUVmax 4.5), especially in the vertebrae and proximal limbs. (H) CT scan showing a few sclerotic lesions. ^{18}F-FDG PET/CT = ^{18}F-fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography, CT = computed tomography.

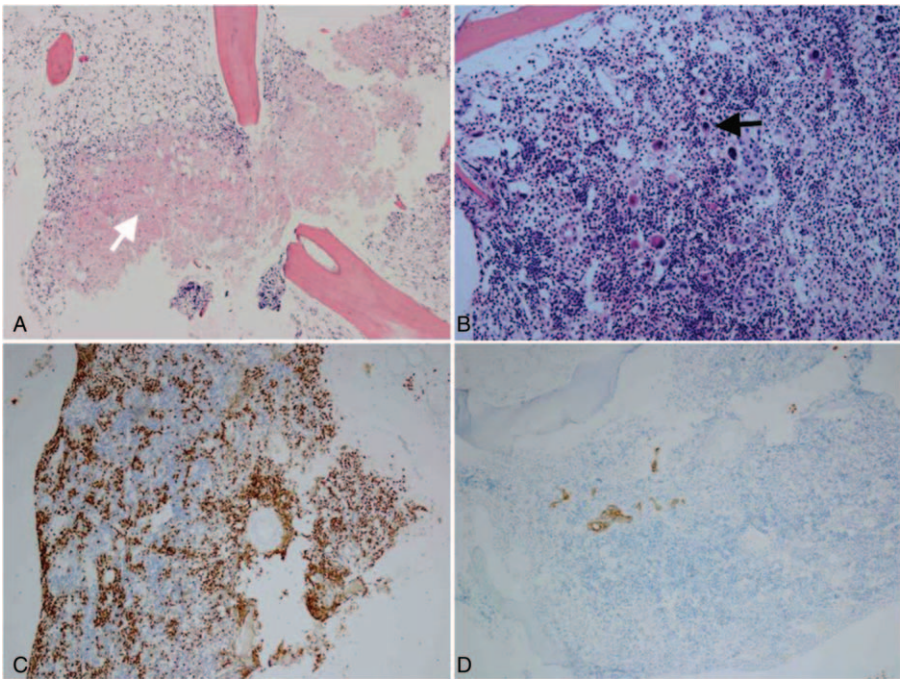

Figure 2. (A, B) Hematoxylin-eosin staining showing areas of coagulation necrosis (white arrow), phagocytic reaction, and scattered alien epithelial cells (black arrow) (100× and 200× magnification, respectively). (C, D) Immumohistochemical staining revealing positive markers CEA and CK7 (100× magnification). CEA = carcino-embryonic antigen, CK7 = cytokeratin 7.

of prognosis in the bone marrow necrosis using ^{18}F-FDG PET/CT. But we speculated that the more extensive BMN, the worse the prognosis may be.

In cases of BMN, kyphoplasty or vertebroplasty might be preferred for pain control instead of radical excision and instrumentation.[5] The prognosis associated with BMN seems to be dependent on the underlying primary clinical condition regardless of the degree of necrosis observed.[2,3]

4. Conclusions

In conclusion, we have described the unusual ^{18}F-FDG PET/CT image with severe extensive BMN caused by metastatic adenocarcinoma. Also, ^{18}F-FDG PET/CT is an useful diagnostic modality in patients with BMN, which can evaluate the involvement of bone marrow and guide the biopsy site. Malignant tumor should always be considered in patients with extensive BMN, even in young people.

Acknowledgments

The authors thank the Sichuan Provincial Department of Science and Technology (2015SZ0128) for the support.

References

[1] Najmaddin SHK, Hisham AA-R, Beston FN. Precursor T-cell acute lymphoblastic leukemia presenting with bone marrow necrosis: a case report. J Med Case Rep 2012;6:349.
[2] Janssens AM, Offner FC, Van Hove WZ. Bone marrow necrosis. Cancer 2000;88:1769–80.
[3] Macfarlane SD, Tauro GP. Acute lymphocytic leukemia in children presenting with bone marrow necrosis. Am J Hematol 1986;22:341–6.
[4] Han A, Xue J, Hu M, et al. Clinical value of 18F-FDG PET-CT in detecting primary tumor for patients with carcinoma of unknown primary. Cancer Epidemiol 2012;36:470–5.
[5] Aras Y, Akcakaya MO, Unal SN, et al. Bone marrow necrosis secondary to imatinib usage, mimicking spinal metastasis on magnetic resonance imaging and FDG-PET/CT. J Neurosurg Spine 2012;16:57–60.
[6] Gaetano P, Georg S, Marco P, et al. Bone marrow involvement in unknown acute myeloid leukemia detected by 18F-FDG PET/MRI. Clin Nucl Med 2015;40:486–7.
[7] Wang YC, Chang PY, Yao NS. Bone marrow necrosis caused by metastatic colon cancer. J Clin Oncol 2009;27:48.
[8] Bhasin TS. A case of bone marrow necrosis of an idiopathic aetiology: the report of a rare entity with review of the literature. J Clin Diagn Res 2013;7:525–8.
[9] Ataga KI, Orringer EP. Bone marrow necrosis in sickle cell disease: a description of three cases and a review of the literature. Am J Med Sci 2000;320:342–7.
[10] Lee YH, Hong YC, Yang CF, et al. Severe extensive bone marrow necrosis from miliary tuberculosis without granulomas and pulmonary presentations. J Chin Med Assoc 2010;73:208–11.
[11] Paydas S, Kocak R, Zorludemir S, et al. Bone marrow necrosis in antiphospholipid syndrome. J Clin Pathol 1997;50:261–2.
[12] Tamura T, Tasaka T, Fujimoto M, et al. Massive bone marrow necrosis in a patient with chronic myelocytic leukemia following imatinib mesylate therapy. Haematologica 2004;89:32.
[13] Rossi D, Ramponi A, Franceschetti S, et al. Bone marrow necrosis complicating post-transplant lymphoproliferative disorder: resolution with rituximab. Leuk Res 2008;32:829–34.
[14] Ramamoorthy SK, Marangolo M, Durrant E, et al. Unusual reaction to Rituximab with intra-vascular hemolysis, rhabdomyolysis, renal failure and bone marrow necrosis. Leuk Lymphoma 2006;47:747–50.
[15] Aboulafia DM, Demirer T. Fatal bone marrow necrosis following fludarabine administration in a patient with indolent lymphoma. Leuk Lymphoma 1995;19:181–4.
[16] Paydas S, Ergin M, Baslamisli F, et al. Bone marrow necrosis: clinicopathologic analysis of 20 cases and review of the literature. Am J Hematol 2002;70:300–5.
[17] Bernard C, Sick H, Boilletot A, et al. Bone marrow necrosis: acute microcirculation failure in myelomonocytic leukemia. Arch Intern Med 1978;138:1567–9.
[18] Osuorji I, Goldman L. G-CSF-associated bone marrow necrosis in AML after induction chemotherapy. Case Rep Hematol 2012;2012:314–278.

[19] Brown CH. Bone marrow necrosis: a study of seventy cases. Johns Hopkins Med J 1972;131:189–203.
[20] Knupp C, Pekala PH, Cornelius P. Extensive bone marrow necrosis in patients with cancer and tumor necrosis factor activity in plasma. Am J Hematol 1988;29:215–21.
[21] Terheggen HG, Lampert F. Acute bone marrow necrosis caused by streptococcal infection. Eur J Pediatr 1979;130:53–8.
[22] Burton C, Azzi A, Kerridge I. Adverse events after imatinib mesylate therapy. N Engl J Med 2002;346:712–3.
[23] Libicher M, Appelt A, Berger I, et al. The intravertebral vacuum phenomen as specific sign of osteonecrosis in vertebral compression fractures: results from a radiological and histological study. Eur Radiol 2007;17:2248–52.
[24] Tang YM, Jeavons S, Stuckey S, et al. MRI features of bone marrow necrosis. AJR Am J Roentgenol 2007;188:509–14.
[25] Sohn MH, Jeong HJ, Lim ST, et al. F-18 FDG uptake in osteonecrosis mimicking bone metastasis on PET/CT images. Clin Nucl Med 2007;32:496–7.