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## CASE REPORT

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# Fluorodeoxyglucose-Positron Emission Tomography–Computed Tomography Features of Atypical Femoral Lesions in Patients Prescribed Bone-modifying Agents: Two Case Reports

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## INTRODUCTION

Atypical femoral fracture (AFF) has been reported in patients prescribed high-dose bisphosphonates or denosumab. Although metastatic bone lesions and pre-fracture AFF lesions are evidenced by abnormal uptake in technetium-99m methylene diphosphonate scintigraphy, pre-fracture AFF lesions are non-fluorodeoxyglucose (FDG)-avid. This is the first report of two cases in which pre-AFF lesions were missed on FDG (positron emission tomography–computed tomography [PET-CT] performed routinely for monitoring of tumour progress). Careful multiplanar reformation (MPR) scrutiny of CT images on FDG-PET-CT might reveal the beaking typical of a pre-AFF lesion in the proximal femur, and thus offer a chance for timely plain radiograph confirmation and consideration of prophylactic fixation based on full assessment of clinical and imaging findings.

left AFF after a fall on level ground. 9 years before this, the patient was diagnosed with carcinoma of the breast, which was treated with mastectomy and chemotherapy. 3 years later, the patient was started on zoledronic acid, initially 4 mg every 3 weeks for 18 months, and then 4 mg every 3 months, continuing to the present (>6 years of zoledronic acid treatment). A retrospective review of an FDG-PET-CT performed 20 months prior to the fall revealed no FDG-avid lesion in either proximal femur. However, MPR of the FDG-PET-CT images showed evidence of lateral cortical beaking at the left proximal femur, corresponding to the site of the subsequent AFF (Figures 1 to 3). The fracture was surgically treated with cephalomedullary nail fixation, and withdrawal of the bone-modifying agent (BMA) / bone-targeted agent (BTA). Histopathology results of bone biopsy were negative for malignant cells.

## CASE REPORTS

### Case 1

In April 2020, a 62-year-old woman presented with a

### Case 2

In October 2018, a 61-year-old woman presented with right hip pain. 6 years before this, the patient was

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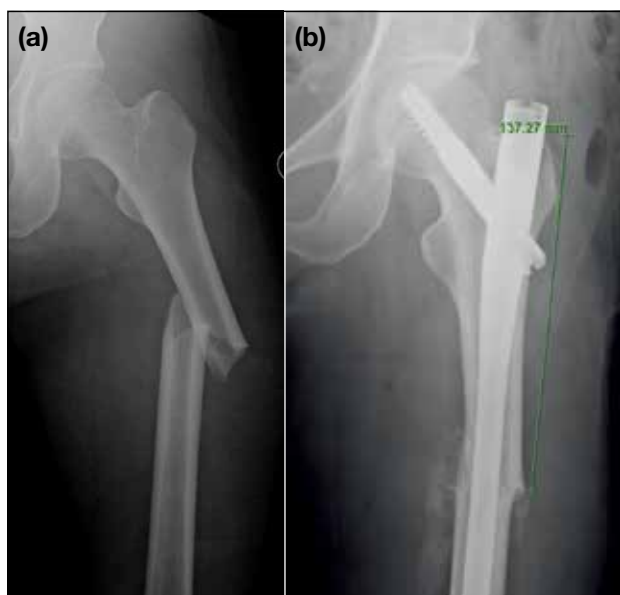
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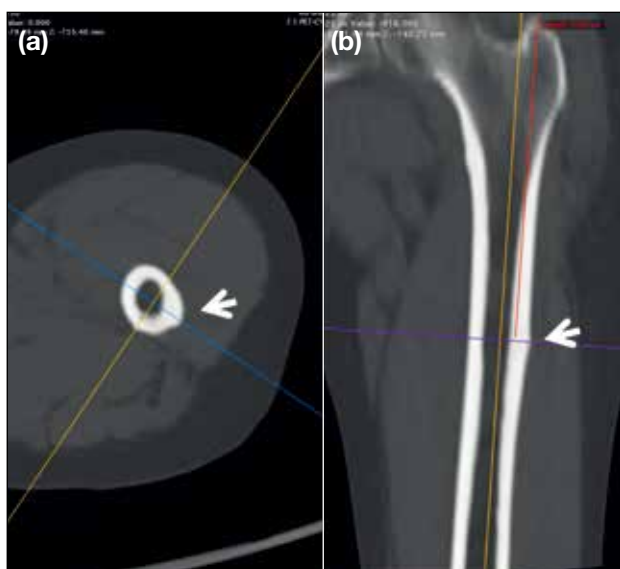
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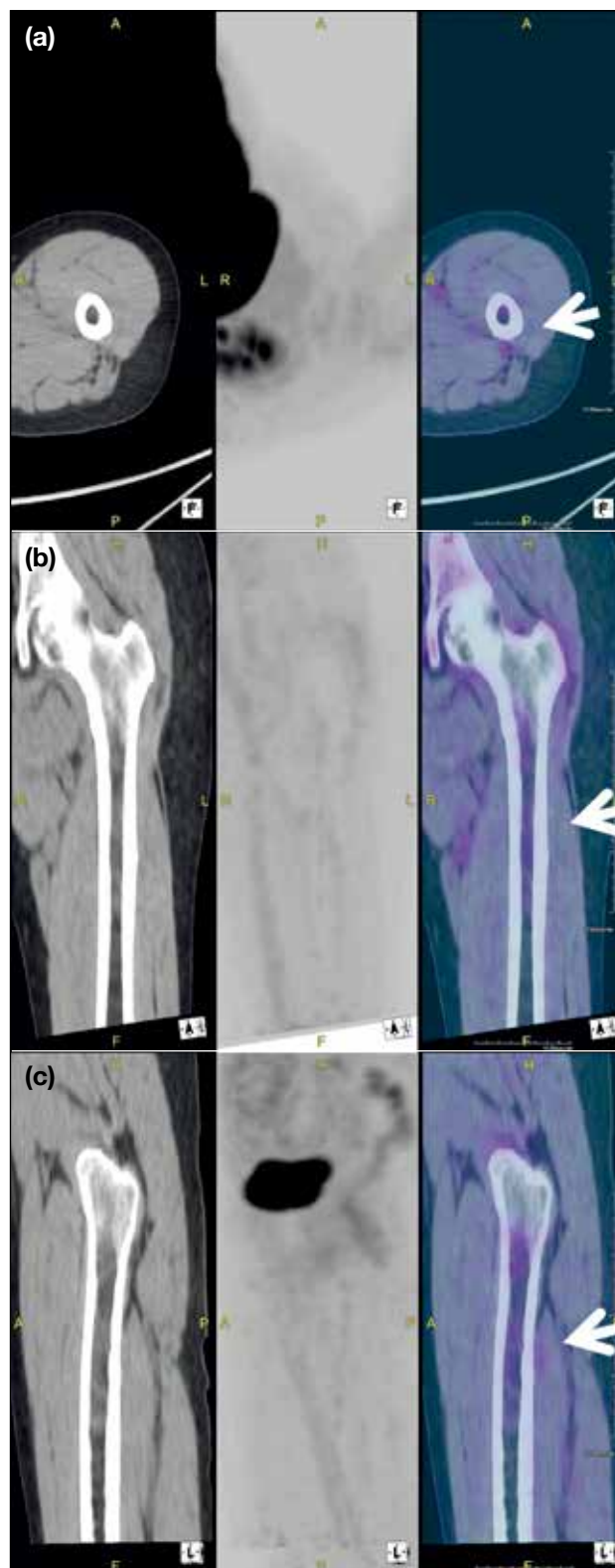


**Figure 1.** Case 1. A 62-year-old woman presenting with left atypical femoral fracture after a fall on level ground. Plain radiographs show fracture (a) before and (b) after fixation.



**Figure 2.** Same patient. Positron emission tomography-computed tomography images taken 2 years before fracture. Multiplanar reformation (a) axial and (b) coronal views showing lateral cortical beaking (arrows) at the level of the fracture shown in Figure 1b.

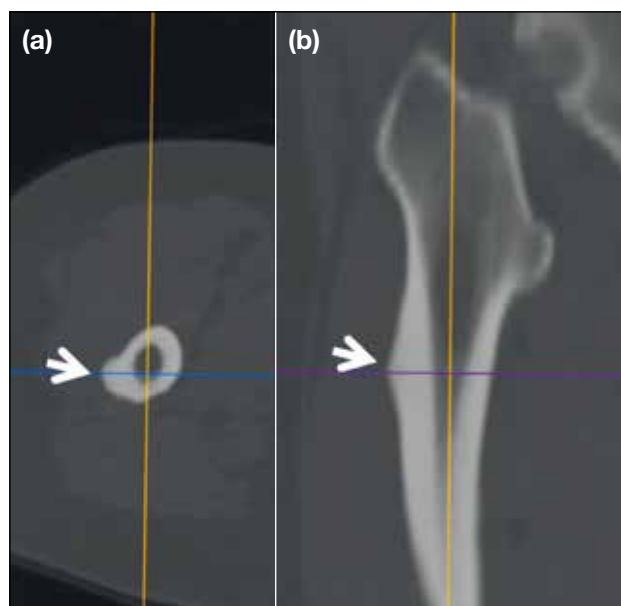
diagnosed with carcinoma of the breast, which was treated with mastectomy and chemotherapy. 1 year later, the patient was started on high-dose denosumab



**Figure 3.** Same patient. Magnified co-registered positron emission tomography-computed tomography images in (a) axial, (b) coronal, and (c) sagittal views showing non-fluorodeoxyglucose-avidity at the corresponding site.



**Figure 4.** Case 2. A 61-year-old woman presenting with right hip pain. Plain radiographs show (a) right femoral beaking; (b) completed atypical femoral fractures a few days later; and (c) after fixation.



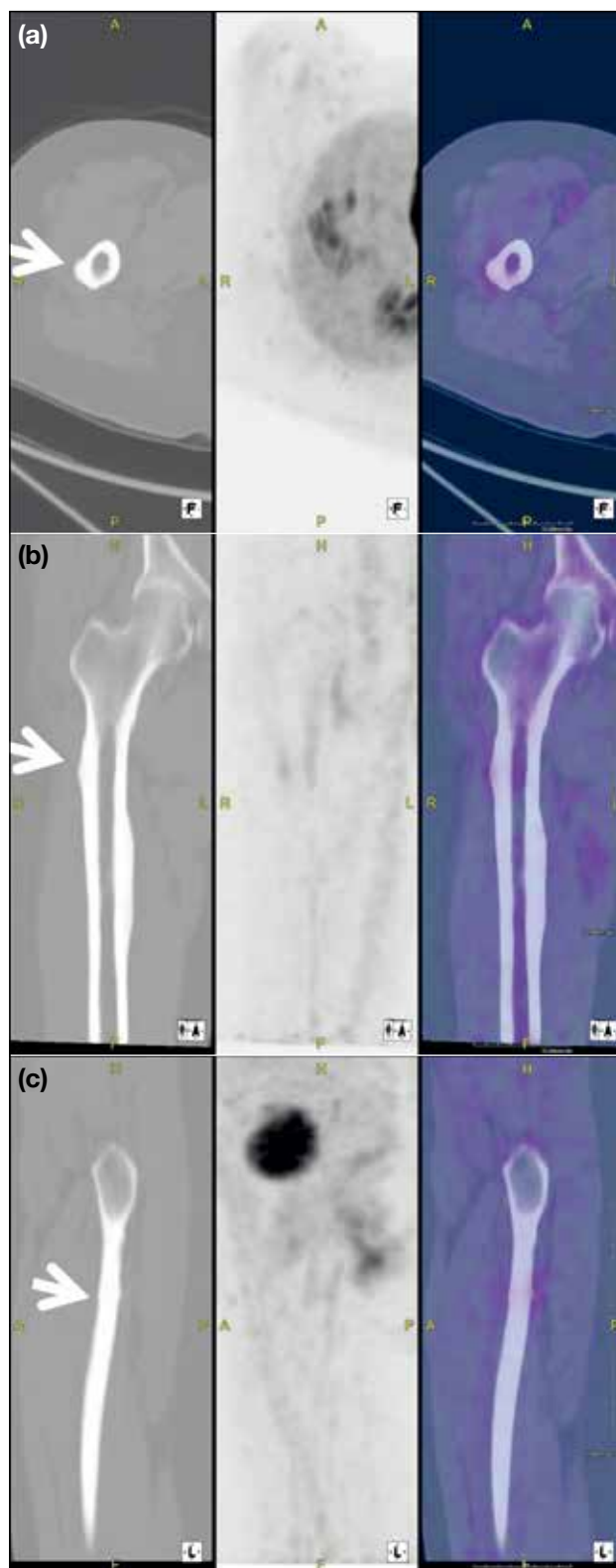
**Figure 5.** Same patient. Positron emission tomography-computed tomography images taken 3 months before fracture. Multiplanar reformation (a) axial and (b) coronal views showing subtrochanteric lateral cortical beaking (arrows) corresponding to the fracture shown in Figure 4c.

(120 mg every 4 weeks), continuing to the present (>5 y of denosumab therapy). Plain radiograph revealed lateral cortical beaking in the proximal femur. A few days

later, she sustained a complete subtrochanteric fracture of the right femur after trivial injury. Retrospective review of the FDG-PET-CT done 3 months prior to the fracture revealed no FDG-avid lesion in either proximal femur, but MPR of the CT images showed evidence of lateral cortical beaking at the right proximal femur (Figures 4 to 6). The fracture was surgically treated with cephalomedullary nail fixation, and withdrawal of the BMA / BTA. Histopathology results of bone biopsy were negative for malignant cells.

## DISCUSSION

AFF is a serious complication of BMAs or BTAs used in the treatment of bone metastases from breast, prostate and other solid malignancies. Osteoclast inhibitors, bisphosphonates and denosumab are powerful BMAs. The incidence of AFF beaking in patients prescribed BMAs has been reported at 12.5% and frank fracture at 7.8%.<sup>1</sup> A recent search of the literature revealed no reports of pre-fracture AFF lesions detected on PET-CT. Takahashi et al<sup>2</sup> mentioned that PET-CT revealed no abnormal uptake although radiographs showed cortical thickening in one of the cases reported, indicating that these pre-fracture AFF lesions might not be FDG-avid. This is the first report that pre-fracture AFF lesions, such as lateral cortical beaking in the femur, can be identified on MPR of PET-CT images.



**Figure 6.** Same patient. Magnified co-registered positron emission tomography–computed tomography images in (a) axial, (b) coronal, and (c) sagittal views showing non-fluorodeoxyglucose-avidity at the corresponding site.

Because PET-CT is regularly used to monitor disease progress in patients prescribed BMAs/BTAs, radiologists should be specifically alerted to their drug history. This should prompt more detailed MPR study of proximal femur CT images to look for the presence of cortical thickening despite the potential absence of FDG-avid lesions.

Radiologically, the earliest suggestion of AFF is a localised lesion with increased thickness of the lateral cortex described as “beaking”. As it progresses, a “dreaded black line” may be seen at the most prominent part of the beak. These radiological features of pre-fracture AFF can be confirmed on timely plain radiograph of the femur and serve as warning signs of an impending AFF. Although different surgeons may have different thresholds for prophylactic fixation, this early finding may alert the clinician to the need for further clinical and imaging assessment of the suspicious lesion.<sup>3</sup> Prophylactic fixation of pre-fracture AFF is highly effective in preventing the agony and complications of a complete AFF.<sup>4</sup> Treatment of completed AFF is more technically demanding and associated with a high risk of delayed union, non-union and implant failures.<sup>5</sup>

Pre-fracture AFF is not evidenced as abnormal uptake in FDG scan but may be detected on detailed MPR scrutiny of CT images. The referring clinician should alert the radiologist of a patient’s drug history in order to make best use of PET-CT for disease progress monitoring.

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