

Case Report

⁶⁸Ga-DOTATATE positron emission tomography/computed tomography to detect the recurrence of phosphaturic mesenchymal tumor-induced osteomalacia

ABSTRACT

⁶⁸Ga-DOTATATE positron emission tomography/computed tomography (PET/CT) has shown superiority over ¹¹¹Indium-octreotide scanning for the detection of phosphaturic mesenchymal tumors (PMTs). We report a case of tumor-induced osteomalacia resulting from PMT which, although initially clinically suspected, was not localized on octreotide scintigraphy performed several years prior. Subsequent surgical excision of a presumed benign osseous lesion a few years later revealed the diagnosis on pathology. Imaging assessment using ⁶⁸Ga-DOTATATE PET/CT following recent clinical suspicion for recurrence revealed an intense tracer-avid lesion at the primary tumor site. DOTATATE imaging plays an important role in localizing tumors with high somatostatin receptor expression, such as neuroendocrine tumors (pheochromocytoma, paraganglioma, and neuroblastoma), meningioma, and mesenchymal tumors, causing oncogenic osteomalacia.

Keywords: ⁶⁸Ga-DOTATATE, phosphaturic mesenchymal tumor, positron emission tomography, somatostatin receptors, tumor-induced osteomalacia

INTRODUCTION

Phosphaturic mesenchymal tumors (PMTs) are very rare tumors, but frequently result in a paraneoplastic syndrome called tumor-induced osteomalacia (TIO).^[1] Tumor cells overproduce fibroblast growth factor 23 (FGF23), which is ultimately responsible for metabolic changes leading to osteomalacia. Patients often present with nonspecific bone pain, gradual-onset muscle weakness, and pathologic fractures. PMTs are usually very small and highly variable in location. The most useful imaging modalities to localize PMTs utilize their expression of somatostatin receptors (SSTRs) 1–5, including octreotide scintigraphy and more recently ⁶⁸Ga-DOTATATE positron emission tomography/computed tomography (PET/CT). ⁶⁸Ga-DOTATATE allows vastly improved spatial resolution and precise tumor localization with PET/CT and has relatively high sensitivity and specificity. Imaging is indicated in patients presenting with TIO or patients with suspected PMT recurrence. The purpose of this case report is

to emphasize the advantage of ⁶⁸Ga-DOTATATE PET/CT over octreotide scintigraphy in localizing PMTs.

CASE REPORT

An elderly male initially presented with bilateral tibial pain 14 years ago. Leg radiographs were negative, but a bone scan was positive for bilateral tibial stress fractures, and bone densitometry revealed diffuse osteopenia. He was found to have hypophosphatemia (1.9 mg/dl; normal 2.5–4.5) and phosphaturia (urine phosphate 1490 mg/24 h; normal

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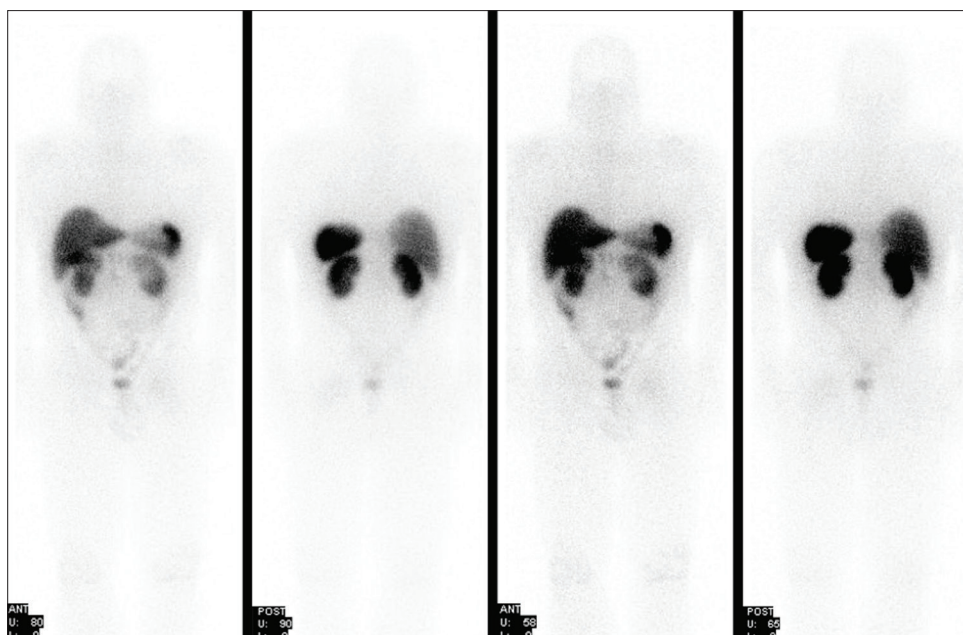


Figure 1: Coronal maximum intensity projection images of the initial octreotide scan. No abnormal octreotide uptake was seen

300–1300). In order to evaluate TIO, an ¹¹¹Indium-octreotide scan was performed 2 years later but returned negative [Figure 1]. FGF23 levels were not measured during the patient’s initial workup. Subsequently, he suffered nontraumatic rib-and-foot fractures. An unenhanced magnetic resonance imaging (MRI) performed for the left hip pain 7 years ago presumed benign fibro-osseous lesion versus enchondroma in the left ischium [Figure 2]. Following surgery for left Cam-type femoroacetabular impingement, he had a femur neck fracture that was instrumented. CT and contrast-enhanced MRI performed for persistent left ischial pain were concerning for chondroid neoplasm [Figure 3]. Incisional biopsy performed 6 years ago revealed mesenchymal tumor, mixed connective tissue type, probably PMT. Hypophosphatemia gradually resolved following surgery, until recently, when serum phosphorus level dropped to 2.3 mg/dl (normal 2.5–4.5 mg/dL). ⁶⁸Ga-DOTATATE PET/CT scan revealed radiotracer uptake in the left ischium suggesting the recurrence of PMT, the initial cause for TIO in this patient [Figure 4].

DISCUSSION

We describe a case of recurrent PMT-related TIO which showed focal uptake on ⁶⁸Ga-DOTATATE PET/CT, but the initial tumor occurred prior to Food and Drug Administration approval of DOTATATE scan and was not localized by octreotide scintigraphy.

While a few hundred cases of TIO have been reported, its true prevalence is unknown. The overexpressed FGF23

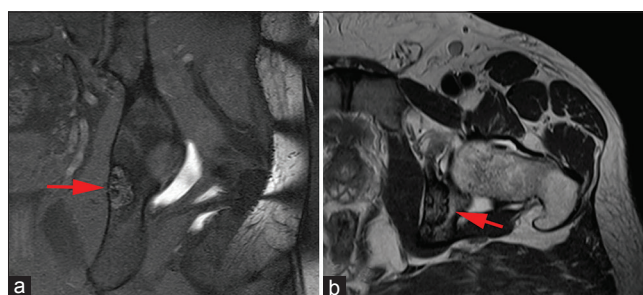


Figure 2: Coronal short tau inversion recovery (a) and axial T2 images (b) of magnetic resonance imaging through left ischium demonstrating slight short tau inversion recovery hyperintense lesion (red arrow)

by mesenchymal tumors is produced by osteogenic cells, osteoblasts, and osteocytes.^[2] FGF23 inhibits renal 1 α -hydroxylation of 25-hydroxyvitamin D, reducing renal phosphate reabsorption and resulting in renal phosphate wasting, osteoblast downregulation, and mobilization of calcium and phosphate from bones.^[2] The mixed connective tissue variant of PMT is the most common subtype and typically benign; however, malignant variants have been described. Patients present with progressive nonspecific symptoms and multiple fractures, often for many years before being diagnosed.^[3]

The tumor can be located anywhere in the body, involving any soft tissue or bone, and its size is usually very small. This makes tumor localization in the body extremely difficult. Any imaging examination performed to localize a PMT needs to cover the entire body, from head to toe. Conventional imaging, including radiographs, CT, and MRI, reveal osteomalacia but rarely localize mesenchymal tumor, as does the bone scintigraphy.^[4]

¹¹¹Indium-octreotide has a high affinity for the somatostatin subtype 2 and 5 receptors, and therefore ¹¹¹Indium-octreotide scintigraphy, combined with single-photon emission CT, can be a valuable modality.^[5] The sensitivity and specificity for this examination, however, are only 36.3% and 80%, respectively.^[6] Fluorodeoxyglucose (FDG)-PET/CT is very sensitive but nonspecific, as increased metabolic uptake related to active fracture healing may also demonstrate increased tracer uptake.^[6]

DOTATATE has a relatively higher affinity for SSTR2 than SSTR5. Immunohistochemical studies have shown that

PMT in TIO demonstrates strong diffuse positive staining for SSTR2A.^[7] Like the octreotide, ⁶⁸Ga-DOTATATE (which uses octreotate instead of octreotide) is an SSTR antagonist which is internalized upon receptor binding.^[8] As a result, there is accumulation of radioactivity within the tumor cells. ⁶⁸Ga being a positron emitter, a type of beta decay, provides greater resolution compared to ¹¹¹Indium, which is a gamma-ray emitter. This high SSTR2 affinity and positron-emitting property of ⁶⁸Ga-DOTATATE provide relatively better sensitivity and specificity in localizing PMTs. In addition, ⁶⁸Ga-DOTATATE PET/CT imaging has a shorter acquisition time as well as a shorter half-life (68 min compared to 2.8 days for ¹¹¹In) and therefore lower radiation exposure.^[9] Sensitivity and specificity of ⁶⁸Ga-DOTATATE have been shown to be 83.3%–100% and 100%, respectively, as compared to 50% for FDG-PET/CT.^[10]

Differential diagnosis for TIO includes renal Fanconi syndrome and heavy metal poisoning. Normal levels of FGF23 can confirm the diagnosis. Treatment relies on complete tumor excision, which is almost always curative and results in rapid resolution of symptoms. However, cases of recurrence and metastases have been reported. Diagnosis is assisted by measuring serum and urine phosphate and FGF23 levels and may suggest TIO, but PMT localization often presents its own challenges.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published

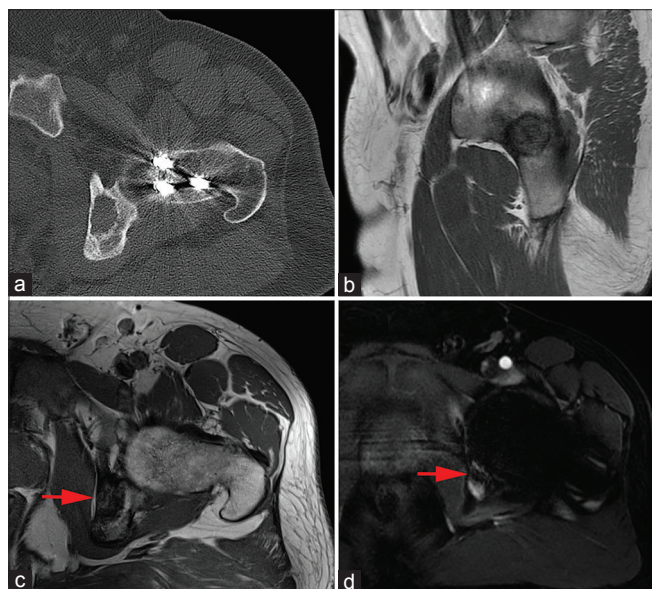


Figure 3: Preincisional biopsy imaging examinations. Axial computed tomography image (a) showing osteolytic lesion in the left ischium with internal matrix small calcifications and disruption of medial cortex. Sagittal T1 (b) and axial T1 (c) magnetic resonance imaging images showing left ischial-enhancing T1 hypointense lesion (orange arrow) (d). Metal-related artifacts on computed tomography and magnetic resonance are noted from left femur neck instrumentation

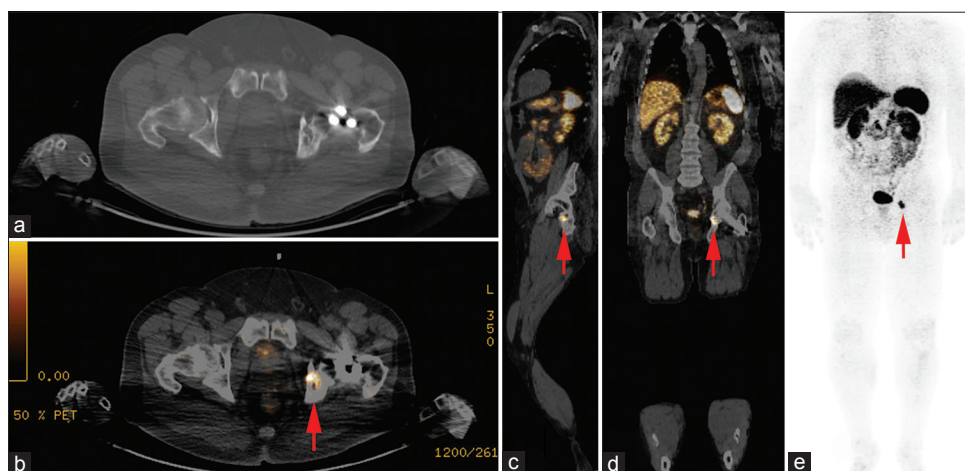


Figure 4: Most recent ⁶⁸Ga-DOTATATE positron emission tomography/computed tomography. Anatomic axial computed tomography image (a) showing mixed lytic and sclerotic focus in the left ischium (orange arrow) that shows corresponding focal increased uptake on the fused positron emission tomography images (b-d) and maximum intensity projection image (e)

and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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