J of Nuclear Medicine Technology, first published online February 23, 2022 as doi:10.2967/jnmt.121.263776

False positive ^{68}Ga-DOTATATE PET-CT in Hereditary hypophosphatemic-osteomalacia mimicking culprit lesions of tumor induced osteomalacia

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Running Title: False positive ^{68}Ga-DOTATATE PET-CT mimicking TIO

Key Words: ^{68}Ga-DOTATATE PET-CT, hypophosphatemia-osteomalacia, Tumor induced osteomalacia (TIO), MRI

Abstract:

The ^{68}Ga-DOTATATE PET-CT is an important imaging modality for detection of culprit lesion of tumor induced osteomalacia (TIO) in clinically symptomatic patient of hypophosphatemia-osteomalacia. Somatostatin receptor (SSTR) expression, may at times be observed in inflammatory/granulomatous conditions and fractures/degenerative bone disease leading to false positive scans finding. A rare case of hereditary hypophosphatemic-osteomalacia is presented, which showed increased false-positive uptake (for possible TIO lesions) in inflammatory condition of maxillary sinus and fracture of tibia in SSTR based ^{68}Ga-DOTATATE PET-CT.

Introduction:

In TIO, culprit lesions are usually mesenchymal tumors with somatostatin receptor (SSTR) expression, and ^{68}Ga-DOTATATE PET-CT playing an important role in tumor localization and management. We herein present a rare case of hereditary hypophosphatemic-osteomalacia, which showed false-positive foci on ^{68}Ga-DOTATATE PET-CT mimicking possible TIO lesions.

Case report:

A 45 years old male complaint of bony pain in chest wall, back and lower limbs regions of 1.5 years duration and found multiple old healed rib fractures. Low level of serum phosphorus of 2.1 mg/dl, raised serum alkaline phosphatase level of 208 IU/L and highly raised blood level of fibroblast growth factor 23(FGF-23) of 1561.5 RU/ml was found on blood investigation. Clinical features, low serum phosphorus and raised level of FGF-23 were highly suspicious of TIO. The patient underwent ^{68}Ga-DOTATATE PET-CT for detection of culprit lesion of TIO. Whole body PET-CT scan was performed 60 minutes after intravenous injection of 74 MBq (2mCi) of ^{68}Ga-DOTATATE on Philips Gemini TF TOF 16 PET/CT scanner. Images were acquired using 3D PET protocol with 3 minutes per bed position acquisition. Data were reconstructed using iterative (RAMLA: 2 iterations, 21 subsets) algorithm. Non-contrast and

low-dose computed tomography (voltage 120kVp, slice thickness 5mm, pitch-0.83, FOV 600mm, rotation time - 0.5sec, 50 mA) was used for anatomical localization and attenuation correction of PET data. The maximum intensity projection image (A) showed abnormal SSTR uptake in maxillary sinus and knee region. Fused transaxial (B) image showed mildly increased SSTR uptake (SUVmax5.42) in left maxillary sinus with mucosal thickening. Fused coronal image (D) showed mild SSTR uptake (SUVmax-3.84 on right) and faint SSTR uptake (SUVmax-2.3 on left) in sclerotic lesion in medial part of upper condyle of bilateral tibia (right > left side). These findings were suggestive of culprit lesions for TIO on ^{68}Ga-DOTATATE PET-CT (shown by green and red arrows in B and D images). In view of doubtful lesions on ^{68}Ga-DOTATATE PET-CT, multiplanar magnetic resonance imaging (MRI) of para-nasal sinus and knee were was performed using spin-echo (SE) T1-weighted (T1W), fast spin-echo (FSE) T2-weighted (T2W), Turbo inversion recovery magnitude (TIRM) and short Tau inversion recovery (STIR) sequences. MRI of maxillary sinus (C) showed moderate T2 hyperintense mucosal thickening in left maxillary sinus with central T2 hypointense areas due to retained secretion. MRI of knee (E) showed fracture along proximal inner medial part of bilateral tibia on T1W coronal view with mild periosteal edema. MRI findings were suggestive of benign disease conditions in both regions. Subsequently, patient was evaluated for hereditary hypophosphatemia. The *SLC2A2* (-) phenotype was identified which is pathogenic for autosomal recessive disorder of Fanconi-Bickel syndrome.

Discussion:

The ^{68}Ga-DOTATATE PET-CT imaging is an important non-invasive imaging modality for detection and localization of culprit lesion in TIO. Other than tumor, SSTR expression is observed in inflammatory/granulomatous conditions and fractures/ degenerative bone disease leading to false positive scans finding in various oncological cases (*1-4*). Raised level of FGF-23 is not specific of TIO and can also be found in hereditary hypophosphatemic and osteomalacia-inducing musculoskeletal disorders, such as X-linked hypophosphatemic rickets, autosomal dominant and recessive hypophosphatemic rickets (*5*). In our case, the patient presented with long standing systemic symptoms of hypophosphatemia with raised level of FGF-23. ^{68}Ga-DOTATATE PET-CT was considered to localize the culprit lesion of TIO in view of clinically

symptomatic and biochemically proven case of hypophosphatemia with increased FGF-23 level. Increased SSTR uptake was seen in maxillary sinus and bilateral tibial regions which on MRI was illustrative of benign etiopathologies. Finally, patient was diagnosed a case of hereditary hypophosphatemia for autosomal recessive disorder of Fanconi-Bickel syndrome.

Conclusion:

The ^{68}Ga-DOTATATE PET-CT is used as first-line imaging modality in suspected cases of TIO. In addition to TIO, raised FGF-23 level can also be found the increased levels in other hypophosphatemic and osteomalacia-inducing musculoskeletal disorders. However, SSTR uptake is also seen in inflammatory/granulomatous conditions and fractures/degenerative bone disease. This should be kept in mind while interpreting ^{68}Ga-DOTATATE PET/CT with equivocal or doubtful lesions in hypophosphatemia-osteomalacia cases.

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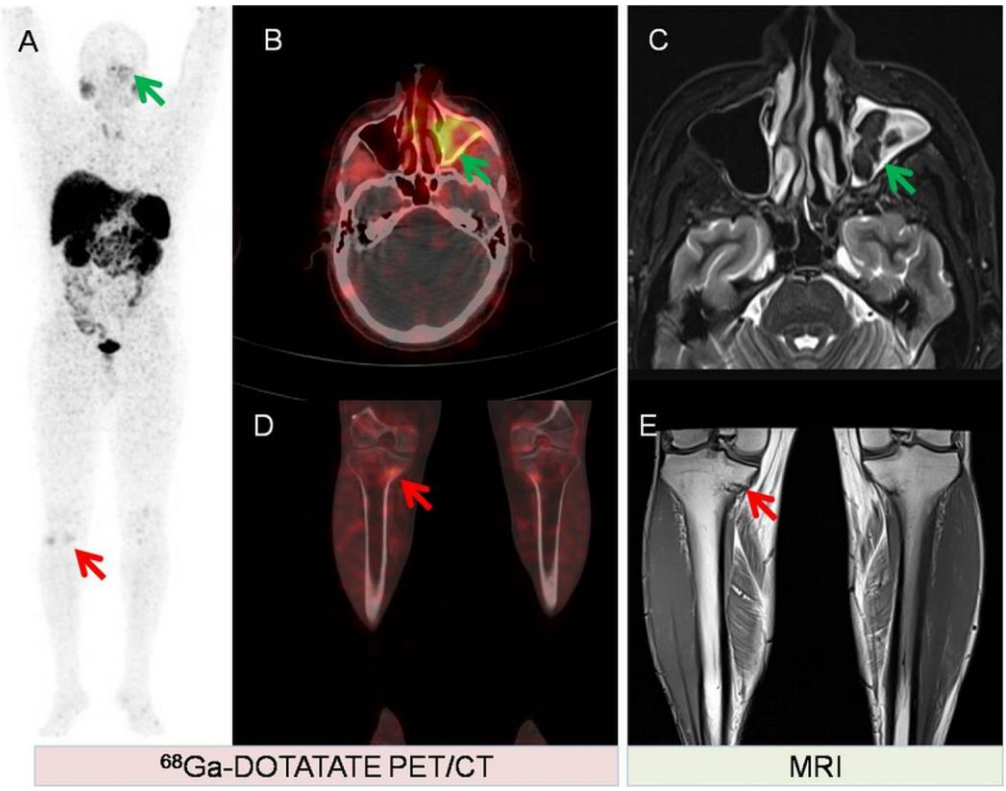

^{68}Ga-DOTATATE PET-CT (Fig.1), demonstrating abnormal SSTR uptake in maxillary sinus and knee regions in the maximum-intensity-projection image (A); fused transaxial image (B) showing mildly increased uptake (SUVmax5.42) in left maxillary sinus with mucosal thickening and fused coronal image (D) showing mildly SSTR avid sclerotic lesion in medial part of upper condyle of right tibia (SUVmax3.84)(shown by green and red arrows in B and D images) and faint SSTR uptake in medial part of upper condyle of left tibia. MRI of maxillary sinus (C) showed moderate T2 hyperintense mucosal thickening in left maxillary sinus with central T2 hypointense areas due to retained secretion and MRI with T1W coronal view of knee (E) showed fracture along proximal inner medial part of bilateral tibia, both were suggestive of benign etiologies.