

F18-fluorodeoxyglucose positron emission tomography/computed tomography for bone hemangiopericytoma

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Abstract. Bone hemangiopericytoma (HPC) is extremely rare, and its clinical manifestations and radiographic features are nonspecific. There are few case reports about application of F18-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) in HPC. A total of four subjects with pathologically diagnosed bone HPC had FDG PET/CT for staging and/or restaging bone HPC. Medical records were retrospectively reviewed for radiological, pathological and follow-up information. All primary bone and metastatic lesions demonstrated high FDG avidity on PET/CT, which also revealed the adjacent soft tissue involvement and synchronous lesion. PET/CT correctly detected metastatic lesions in 1 patient. Furthermore, 3/4 patients with available laboratory data had hypocalcemia, but normal phosphorus levels when HPC existed as primary lesions or metastatic disease; however, normalization of calcium levels when they were disease-free. The results suggested that FDG PET/CT could be effectively used for staging, surveillance and detection of recurrent/metastatic disease in HPC. There may be an association between bone HPC and hypocalcemia.

Introduction

Hemangiopericytoma (HPC) is a malignant vascular tumor arising from mesenchymal cells that surround endothelial tissue, which is known as Zimmerman's pericytes (1). HPC was first reported by Stout and Murray in 1942 and represents only <1% of all vascular neoplasms (1). Most of HPC are in soft tissues and can be reclassified as a fibroblastic neoplasm similar to a solitary fibrous tumors (2-4). The most common sites of HPC are the lower extremities, followed by the pelvis

and head and neck (5,6). HPC has non-specific image features and clinical manifestations. Pathological confirmation combined with immunochemical analysis is mandatory for diagnosis of HPC (2). The histological appearance does not reliably predict the biologic behavior of the tumor.

Primary bone HPC is extremely rare. In the radiology literature, there are only case reports or small case series reports of bone HPC (7-13). Although most of bone HPC demonstrate as destructive or lytic lesions (7-13), radiographic findings are non-specific as well (14).

Currently F18-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) imaging is standard care for staging, restaging and surveillance of primary malignant bone neoplasms, but there is very little information about its application in bone HPC. There were only limited case reports about FDG PET/CT image findings of HPC, mostly non-osseous lesions (15-20). This retrospective study presents FDG PET/CT findings in 4 patients with primary bone HPC.

Patients and methods

Ethics. This retrospective study was approved by the Institutional Review board. Relevant cases were identified through a search of a computerized database of patients who underwent PET/CT imaging at the Advanced Imaging Center, University Hospital between January 2010 and June 2016.

Patients. The study group consisted of 4 subjects with pathologically diagnosed bone HPC, who had FDG PET/CT for staging and/or restaging or surveillance. Non-osseous HPCs were excluded from the study.

Method. FDG PET/CT. Combined PET-CT was performed using a PET-CT scanner (Discovery LS, GE Healthcare, Milwaukee, WI, USA) and standard techniques. The patients had fasted for at least 6 h prior to examination and their blood glucose level was <200 mg/dl. The patients received oral but not intravenous contrast media. Spiral low-dose CT (80 mA, 140 kV and 4 mm section thickness) was performed with the cranio-caudal direction covering the areas from the vertex to the toes for the purpose of attenuation correction and anatomic localization. Thereafter, emission scan was conducted in a reverse direction.

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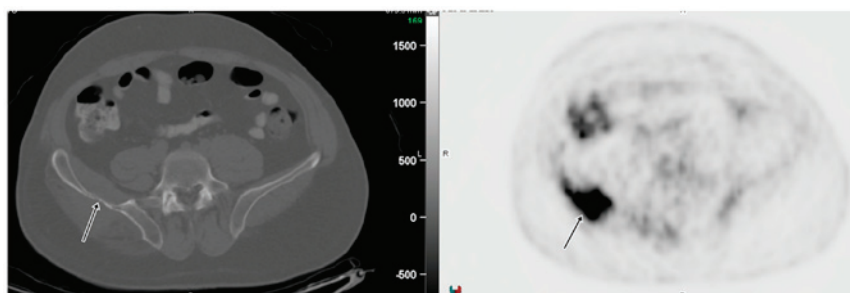


Figure 1. Axial FDG PET/CT images of Patient 1. There was destructive lesion with intense FDG uptake (arrows) in the right ilium with both sided soft tissue invasion.

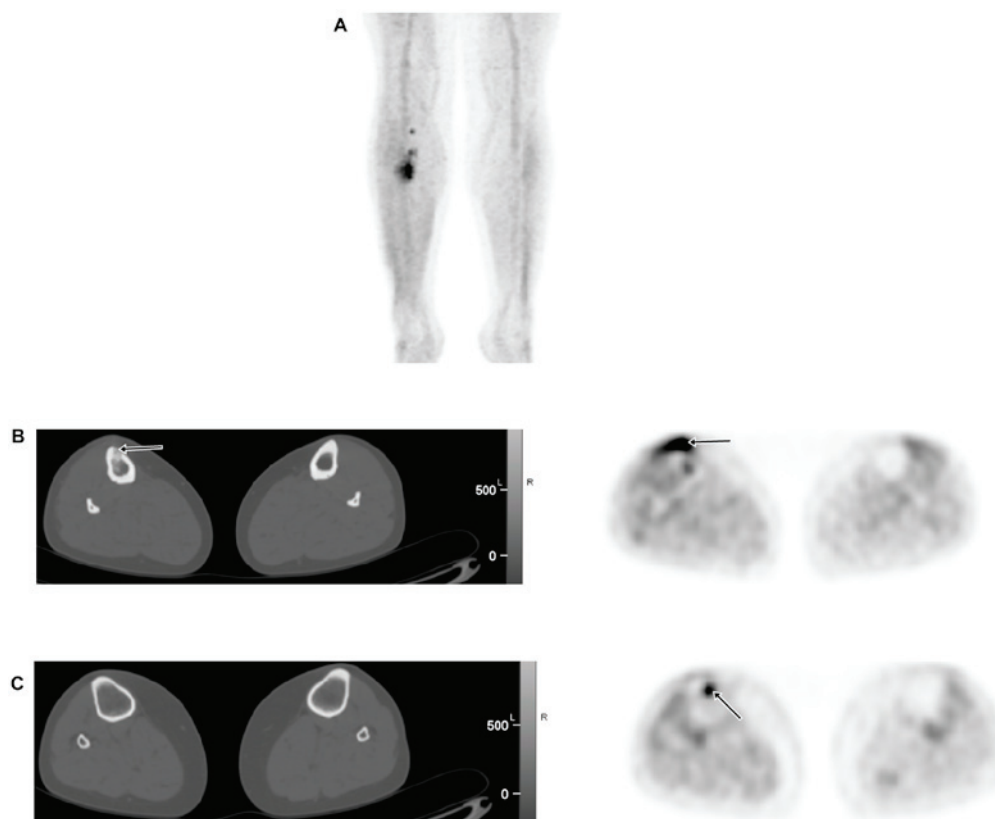


Figure 2. Maximum intensity projection (A) and axial images (B and C) of the lower extremity FDG PET/CT of Patient 3. There was a highly FDG avid destructive lesion in the left tibia with adjacent soft tissue involvement (B, arrows) There was another smaller focus of intense uptake proximal to the known HPC lesion in the left tibia (C, arrow), suspicious for a synchronous lesion. Surgical pathology confirmed multifocal HPC.

Image analysis. An image software Mim (Mim Software Inc, Cleveland, OH, USA) was used for image display and analysis. The whole-body maximum-pixel-intensity projection was used for visual evaluation. Maximum standardized uptake value (SUV_{max}) of lesions was recorded.

PET/CT findings were correlated with the patients' medical records including radiological, laboratory, pathologic and follow-up information.

Results

Table I summarizes patients' characteristics and clinical data including sites of the bone lesions, purpose of FDG PET/CTs, SUVs of the lesions, adjacent soft tissue involvement, and metastatic disease.

All 4 patients had surgical pathological diagnoses of bone HPC, including positive CD34 immunochemical stain analyses.

Patient 1 was a 54-year old man with the right hip pain. CT and radiographs showed a large destructive lesion of the right iliac wing with adjacent soft tissue involvement. Biopsy suggested HPC. Staging FDG PET/CT showed a large, intensely FDG avid (SUV_{max} 11.8) right iliac lesion with adjacent soft tissue components (Fig. 1). The patient underwent radical resection, plate/screw fixation and bone graft reconstruction. Afterwards, 5 postoperative surveillance PET/CTs were all negative for recurrent or metastatic disease. The patient was disease-free for >3 years. On laboratory data, the patient had persistent preoperative hypocalcemia (the lowest serum calcium level 6.9 mg/dl), which was normalized 1 week postoperatively.

Table I. Patients' characteristics and FDG PET/CT findings.

Patient	Sex/age	Location	Bone change	PET indication	SUV _{max}	Soft tissue involvement	Metastasis
1	Male/54	L. Ilium	Destructive	Staging Restaging	11.8	Yes	No No
2	Female/88	R. Femur	Destructive	Staging	9.0	Yes	No
3	Female/30	R. Tibia	Lytic	Staging	14	Yes	No, but 1 synchronous lesion
				Restaging			No
4	Female/78	L. Femur	Lytic	Restaging	Varied, max. 8	Yes (CT)	Yes on Restaging

Patient 2 was an 88-year-old woman with pain of the right lower extremity. Radiographic images showed a destructive mass of the right femur. Staging FDG PET/CT demonstrated a large lytic lesion with intense uptake (SUV 9.0) in the right distal femur and adjacent posteromedial soft tissue. Surgical pathology indicated HPC. The patient was lost to follow-up postoperatively. No laboratory data were available on the medical record.

Patient 3 was a 30-year-old woman with newly diagnosed HPC of the right tibia. Staging FDG PET/CT showed abnormal uptake (SUV 14) in the known lesion of the right proximal tibia. There was an additional 1.1 cm focus of uptake (SUV 9.0) in the right proximal tibial metaphysis suspicious for synchronous lesion, although no corresponding bone lesion was seen on the integrated CT (Fig. 2). The patient underwent radical resection and pathology confirmed multi-focal lesions of HPC. Postoperative surveillance PET/CT were all negative for recurrent or metastatic disease. The patient were disease-free for 6.5 years. The patient had temporary mild hypocalcemia (serum calcium level 8.3 mg/dl) preoperatively, but normal serum calcium level 2 days postoperatively.

Patient 4 was a 78-year-old woman with a destructive lesion and pathologic fracture of the left proximal femur. Surgical pathology suggested bone HPC. There was no pre-surgical staging PET/CT. Postsurgical surveillance PET/CTs were negative until 2 years later when FDG PET/CT showed positive left inguinal lymphadenopathy and new pulmonary nodules. Excisional biopsy of the left inguinal lymph node was positive for HPC metastasis. Afterwards, the patient underwent chemotherapy with different regimens (Doxil, Temodar, Avastin and irinotecan). Post-therapeutic PET/CTs demonstrated continuous progression of metastatic disease with new lesions in the lungs, liver, muscle and bone (Fig. 3). The patient declined further treatment and was enrolled in hospice care. The patient had persistent hypocalcemia (the lowest calcium level 7.0 mg/dl) preoperatively, within 5 months postoperatively and 1 months after metastases were diagnosed.

In the current case series, 3 had lesions in the lower extremities (femora and tibia) and 1 had lesion in the pelvis (ilium). All had destructive or lytic lesions on radiographic images. All 3 primary bone HPC lesions (patients 1-3) and multiple metastatic HPC lesions (patient 4) demonstrated high FDG avidity on PET/CT imaging. The adjacent soft tissue involvement or invasion was present in all 3 staging PET/CT images. One patient had a synchronous lesion in the same bone

on PET/CT. FDG PET/CT was accurate in staging 3 patients (patient 1-3) and restaging 3 patients (patient 1, 3 and 4).

Three of four patients with available laboratory data had hypocalcemia when HPC existed either as primary lesions (patients 1, 3 and 4) or metastatic disease (patient 4), but normal calcium levels when they were disease-free. All patients had normal serum phosphorus levels when hypocalcemia existed. Unfortunately, no patient had further evaluation of the other laboratory profile such as parathyroid hormone or vitamin-D.

Discussion

Primary bone HPC is extremely rare, comprising only 0.1% of malignant primary bone tumors (14). Patient's symptoms and signs are nonspecific in HPC. In current 4 cases, 3 patients had pain and 1 patient presented with pathological fracture. For the lesion sites, 2 were in the femur, 1 was in the tibia and 1 was in the ilium. Findings are consistent with observation of previous case reports that the lower extremities are the most common site of bone HPC (14,21). On radiographic images including plain X-ray, CT and/or MRI, all lesions were destructive or osteolytic with cortical disruption and extension to the adjacent soft tissue. However these features were nonspecific for HPC and indistinguishable from either more benign-appearing tumors such as giant cell tumor, chondromyxoid fibroma, or more malignant-appearing tumors such as fibrosarcoma, angiosarcoma and metastasis (14). HPC could not be diagnosed until surgical pathology from biopsy or resection was obtained. In all cases, final diagnoses were based on the architectural pattern on pathology and immunohistochemical stain. In addition to initial workup, CT and/or MRI are often used to define the extent of bone lesion and soft tissue involvement.

The current data demonstrated high FDG avidity of both primary bone and metastatic lesions of HPC. All lesions had intense uptake on FDG PET/CT and adjacent soft tissue involvements. In the patient 3, PET detected an additional small synchronous lesion in the same bone as the original. In the patient 4, FDG/CT accurately diagnosed multiple metastatic nodal, pulmonary, hepatic, bone and muscle lesions which were all highly FDG avid. Therefore, FDG PET/CT is a useful image modality for staging, surveillance and detection of recurrent/metastatic disease in bone HPC.

Radical resection of the lesion is a mainstay of treatment of HPC. In 3 of 4 patients with available follow-ups,

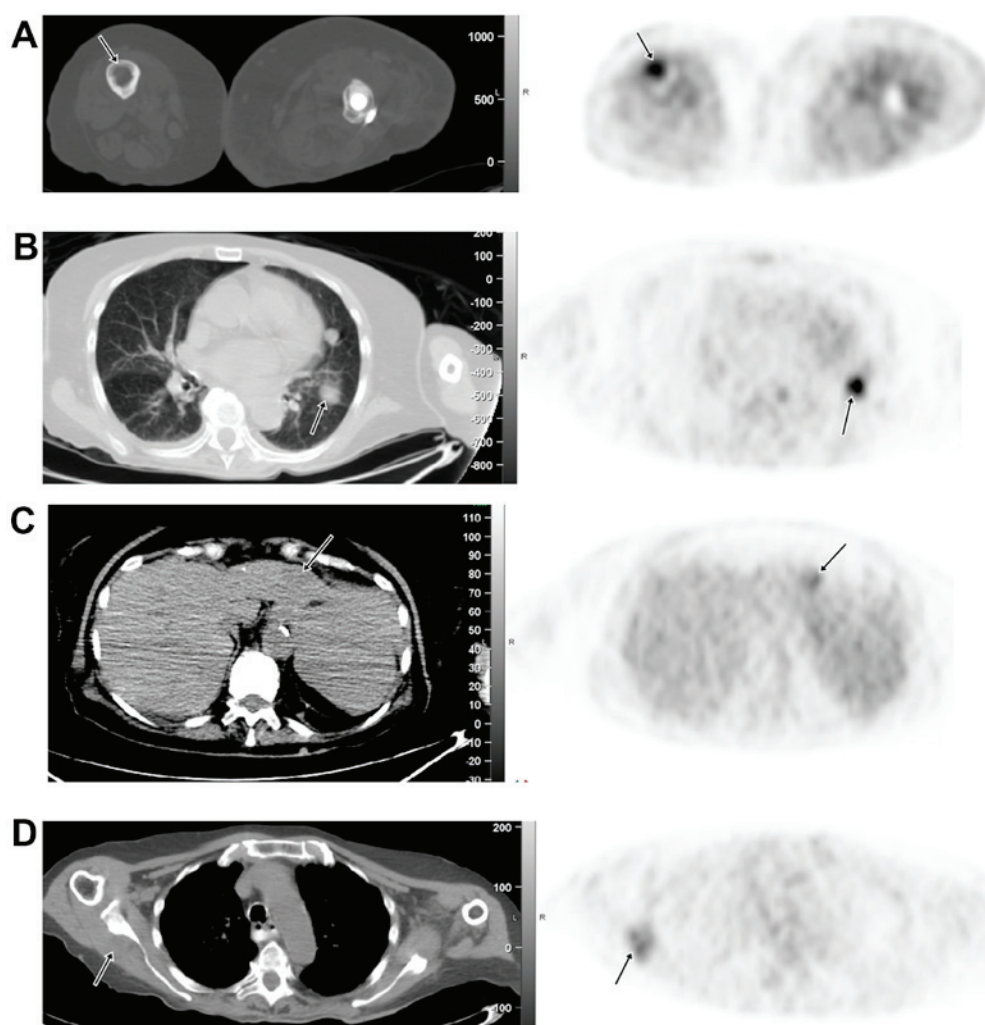


Figure 3. Axial FDG PET/CT images of patient 4. Hardware with mild reactive uptake was in the left femur, representing previous primary HPC site and postoperative change (A) However, there were multiple FDG avid lesions (arrows) in the bone (A) lung (B) liver (C) and muscle (D) maximum uptake was in the lung lesion with SUV 8.0.

the patient 1 and 3 were disease-free 3 years and 6.5 years postoperatively without any adjunct therapy, respectively. The patient 4 developed metastases 2 years after surgical resection of bone HPC and the metastatic lesions were irresponsive to chemotherapy. Except for regional lymph nodes, the first and main site of distant metastasis was the lung.

Tumor-induced osteomalacia (TIO) has been reported to occur in HPC (14,15,20). TIO is a rare paraneoplastic syndrome characterized by hyperphosphaturia, hypophosphatemia, decreased serum Vitamin D3 and osteomalacia. There were a few case reports that TIO was in association with HPC and the serum and urine phosphate levels returned to normal after excision of the tumors (14,15,20,22). It was hypothesized that these tumors elaborate a substance that decreases or interrupts the synthesis of 1, 25-dihydroxycholecalciferol, resulting in reduced tubular reabsorption of phosphorus, which in turn induces osteomalacia (14). There was also a case report about association between HPC and hypoglycemia, which was caused by increased circulating insulin-like activity from elevated free insulin-like growth factor II (IGF-II) stimulating glucose uptake primarily into muscle tissue (23). However, the current case series, for the first time, demonstrates different

laboratory findings than that of TIO or paraneoplastic syndrome. All 3 patients with available laboratory data had hypocalcemia prior to treatment, and normalization of serum calcium levels days or months after surgical resections of the HPC lesions or when they were disease-free. Patient 4 had recurrent hypocalcemia after development of metastatic disease. No patient had hypophosphatemia. Unfortunately, no further laboratory workups were obtained for these patients, such as parathyroid hormone, urine calcium or phosphate clearance or serum/urine vitamin D analyses. The mechanism of hypocalcemia in bone HPC is not clear. It is reasonable to assume that both primary bone HPC lesion and metastatic HPC lesions might produce a substance which could interfere or damage normal metabolism of calcium. Further biochemistry investigation is needed to clarify the association between bone HPC and hypocalcemia.

In conclusion, bone HPC is extremely rare. Radiographic features of the lesions are nonspecific and pathologic diagnosis is warranted. Both primary bone and metastatic HPC lesions demonstrated high FDG avidity on PET/CT, which could be effectively used for staging, surveillance and detection of recurrent/metastatic disease. On pre-therapeutic

imaging, PET/CT could reveal soft tissue involvement and synchronous lesion. All three patients with available laboratory data had hypocalcemia prior to treatment but normalization of serum calcium levels days or months after surgical resections of the HPC lesions or when they were disease-free. Recurrent hypocalcemia occurred after development of metastatic disease in 1 patient. The findings are different from that reported in the literature regarding tumor-induced osteomalacia or paraneoplastic syndrome. Both primary bone HPC lesion and metastatic HPC lesions may produce a substance which could interfere or damage normal metabolism of calcium.

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