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PET-positive fibrous dysplasia - a potentially misleading incidental finding in a patient with intimal sarcoma of the pulmonary artery

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Abstract Benign bone tumors can show an increased FDG uptake in FDG-PET/CT investigations. In the presented case, an incidentally detected PET-positive asymptomatic fibrous dysplasia was initially misinterpreted as a metastasis in a patient with intimal sarcoma of the pulmonary artery.

Introduction

Fibrous dysplasia (FD) is a developmental disorder in which normal bone marrow is replaced with fibro-osseous tissue. Patients are often asymptomatic, and FD is often detected incidentally on radiographs, computed tomography (CT) or bone scans. FD can lead to complications like deformity, pathologic fractures and—rarely—malignant transformation. FD can be monostotic or polyostotic. Polyostotic FD may be a component of the McCune-Albright syndrome [1–4]. 18-fluoro-deoxyglucose positron emission tomography (FDG-PET/CT) is increasingly used for the staging of different malignant diseases [5, 6]. FDG is not a tumor-specific agent, and an increase in FDG uptake can be shown by many benign or physiologic “disorders”, such as infections and inflammations [7, 8], brown fatty tissue [9], traumatic lesions [10], ovaries [11] and benign tumors like Warthin’s tumor of the parotid

gland [12]. If PET/(CT) is performed to stage malignancies, an FDG uptake in benign lesions can lead to their misinterpretation as metastases. To our knowledge, there is no report in the literature of a biopsy-proven PET/CT-positive fibrous dysplasia.

Case report

A 40-year-old male non-smoker was presented who had had a cough for 3 months and suffered from weight loss, night sweat and recurrent haemoptysis. A chest X-ray and a contrast-enhanced chest CT scan showed a mass at the left hilus, most likely arising from the left pulmonary artery. The differential diagnosis of a tumor of the intima of the pulmonary artery, a bronchial carcinoma, tuberculosis or other tumor was established. A bronchoscopy was not conclusive. The patient was referred to us with suspicion of

a pulmonary artery intimal sarcoma, and ^{18}F -FDG-PET/CT (combined PET/CT in-line system; Discovery ST, GE Health Systems, Milwaukee, WI, USA) was performed for staging. The central lung lesion at the left hilus showed an increased FDG uptake (SUV max. 4.1) (Fig. 1a-c). Another asymptomatic FDG-active lesion was found in the proximal diaphysis of the left femur (SUV max. 2.9; Fig. 1d). Because of the increased FDG uptake, this lesion was initially interpreted as suspicious for a metastasis of the lung tumor.

However, due to the recurrent character of the hemoptysis, and due to the absence of effective induction therapy for intimal sarcomas, a lung resection was performed with a palliative intention. The patient underwent extended left pneumonectomy. The histology confirmed the presumed diagnosis of a high-grade intimal sarcoma of the left pulmonary artery (Fig. 2).

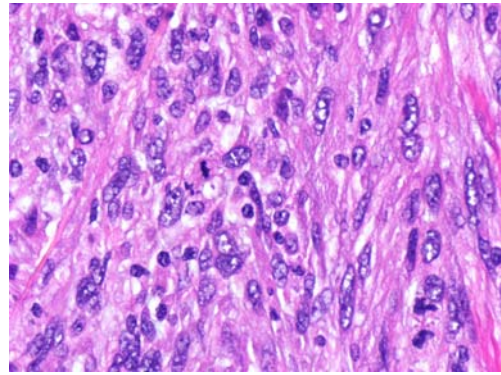
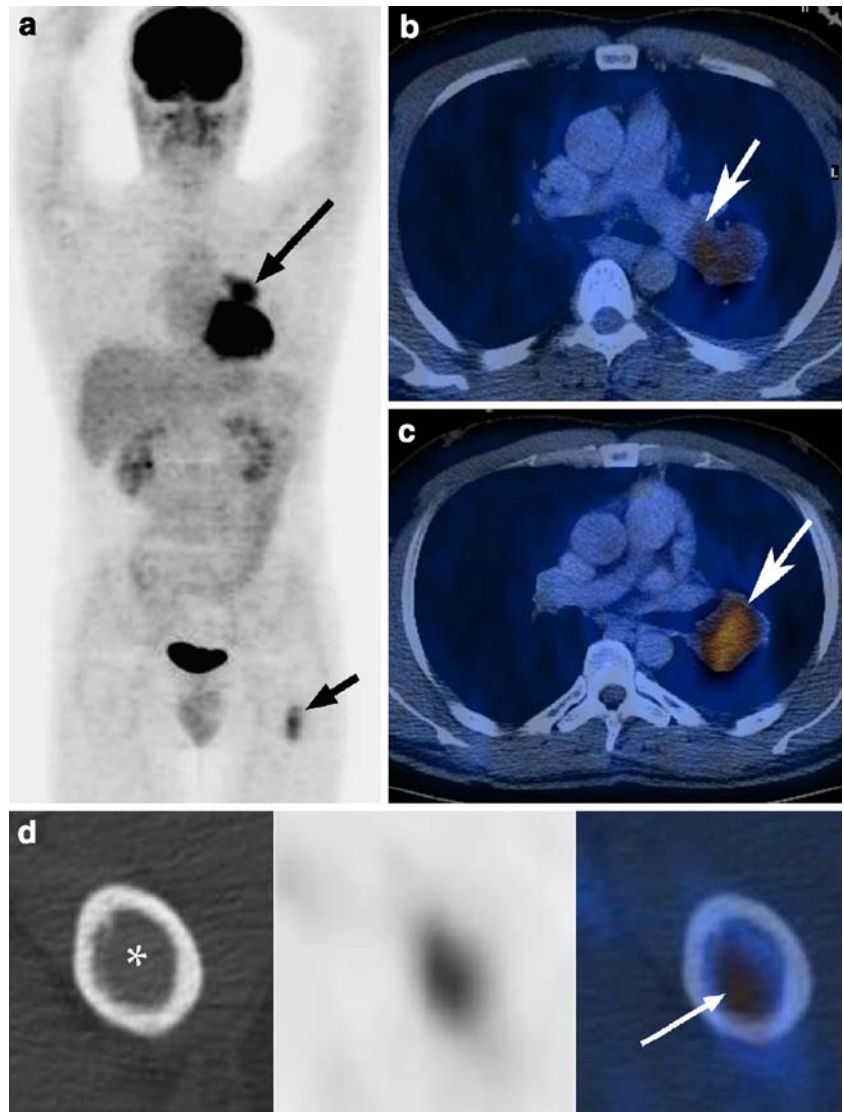


Fig. 2 Hematoxylin and eosin staining (original magnification 400 \times) of the centrally located, intraluminal tumor of the pulmonary artery, in a pneumonectomy specimen showing highly pleomorphic and mitotically active malignant tumor tissue corresponding to a high-grade spindle-cell intimal sarcoma

Fig. 1 MIP image (a) demonstrating an increased FDG uptake (SUV max. 4.1) centrally in the left lung (*long arrow*) and in the proximal left femur diaphysis (*short arrow*). Axial fused PET/CT images show that the tumor has a close relationship to the left pulmonary artery (b, c; *arrow*). On axial images (d) of the lesion in the femur, “ground-glass” appearance (*asterisk*) of the lesion is visible with increased FDG-uptake (SUV max. 2.9)



The bone lesion was further evaluated by means of conventional X-rays (Fig. 3) and MRI (Fig. 4). The X-ray demonstrated a homogeneous grayish lesion with a “ground-glass” pattern in the femur. There were no visible periosteal reactions or destructions, and no deformity could be detected. MR images presented a T1-hypointense lesion in the diaphysis with sharp borders and homogenous contrast enhancement on fat-suppressed T1-weighted images. All images were reviewed by an experienced musculoskeletal radiologist together with a nuclear physician. Because of the typical pattern, the most likely diagnosis of incidentally detected FD was established. The lesion was biopsied under fluoroscopic guidance, and the histology confirmed the diagnosis of FD (Fig. 5).

Discussion

This case demonstrates that an increased FDG uptake in a clinically occult fibrous dysplasia can be misleading in the evaluation of a patient with a malignant primary tumor. The literature on PET and fibrous dysplasia is very limited. Aoki et al. evaluated primary benign and malignant bone tumors, and found an increased FDG uptake (SUV max. >2.0) in three of six patients with fibrous dysplasia. There was no statistically significant difference in SUV between FD ($n=6$; SUV max. 2.05 ± 0.98) and osteosarcoma ($n=6$; SUV max. 3.07 ± 0.96) or chondrosarcoma ($n=7$; SUV max. 2.23 ± 0.74) [13]. With a cut-off SUV max. of 2.0,

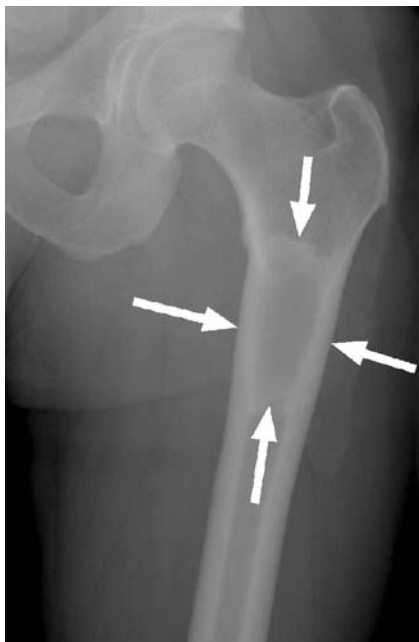


Fig. 3 X-ray of the bone lesion (*arrows*) showing a slightly expansile subtrochanteric lesion in the left femur without periosteal reactions or destruction of the cortex indicating a benign tumor. Homogeneously increased density of the lesion compared with surrounding normal bone structure



Fig. 4 Coronal contrast-enhanced, fat-suppressed MR image showing a homogeneous contrast enhancement of the well-defined lesion (*arrows*)

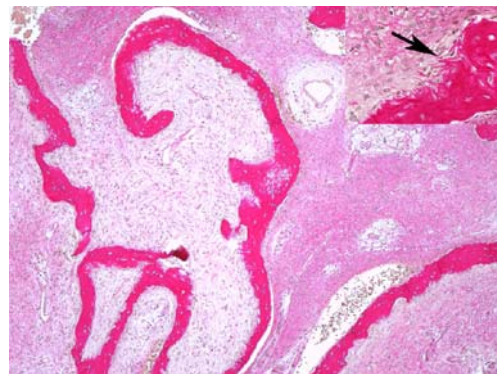


Fig. 5 Elastica and van Gieson staining (original magnification 50 \times) of the fluoroscopically guided biopsy of the left femur lesion: bland spindle-cell proliferation with bone trabeculae without osteoblastic rimming and directly ingrowing collagen bundles (*arrow*) characteristic of fibrous dysplasia

only 64% of the 52 cases were classified correctly as benign or malignant. They found out that histiocytic and giant cell-containing benign bone lesions in particular can show a high FDG uptake. In another publication, the authors described a case of a female patient with breast cancer, where the bone scan showed multiple focal uptakes due to polyostotic FD. All of the lesions were PET-negative [14]. Toba et al. described a case of a patient with FD in the craniofacial bone without an increased FDG uptake [15]. It is generally accepted that FD is a developmental failure in the remodeling of primitive bone to mature lamellar bone. One explanation for the different degrees of FDG metab-

olism of FD may be that the turnover of the remodeling process may have various velocities in different patients in different stages of the disease. Fibroblasts are the predominant proliferating cells in FD lesions, and the difference in SUV among FD may be due to the difference in the amount of proliferating fibroblasts or their metabolic turnover. Furthermore, a bone reaction may be influenced by the mechanical stress on the lesion, which may be higher in weight-bearing bones like the proximal femur than in the face. Experience with FDG-PET and other fibrous lesions, such as cortical desmoid, desmoplastic fibroma, nonossifying fibroma and osteofibrous dysplasia, is also very limited.

A malignant transformation of FD is rare, with reported prevalences ranging from 0.4% to 4% [16–18]. The most common malignant tumors reported are osteosarcoma, fibrosarcoma and chondrosarcoma. The FDG uptake correlates with the grade of bone sarcomas, and it is possible that an increased FDG uptake is a sign of the transformation of a benign tumor into a malignant one, but this hypothesis has not been proven yet [19, 20]. Unfortunately, because the differentiation, for example, between enchondroma and low-grade chondrosarcoma is sometimes impossible even for the pathologist, one can not expect FDG-PET or PET/CT studies to provide a solution to this problem.

Other benign conditions with an increased uptake in the bone are fractures, which can be misleading in tumor patients. The amount of the FDG uptake of fractures depends on the time interval between trauma and PET imaging. In most cases, the different pattern of uptake and clinical correlation allows an accurate differentiation of a fracture from malignant tumors [10, 21, 22].

This case also shows that thorough interpretation of the CT information from the PET/CT study with the help of an experienced musculoskeletal radiologist is essential to making a correct diagnosis. CT is still the best technique for demonstrating the typical radiographic findings of FD: the “ground-glass” pattern of the bone, the lesion being characteristically surrounded by a distinct rim of reactive bone, the endosteal scalloping. With CT, the extent of the lesion becomes clearly visible.

There are reports suggesting that FD accumulates other PET tracers: Tsuyuguchi et al. described two cases of FD of the skull base with mild accumulation (SUV values were about 2.0) of ^{11}C -methyl-L-methionine on PET [23]. ^{11}C Met PET is clinically used for the evaluation of brain tumors [24]. Tsuyuguchi and his colleagues speculated that “the mechanism of ^{11}C Met uptake in FD is due to increased metabolism and active transport of this amino acid because of the increased density of spindle cells”.

We found no publications on FD and ^{18}F -fluoride-PET. First studies indicate that ^{18}F -fluoride is more sensitive than a conventional bone scan for detecting skeletal metastases in patients with prostate, lung or thyroid cancer [25]. Because ^{18}F -fluoride-PET is also cost-effective, some authors expect that “classic” bone scans will be replaced with ^{18}F -fluoride PET completely in the next few years [26, 27]. ^{18}F -fluoride is a very potential non-specific bone tracer. Because ^{18}F -fluoride is a bone agent with an accumulation mechanism that is similar to methylene diphosphonate (MDP), one might expect that FD would show a significant uptake, even higher than in FDG-PET examinations.

The findings of whole-body integrated PET/CT imaging can clearly affect therapeutic management. Lardinois and colleagues found extrapulmonary lesions in 110 out of 250 NSCLC patients with PET/CT. In 72 patients, solitary lesions were present. 32 (46%) of these lesions were unrelated to the lung primary. In 26 patients, the extrapulmonary lesion was caused by a benign tumor or an inflammatory lesion [12]. An extrathoracic solitary FDG accumulation in a patient with a lung tumor requires a histopathologic diagnosis, not only to exclude a false positive result or to confirm an occult metastasis, but also to diagnose lesions that are not related to the primary.

In conclusion, PET-CT readers should be aware of FDG-positive benign bone tumors, and should be familiar with the typical CT appearance of these lesions.

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