CASE REPORT

A Solid brown Fat Tumour-Hibernoma in a Patient with a Non-small Cell Lung Cancer: Benign Versus Malignant Molecular Phenotype

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ABSTRACT

BACKGROUND: Pitfalls in Fluorine 18 Positron Emission Tomography Computed Tomography (18F FDG PET-CT) could mislead an appropriate treatment plan by an inexperienced PET reader.
METHODS: An incidental finding of a false-positive FDG-avid fatty lesion in the right gluteal region was observed on PET-CT evaluation performed for post-treatment non-small cell lung carcinoma (NSCLC) in a 40-year-old man. Post-treatment monitoring with 18F FDG PET-CT revealed partial remission of the right upper lobe mass, progressive metabolic activity in mediastinal lymphadenopathy, and new metastatic lesions in the left upper lobe and at the T12 vertebra. There was also increased FDG-avidity in the previously noted right gluteal fatty lesion, raising suspicion for metastasis.
RESULTS: A biopsy of the right gluteal lesion confirmed a hibernoma. The patient opted for conservative management with maintenance chemotherapy (erlotinib 150 mg once daily).
CONCLUSION: Pitfalls in 18F FDG PET-CT interpretation may mislead treatment decisions in cancer patients. Careful characterization of benign versus malignant lesions is essential to avoid inappropriate therapy.
KEYWORDS: hibernoma; 18F FDG PET-CT; gluteal region; lung carcinoma; NSCLC

INTRODUCTION

Brown adipose tissue (BAT) glucose uptake can be measured using 18F FDG PET-CT. BAT is a thermogenic tissue activated by sympathetic nervous stimulation, such as cold exposure, β3-adrenergic receptor agonists, or neuroendocrine tumors (1). Hibernoma is a rare benign fatty tumor arising from vestiges of fetal brown fat. It is a slow-growing, hypervascular soft tissue mass most commonly seen in adults, particularly in women (1).
Unlike BAT, which regresses with age, hibernomas present as slowly enlarging masses that may become large and often require surgical excision, although they do not metastasize. Histologically, hibernomas have four variants: typical (82%), myxoid (8%), lipoma-like (7%), and spindle cell (2%) (1).

Moreover, 18F FDG PET-CT is increasingly used for diagnosis and staging across various tumor types in phenotyping cellular reprogramming albeit abnormal metabolic activity in malignant cells that may not be morphologically evident (2–4). It serves as a marker of glucose uptake via facilitated transport through glucose transporters (GLUT). However, 18F FDG PET-CT is non-specific, and differentiation between malignant and benign lesions—such as liposarcoma, fibroma, or BAT—may be uncertain in some cases (2,3,5,6).

Most previous reports describe sporadic occurrences of hibernomas in various tumor cell lineages, particularly in association with MEN1 (7). We present a rare case of hibernoma detected on 18F FDG PET-CT and discuss its differentiation from BAT and malignant tumors, highlighting its importance in preventing misdiagnosis and inappropriate treatment planning.

CLINICAL DESCRIPTION

A 40-year-old man with NSCLC showed progressive metabolic disease on 18F FDG PET-CT, along with altered glucose metabolism in a fatty lesion in the right gluteal region. The scan (Discovery RX 690, WI, USA) was performed from the skull base to the upper thighs following intravenous administration of 294 MBq of 18F-FDG. A contemporaneous non-contrast low-dose CT scan was obtained for attenuation correction.

The PET-CT revealed an FDG-avid mass in the right upper lung lobe and multiple FDG-avid mediastinal lymph nodes. The SUVmax, defined as the highest pixel value within the tumor, was calculated using the following equation:
SUVmax = [tumor maximum radioactivity concentration (Bq/mL)] / [injected dose (MBq) × body weight (g) × (g/mL)]

A repeat scan performed 3 months after chemotherapy demonstrated a partial metabolic response in the right upper lobe mass but progressive disease in the mediastinal lymph nodes. New FDG-avid lesions were also identified in the left lung and at the T12 vertebra.

The previously noted right gluteal fat lesion showed altered glucose metabolism and was initially suspected to represent a poorly differentiated tumor (Figure 1). However, biopsy confirmed the diagnosis of hibernoma (Figure 2).

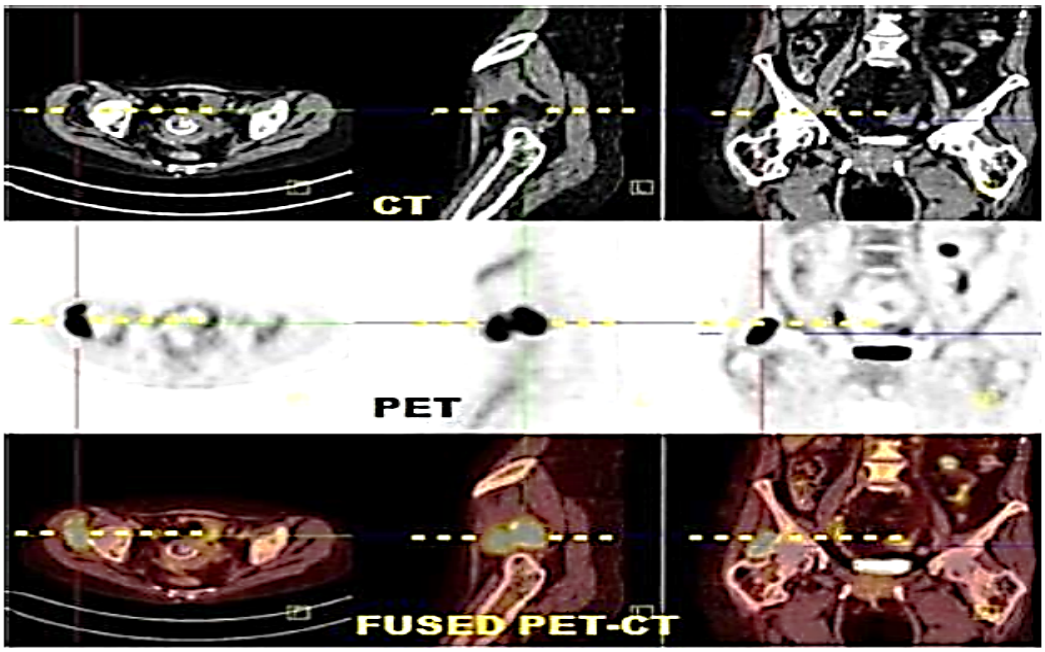

***Figure 1**: Fused 18F FDG PET-CT (multiplanar), 3 months post-treatment: FDG-avid fat-density lesion in the right gluteal region with SUVmax of 9.9 g/dL*

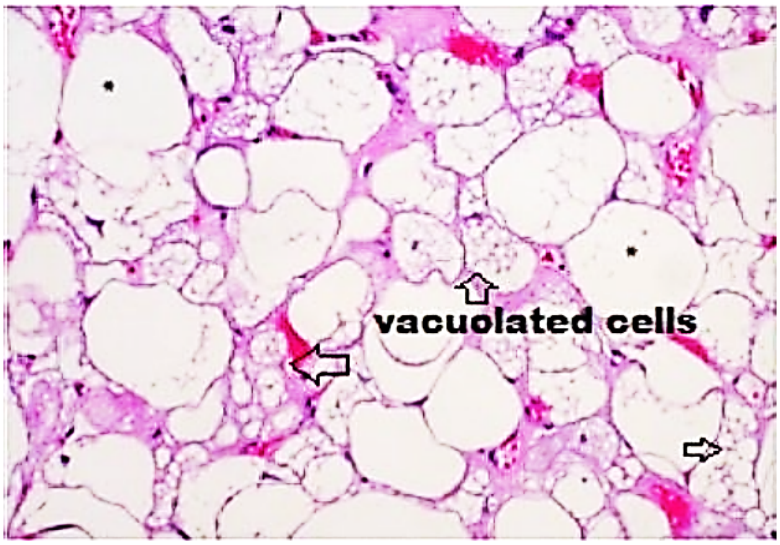

***Figure 2**: Photomicrograph (H&E, ×200): Hibernoma tissue showing small, round, brown fat-like cells with uniform cytoplasmic vacuoles (arrowhead) and small, regular nuclei, without lymphoblastic infiltration*

At 6-month follow-up, the patient appeared pale and anorexic and reported a 3 kg weight loss. Despite these symptoms, he chose to continue conservative management with maintenance chemotherapy (erlotinib 150 mg once daily), and treatment was adjusted according to clinical status.

DISCUSSION

Structural imaging techniques, such as computed tomography (CT) and magnetic resonance imaging (MRI), play an important role in characterizing the relative proportions of brown and white adipose tissue within a hibernoma lesion (8–9). When typical imaging features are recognized, a preoperative diagnosis of hibernoma may occasionally be achieved.

On CT, the lesion typically appears as a solid, well-marginated mass that is slightly hyperdense compared to subcutaneous fat. This increased attenuation reflects its composition, with values that are intermediate between those of fat and skeletal muscle. Hibernoma can be distinguished from physiological (BAT), which is normally distributed in characteristic locations such as the supraclavicular, paraspinal, and anterior chest wall regions. Unlike hibernoma, BAT represents normal fatty tissue and exhibits physiological metabolic properties associated with sympathetic nervous system activity.

Additionally, 18F-FDG PET revealed altered glucose metabolism in the hibernoma, which is primarily due to its brown fat component, reflecting an increased number of mitochondria that utilize glucose (3, 10, 11). This report highlights that the hibernoma showed high FDG accumulation (SUVmax: 9.9 g/dL) with a homogeneous pattern. This finding is consistent with other reports where the SUVmax of typical hibernomas ranges from 7.3 to 26.7 g/dL. In contrast, liposarcomas and fibrosarcoma typically present with heterogeneous fat mixed with soft tissue on CT and have a lower SUVmax (less than 2.0 g/dL) compared to hibernomas (12-15). However, further experimental research is required to establish cut-off SUVmax values for distinguishing hibernomas from other malignant sarcomas, as this remains a challenge.

An interesting observation in this case is the fluctuation in FDG avidity, which helps distinguish hibernoma from liposarcoma and fibrosarcoma, the latter typically demonstrating progressive FDG accumulation over time. The increased FDG uptake observed on the second 18F-FDG PET-CT scan was likely attributable to chemotherapy-induced activation of brown adipose tissue. Such activation

is known to occur in response to sympathetic stimulation, as seen in neuroendocrine tumors, or following exposure to cold temperatures (5) (Figure 3).

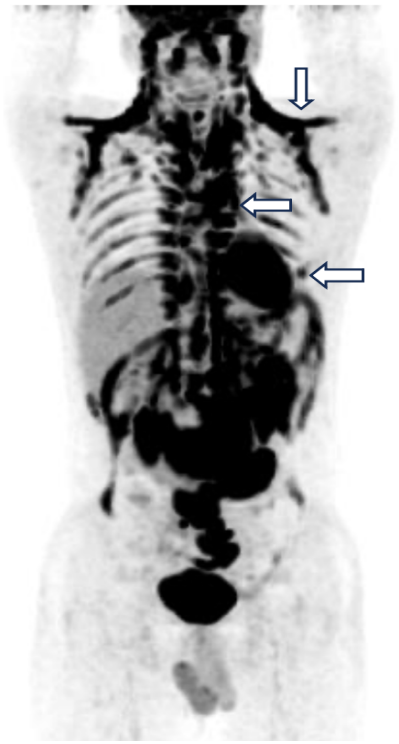

***Figure 3**: MIP image of BAT: A 30-year-old patient with metastatic gastro-pancreatic neuroendocrine tumor demonstrating multiple FDG-avid BAT deposits in the paraspinal, supraclavicular, and anterior chest wall regions (white arrows).*

Furthermore, the FDG avidity of hibernomas decreases with the administration of beta-blockers, in contrast to other sarcomas, which continue to exhibit persistently high FDG uptake (10) (Table 1).

Table 1: Phenotypes of the altered glucose metabolic changes of different brown fat tissues.

Cell lineage	CT features	18F FDG features	Glycolytic Phenotype
Hibernoma	Hypodense tumor with or without septation	Fluctuation of FDG avidity	Chemotherapy upregulation Down regulated by beta antagonist agent
Liposarcoma Fibrosarcoma	Hypodense tumor with internal septation	Progressively increase FDG avidity	Not sensitive to alfa-agonist or antagonist
BAT	Normal fatty tissue in the supraclavicular, paraspinal or in the anterior chest wall (HU < -1)	Activated FDG uptake by sympathetic nervous system	Down regulated by beta antagonist agent Upregulated by alfa-agonist agent

In conclusion, a key teaching point from this study is the importance of characterizing hibernoma features using both computed tomography (CT) and 18F-fluorodeoxyglucose positron emission tomography imaging. When a new lesion demonstrates increased uptake on 18F-FDG PET-CT, the corresponding CT findings are essential for identifying structural characteristics. These structural features may share phenotypic similarities with malignant lesions, potentially leading to diagnostic confusion.

Notably, the fluctuation in glucose metabolism observed on serial 18F-FDG PET scans is a distinctive feature of hibernomas and is thought to reflect cellular reprogramming of brown adipose tissue. This metabolic variability can help differentiate hibernomas from malignant tumors,

which typically exhibit more consistent patterns of FDG uptake over time.

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