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A GLUTEAL HIBERNOMA MASQUERADES AS A METASTATIC TUMOR IN POST-TREATMENT ^{18}F FDG PET-CT

T.H. HASSAN MAHGOUB[1], F.F. AHMAD SAAD[2], S. RAMDAVE[3]

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[1]Department of Radiology, Federal Central Police Hospital, JH65+FVH, Al Khurtum, Sudan
[2]Centre for Diagnostic Nuclear Imaging, Universiti Putra Malaysia, Serdang, Malaysia
[3]Department of Nuclear Medicine and PET, Monash Medical Centre, Monash University, Victoria, Australia

Corresponding Author
Thuraia Hatim Hassan Mahgoub, MD; email: Thuraia.hatim@gmail.com

ABSTRACT – ***Background:*** Pitfalls in ^{18}F Fluorodeoxy-glucose Positron Emission Tomography Computed Tomography (18F FDG PET-CT) can mislead PET readers to interpret images incorrectly, particularly in oncologic staging and restaging. Although FDG uptake reflects increased glucose metabolism, it is not specific for malignancy. Hibernoma, a rare benign tumor arising from brown adipose tissue, may show intense FDG avidity and closely mimic metastatic disease, representing an important diagnostic pitfall.

Case Presentation: A 45-year-old man with stage IIIB non-small cell lung carcinoma (NSCLC) underwent PET-CT for post-treatment re-staging. An incidental, false-positive FDG-avid fatty lesion was found in the right gluteal region. Follow-up ^{18}F FDG PET-CT showed partial remission of the right upper lobe lung mass and mediastinal lymphadenopathy, but metastatic lesions progressed in the left upper lobe and T12 vertebra. The prior right gluteal fatty lesion showed altered glucose metabolism with FDG avidity, suspicious for metastasis.

A biopsy of the right gluteal lesion confirmed a hibernoma. The patient was started on the standard doses of the cyclophosphamide, doxorubicin, and etoposide (CAE) regimen (1,000 mg/m^2 cyclophosphamide, 60 mg/m^2 doxorubicin, and 50 mg/m^2 vincristine) for six cycles, at 4-week intervals. The patient opted for conservative treatment with maintenance dose chemotherapy tablets (erlotinib 150 mg once/day).

Conclusions: An appropriate ^{18}F FDG PET-CT characterization of a hibernoma in a patient with NSCLC may avert futile treatment, as it potentially resembles a false-positive malignant lesion.

KEYWORDS: Hibernoma, ^{18}F FDG PET-CT, Gluteal region, Lung carcinoma, NSCLC, ^{68}Ga-FAPI.

INTRODUCTION

A hibernoma is a rare benign fatty tumor that arises from the vestiges of fetal brown fat. It is a slow growing, hypervascular soft tissue mass that is most prevalent in adults, particularly in women. It has four histologic variants: typical (82%), myxoid (8%), lipoma-like (7%), and spindle cell (2%)[1]. Moreover, ^{18}F FDG PET-CT has increasingly been used for the diagnosis and staging across various tumor types, as it can demonstrate abnormal metabolic activity in malignant cells that is indiscernible morphologically[2-4]. It reflects increased glucose uptake in tumor cells mediated by glucose transporters (GLUT). Nevertheless, ^{18}F FDG PET-CT is a non-specific marker, and distinguishing malignant from benign lesions may at times be impossible[5,6]. Previous scholars[7] describe the sporadic occurrence of hibernomas across various tumor cell lineages, particularly in association with MEN1. Here, we document a case of hibernoma on ^{18}F FDG PET-CT that resembles a malignant lesion. To our knowledge, no previous reports have described the evolution of a hibernoma on serial ^{18}F-FDG PET-CT, as observed in our case.

CASE REPORT

A 45-year-old man diagnosed with stage IIIB non-small cell lung cancer (NSCLC) underwent PET-CT for disease re-staging after chemoradiation. He was afebrile and had stable vitals on admission. On examination, occasional rhonchi were heard in both lungs. The ^{18}F-FDG PET-CT (Discovery RX, 690, WI, USA) showed an FDG-avid mass in the right upper lung and multiple FDG-avid mediastinal lymph nodes (Figure 1A-B). A non-FDG avid fatty lesion with fine septation but without calcification or necrosis was seen in the right gluteal region. SUVmax, the highest pixel value of the tumor lesion, was calculated as follows: SUVmax = [tumor maximum radioactivity concentration (Bq/mL)] / [injected dose (MBq) × body weight (g) × (g/mL)].

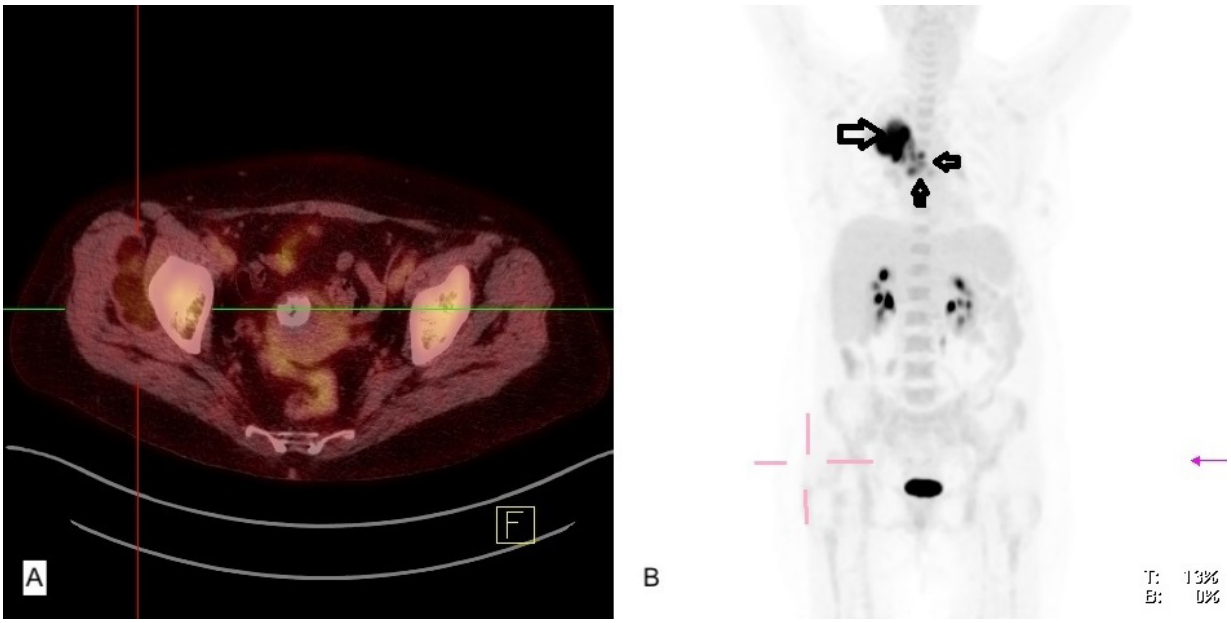

Figure 1. A, The axial fused ^{18}F-FDG PET-CT shows a non-FDG-avid fatty mass in the right gluteal region (hairline marker). A 45-year-old man with stage IIIB non-small cell lung cancer (NSCLC) underwent ^{18}F-FDG. **B,** (MIP PET): The first PET imaging on re-staging using ^{18}F-FDG PET-CT reveals an FDG-avid mass (SUVmax: 26.8 g/mL), measuring 6.9 cm × 6.0 cm in the upper lobe of the right lung (head arrow), along with multiple areas of FDG-avid mediastinal lymphadenopathy (small head arrows).

A repeat ^{18}F-FDG PET-CT was performed 3 months post-chemotherapy, which indicated a partial metabolic response in the right upper lobe mass and the adjacent mediastinal lymph nodes, with new FDG-avid lesions observed in the left lung and at the T12 vertebra, suggesting further disease progression (Figure 2A-B). The previously noted right gluteal fatty lesion demonstrated altered glucose metabolism with FDG avidity, suspicious for metastasis. A biopsy of the lesion revealed a benign hibernoma (Figure 3). He was started on the standard doses of CAE regimen (1,000 mg/m^2 cyclophosphamide, 60 mg/m^2 doxorubicin, and Etoposide 50 mg/m^2) for six cycles, at 4-week intervals

During the 6-month follow-up, the patient appeared pale and anorexic, reporting a weight loss of 3 kg. Despite these symptoms, the patient opted for conservative treatment, continuing with a maintenance dose of chemotherapy tablets (erlotinib 150 mg once per day).

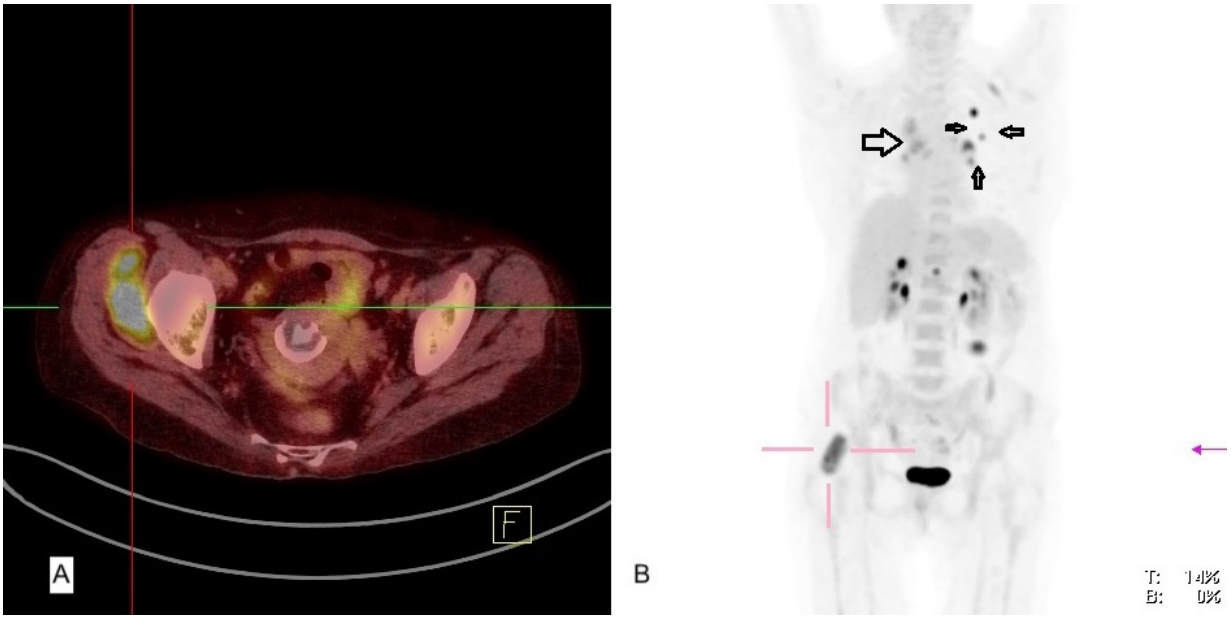

Figure 2. A, Axial: Fused ^{18}F-FDG PET-CT reveals that the previously noted fat-density lesion in the right gluteal region is now FDG-avid (hairline). The lesion in the right gluteal region demonstrated further avidity on the ^{18}F-FDG PET-CT. **B,** (MIP PET) – Post-treatment ^{18}F-FDG PET at 3 months. The post-treatment ^{18}F-FDG PET-CT shows a partial metabolic response of the previously noted right upper lobe mass (SUVmax: 5.6 g/mL, previously 26.8 g/mL) and the adjoining areas of mediastinal lymphadenopathy (head arrows). New FDG-avid lesions are noted in the left lung and at the T12 vertebra (small arrows).

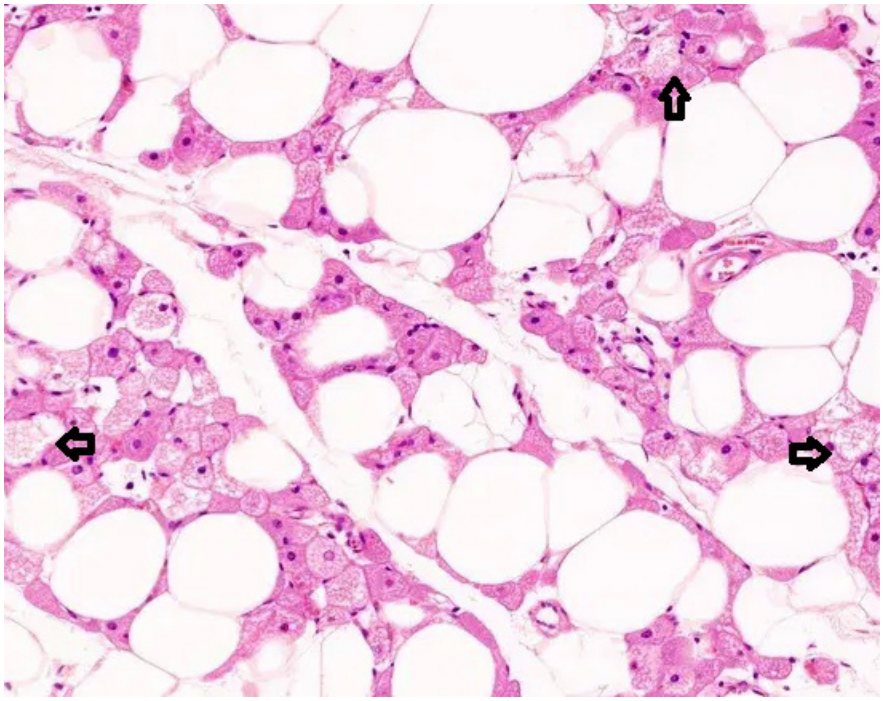

Figure 3. Photomicrograph (H&E, Mag × 200): The hibernoma tissue displays small, round, brown, fat-like cells with uniform, small cytoplasmic vacuoles (arrowhead) and regular, small, round nuclei. There are no lymphoblastic infiltrates, indicating the absence of inflammatory changes.

RESULTS

Extrathoracic hibernoma co-existing with non-small cell lung cancer (NSCLC) is extremely rare; fewer than 250 cases have been reported in intrathoracic locations[2]. This case provides new insights into the extrathoracic location of hibernoma in NSCLC patients. Structural imaging tools such as CT and MRI help distinguish brown and white fat in hibernoma lesions[8,9].

The hibernoma in this case showed hypermetabolic changes on ^{18}F FDG PET-CT, with internal septation. This appearance is indistinguishable from a malignant liposarcoma. However, the presence of a fatty component was confirmed by the negative Hounsfield value (Table 1). The *in vivo* FDG avidity (SUVmax 9.9 g/ml) matches other reported cases, indicating brown fat sympathetic activity and increased mitochondrial glucose use[10,11].

Table 1. Different characterization of glucose cellular reprogramming given the uncertainty in the altered glucose metabolic changes of the right gluteal lesion, prompting biopsy.

Cell lineage	Altered ^{18}F-FDG uptake pattern & CT	^{18}F-FDG intensity	Glucose regulation in cells
Hibernoma	Fluctuation of FDG avidity with or without septation	Very high > 7.3 g/ml	Chemotherapy upregulation Beta-blocker downregulation
Liposarcoma Fibrosarcoma	Progressively increase FDG avidity with internal septation	Low < 2.0 g/ml	Not sensitive to beta-blocker

Malignant liposarcomas commonly have lower metabolic activity (less than 2.0 g/mL) and heterogeneous fat admixed with soft tissue on CT[12,13]. Similarly, in fibrosarcoma, histology shows low glucose uptake, a lack of spindle fibroblast proliferation, and Teuton-type giant cells, which on histology exclude the diagnosis[14,15].

In particular, the hibernoma-induced alteration in glucose metabolism in our case could help differentiate it from liposarcoma and fibrosarcoma. The increased FDG uptake observed on the second ^{18}F-FDG PET-CT scan was likely due to chemotherapy-induced upregulation of glutathione-1 that transduces glucose transportation in the form of brown fat. Activation of brown fat is known to occur in response to sympathetic stimulation or exposure to cold[5]. The FDG avidity of a hibernoma also decreases with beta-blocker use, in contrast to other sarcomas, which continue to show high FDG uptake[10]. The promising molecular tracer ^{68}Ga-FAPI may help differentiate malignant tumors from benign lesions such as hibernoma by targeting fibroblast activation protein (FAP) expressed in the tumor microenvironment[16].

CONCLUSIONS

A key teaching point is the ability to differentiate hibernomas from liposarcomas using FDG imaging. This can help avoid unnecessary surgery or toxic chemotherapy. When a new ^{18}F-FDG-avid lesion is detected, it should be correlated with the corresponding CT findings to assess its morphological characteristics. Here, CT revealed a fatty origin in the right gluteal region. Fluctuation in glucose metabolism on serial PET scans further supports a benign diagnosis, consistent with hibernoma or brown fat.

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Conflict of Interest:
The authors declare no conflict of interest.

ORCID ID:
Thuraia Hatim Hassan Mahgoub: 0009-0000-5233-4828
Fathinul Fikri Ahmad saad: 0000-0002-0499-7747
Ramdave Shakher-: 0000-0003-1469-2258

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