


Asymmetric 18F-FDG Uptake in the Infradiaphragmatic Brown Adipose Tissue (BAT) Mimicking Adrenal Metastasis: A Relatively Rare Site of Brown Fat and a Potential Source for False Positive FDG-PET Study

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ABSTRACT

FDG uptake in the metabolically active brown adipose tissue (BAT) is a source of significant concern while interpreting FDG-PET studies. It is also of great interest due to its potential implications for obesity research. In this communication, we describe hitherto unreported asymmetric BAT uptake in the abdomen, persisting after diazepam intervention in the repeat PET study on a separate day. The patient did not have any evidence of disease even at 24 months' follow up. The present case is a useful addition to the current body of literature of false positive FDG-PET due to BAT uptake in unusual location and underscores the importance of high index of suspicion and careful correlation, whenever one comes across an unusual PET finding in a given clinical situation. This assumes important diagnostic value particularly when it coexists in the setting of malignancy where the disease can be falsely upstaged by misinterpretation. The literature relevant to the report is discussed and a schema is suggested for correct interpretation.

CASE REPORT

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A 12 year old female, diagnosed to have Ewing's sarcoma of left suprapubic ramus was referred for whole body FDG-PET for metastatic survey and disease evaluation following surgery, chemotherapy and local external radiotherapy. The baseline FDG PET (Fig. 1a) showed intense FDG uptake in bilateral neck and paraspinal regions. There was, however, no clinicoradiological evidence of disease in the neck to account for such avid uptake. This, alongwith the bilaterally symmetrical uptake pattern indicated that the hypermetabolism in all probability was due to the brown adipose tissue. Solitary

intense focus was also noted in the left side of the abdomen posteriorly, which gave an initial impression of left adrenal involvement. That the rest of the whole body survey was unremarkable was the reason why strenuous efforts were undertaken to elucidate the abovementioned uptake. Correlative anatomic imaging modalities (USG and CT of the abdomen) did not reveal any evidence of adrenal metastasis. Repeat intravenous diazepam primed FDG PET (Fig. 1b) was carried out to settle the BAT uptake. The uptake, however, persisted in the repeat scan, indicating the BAT uptake to be "diazepam resistant". Hence, it was concluded that the uptake was due to uptake in the metabolically active

infradiaphragmatic brown fat. The patient did not have any evidence of disease even at 24 months' follow up.

DISCUSSION

Adrenal involvement is a major issue in the clinical decision making process in oncology practice. FDG-PET has been found extremely effective in detecting adrenal involvement not identified or not meeting size criteria for malignancy with CT. FDG-PET detects the presence of metastatic lesions by directly documenting metabolic activity in the tumor and is being increasingly incorporated in the management protocols of cancer patients. However, potentially misleading falsely elevated FDG uptake can arise from various anatomical variants, physiological processes and benign pathologies unrelated to the primary disease processes and with its increasing use in current practice, these are increasingly recognized. Uptake in brown adipose tissue poses a significant challenge to interpreting physicians. This is particularly problematic while evaluating the neck, where it can mask or mimic nodal disease leading to erroneous interpretation (1,2). The literature, hence, is mainly restricted to addressing the difficulty posed by it in neck evaluation in cancer patients undergoing PET studies. Several interventions have been proposed to reduce this uptake with varying degree of success (3-8).

Brown fat is a type of adipose tissue and regulates body temperature by non-shivering thermogenesis. It has dense mitochondria in the cells, is especially described in underweight patients and activated during increased sympathetic nerve system activity due to cold stress. Avid FDG uptake is encountered in this metabolically active brown adipose tissue (BAT) and poses a major diagnostic challenge in disease evaluation in oncology practice. It is important to recognize this to obviate false interpretation of this benign normal variant as a malignant focus in FDG-PET. The usual distribution includes neck and shoulder region, axillae, mediastinum, retrocrural and paravertebral regions (3). (Other radiopharmaceuticals that have been described to show uptake in the BAT are 123I-metaiodobenzylguanidine (MIBG), 99mTc-tetrofosmin, 18F-6-fluorodopamine (F-DA) and 11C-meta-Hydroxyephedrine.) This has been also termed as "USA Fat" by some authors to emphasize the localization of FDG to the supraclavicular area fat, which has been extremely problematic in differentiating from metastatic lymph nodes in the neck and can lead to false positive (by mimicking) or false negative (by masking) results. Hence BAT uptake in this region has been the concern of majority of the published studies till date.

The uptake pattern is often very characteristic: typically bilateral and symmetric, intense, more often multifocal than linear (Fig. 2). Secondly, pharmacologic intervention with various agents to block FDG uptake in the BAT: Premedication with (a) diazepam (both low and moderate dose), (b) propranolol, (c) reserpine and (d) intravenous fentanyl all have been tried with varying success rates (3-8). The tumour FDG uptake, however, is unaffected with such premedication. Uptake of FDG into BAT increases by intraperitoneal injections of nicotine and ephedrine and this effect were further enhanced when both these drugs are

administered in combination (9). Thirdly, temperature-controlled environment settings during FDG uptake phase is another effective method to minimize the USA-Fat artifact (2,3,8). With the advent of precise localization with fusion PET/CT (2,3,5), it has been now possible to resolve this issue by accurate anatomic localization of this hypermetabolic fat. In a recently published retrospective study, patients who were prepared with the high-fat low-carbohydrate diet had a significantly lower frequency of hypermetabolic BAT uptake on FDG PET scans during the winter months ($p < 0.0002$) compared to those patients who were prepared by fasting (10).

In one report regarding the FDG uptake in the infradiaphragmatic brown fat identified by PET/CT imaging, the importance of recognizing this entity was highlighted (11). The present case draws attention to an important issue regarding interpretation of whole body FDG-PET. The uptake may not be always bilaterally symmetrical. Solitary focus of FDG hypermetabolism in and around the location of the adrenal gland, even though asymmetric, should not be interpreted straightaway as disease involvement. With the given intensity of the uptake in the present case, the lesion could have been easily mistaken as a metastatic focus in the adrenal gland. Secondly, even after benzodiazepine premedication the uptake may persist as evidenced by this case. BAT has been reported to have benzodiazepine receptors, to which diazepam binds as an agonist (12). It is possible that in humans the central antianxiety effect of diazepam may relieve the sympathetic nervous system activity and thus reduce 18F-FDG uptake in BAT. In general, the experience in the clinics shows that propranolol or reserpine appears to be considerably more suitable than diazepam in reducing 18F-FDG uptake in BAT. Hence, the interpreting physician must consider the focus in the background of FDG uptake in the BAT and the disease status in the rest of the body. In this case, the disease free status in the rest of the whole body survey and the presence of extensive BAT uptake in other areas made it imperative to rule out the same in the abdomen. A further careful correlation is essential for an accurate diagnosis as well as therapeutic decision making in these patients.

TEACHING POINT

Recognizing FDG uptake in infradiaphragmatic brown fat is important while interpreting PET study and the uptake may not be always bilaterally symmetrical. Benzodiazepine premedication is not 100% efficacious in abolishing the aforementioned activity.

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FIGURES

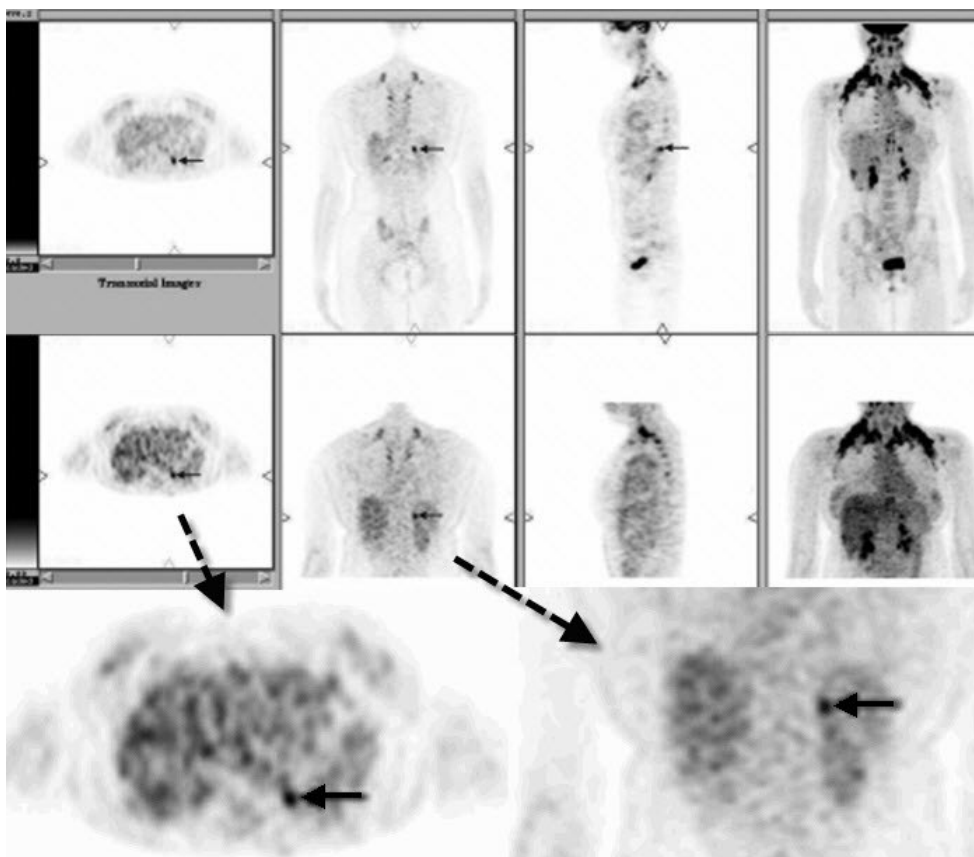


Figure 1: Whole body FDG-PET imaging was performed sixty minutes after the intravenous injection of 0.14mCi/kg of FDG. Emission and transmission data was acquired with successive overlapping axial frames. Two dimensional acquisition technique was adopted which allows use of a lower dose of radiotracer. The ordered-subsets expectation maximization (OSEM) method was used to reconstruct the PET images.

The baseline FDG PET (upper panel) showed intense FDG uptake in bilateral neck and paraspinal regions. Solitary intense focus was also noted in the left side of the abdomen posteriorly (arrow). The uptake persisted in the repeat scan after diazepam intervention (middle panel, lower panel magnification), indicating the BAT uptake to be "diazepam resistant".



ABBREVIATIONS

BAT = Brown adipose tissue
FDG-PET = Fluorodeoxyglucose positron emission tomography
USA Fat = Upper Supraclavicular area Fat

KEYWORDS

Brown Fat, FDG-PET, adrenal metastasis

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Figure 2: Typical pattern of FDG uptake in the brown adipose tissue: avid bilateral and symmetric, intense, more often multifocal than linear and distributed over neck, supraclavicular and paravertebral region.