

Imaging of Pulmonary Tuberculosis with ^{18}F -Fluoro-Deoxy-Glucose and ^{18}F -Ethylcholine

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Abstract: *Introduction:* A 37-year-old man was referred for PET/CT with the following diagnostic challenge: a longstanding smoking history, histologically confirmed TB and sarcoidosis with worsening chest-related symptoms and a non-responsive right upper lobe lung lesion (as detected on CT).

Materials and Methods: PET/CT imaging was performed with ^{18}F -FDG and followed by imaging with ^{18}F -fluoroethyl-choline in an attempt to better characterize the lung lesion. This was followed by biopsies of the right upper lobe nodule, the pleura and a brain lesion.

Results: Both tracers demonstrated increased uptake in the lung lesion and in multiple lymph node groups. Histology revealed the presence of a granulomatous disease in the lung lesion, the pleura and in the brain. Follow-up evaluation with ^{18}F -fluoroethyl-choline PET/CT demonstrated some improvement, which correlated with clinical improvement.

Conclusion: Tuberculous lesions demonstrate increased accumulation of ^{18}F -fluoroethyl-choline on PET/CT, which may be useful in the evaluation of treatment response. When used in combination with ^{18}F -FDG, it could be of value in distinguishing malignant lesions from tuberculosis.

Keywords: ^{18}F -fluoroethyl-choline, ^{18}F -FDG, functional imaging, lung lesions, PET/CT, sarcoidosis, tuberculosis.

INTRODUCTION

A 37-year-old man with a long-standing smoking history presented with worsening chest-related symptoms on anti-Tuberculosis treatment. Rifampin therapy had been re-started empirically three months prior to the initial PET/CT after histological confirmation of Tuberculosis (TB) from pleural and liver tissue. At the time of investigation, sarcoidosis had also been confirmed histologically from enlarged abdominal lymph nodes (which were discovered on CT). Steroid therapy was started in order to treat the sarcoidosis. However, this had to be discontinued after six months following the occurrence of unacceptable side effects. A follow-up CT revealed a collapsed right lung with a large pleural effusion (for which an intercostal drain was inserted) and a lesion in the right upper lung that had not responded to treatment.

The diagnostic challenge, therefore, was one of a patient with histologically proven TB (pleura & liver) and sarcoidosis (abdominal lymph nodes) with worsening chest-related symptoms (after three months of Rifampin treatment) and a non-responsive lung lesion. Taking into account the long-standing smoking history, a malignant lung lesion was also possible. Mycobacterial culture and sensitivity studies

demonstrated sensitivity of acid-fast bacilli (AFBs) to Rifampin and patient compliance to treatment was good.

It is well known that imaging with ^{18}F -FDG PET/CT (including dual-phase imaging) is unable to distinguish malignant lesions from granulomatous disease in countries where these diseases are highly prevalent [1-3]. We subsequently decided to image the patient first with ^{18}F -FDG, followed by ^{18}F -fluoroethyl-choline (FEC) five days later in order to try and better characterize the right upper lung lesion.

MATERIALS & METHODOLOGY

Approval was obtained from the university and hospital's research ethics committee as well as written informed consent from the patient.

PET/CT imaging was performed with ^{18}F -FDG (FDG) first, followed by imaging with ^{18}F -fluoroethyl-choline (FEC) five days later, in an attempt to better characterize the lung lesion.

Routine PET/CT imaging protocols were followed after IV administration of 305 MBq (8.2 mCi) of ^{18}F -FDG and 104 MBq (2.8 mCi) of ^{18}F -fluoroethyl-choline. The uptake time was 60 min for FDG with IV contrast given, whereas the uptake time for the ^{18}F -fluoroethyl-choline PET was 90 min with no IV contrast. Follow-up evaluation with ^{18}F -Ethylcholine PET/CT was performed eight months later.

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Biopsies and tissue analysis of the right upper lobe nodule, the pleura and brain lesion, were performed following the baseline imaging.

RESULTS

^{18}F -FDG-PET (FDG PET) images demonstrated an intensely FDG-avid pulmonary nodule with left supraclavicular as well as multiple mediastinal-, abdominal- and pelvic lymph node involvement. Hyper-metabolic liver lesions were also noted. The high intensity brain uptake, which is normally seen with FDG PET, limits the detectability of hyper-metabolic brain lesions (see Fig. 1a).

The initial ^{18}F -fluoroethyl-choline PET (FEC PET) images demonstrated a similar pattern of abnormal tracer accumulation in the mediastinum, although this was less extensive and much less intense (see Figs. 1b, 2). Uptake in the right upper lobe nodule demonstrated a SUVmax of 3.25. The normal tracer bio-distribution of ^{18}F -fluoroethyl-choline results in high intensity liver uptake, which limits the detection of liver involvement.

A repeat biopsy of the lung lesion, pleura and brain revealed granulomatous inflammation with caseous necrosis. Langerhans giant cells were present and special stains for AFBs were strongly positive. No evidence of an underlying neoplastic process could be found. The combined findings of high ^{18}F -FDG uptake and relatively low ^{18}F -fluoroethyl-choline uptake may indicate granulomatous disease rather than malignancy (in which case high uptake would be expected with both tracers.)

Anti-TB therapy was subsequently started and follow-up imaging with ^{18}F -Choline-PET/CT was performed eight months after the initial scan to assess treatment response. Image findings suggested a good response to therapy, which corresponded to the clinical improvement (see Fig. 1c).

Both tracers demonstrated increased uptake in the lung lesion and in multiple lymph node groups. Due to the differences in the normal tracer bio-distribution, liver involvement could be detected on FDG PET, whilst brain involvement could be detected on FEC PET (see Fig. 3). The mediastinal involvement on FEC PET appeared less extensive and less intense than what was demonstrated on FDG.

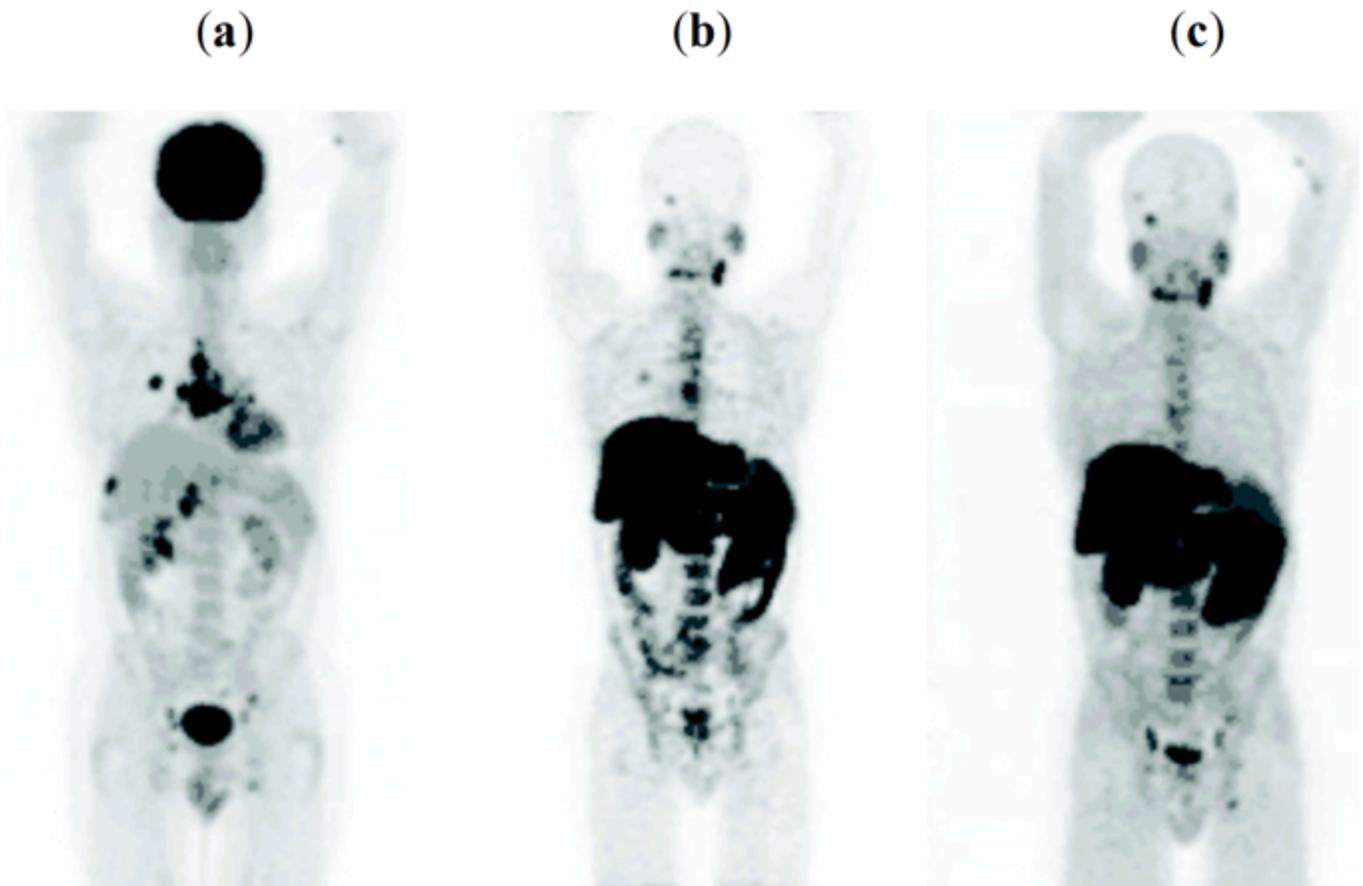


Fig. (1). (a) ^{18}F -FDG Maximum Intensity Projection (MIP) 305 MBq (8.2 mCi) of ^{18}F -FDG was administered IV. Uptake time: 60 min, IV contrast given. ^{18}F -FDG demonstrates intense uptake in the right upper lobe nodule (SUVmax 9.48), which corresponded to a spiculated pleural-based right upper lobe nodule (14.3x15.3 mm) on CT. (b) FEC MIP 104 MBq (2.8 mCi) of ^{18}F -Choline was administered IV. Uptake time 90 min, no IV contrast given. This image demonstrate tracer uptake in the lung nodule and mediastinal lymph nodes, which appear less extensive and less intense when compared to the FDG MIP. (c) Anti-tuberculosis treatment was re-started and follow-up imaging with ^{18}F -Choline-PET/CT was performed eight months after the initial scan to assess treatment response. Image findings indicated a good response to therapy, which corresponded to clinical improvement. On the FEC MIP image the nodule in the right upper lobe is no longer clearly visualized and the previously noted lymph node involvement appears less intense.

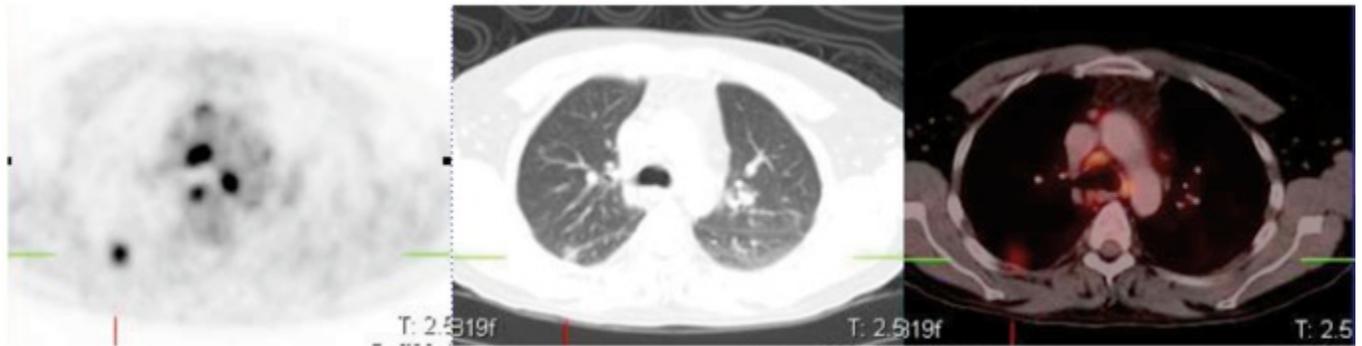


Fig. (2a). The right-sided lung nodule and metabolically active mediastinal lymph nodes are demonstrated on ^{18}F -FDG PET with their respective SUVmax values: Anterior mediastinal lymph node group: SUVmax 8.44, Middle mediastinal group SUVmax 14.47, and Posterior mediastinal group: SUVmax 16.0.

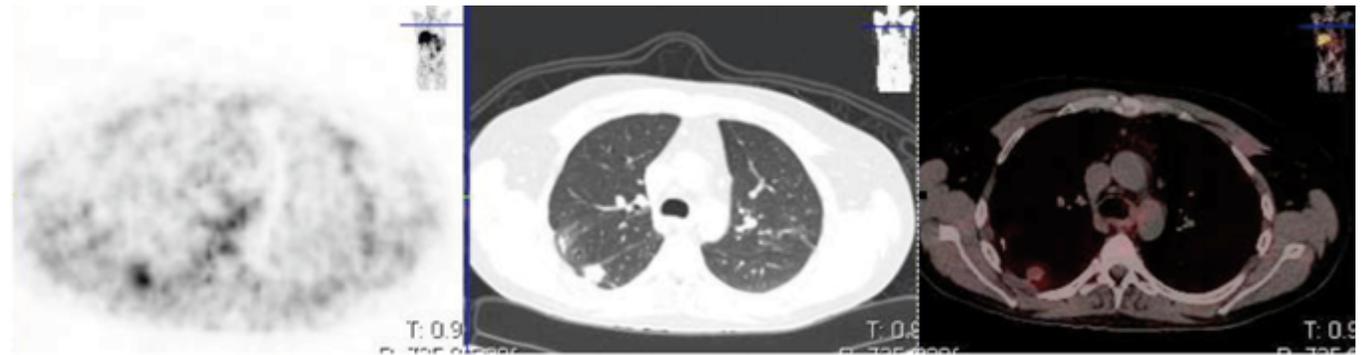


Fig. (2b). Lung nodule and mediastinal lymph node involvement demonstrated on ^{18}F -fluoroethyl-choline PET with their respective SUVmax values: Anterior mediastinal lymph nodes: SUVmax 3.40, Pre-tracheal lymphadenopathy: SUVmax 3.89. The involvement on these images appear less extensive and less intense.



Fig. (2c). ^{18}F -fluoroethyl-choline PET/CT images demonstrate mediastinal lymph node involvement, which appears less pronounced (both in extent and intensity) when compared to the ^{18}F -FDG PET images.

DISCUSSION

Abnormal choline metabolism is associated with neoplastic processes and results from changes in the enzymes that control anabolic- and catabolic pathways. This leads to increases in choline-containing precursors and phospholipid breakdown products, which provides an estimation of the degree of membrane proliferation [4].

Choline can be labeled to either ^{11}C - or ^{18}F - as ^{18}F -fluoroethyl-choline (FEC) or ^{18}F -fluoromethyl-choline (FCH) respectively, and is biochemically indistinguishable from the natural form of choline as a component of cell membranes. There are small differences with regards to the bio-kinetics, bio-distribution and intensity of uptake in

lesions between these two tracers, which have not been found to be clinically relevant [5].

The use of ^{18}F -fluoroethyl-choline in the setting of prostate cancer is well known. However, several authors have also evaluated its use in other malignancies [6-8]. Superiority of FEC PET over FDG PET has been demonstrated in differentiating low-grade glioblastomas from high-grade lesions, in detection of tumor recurrence and in guiding brain biopsies. Its use in the management of other tumors is evolving with reports of high accuracy in distinguishing benign from malignant thoracic lesions as well as in staging of lung cancers. Readers are hereby referred to a comprehensive systematic review by Treglia *et*

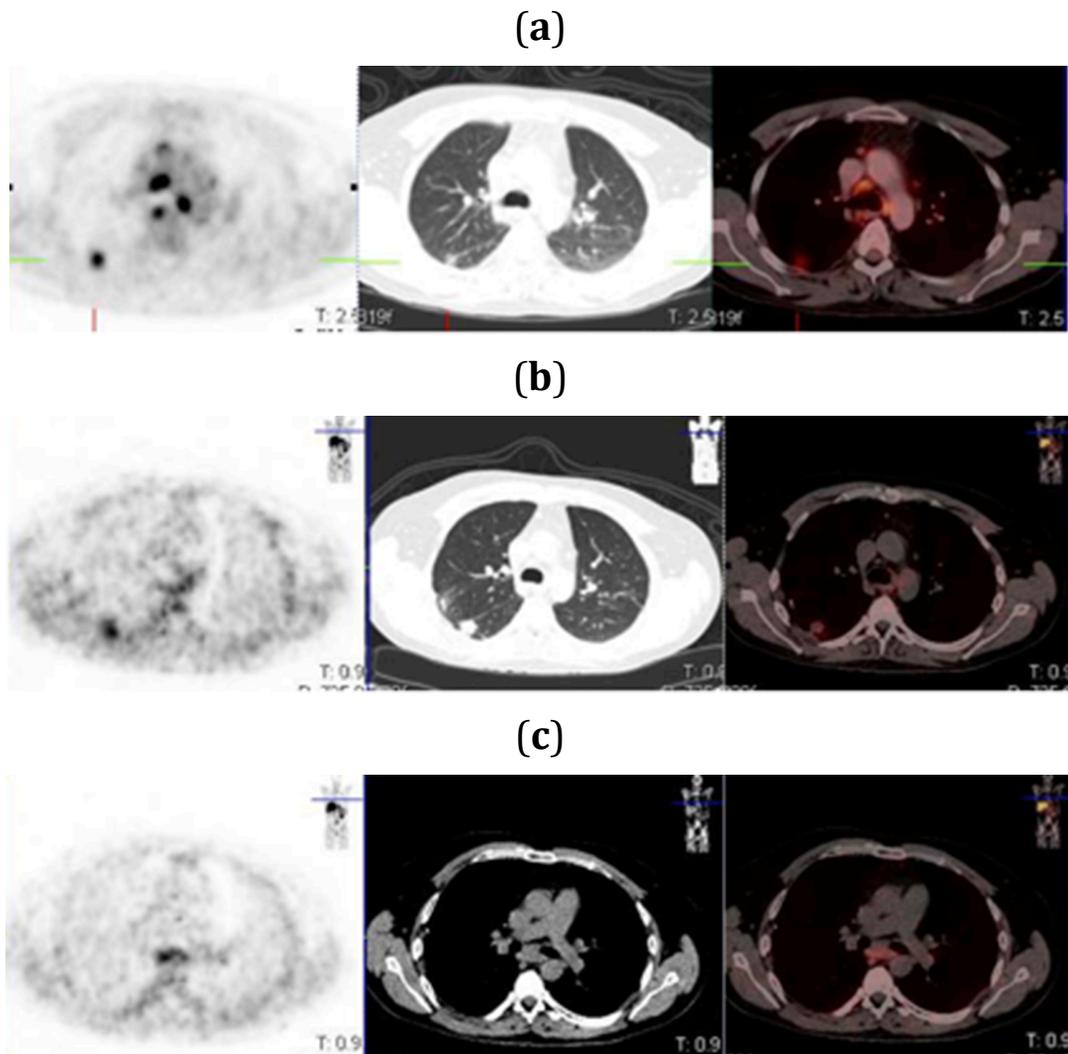


Fig. (3). ¹⁸F-fluoroethyl-choline PET/CT images demonstrate very low uptake in normal brain tissue, the venous sinuses and lateral ventricles, which allow for better detection of tuberculous brain involvement when compared to ¹⁸F-FDG.

al. on the use of choline PET imaging in tumors other than prostate cancer [6].

In the setting of lung- and mediastinal pathology, various studies have been conducted, of which we will briefly mention the ones most relevant to this case. Liu *et al.* (2006) investigated the role of ¹¹C-Choline in the characterization of mediastinal masses in 32 patients and found an accuracy of 75% in distinguishing benign from malignant lesions [9]. The authors described higher tracer accumulation in malignant lesions, compared to benign lesions and suggested dual-time point imaging (5-10 minutes and 25-30 minutes) in order to highlight differences even further.

Hara *et al.* (2000) compared the diagnostic accuracy of ¹¹C-choline and ¹⁸F-FDG PET in the detection of mediastinal lymph node metastases from non-small cell lung cancer and reported a 100% detection rate with ¹¹C-choline [10]. The same group later investigated the combined use of ¹⁸F-FDG and ¹¹C-choline in the differentiation between lung cancer and TB. The authors found that both tracers demonstrated high accumulation in malignant lesions. In TB, however,

FDG demonstrated significantly higher uptake than choline [11]. This is similar to what we have found.

Various other groups have also confirmed the value of choline PET imaging in the staging of lung cancer, especially with regards to assessment of mediastinal lymph node- and brain metastases [12-14].

To date, no clear superiority of choline over FDG imaging has been demonstrated with regards to chest pathology and combining these tracers may be of value.

CONCLUSION

This patient with histologically confirmed granulomatous disease demonstrated increased tracer accumulation with both ¹⁸F-FDG and ¹⁸F-fluoroethyl-choline in the lung nodule and mediastinal lymph nodes, which differed in terms of the extent and intensity of the involvement. Brain involvement could be better detected with FEC PET, whilst liver involvement was better appreciated on FDG PET.

Our findings suggest that ¹⁸F-fluoroethyl-choline may be used in the evaluation of treatment response. Furthermore,

that the combined findings of high ¹⁸F-FDG uptake and relatively low ¹⁸F-choline uptake may indicate granulomatous disease rather than malignancy (in which case high uptake would be expected with both tracers.) Further investigations are needed in order to establish a possible SUV cut-off.

LIST OF ABBREVIATIONS

AFB	=	Acid Fast Bacilli
Choline	=	¹⁸ F-Fluoroethyl-choline
CT	=	computed tomography
FDG	=	¹⁸ F-fluoro-deoxy-glucose
IV	=	Intravenous
MBQ	=	MegaBequerel
mCi	=	miliCurie
MIP	=	Maximum Intensity Projection
PET	=	Positron Emission Tomography
SUV	=	Standardized Uptake Value
TB	=	Tuberculosis

CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

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