

# Mediastinal lymphadenopathy detected with an integrated positron emission tomographic/computed tomographic scan: a differential diagnosis to consider before minimally invasive staging

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Integrated positron emission tomography combined with plain computed tomography is commonly employed as the diagnostic tool for patients presenting with lung opacities. This technology is non-invasive and does not put the patient at risk of contrast reaction. We report a case of a man who presented with fever, septicaemia, and a left apical lung opacity on chest radiography. His positron emission tomography and plain computed tomography scans showed increased uptake by the left apical lung opacity together with a huge anterior mediastinal mass, suggestive of lung cancer with mediastinal lymph node involvement, and a right upper lobe shadow. After an initial futile bronchoscopy, an endobronchial ultrasound-guided transbronchial needle aspiration of the mediastinal node was planned but a contrast computed tomographic scan of the thorax revealed no significantly enlarged mediastinal lymph nodes. The differential diagnoses of these findings, together with the limitations of positron emission tomography and plain computed tomography, are discussed.

## Introduction

In lung cancer patients whose initial diagnosis has been made by chest radiography or computed tomography (CT), histological confirmation of the tumour cell type is necessary to guide the mode of treatment. In patients with non-small cell lung cancers, the disease stage and hence operability will depend on the extent of hilar and mediastinal lymph node involvement. Positron emission tomography (PET) using  $^{18}$ fluorodeoxyglucose (FDG) enables detection of increased glucose metabolic uptake, a characteristic of most cancers. Integrated PET and CT imaging allows the location of FDG uptake to be determined using a plain CT scan. The latest international guidelines advise that staging the mediastinal nodes using CT or PET is not sufficiently accurate.<sup>1</sup> Mediastinoscopy has been the gold standard for this type of staging.<sup>2</sup> Recently, endobronchial ultrasound (EBUS)-guided transbronchial needle aspiration (TBNA) has emerged as a safe, minimally invasive and now widely accepted alternative to lymph node staging by mediastinoscopy.<sup>1,3</sup> Endobronchial ultrasound-guided TBNA of the enlarged mediastinal lymph nodes can provide both confirmation of the histological cell type and confirmation of the nodal disease at the same time. We report a case illustrating the possible pitfalls of using integrated PET/CT scanning to guide mediastinal lymph node staging.

## Case report

A 76-year-old non-smoking man with a history of hypertension and chronic renal failure presented with dizziness due to iron deficiency anaemia. An oesophago-gastro-duodenoscopy (OGD) was performed and a gastric ulcer was diagnosed. He was admitted to hospital 2 weeks after his OGD for fever and poor general condition. He also gave a 6-month history of left-sided chest pain. A physical examination revealed finger clubbing and a post-herpetic eruption scar over the left T5 dermatome.

### Key words

Aortic aneurysm; Endosonography;  
Mediastinum; Positron-emission  
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computed

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## Investigations

Blood tests showed a leucocytosis, with a total white cell count of  $17.6 \times 10^9$  /L (94% neutrophils), a creatinine of  $324 \mu\text{mol/L}$ , a normochromic normocytic anaemia with a haemoglobin of  $81 \text{ g/L}$ , a C-reactive protein level of  $210 \text{ mg/L}$ , a serum iron level of  $7 \mu\text{mol/L}$  and a total iron binding capacity of  $50 \mu\text{mol/L}$ , and a serum ferritin of  $85 \text{ ng/mL}$ . Sputum and urine cultures were negative but blood cultures grew methicillin-sensitive *Staphylococcus aureus* (MSSA).

Chest radiography (Fig 1a) showed a left apical opacity and cardiomegaly

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(cardiothoracic ratio, 0.6). The patient was commenced on intravenous amoxicillin/clavulanate before the blood culture results were available. His fever and leucocytosis both responded to antibiotics. The blood cultures were repeated thrice and all were negative. No significant valvular lesions and no vegetations were detected on transthoracic echocardiography.

In an attempt to localise the source and complications of his MSSA septicaemia and to investigate possible malignancy, a PET/CT scan was arranged in the private sector. Intravenous contrast was not requested in view of his impaired renal function and the additional financial burden it would impose on the patient. The PET/CT scan showed a hypermetabolic soft tissue shadow (max diameter, 2.2 cm) with a standard uptake value (SUV) max 12.35 in the left lung apex. A right upper lobe lesion of SUV 2.8 was suggestive of fibrosis/mass. An enlarged hypermetabolic soft tissue mass at the anterior mediastinum measuring 4.8x4.5x6.8 cm and SUV 9.54, likely to be lymphadenopathy, was reported (Figs 1b-1f).

Bronchoscopy failed to yield histologic specimens for diagnosing the right upper lobe lesion. The patient was referred to the authors for EBUS-guided TBNA of his mediastinal lymphadenopathy.

At the same time, a gallium scan was arranged to monitor his MSSA septicaemia 2 months after the

### 正電子及電腦斷層造影術 (PET/CT) 對縱隔淋巴結病的檢測：微創分期前可考慮的一種鑒別診斷

結合正電子和電腦斷層造影術 (PET/CT) 對有肺影的病人已成為一種普遍的診斷工具。此技術的非侵入性避免病人對造影劑出現反應。本文報告一名有發燒及敗血病的男性，其胸部X綫影像顯示左肺尖端有肺影。PET及CT均顯示左肺尖端有攝取增加現象，並發現前縱隔腔腫瘤及右肺葉上端有影。起初的支氣管鏡檢未有發現，原本計劃對縱隔淋巴結作支氣管內視鏡超聲波指引經氣管細針抽吸檢測，但顯影CT影像並未發現大型縱隔淋巴結。本文討論不同技術的鑒別診斷結果，以及PET/CT技術的限制。

onset. A contrast CT thorax was also performed at this time to enable localisation of the abnormalities. In brief, the left apical lung opacity showed increased focal uptake in the gallium scan and irregular enhancement after injection of contrast. These findings were suggestive of lung carcinoma of the left upper lobe. The right upper lobe lesion showed mild increased uptake corresponding with the fibrosis/consolidation changes seen on the contrast CT scan. Nonetheless, no mediastinal lymphadenopathy was reported. The contrast CT scan detected only small lymph nodes with a maximal short axis of 0.64 cm,

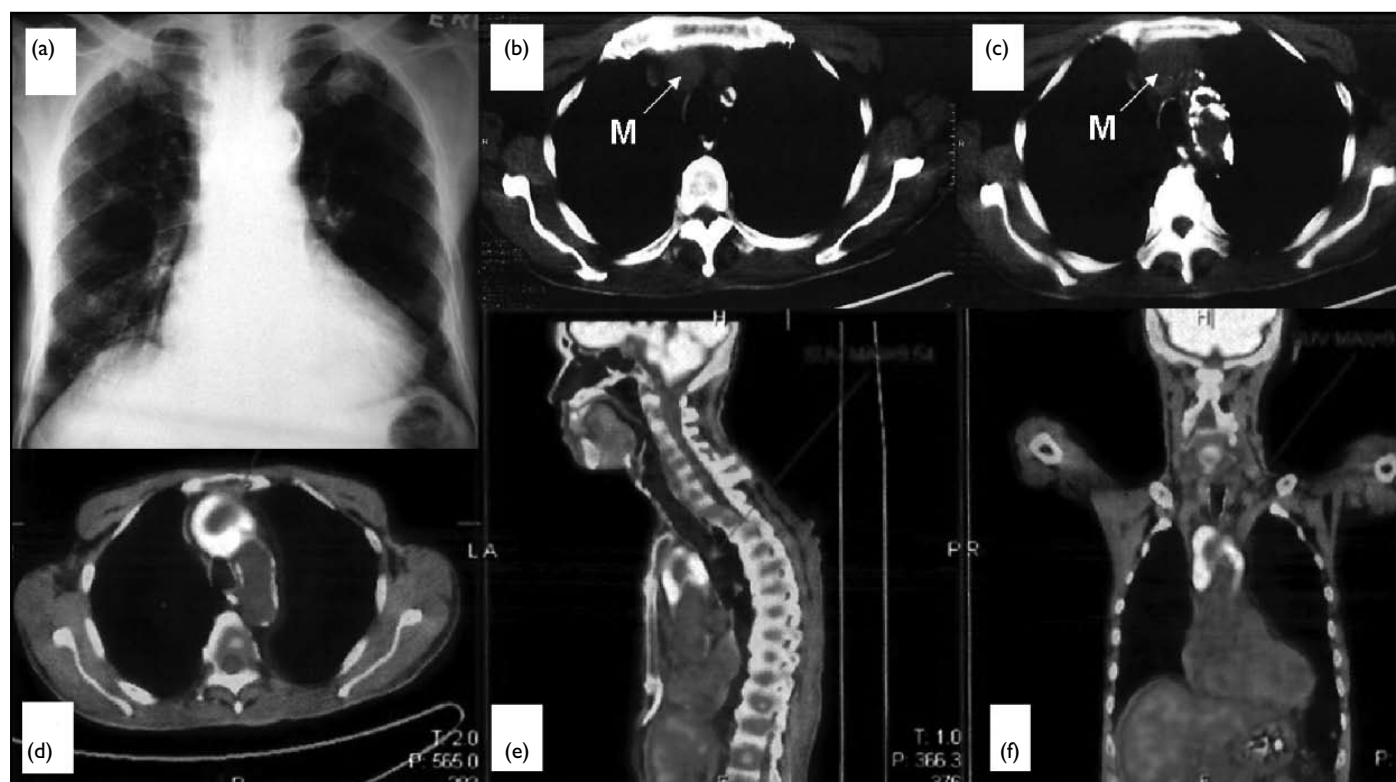
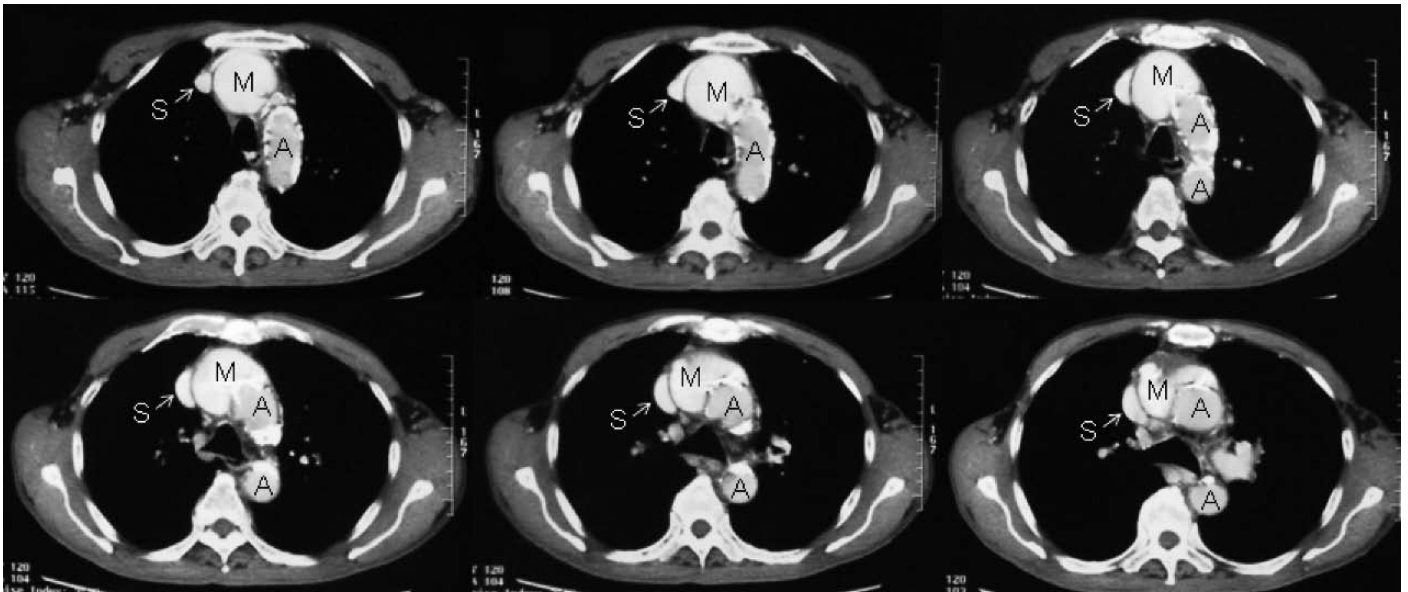


FIG 1. (a) Chest radiography of the patient. (b, c) Plain computed tomography (CT) of the thorax showing a right paratracheal mass (denoted by "M"). (d-f) Positron emission tomography/CT images showing an enlarged hypermetabolic soft tissue mass at the anterior mediastinum measuring 4.8x4.5x6.8 cm with standard uptake value of 9.54



**FIG 2. Contrast computed tomography of the thorax**

The anterior mediastinal mass (denoted by "M") was at the right paratracheal region and intensely contrast-enhanced. It was an aortic aneurysm arising from the aorta (denoted by "A"). "S" denotes superior vena cava

with no uptake in the gallium scan at the precarinal region.

The authors reviewed the two sets of CT films while the patient was being prepared for EBUS-guided TBNA. The 4.5-cm mediastinal lymphadenopathy described in the first plain CT was enhanced by contrast and was seen to be contiguous with the ascending aorta in the second set of CT films (Fig 2). The coronal reconstruction by contrast-enhanced CT showed that the mass was part of the aorta and connected with the great vessels supplying the upper part of the body. In retrospect, the PET images also suggested that the mediastinal mass was contiguous with the aorta (Figs 1d-f). The mediastinal mass reported in the PET/CT scan was an aneurysm of the ascending aorta. The EBUS/TBNA was cancelled.

The patient did not report any adverse reaction after the contrast injection and his renal function remained static. A CT-guided transthoracic needle aspiration of the left apical lung opacity showed adenocarcinoma. Serology for syphilis was negative but a sputum culture yielded *Mycobacterium tuberculosis*. The patient was put on anti-tuberculous medications. He refused to consider surgical resection of his lung cancer due to his age and his co-morbidities.

## Discussion

In our patient, a plain CT film accompanying the PET scan failed to reveal that the mediastinal mass was an aneurysm of the ascending aorta, underlining the importance of using a contrast study. Naidich et al<sup>45</sup>

have pointed out that lymphadenopathy restricted to the anterior portions of the hila is more difficult to define than that affecting posterior nodes, especially without intravenous contrast, because the anterior pulmonary/hilar interface is less characteristic than the same posterior interfaces.

The intense and diffuse FDG uptake seen on the PET images of our patient's anterior mediastinum could have been due to MSSA aortitis or a mycotic aneurysm. Other possibilities would include aortitis due to syphilis or autoimmune diseases such as giant cell arteritis. Although increased FDG uptake occurs in aortic aneurysms and atherosclerosis, in our case the FDG uptake (SUV 9.54) was much higher than the FDG uptake reported previously for aortic aneurysms (SUV 2.52±0.52).<sup>6</sup> A PET scan seems to be a more sensitive investigation than a gallium scan for identifying vasculitis of the large arteries.<sup>7</sup> Despite this, an active infection at the time of the PET scan is the more likely explanation for the intense FDG uptake at the ascending aorta, given his MSSA septicaemia and subsequent clinical response to therapy. Positron emission tomography/CT is the tool used to investigate pyrexia of unknown origin most frequently. Our case exemplifies the superiority of PET over gallium scanning for detecting both malignancies and inflammatory diseases, as previously reported.<sup>7</sup> Nevertheless, interpretations should be guided by the reasons for ordering PET/CT. In our case, PET/CT was done to screen for the source of septicaemia with an incidental finding of a malignancy; thus FDG uptake foci should not be interpreted solely as metastatic diseases without

histologic confirmation. Tumour staging using PET/CT should be postponed during active infection as this may lead to false-positive tumour involvement.

Pulmonary tuberculoma commonly causes an increase in FDG uptake. Hong Kong is one of the Asian regions with a high prevalence of tuberculosis, and thus positive FDG uptake results should be interpreted with caution.<sup>8,9</sup> In our patient, it was assumed that the right upper lobe lesion, with an FDG uptake of SUV 2.8, was due to tuberculous infection. This was based on the sputum culture result, even though a synchronous tumour or metastatic disease could not be ruled out without an excisional biopsy. The SUV seen in our patient was in keeping with the SUV of 4.2±2.2 found in the tuberculomas of 10 patients in a Korean study.<sup>9</sup>

With the introduction of EBUS/TBNA, tissue sampling of PET positive lymph nodes can be performed under conscious sedation. The convex probe EBUS (Olympus Ultrasonic bronchofiberscope BF UC260F-OL8, Tokyo, Japan) provides B-mode imaging of the peribronchial structures so the anatomical relationship between the 'mediastinal mass' and the aorta will be revealed. Any blood flow inside the 'mass' will also be detected by the power doppler<sup>10</sup> although blood flow may be totally absent in the thrombosed region of the aneurysm. On the other hand, if blind TBNA was attempted in this case, the

outcome could have been disastrous especially with repeated punctures.

Emerging data suggest that use of a combination of an endoscopic ultrasound-guided needle aspiration (EUS-NA) and an EBUS-NA may allow nearly complete access to all mediastinal lymph nodes.<sup>11</sup> This technique (EUS-NA) is a minimally invasive method performed via the oesophagus to sample posterior mediastinal lymph nodes while EBUS-TBNA is best suited for anterior mediastinal lymph nodes.<sup>1,11</sup>

In summary, we report on a patient with carcinoma of the lung, pulmonary tuberculosis and an aortic aneurysm presenting with MSSA septicaemia. All these lesions showed increased FDG uptakes on PET/CT scanning. In regions where tuberculosis is prevalent, clinical judgement must be exercised when interpreting positive FDG uptakes. A contrast CT of the thorax can distinguish the presence of anterior mediastinal lymphadenopathy from vascular abnormalities. An EBUS study of the peribronchial lesion will provide additional information on the anatomical relationship between the mass and the aorta and detect the blood flow around the thrombosed part of the aneurysm. Aortic aneurysms should always be considered when an integrated PET/CT scan is used as the sole imaging investigation for making an invasive or minimally invasive diagnosis of mediastinal masses.

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