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Intense uptake of [F-18]-fluoro-2 deoxy-D-glucose in active pulmonary tuberculosis

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FDG PET is well recognized for its utility in cancer workup. Nonetheless, the differentiation between malignant and benign pulmonary lesions by FDG PET is challenging. The authors report three proved cases of pulmonary tuberculosis in acute active and open stages. The activities and extents of infection were demonstrable in FDG PET, which could not be observed in either chest radiograph or computed tomography.

Key words: FDG PET scintigraphy, tuberculosis

INTRODUCTION

[F-18]-fluoro-2 deoxy-D-glucose (FDG) in conjunction with positron emission tomography (PET) is a novel modality in tumor detection, staging, and therapeutic monitoring. Its non-specificity remains a difficulty in differentiating malignant from benign pathological variants which occasionally mimic malignancy. In acute infectious and non-infectious inflammatory processes, activated leukocytes ignite a metabolic burst during which they utilize an increased amount of glucose and FDG may also accumulate in the infectious agent itself.[1]

Previous reports demonstrated the usefulness of FDG PET in the detection of infectious foci and the assessment of lesion activities.[2] Focal uptakes of FDG in tuberculous lymphadenitis in mediastinal, supraclavicular, and paraaortic regions, and in tuberculous pneumonitis had been reported.[3–5] Tuberculosis (TB) is a chronic granulomatous inflammation in which macrophages are the first line of defense; after phagocytosis, macrophages produce cytokines that recruit peripheral lymphocytes and monocytes at the site of inflammation.[6] The subsequent formation of granulomas provides the critical environment in which the host limits TB infection by suppressing bacterial replication and facilitate intracellular killing; only 5% of people infected with TB fail to contain the initial infection and go on to develop active TB disease.[7]

We report three proved cases of pulmonary TB in acute active and open stages. The activities and extents of infection were demonstrable in FDG PET, which could not be observed in either chest radiograph or computed tomography (CT).

CASE REPORT

The first case was a 69-year-old female patient admitted with the chief complaint of fever and cough. Chest radiograph revealed multiple ill-defined, radio-opaque masses in both upper and middle lung fields, and a large cavitated mass in the left para-hilar region (Fig. 1A). Chest CT scan showed multiple ill-defined, various-sized masses in bilateral upper lobes of the lungs. The largest one involved the anterior segment of left upper lobe and part of the left lingular lobe with irregular-walled cavities (Fig. 1B). The radiologist's comment was that infections such as pulmonary TB or lung cancer with intrapulmonary metastases should be considered. Bronchoscopic findings included bloody sputum, redness and swelling of left upper bronchial trees, without sign of endobronchial lesion or external compression.

Whole body and brain PET imaging was performed at 45 minutes after intravenous injection of 370 MBq (10 mCi) of [F-18]FDG on a Siemens ACCEL PET scanner. Fasting for 6 hours was required prior to the scanning.

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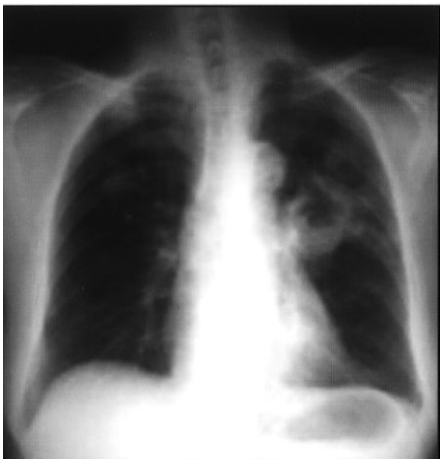

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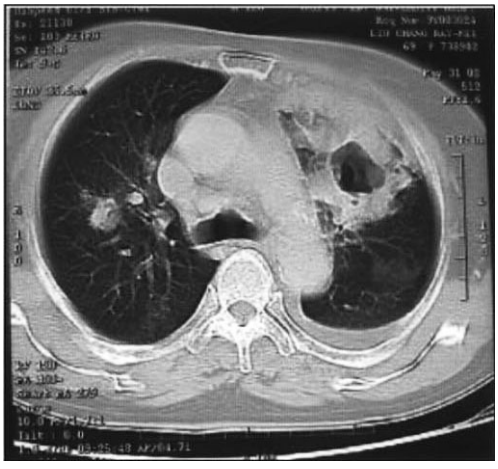

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C

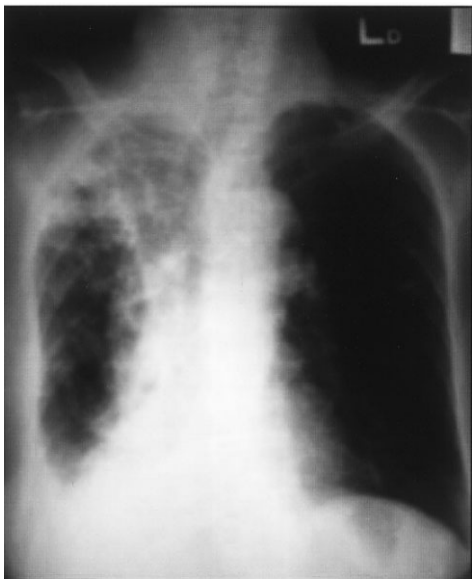
Fig. 1 (A) The chest radiograph shows multiple ill-defined masses in both upper and middle lung zones, and a large cavitated mass at the left para-hilar area. (B) Chest CT scan shows bilateral upper lobes multiple ill-defined masses with cavitations. (C) There is a huge hypermetabolic mass with the central area devoid of radioactivity in the left middle lung field of the PET image. The main mass has non-viable, probably necrotic, tissue in the central area. In addition, there are seven additional focal nodules in the bilateral lung fields.

Images were reconstructed iteratively with attenuation correction. There is a huge hypermetabolic mass with the central area devoid of radioactivity in the left middle lung field, the corresponding area seen on the chest radiography and CT scan. In addition, there are seven additional focal nodules in the bilateral lung fields. The standard uptake value (SUV) of the main mass is about 7.5 and those of the other nodules are about 4.9, 5.8, 1.4, and 9.5 respectively. The main mass occupying the left upper and middle lung fields has non-viable, probably necrotic, tissue in the central area. The PET findings (Fig. 1C) are compatible with active infection, TB or fungus, of the lungs.

CT guided biopsy was subsequently executed. Pathology report indicated caseous necrotic granulomatous inflammation. Although no bacillus was found by the acid-fast stain, TB was still the most likely etiology as suggested by the pathologist. The sputum culture was positive for mycobacterium.

The second case was an 83-year-old female patient admitted to our hospital due to fever and chillness. Chest radiograph showed ill-defined radio-opaque patches in the right middle and lower lung fields (Fig. 2A), and those patches were suggested to be some alveolar processes of various etiologies by the radiologist. Because the patient was unable to expectorate sputum, neither sputum smear nor sputum culture was obtained during this admission. PET scan with the same technique as described in the previous case indicated a discrete distribution of increased uptakes of FDG in the right lung with areas devoid of radioactivities (Fig. 2B). Our impression was also an active infectious process. The patient was then put on tentative anti-TB treatment and discharged. She was readmitted 2 months later due to consciousness changes. Sputum acid fast stain (AFS) was found to be positive in the subsequent admission.

The third case was a 32-year-old female patient who was sent to the emergency room due to short of breath and severe chest pain, and subsequently admitted. This patient had been an intravenous substance addict and suffered from infective endocarditis about 2 months prior to this admission. Chest radiograph revealed consolidations in bilateral lower lung fields with cavitary lesions in the right



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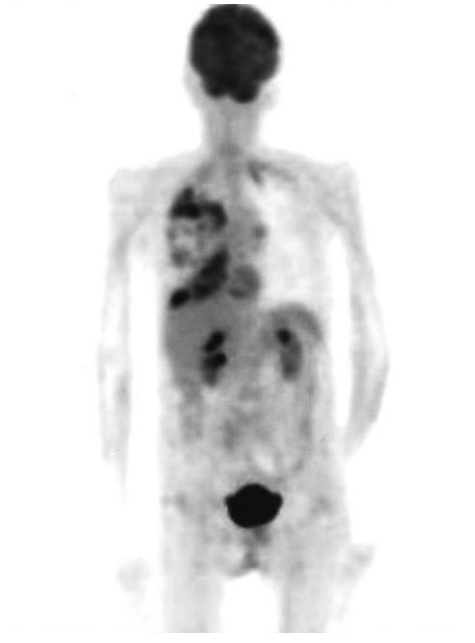
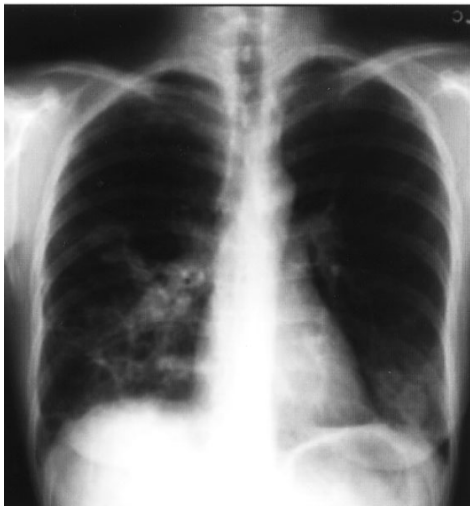


B

Fig. 2 (A) The chest radiograph shows large ill-defined consolidations in right upper and lower lung zones with multiple areas of cavitations. Note right pleural effusion. (B) PET scan indicated a discrete distribution of increased uptakes of FDG in the right lung with areas devoid of radioactivities.

middle lung field (Fig. 3A). Sputum AFS smears were negative; however, sputum mycobacterial cultures were positive. A PET scan was then administered. Several hypermetabolic areas were detected, in which cavity-like lesions located in both right and left middle to lower lung fields were demonstrated. The SUVs of the lesions were approximately 1.6 to 4.7. The hyper-uptake areas were more extensive than the radio-opaque areas demonstrated



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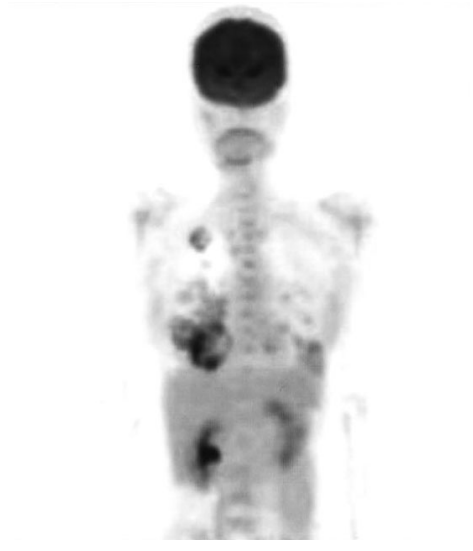

B

Fig. 3 (A) The chest radiograph shows multiple ill-defined cavitated pulmonary masses in both lower lung zones. (B) Several hypermetabolic areas were detected in bilateral upper and lower lung fields of the PET image. A cavity like lesion, which was not shown in the chest radiograph, was found in the right upper lung field.

in the chest radiograph. For instance, a cavity like lesion, which was not shown in the chest radiograph, was found in the right upper lung field (Fig. 3B).

DISCUSSION

FDG PET is well recognized for its utility in cancer work-up. Nonetheless, the differentiation between malignant and benign pulmonary lesions is challenging. Semiquantitative analyses, such as the SUV, are regularly used as supplementary tools for decision making in the interpretation of FDG PET. The cut-off value of 2.5 for SUV

is usually suggested for discrimination, i.e., greater than 2.5 for malignant lesions.[8] However, FDG has also been proven to be able to accumulate in both acute inflammatory tissues[9] and chronic inflammatory processes.[10] Even in tumors, it has been indicated that as much as 29% of the FDG uptake could derive from nontumor tissues.[11]

Various intensities described as weak, intermediate, and strong uptakes of FDG in tuberculosis infection were reported previously.[3,4,8,12] *Mycobacterium tuberculosis* infection is a high prevalence disease in low socio-economic areas and immune-compromised patients. Pulmonary tuberculosis in the acute active state also has intense glucose hypermetabolism. Our report reveals that the extent of infectious process and viability of involved tissue, which cannot be completely identified in morphological imaging modalities, are demonstrable in PET.

Scientists have tried various approaches in order to increase TB diagnosis accuracy by the PET. For instance, the combined use of F-18 FDG and C-11 acetate (ACE) helps differentiate TB from cancer. In a study done in Taipei's Veteran General Hospital, the investigators found out that the sensitivity and specificity of F-18 FDG PET in detecting active pulmonary TB were 100% and 44% respectively, whereas the sensitivity of combined F-18 FDG and C-11 ACE PET scan was still 100% and, more importantly, the specificity increased to 83%.[13]

The use of PET scanning in infections has been an interesting research subject. It has been argued that FDG scanning is particularly useful in patients with human immunodeficiency virus (HIV) infection or fever of unknown origin in that FDG scanning allows rapid evaluation of the whole body with a report potentially available within 4 hours of injection.[14] Especially, HIV infection has fueled a resurgence in the incidence of TB over the past decade. HIV-associated impairments of immunological mechanisms contributes to the increased risk of active TB, which include impairment of pulmonary innate immune defense; impairment of cellular recruitment and establishment of the cell-mediated granulomatous response to recent TB infection; and functional impairment of established granulomas containing latent TB infection.[7] Although all of our three cases are not immune-compromised, it is worthwhile keeping in mind the potential utility of PET in this area.

It is important in the interpretation of a FDG PET study to aware of the possible pulmonary TB pitfalls and to apply sputum or bronchial brushing cytology examination in TB susceptible subjects.

REFERENCES

1. Gutowski TD, Fisher SJ, Moon S, Wahl RL. Experimental studies of 18-F-2-fluoro-2-deoxy-d-glucose (FDG) in infection and in reactive lymph nodes. *J Nucl Med* 1992; 33: 925. (abstract)
2. Ichiya Y, Kuwabara Y, Sasaki M, Yoshida T, Akashi Y, Murayama S, et al. FDG-PET in infectious lesions: The detection and assessment of lesion activity. *Ann Nucl Med* 1996; 10: 185–191.
3. Bakheet SM, Powe J, Ezzat A, Rostom A. F-18-FDG uptake in tuberculosis. *Clin Nucl Med* 1998; 23: 739–742.
4. Yen RF, Chen ML, Liu FY, Ko SC, Chang YL, Chieng PU, et al. False-positive 2-[F-18]-fluoro-2-deoxy-D-glucose positron emission tomography studies for evaluation of focal pulmonary abnormalities. *J Formos Med Assoc* 1998; 97: 642–645.
5. Cook GJ, Fogelman I, Maisey MN. Normal physiological and benign pathological variants of 18-fluoro-2-deoxyglucose positron-emission-tomography scanning: potential for error in interpretation. *Semin Nucl Med* 1996; 26: 308–314.
6. Mariani F, Goletti D, Ciaramella A, Martino A, Colizzi V, Fraziano M. Macrophages response to *Mycobacterium tuberculosis* during HIV infection: relationships between macrophage activation and apoptosis. *Current Molecular Medicine* 2001; 1: 209–216.
7. Lawn SD, Butera ST, Shiunick TM. Tuberculosis unleashed: the impact of human immunodeficiency virus infection on the host granulomatous response to *Mycobacterium tuberculosis*. *Microbes and Infection* 2002; 4: 635–646.
8. Knight SB, Delbeke D, Stewart JR, Sandler MP. Evaluation of pulmonary lesions with FDG-PET. Comparision of findings in patients with and without a history of prior malignancy. *Chest* 1996; 109: 982–988.
9. Ishimori T, Saga T, Mamede M, Kobayashi H, Higashi T, Nakamoto Y, et al. Increased ^{18}F-FDG uptake in a model of inflammation: Concanavalin A-mediated lymphocyte activation. *J Nucl Med* 2002; 43: 658–663.
10. Yamada S, Kubota K, Kubota R, Ido T, Tamahashi N. High accumulation of fluorine-18-fluorodeoxyglucose in turpentine-induced inflammatory tissue. *J Nucl Med* 1995; 36: 1301–1306.
11. Kubota R, Yamada S, Kubota K, Ishiwata K, Tamahashi N, Ido T. Intratumoral distribution of fluorine-18-fluorodeoxyglucose *in vivo*: High accumulation in macrophages and granulation tissues studied by microautoradiography. *J Nucl Med* 1992; 33: 1972–1980.
12. Knopp MV, Bischoff HG. Evaluation of pulmonary lesions with positron emission tomography. *Radiologe* 1994; 34: 588–591.
13. Liu RS, Shei HR, Feng CF, Chang CP, Liao SQ, Yeh SH. Combined ^{18}F FDG and ^{11}C acetate PET imaging in diagnosis of pulmonary tuberculosis. Proceedings of the SNM 49th Annual Meeting. *J Nucl Med* 2002; 43: 127–128. (abstract)
14. O'Doherty MJ, Barrington SF, Campbell M, Lowe J, Bradbeer CS. PET scanning and the human immunodeficiency virus-positive patient. *J Nucl Med* 1997; 38: 1575–1583.