Uptake of Fluorine-18-Fluorodeoxyglucose in Pulmonary Mycobacterium avium Complex Infection

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Abstract

Two patients showing abnormal fluorine-18-fluorodeoxyglucose (FDG) uptake due to Mycobacterium avium complex (MAC) infection are presented. Intense focal FDG uptake in the lung field could have been caused by an infectious disease such as MAC. This should be considered as a possibility when FDG whole-body scans of patients with pulmonary nodules are interpreted. To our knowledge, this is the first description of an FDG-positron emission tomography (FDG-PET) image of MAC infection of the lung.

(Key words: MAC, FDG-PET, non-tuberculous mycobacteria, pulmonary nodule, lung cancer, inflammation)

Introduction

Pulmonary disease from non-tuberculous mycobacteria (NTM) has a wide spectrum of clinical presentations, from simple pneumonic infiltrates to progressive destructive disease (1–3). The majority of patients with pulmonary disease due to NTM have chronic underlying lung diseases such as pneumoconiosis, bronchiectasis, chronic bronchitis, and emphysema (1, 4). Although exposure to NTM often occurs without any clinical manifestation, there are differences in the virulence of these mycobacteria, and clinical manifestations may range from no symptoms or signs to destructive or even fatal disease (1). Among the NTM, Mycobacterium avium-intracellulare complex (MAC) disease has been increasingly recognized as an infective agent in immunocompetent patients without preexisting pulmonary disease (4). The most common radiographic findings have been relatively nonspecific alveolar or nodular infiltrates, with the nodules frequently cavitated (5–8). In addition, solitary or multiple pulmonary nodules discovered on routine chest roentgenogram are often due to NTM infection, particularly MAC infection (9). It is important to distinguish between MAC and lung cancer in such cases.

In the field of nuclear medicine, fluorine-18 fluorodeoxyglucose positron emission tomography (FDG-PET) has emerged as an important clinical tool for diagnosing, staging, and monitoring the therapy of cancer over the past several years (10, 11). FDG-PET is a molecular whole-body imaging modality that allows for noninvasive imaging of biological processes such as glucose use by tumors. Numerous studies have shown that FDG-PET is highly accurate for diagnosing and staging lung cancer (12). FDG-PET provides diagnostic information beyond that obtained through standard anatomic imaging modalities such as CT or MRI. In addition, thoracic PET imaging has proven to be a very powerful tool in the evaluation of pulmonary nodules. Among patients with a solitary pulmonary nodule more than 1cm, sensitivities and specificities are reported between 90–95% (13, 14).

In this report, we present two cases of intense FDG uptake related to MAC infection. These cases suggest potential pitfalls of FDG-PET assessments in evaluating pulmonary nodules.

Case Reports

Case 1

A 67-year-old man was admitted to our hospital for further evaluation because of progressive emaciation, low-grade fever and elevation of tumor marker (CA19-9: 167 U/ml). He had already been diagnosed with MAC disease in bilateral lungs and treated with clarithromycin, rifampicin and ethambutol hydrochloride. In a laboratory examination, the white blood cell count was 8,800/μl with a normal differential. CRP was 2.01 mg/dl. Chest radiograph and computed tomography (CT) scan of the thorax revealed multiple nodule-
Figure 1. Chest images of Case 1. (A) Chest radiograph on admission shows multiple hazy infiltrates in bilateral lungs. (B) High resolution CT scan of the right lung shows multiple nodular infiltrates with or without cavity. Centrilobular nodules are also demonstrated. (C) FDG-PET image shows intense multifocal uptake corresponding to the lesion of MAC infection, demonstrated by CT scan in Fig. B. SUVs for the lateral cavitary lesion (arrowhead) and the medial cavitary lesion (arrow) were 3.01 and 3.06, respectively.

In our hospital was obtained on a high-resolution dedicated system (ECAT HR+; Siemens Medical Systems, Inc., Hoffman Estates, IL). The resolution for reconstructed images was 10 mm. The patient fasted for at least 5 hours before receiving an intravenous injection of 18F–FDG. A standard whole-body imaging protocol commencing 60 minutes after injection was used. As a result, there was intense multifocal uptake in bilateral lungs that corresponded to the lesion demonstrated by chest X-ray and CT scan as MAC
infection (Fig. 1C). Standardized uptake values (SUVs) for these lesions were varied from 2.08 to 3.36. Cavitary lesions and nodular lesions more than 1 cm in diameter showed high SUV of greater than 2.5. However, most centrilobular nodules less than 1 cm showed low SUVs of less than 2.5.

**Case 2**

A 70-year-old woman was admitted to our hospital for further evaluation because of progressive emaciation, cough and elevation of tumor marker (CA19–9; 195 U/ml). In a laboratory examination, the white blood cell count was 5,800/μl with a normal differential. CRP was 0.67 mg/dl. Chest X-ray showed a solitary nodular lesion in the left upper lung field. CT scan revealed a nodular infiltrate surrounded by centrilobular micronodules in the left upper lobe (Fig. 2A). Repeated sputum culture and cytology revealed presence of *Mycobacterium intracellulare* and absence of malignancy. An FDG-PET whole-body scan was performed to examine for malignancy other than lung cancer. It showed intense uptake that corresponded to the nodular infiltrate demonstrated by chest X-ray and CT scan (Fig. 2B). SUV for this lesion was 3.14.

**Discussion**

The FDG-PET literature has previously suggested that significant uptake of FDG is indicative of malignant neoplastic tissue including lung cancer (10–12). Therefore FDG-PET scanning has increasingly been proposed as a method of differentiating benign and malignant lesions. However, increased FDG uptake is not limited to malignant tissue. It is taken up not only by viable tumor cells, but also by inflammatory cells (15). FDG has been seen in vitro to be accumulated by leukocytes, lymphocytes, and macrophages. Activated inflammatory cells have markedly increased glycolysis, and thus avid FDG uptake is the rule in inflammatory tissue (15). Therefore, FDG uptake may be seen in vivo at sites of variable inflammatory changes including granulomatous inflammation. In the thorax, several benign inflammatory diseases have been reported to be associated with increased FDG accumulation. False-positive findings have been reported in inflammatory and granulomatous processes such as bacterial pneumonia (16), aspergillosis, cryptococcosis, histoplasmosis (17, 18) sarcoidosis (19), and tuberculosis (20). In the present cases with MAC infection, granulomatous inflammation was presumed to be the cause of increased FDG accumulation. To our knowledge, this is the first description of an FDG-PET image of MAC infection of the lung.

Tissue inflammation may manifest increased glycolysis, but the increase in metabolic rate due to inflammatory changes is usually substantially less than that of neoplastic tissue. Inflammation and malignancy generally are differentiated on the basis of standardized uptake value (SUV), which allows a numerical comparison of areas of abnormally increased FDG uptake with areas of normal tissue (14, 21, 22).

A SUV threshold of 2.5 has been empirically determined to provide both good sensitivity and specificity in differentiating benign and malignant lesions in patients with pulmonary nodules (21–23). In the present cases, the SUV of most nodular infiltrates were more than 2.5, suggesting potential pitfalls of quantitative FDG-PET assessments in evaluating pulmonary nodules.

Gribetz et al have reported that a solitary pulmonary nodule discovered on routine chest roentgenogram is often the result of a granulomatous reaction to MAC infection (9). However, FDG whole-body scanning to differentiate between MAC infection and lung cancer may be considerably limited. Physicians should be aware of this nonspecificity when using FDG-PET scanning to assess pulmonary nod-
ules. Further studies are necessary to assess and compare the intensity and patterns of FDG uptake in MAC infection and lung cancer. The knowledge of these potential pitfalls will decrease the false-positive results of FDG-PET scan.

References