Usefulness of Respiratory-Gated ^{18}F -FDG PET/CT in Detecting Upper Abdominal Fever Focus

Sungwoo Bae¹ · Ji-In Bang² · Yoo Sung Song¹ · Won Woo Lee^{1,3}

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Abstract

Respiratory-gated ^{18}F -fluorodeoxyglucose (^{18}F -FDG) PET/CT has been successfully used to better localize malignancies in the lung or upper abdominal organs. However, clinical usefulness of respiratory-gated ^{18}F -FDG PET/CT in detection of fever focus has not been reported yet. A 68-year-old male patient with a history of living donor liver transplantation and biliary stenting was referred for ^{18}F -FDG PET/CT due to fever of unknown origin (FUO). To find the accurate fever focus, respiratory-gated and non-gated ^{18}F -FDG PET/CT was performed. Respiratory-gated PET/CT readily revealed prominent hypermetabolic lesion in the distal common bile duct (CBD) area where previous surgical graft was in situ. Maximum standardized uptake value (SUVmax) and SUV ratio (SUR) were greater in the gated PET/CT (SUVmax 5.4 and SUR 3.5) than in the non-gated PET/CT (SUVmax 4.6 and SUR 3.0). Fever dramatically subsided after removal of the graft in the CBD. This case report implies that respiratory-gated ^{18}F -FDG PET/CT can visualize upper abdominal fever focus with better contrast than the conventional non-gated method.

Keywords Respiratory-gated imaging techniques · Positron emission tomography · Computed tomography · Fever of unknown origin · Fluorodeoxyglucose ^{18}F

Introduction

Computed tomography (CT) is instantaneously acquired but positron emission tomography (PET) takes several minutes per each bed position. Thus, PET emission signals from organs close to the diaphragm are greatly affected by respiratory motion. Blurring effect due to respiratory motion disturbs not only the image quality but also quantification data from PET. Various gating methods have been used to mitigate the effect of respiratory motion. Hardware-based methods employ external devices that trail the movement of the chest or upper abdomen [1, 2]; the obtained respiratory signals are gated

vertically phase-by-phase between end-inspiratory peaks (phase-based gating) [1] or selected horizontally from lowest respiratory amplitude up to preset counts (amplitude-based gating) [2]. Cine CT-based 4D-PET/CT is another promising approach [3]. Data-driven respiratory gating methods without external devices are under active investigation [4].

Numerous studies demonstrated better performance of respiratory-gated ^{18}F -fluorodeoxyglucose (^{18}F -FDG) PET/CT in localizing lung or upper abdominal tumors compared with non-gated PET/CT [1–3, 5, 6]. However, to the best of our knowledge, non-tumorous infectious diseases have not been investigated using respiratory-gated ^{18}F -FDG PET/CT. Herein, we present a case of fever of unknown origin (FUO) in which respiratory-gated ^{18}F -FDG PET/CT played a crucial role for detection of the fever focus in the upper abdominal area.

✉ Won Woo Lee
wwlee@snu.ac.kr

¹ Department of Nuclear Medicine, Seoul National University Bundang Hospital, Seoul National University College of Medicine, 82, Gumi-ro 173 Beon-gil, Bundang-gu, Seongnam-si, Gyeonggi-do 13620, South Korea

² Department of Nuclear Medicine, Ewha Womans University School of Medicine, Seoul, South Korea

³ Institute of Radiation Medicine, Medical Research Center, Seoul National University, Seoul, South Korea

Case Report

A 68-year-old male patient was admitted to the (anonymous) hospital due to FUO in August 2017. The fever had lasted for about a week before admission. He had a history of hepatocellular carcinoma with alcoholic liver cirrhosis and

underwent living donor liver transplantation in 2010. Subsequently, he had biliary stricture as a complication of the surgery. This led to repetitive stent insertion to the common bile duct (CBD) area over a period of several years. In October 2015, all of the CBD stents were removed and there was no evidence of infection in the bile duct, thereafter.

At the time of current admission for FUO work-up, physicians could not find the cause of fever. Therefore, empirical antibiotics were prescribed, and the patient was discharged. However, the fever did not subside and the patient was readmitted to the Department of Internal Medicine in September 2017. At this time, potential differential diagnosis of FUO was *Clostridium difficile*-associated disease, small liver abscess, or tuberculosis.

Toxin assay for *Clostridium difficile*, antibody assay for *Orientia tsutsugamushi*, and blood culture were negative. C-reactive protein levels were elevated but other laboratory findings were not specific for any disease. Attending physicians consulted with the Department of Nuclear Medicine regarding

appropriate imaging modality for identifying the fever focus and ^{18}F -FDG PET/CT with respiratory gating was recommended.

PET/CT was conducted using a PET scanner with 40-channel CT and capability of time-of-flight (TOF) and point-spread-function (PSF) (Biograph mCT flow, Siemens). Fifty minutes after injection of 10.6 mCi ^{18}F -FDG, PET/CT was performed. Whole blood glucose level was 89 mg/dl at the time of ^{18}F -FDG injection. Helical CT was first performed with the following parameters: Caredose 4D/CareKv 120 with quality reference of 100 mAs, tube rotation time of 0.5 s, and pitch of 1.0 mm. CT images were reconstructed using an iterative CT dose-reduction technique (Sinogram Affirmed Iterative Reconstruction, SAFIRE, Siemens). Then, PET images were acquired using the flow mode with a scan speed of 1.5 mm/s caudo-cranially. For respiratory gating, the scan speed was reduced to 1.0 mm/s at the upper abdominal area and respiratory signal was obtained using a belt gating system (AZ-733V, Anzai, Japan) wrapped around the upper abdomen. The scan

Fig. 1 Non-gated versus gated ^{18}F -FDG PET/CT. **a** Axial CT showing a surgical graft in the common bile duct area. **b**, **d**, and **f** Non-gated PET and PET/CT at the same level of the axial CT. **c**, **e**, and **g** Respiratory-gated PET and PET/CT showing prominent hypermetabolism at the graft insertion site

Fig. 2 The infected surgical graft. **a** Endoscopic image showing the graft inserted in the common bile duct (CBD). Arrow points the graft in the CBD. **b** Removed infected graft

speed was reset to 1.5 mm/s beyond the upper abdominal area. Non-gated PET images were reconstructed using the vendor-provided iterative reconstruction algorithm with two iterations and 21 subsets (True X + TOF, Ultra HD-PET, Siemens), Gaussian filter of 5 mm FWHM, matrix of 256×256 , and zoom factor of 1. For the gated PET images, respiratory gating technique (HD-Chest, Siemens) was applied to the upper abdominal area with the automatic amplitude-based gating method using duty cycle of 35% from 0–4 to 0–10% amplitude. For quantitative assessment, maximum standardized uptake value (SUVmax) was defined as the maximum lesion radioactivity normalized by injected activity and body weight, and SUV ratio (SUR) as SUVmax divided by SUVmean of the liver. The quantification data were measured using a dedicated analysis system (Syngovia MM oncology, Siemens).

Figure 1 shows non-gated and gated images of ^{18}F -FDG PET/CT. In the axial CT image (Fig. 1a), a surgical graft from the previous liver transplantation was observed in the CBD area. In the non-gated axial PET (Fig. 1b) and PET/CT fusion (Fig. 1d, f) images, mild hypermetabolism was poorly visible around the graft area, with an SUVmax of 4.6 and an SUR of 3.0. On the other hand, respiratory-gated axial PET (Fig. 1c) and PET/CT fusion (Fig. 1e, g) images showed more prominent hypermetabolism at the graft area, with an SUVmax of 5.4 and an SUR of 3.5. The gated PET/CT images (Fig. 1c, e, g) were noisier than the non-gated counter parts (Fig. 1b, d, f). Based on the characteristics in the respiratory-gated images, the graft insertion site was determined as the possible fever focus.

Subsequently, the attending physicians removed the graft using endoscopic retrograde cholangiopancreatography (ERCP). During the graft removal procedure, malodorous pus was drained from the graft insertion site (Fig. 2). Microbiologic culture study from the pus revealed growth of *Citrobacter freundii*, which can cause biliary tract infection [7].

The fever subsided and the patient's general condition recovered a few days after removal of the graft, confirming the infected graft in the CBD area as the fever focus.

Discussion

^{18}F -FDG PET/CT has been utilized as a diagnostic tool in patients with FUO and reported to have high sensitivity with low specificity for detection of the fever focus [7–9]. Due to its high sensitivity, ^{18}F -FDG PET/CT has been recommended as a screening tool of FUO in the diagnostic work-up. If there is a suspicious hypermetabolic lesion, nuclear medicine physicians can recommend further examination to confirm the ^{18}F -FDG PET/CT findings, as was done in our case.

In this case study, we employed the amplitude-based respiratory gating method using an external device and compared gated PET/CT with non-gated PET/CT. Since not all of the PET emission data are utilized in the respiratory gating, finally processed PET images had poorer signal-to-noise ratio than the non-gated images. However, lesion contrast substantially improved by visual assessment (Fig. 1c, e) and quantification of SUVmax and SUR. These findings were used in patient management procedures. Subsequent graft removal confirmed the usefulness of the respiratory-gated ^{18}F -FDG PET/CT.

Traditionally, respiratory-gated ^{18}F -FDG PET/CT has been advocated as a tool for the more relevant quantitation of metabolic activity or lesion size, leading to more accurate diagnoses of malignancy in the lung, liver, and upper abdominal area [1–3, 5, 6]. Based on the findings of the current case report, the application of respiratory gating can be recommended for localizing upper abdominal fever foci.

Compliance with Ethical Standards

Conflict of Interest Sungwoo Bae, Ji-In Bang, Yoo Sung Song, and Won Woo Lee declare that there is no conflict of interest. There was no funding source in this study.

Ethical Approval The study was approved by our Institutional Review Board and was performed in accordance with the ethical standards of the 1964 Declaration of Helsinki and its later amendments.

Informed Consent The need for patient's informed consent was waived by the IRB.

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