# High myocardial $^{18}$F-FDG uptake after chemotherapy in the presence of left ventricular dysfunction as well as 3-month later with no left ventricular dysfunction

Case Report

**Joon Hyouk Choi[1], Chang Lim Hyun[2], Heesung Song[3]**

[1]Division of Cardiology, Department of Internal Medicine, School of Medicine, Jeju National University, Jeju, Republic of Korea
[2]Department of Pathology, School of Medicine, Jeju National University, Jeju, Republic of Korea
[3]Department of Nuclear Medicine, School of Medicine, Jeju National University, Jeju, Republic of Korea

(Received 8 May 2017, Revised 22 August 2017, Accepted 26 August 2017)

## ABSTRACT

Diffusely increased glucose metabolic activity in the right and left ventricles using 2-deoxy-2-(F-18) fluoro-D-glucose positron emission tomography/computed tomography ($^{18}$F-FDG PET/CT) and global left ventricular hypokinesia at echocardiography can be evident in acute myocarditis. But, there has been no case report that the ventricular $^{18}$F-FDG uptake remains unchanged even after recovery of ventricular hypokinesia. A 60-year-old female with primary pleural effusion lymphoma underwent echocardiography and electrocardiography due to fever and elevated cardiac marker after chemotherapy. The electrocardiography showed global hypokinesia suggesting heart failure and the managements were performed. After 20 days $^{18}$F-FDG PET/CT for assessing the extent of lymphoma demonstrated that newly appeared high $^{18}$F-FDG uptake in the myocardium suggesting pathologic lesions. To evaluate malignancy a cardiac biopsy was performed. Myocarditis was confirmed pathologically. Three months later, improved ventricular function was confirmed by echocardiography, but the metabolic activity in the ventricles was not decreased at follow-up $^{18}$F-FDG PET/CT.

**Key words:** Myocarditis; Chemotherapy; Fluorodeoxyglucose

**Iran J Nucl Med 2018;26(1):54-57**
Published: January, 2018
http://irjnm.tums.ac.ir

**Corresponding author:** Heesung Song, Department of Nuclear Medicine, School of Medicine, Jeju National University, Jeju, Republic of Korea. E-mail: heesung119@gmail.com

## INTRODUCTION

Patients being treated for lymphoma are prone to myocarditis due to drug toxicity and decreased immunity [1-2]. 2-Deoxy-2-(F-18) fluoro-D-glucose positron emission tomography/computed tomography ($^{18}$F-FDG PET/CT) is useful for detecting inflammation and infection, as well as malignant lesions. $^{18}$F-FDG PET/CT is a useful test in oncology, and is also helpful to diagnose related diseases due to the uptake of $^{18}$F-FDG at sites of inflammation and infection. Several reports have described the usefulness of $^{18}$F-FDG PET for detecting myocarditis [3-6]. Diffusely increased metabolic activity is evident in the right and left ventricles using $^{18}$F-FDG PET/CT and global left ventricular hypokinesia in echocardiography in patients with myocarditis. But, there was no report about the change of metabolism on the ventricles using $^{18}$F-FDG PET/CT after ventricular hypokinesia has improved based on echocardiography. In the present case, we sequentially performed echocardiography and $^{18}$F-FDG PET/CT in a patient who received chemotherapy.

## CASE REPORT

A 60-year-old female with primary pleural effusion lymphoma visited the emergency room because of a fever after chemotherapy (rituximab, cyclophosphamide, doxorubicin (cumulative dose 237 mg/m2), vincristine, and prednisone). She was diagnosed with neutropenic fever (absolute neutrophil count: 100/μl) and underwent echocardiography due to an elevated level of the cardiac marker creatine kinase-MB (CK-MB 18.26 ng/dl) followed by electrocardiography (ECG; deep T wave inversion of V1~V6 lead) (Figure 1b). No cardiac symptoms were evident. Decreased left ventricular (LV) systolic function (ejection fraction (EF) by Simpson's method: 32%), global hypokinesia and myocardial hypertrophy were observed by echocardiography, suggesting the possibility of acute myocarditis. Conservative management involving diuretics, angiotensin-converting enzyme inhibitor and beta blocker was performed for the neutropenic fever. After recovery of the neutrophil count, $^{18}$F-FDG PET/CT was performed to assess the extent of lymphoma (serum glucose level; 93mg/dl). Newly appeared intense $^{18}$F-FDG uptake with diffuse pattern in the left and right ventricles was identified (Figure 2b), which the previous $^{18}$F-FDG PET/CT for staging before chemotherapy did not show (serum glucose level; 109 mg/dl, Figure 2a). Because new high $^{18}$F-FDG uptake with diffuse pattern on the myocardium suggested pathologic lesions such as cardiac malignancy or lymphoma involvement, endomyocardial biopsies on the LV were performed. The pathological specimen demonstrated heavy inflammatory cell infiltration between degenerative cardiomyocytes with fibrinous necrotic materials and inflammatory exudates, suggesting active myocarditis (Figure 3).

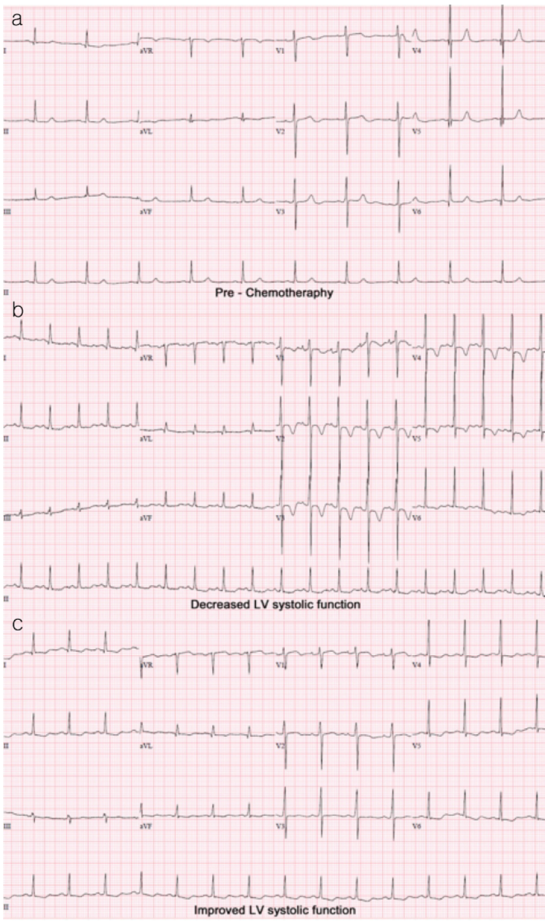


**Fig 1.** ECG of pre-chemotherapy was normal (a). ECG of decreased LV systolic function was T wave inversion at V1~V6. Three month later (improved LV systolic function) (b), deep T wave inversions of V1~V6 leads were resolved in a follow-up ECG (c).

Three months later, the improved ventricular function was confirmed by echocardiography (LVEF by Simpson's method: 52%), and deep T wave inversions of V1~V6 leads were resolved in ECG (Figure 1c). But, the metabolic activity in the ventricles was not decreased at follow-up $^{18}$F-FDG PET/CT with SUVmax from 25.4 to 21.8 (serum glucose level; 79mg/dl, Figure 2c). Flow sheet showed main events according to the level of CK-MB (Figure 4).

## DISCUSSION

The adverse cardiac effects associated with chemotherapy vary and clinically evident heart failure occurs in 1 to 5% of patients receiving chemotherapy and the other 5 to 20% experience asymptomatic decline of left ventricular function [2, 7]. Infectious myocarditis is a serious complication detected in

oncologic patients because of their compromised immune status.

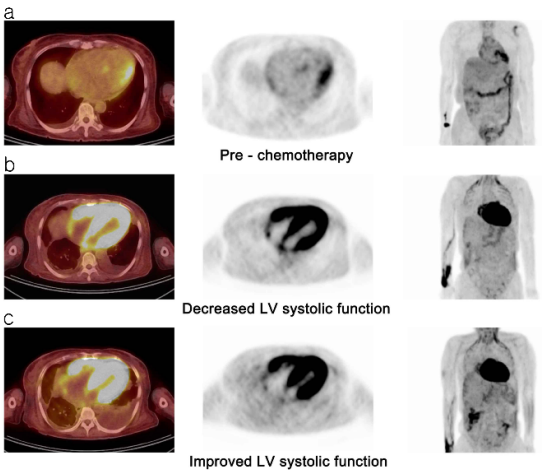


**Fig 2.** $^{18}$F-FDG PET/CT of pre-chemotherapy revealed no abnormal $^{18}$F-FDG uptake in the myocardium (a). $^{18}$F-FDG PET/CT of decreased LV systolic function revealed intensely increased $^{18}$F-FDG uptake with a diffuse pattern in the left and right ventricles (b). Three months later when LV systolic function had improved, metabolic activity in the ventricles was not decreased (SUVmax from 25.4 to 21.8) (c).

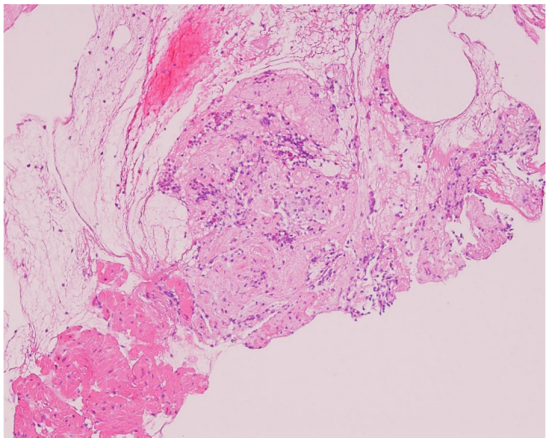

**Fig 3.** Endomyocardiac biopsy results. Microscopically, heavy inflammatory cell infiltration between degenerative cardiomyocytes with fibrinous necrotic materials and inflammatory exudates were observed (H&E stain, 100x).

Wide-ranging virus types have been related with viral infectious cardiomyopathy and the development of dilated cardiomyopathy, which can occur as a result of viral myocarditis [6, 8]. Diffusely increased metabolic activity in the right and left ventricles at $^{18}$F-FDG PET/CT and global left ventricular hypokinesia at echocardiography can be evident in acute myocarditis [4-6]. But, after ventricular hypokinesia improves, no changes of the metabolic activity in the ventricles at follow-up $^{18}$F-FDG PET/CT have been apparent.

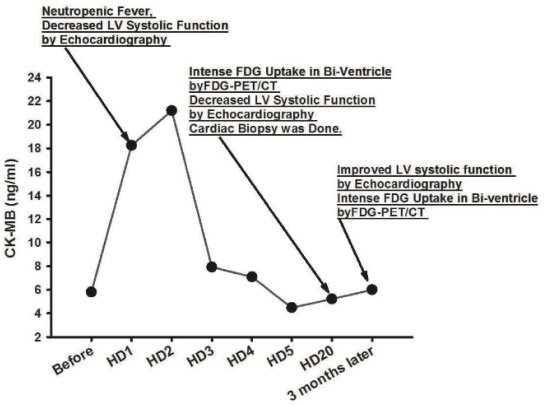


**Fig 4.** Flow sheet showed main events according to the level of CK-MB.

The current case involved a patient suffering from lymphoma. After chemotherapy, she had neutropenic fever without cardiac symptoms. Echocardiography is relatively nonspecific and is recommended in the initial diagnostic evaluation of patients with suspected myocarditis. CK-MB level is very specific but of limited sensitivity for the diagnosis of myocarditis [9]. Considering the result of several modalities such as ECG (deep T wave inversion of V1~V6 lead), cardiac markers (elevated CK-MB), neutropenia and the history of cardiotoxic agent of chemotherapy, acute myocarditis could be diagnosed clinically. After 20 days the conservative management of the cardiomyopathy, $^{18}$F-FDG PET/CT for assessing the extent of lymphoma showed newly appeared intense $^{18}$F-FDG uptake with diffuse pattern in the ventricles, which was suspicious of pathologic lesions such as malignant lymphoma involvement or cardiac malignancy rather than physiologic radioactivity. A myocardial biopsy was performed to evaluate malignancy and acute myocarditis was confirmed pathologically. The assessment of cardiac disease by $^{18}$F-FDG PET/CT can be challenging because the radiotracer accumulates in normal myocardium. Physiologic $^{18}$F-FDG uptake in myocardium can range from non to diffuse or focal uptake in the same patient under a variety of physiologic conditions, since normal myocardial $^{18}$F-FDG uptake depends on the patient's fasting state [3, 10]. Obviously increased metabolic activity in the myocardium can be observed on normal myocardium as well as pathologic lesions such as myocarditis or cardiac malignancies. But, the two pathologic lesions can be differentiated by $^{18}$F-FDG uptake patterns. Myocarditis displays diffuse uptake, while malignancy is associated with focal uptake generally [3-6, 10]. Myocarditis that results from radiation treatment, chemotherapy or viral infection may also produce increased metabolic

activity in the myocardium due to a combination of microvascular damage, myocyte damage and changes in fatty-acid metabolism [1]. In this case, the results of the echocardiography, biopsy specimens and $^{18}$F-FDG PET/CT revealed myocardial inflammation that was suggestive of myocarditis. Three months later, the improved ventricular function was confirmed by echocardiography, but the metabolic activity in the ventricles was not decreased at $^{18}$F-FDG PET/CT. After ventricular hypokinesia had improved, we could not find the cause of the unchanged metabolic activities. If an additional $^{18}$F-FDG PET/CT was done 3-6 months after the follow-up $^{18}$F-FDG PET/CT, the possible causes would have been clearer. But, we were no longer able to follow the patient. It is assumed that she refused treatment or went to another hospital. If the myocardial $^{18}$F-FDG uptake returns to be normal on an additional $^{18}$F-FDG PET/CT after 3-6 months, we can assume that the motor function of a myocardium is restored prior to normalization of glucose metabolism like 'reverse pattern of hibernating myocardium'. On the contrary, if there is no significant change of diffuse and intense $^{18}$F-FDG uptake on the myocardium, we can suppose that acute myocarditis cause a prolonged impairment of metabolism on the myocardium because cardiac toxic agents can produce irreversible heart failure [2]. There has been no case report that the ventricular $^{18}$F-FDG uptake remains unchanged even after recovery of ventricular hypokinesia in the acute myocarditis. Even if an abnormal $^{18}$F-FDG uptake of myocardium is found incidentally, more precautions are needed to distinguish the cause.

## CONCLUSION

This is the first report describing that high myocardial FDG uptake after chemotherapy in the presence of left ventricular dysfunction as well as 3-month later with no detectable left ventricular dysfunction.

## Acknowledgement

No work resembling the enclosed article has been published or is being submitted for publication elsewhere. We certify that we have each made a substantial contribution so as to qualify for authorship and that we have approved the contents. We have disclosed all financial support for our work and other potential conflicts of interests.

## REFERENCES

1. Jingu K, Kaneta T, Nemoto K, Ichinose A, Oikawa M, Takai Y, Ogawa Y, Nakata E, Sakayauchi T, Takai K, Sugawara T, Narazaki K, Fukuda H, Takahashi S, Yamada S. The utility of 18F-fluorodeoxyglucose positron emission tomography for early diagnosis of radiation-induced myocardial damage. Int J Radiat Oncol Biol Phys. 2006 Nov 1;66(3):845-51.
2. Volkova M, Russell R 3rd. Anthracycline cardiotoxicity: prevalence, pathogenesis and treatment. Curr Cardiol Rev. 2011 Nov;7(4):214-20.
3. James OG, Christensen JD, Wong TZ, Borges-Neto S, Koweek LM. Utility of FDG PET/CT in inflammatory cardiovascular disease. Radiographics. 2011 Sep-Oct;31(5):1271-86.
4. Takano H, Nakagawa K, Ishio N, Daimon M, Daimon M, Kobayashi Y, Hiroshima K, Komuro I. Active myocarditis in a patient with chronic active Epstein-Barr virus infection. Int J Cardiol. 2008 Oct 30;130(1):e11-3.
5. Maurer AH, Burshteyn M, Adler LP, Steiner RM. How to differentiate benign versus malignant cardiac and paracardiac 18F FDG uptake at oncologic PET/CT. Radiographics. 2011 Sep-Oct;31(5):1287-305.
6. Miyagawa M, Yokoyama R, Nishiyama Y, Ogimoto A, Higaki J, Mochizuki T. Positron emission tomography-computed tomography for imaging of inflammatory cardiovascular diseases. Circ J. 2014;78(6):1302-10.
7. Albini A, Pennesi G, Donatelli F, Cammarota R, De Flora S, Noonan DM. Cardiotoxicity of anticancer drugs: the need for cardio-oncology and cardio-oncological prevention. J Natl Cancer Inst. 2010 Jan 6;102(1):14-25.
8. Kühl U, Pauschinger M, Noutsias M, Seeberg B, Bock T, Lassner D, Poller W, Kandolf R, Schultheiss HP. High prevalence of viral genomes and multiple viral infections in the myocardium of adults with "idiopathic" left ventricular dysfunction. Circulation. 2005 Feb 22;111(7):887-93.
9. Magnani JW, Dec GW. Myocarditis: current trends in diagnosis and treatment. Circulation. 2006 Feb 14;113(6):876-90.
10. Fukuchi K, Ohta H, Matsumura K, Ishida Y. Benign variations and incidental abnormalities of myocardial FDG uptake in the fasting state as encountered during routine oncology positron emission tomography studies. Br J Radiol. 2007 Jan;80(949):3-11.