Radiation-Induced Cardiomyopathy Incidentally Detected on Oncology ^{18}F -Fluorodeoxyglucose Positron Emission Tomography

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Figure 1. (A) Main radiation fields and dose distribution. Mediastinal radiotherapy was performed using (solid line area) anterior-posterior fields with 40 Gy and (dashed line area) parallel-oblique fields with 20 Gy. Thus, total radiation dose in the red, blue, and green regions corresponds to 60, 40, and 0 Gy, respectively. (B) ^{18}F -fluorodeoxyglucose (FDG) uptake by the esophageal cancer before radiotherapy. (C) FDG uptake in the left ventricle. Note the uptake territory and radiation dose. (D) Fusion of cardiac computed tomography and FDG-positron emission tomography/computed tomography.

A 54-year-old man was referred to Ehime Prefectural Central Hospital because of dysphagia. After several examinations, he was diagnosed with unresectable stage IV esophageal cancer. The patient received chemotherapy (5-fluorouracil+cisplatin) and mediastinal radio-

therapy (RTx) with a total dose of 60 Gy for the tumor and lymph nodes, with 40 Gy and 20 Gy using anterior-posterior and parallel-oblique fields, respectively (**Figure 1A**). Before RTx, ^{18}F -fluorodeoxyglucose (FDG) positron emission tomography (PET)/computed tomography (CT)

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Figure 2. (A) Bull's eye image of the longitudinal strain of the left ventricle showing preserved global longitudinal strain with a localized decrease, predominantly in the basal segments corresponding to radiation fields. (B) Short axis image of cardiac magnetic resonance imaging (MRI). No late gadolinium enhancement was detected on cardiac MRI. Ant, anterior; Inf, inferior; Lat, lateral; Post, posterior; Sept, septal.

>12h after overnight fasting showed FDG uptake from the thoracic to the lower esophagus (**Figure 1B**). Eight months after RTx, however, FDG-PET/CT >12h after overnight fasting showed FDG uptake in the basement of the left ventricle (LV; **Figure 1C,D**; **Movie S1**), while the uptake from the thoracic to the lower esophagus could not be observed. Thus, he was referred to the cardiology department. Transthoracic echocardiography showed slightly reduced LV wall motion in basal segments and moderate pericardial effusion (**Movie S2**). Two-dimensional speckle-tracking echocardiography indicated preserved global longitudinal strains (-17.9%) with a regional decrease predominantly in the basal segments (**Figure 2A**). No late gadolinium enhancement was detected on cardiac magnetic resonance imaging (MRI; **Figure 2B**). Coronary angiography showed no significant stenosis. Accordingly, we diagnosed this condition as radiation-induced cardiomyopathy, and the patient was treated with β -blockers and angiotensin-converting enzyme inhibitors (ACEI). His course was uneventful thereafter, and regional LV dysfunction was restored.

RTx is one of the cornerstones of treatment for cancer. RTx improves survival, but normal tissue toxicity is a matter of concern. In particular, cardiac toxicity is one of the most concerning side-effects of RTx. The correlation between the incidence of cardiovascular disease and radiation dose is well established.^{1,2} Diagnosis of radiation-induced cardiomyopathy is challenging and usually is a diagnosis of exclusion. Therefore, diagnosis of radiation-induced cardiomyopathy needs multimodality assessment using echocardiography,² cardiac MRI,³ and myocardial perfusion imaging.⁴ Late gadolinium enhancement has been detected in half of patients who received RTx for esophageal cancer.³ The present patient did not develop myocardial fibrosis. The tolerance dose of myocardium is estimated to be 30–40 Gy.^{2,3} In contrast, in the present case there was no dermatitis during follow-up, although the risk of severe skin damage such as ulceration increases at >40–45 Gy.⁵ Thus, the adverse effects of RTx might depend on the susceptibility of each organ. There are no drugs specifically approved to treat RTx-induced cardiomyopathy.⁶

Treatment for RTx-induced cardiomyopathy is the same as that for heart failure, and involves ACEI, angiotensin receptor blockers, aldosterone antagonists and β -blockers. FDG-PET/CT has been widely used to evaluate cancer and inflammatory cardiovascular diseases. These conditions reflect enhanced glucose utilization in tumor cells or inflammatory cells. In contrast, in normal myocytes, free fatty acid (FFA) is the main substrate of energy production in the fasting state, whereas the predominant substrate during ischemia is glucose because β -oxidation of FFA is susceptible to ischemia.⁷ Yan et al investigated RTx-induced microvascular damage and mitochondrial injury in an experimental study.⁸ These alternations may cause ischemia and diminished energy production, resulting in regional metabolic shift from FFA to glucose and contractile dysfunction. It is well known, however, that non-specific FDG uptake is occasionally observed even under fasting conditions, leading to misinterpretation.^{9–11} There are several methods to suppress glucose uptake (i.e., heparin loading, low-carbohydrate/high-fat diet, prolonged fasting) to facilitate diagnosis of cardiac sarcoidosis on FDG-PET.⁷ Routine oncology PET (including in the present case), however, does not involve these methods. Although the fasting condition at PET acquisition was almost the same before and after RTx, the modification of physiological FDG uptake could not be completely excluded. Nevertheless, if incidental FDG uptake is detected in the myocardium after RTx, cardiac screening on multimodality imaging is mandatory to facilitate early identification of cardiac complications.

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Supplementary Files

Supplementary File 1

Movie S1. Fusion of 3-D cardiac computed tomography and ¹⁸F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG-PET/CT) showing accumulation of FDG that crossed the left ventricle obliquely.

Supplementary File 2

Movie S2. Transthoracic echocardiography from the apex showing slightly reduced left ventricular wall motion in the basal segment and moderate pericardial effusion. 2CV, 2-chamber view; 3-CV, 3-chamber view; 4CV, 4-chamber view.

Please find supplementary file(s);
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