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CASE REPORT
Cardiac imaging

Activation of cardiac sarcoidosis associated with development of gastric cancer: a case report

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Background The high ^{18}F-fluorodeoxyglucose (FDG) uptake in sarcoidosis lesions reflects infiltration of inflammatory cells such as macrophages. An increased incidence of cancer in patients with sarcoidosis has been suggested, and some combination of the following mechanisms has been proposed: chronic inflammation, immune dysfunction, shared aetiologic agents, and genetic susceptibility to both cancer and autoimmune diseases.

Case summary A 73-year-old man was admitted to our hospital due to effort dyspnoea. Initial investigations showed complete atrioventricular block on electrocardiography, basal thinning of the interventricular septum, and preserved left ventricular (LV) systolic function on echocardiography, and late gadolinium enhancement (LGE) in all layers of the basal interventricular septum on cardiac magnetic resonance imaging. FDG positron emission tomography/computerized tomography (FDG-PET/CT) showed no abnormal uptake in the whole-body including myocardium. After discussion, corticosteroid was not initiated then. One year later, he developed stomach adenocarcinoma. Repeated investigations demonstrated enlargement of the LV (LV diastolic diameter 63 mm) and diffuse systolic impairment of LV function (LV ejection fraction 31%) on echocardiography, and abnormal focal uptake at the lateral walls of LV and hilar lymph nodes on FDG-PET/CT imaging. One more year after the surgery for gastric cancer and corticosteroid initiation, echocardiography showed recovery of systolic function and FDG-PET/CT showed no uptake in either the myocardium or hilar lymph nodes.

Discussion In the present case, it is speculated that the first inflammation which left scarred areas showing LGE was already completed before the first FDG-PET/CT. The development of gastric cancer may be associated with the reactivation of cardiac sarcoidosis.

Keywords Case report • Cardiac sarcoidosis • PET-CT • ^{18}F-FDG • Malignant tumour

Learning points

- Multimodality cardiac imaging is essential for identification of patients with the early stage of cardiac sarcoidosis (CS).
- In the present case, the development of gastric cancer may be associated with the reactivation of CS.
- Cardiac re-evaluation in patients with CS may be needed before cancer surgery.

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Introduction

Sarcoidosis, characterized by non-caseating granulomas, is a multisystem chronic condition of unknown aetiology, but in which some combination of infectious, genetic, and environmental factors is suspected. It has been estimated that two of three patients with sarcoidosis die of cardiac involvement.[1] Despite the need for early diagnosis and therapeutic interventions, diagnostic confirmation of cardiac sarcoidosis (CS) is difficult because endomyocardial biopsy has low sensitivity (less than 20%) due to the focal nature of the disease.[2,3] That is the reason why multimodality cardiac imaging is essential for identification of patients with the early stage of CS.

^{18}F-fluorodeoxyglucose (^{18}F-FDG) is a glucose analogue that is taken up by cells that have increased glucose use such as brain cells, myocytes, cancer cells, and inflammatory cells, and positron emission tomography (PET) delineates areas of high ^{18}F-FDG uptake. The high ^{18}F-FDG uptake in sarcoidosis lesions reflects infiltration of inflammatory cells such as macrophages.[4,5] Meanwhile, an increased incidence of cancer in patients with sarcoidosis compared with the general population has been suggested.[6] We report a case with worsening left ventricular (LV) contraction on echocardiography and newly developed myocardial focal uptake on repeated ^{18}F-FDG PET/computerized tomography (FDG-PET/CT) images before surgery for gastric cancer.

Timeline

December 2016	Effort dyspnoea
	Electrocardiogram: complete atrioventricular block
	Transthoracic echocardiogram (TTE): basal thinning of interventricular septum, 59% of left ventricular ejection fraction (LVEF), and 50 mm of left ventricular diastolic diameter (LVDd)
	Cardiac magnetic resonance imaging: late gadolinium enhancement in all layers of basal interventricular septum
	Permanent pacemaker implantation
	Fluorodeoxyglucose-positron emission tomography/computerized tomography (FDG-PET/CT): no uptake in the whole-body including myocardium
	Endomyocardial biopsy: non-caseating granuloma
March 2018	Epigastric discomfort
	Diagnosed as gastric cancer
	TTE: 31% of LVEF and 63 mm of LVDd
	FDG-PET/CT: abnormal focal uptake at the lateral walls of left ventricle and hilar lymph nodes
May 2018	Gastric surgery
June 2018	Oral corticosteroid initiation
July 2019	TTE: 52% of LVEF and 49 mm of LVDd
	FDG-PET/CT: no uptake in either myocardium or hilar nodes

Case presentation

A 73-year-old man was admitted to our hospital due to effort dyspnoea. Since he was suffering from diabetes, dyslipidaemia, and hypertension, he was taking Irbesartan, Amlodipine, Aspirin, Rosuvastatin, Tamsulosin, Sitagliptin, and Ipragliflozin at the time of admission. Upon admission, the patient was alert and conscious, with a blood pressure of 151/53 mmHg, heart rate 39 beats per minute, and oxygen saturation of 97% on room air. No murmur and no crepitations on auscultation, and no peripheral oedema. A 12-lead electrocardiogram revealed complete atrioventricular block (*Figure 1A*), and chest X-ray was almost normal. A transthoracic echocardiogram (TTE) showed basal thinning of the interventricular septum, dilatation of left atrium (43 mm), and preserved LV ejection fraction (LVEF) of 59% with normal LV diastolic diameter (LVDd) of 50 mm (*Figure 1B*, *Video 1A*). Laboratory analysis showed normal level of angiotensin-converting enzyme activity (15.0 U/L), normal cardiac troponin I (<0.006 ng/ml), and slightly elevated brain natriuretic peptide level [89.7 pg/mL (normal reference range ≤18.4 pg/mL)]. After excluding coronary artery disease by invasive coronary angiography, endomyocardial biopsy was performed: non-caseating granuloma was not identified. Three-tesla cardiac magnetic resonance imaging showed diffuse patchy late gadolinium enhancement (LGE) in the basal interventricular septum (*Figure 1C and D*). Furthermore, FDG-PET/CT was performed after taking a low-carbohydrate, fat-rich, and protein-permitted diet, followed by an 18 h fast and administration of heparin: no uptake in the whole-body including myocardium. Extra-cardiac involvement was not identified either by ophthalmologic, skin, or any other examinations (*Figure 2A–C*). A permanent pacemaker had been implanted in the patient. He was not definitely diagnosed with CS because of a lack of evidence of extracardiac sarcoidosis and meeting only the following three major criteria for cardiac involvement: high-grade atrioventricular block, basal thinning of the ventricular septum, and LGE positivity.[1] So after discussion corticosteroid was not initiated.

One year later, he became conscious of epigastric discomfort, with upper gastrointestinal endoscopy revealing stomach adenocarcinoma. Before the surgery for it, re-evaluation for cardiac risk was performed. Repeated echocardiography demonstrated enlargement LV (63 mm of LVDd) and diffuse systolic dysfunction of LV wall motion (31% of LVEF) (*Video 1B*). After excluding the development of coronary artery disease by coronary CT angiography, FDG-PET/CT was repeated and showed abnormal focal uptake at the lateral walls of LV and hilar lymph nodes (*Figure 2D–F*). After repeated systemic examinations, extra-cardiac involvement was not identified again. Regardless, he was clinically diagnosed to have CS because he fulfilled five major criteria including LV contractile dysfunction (<50% LVEF) and abnormally high tracer accumulation in the heart on ^{18}F-FDG PET.

After the surgery for gastric cancer, prednisolone was orally initiated at a dose of 30 mg/day, then tapered by 5 mg/day at intervals of 4 weeks, and maintained at 5 mg/day. One year after corticosteroid initiation, echocardiography showed recovery of systolic function (*Video 1C*), and FDG-PET/CT showed no uptake in either the myocardium or hilar lymph nodes (*Figure 2G–I*). The patient was asymptomatic from CS both before and after corticosteroid initiation and the clinical course remained stable throughout.

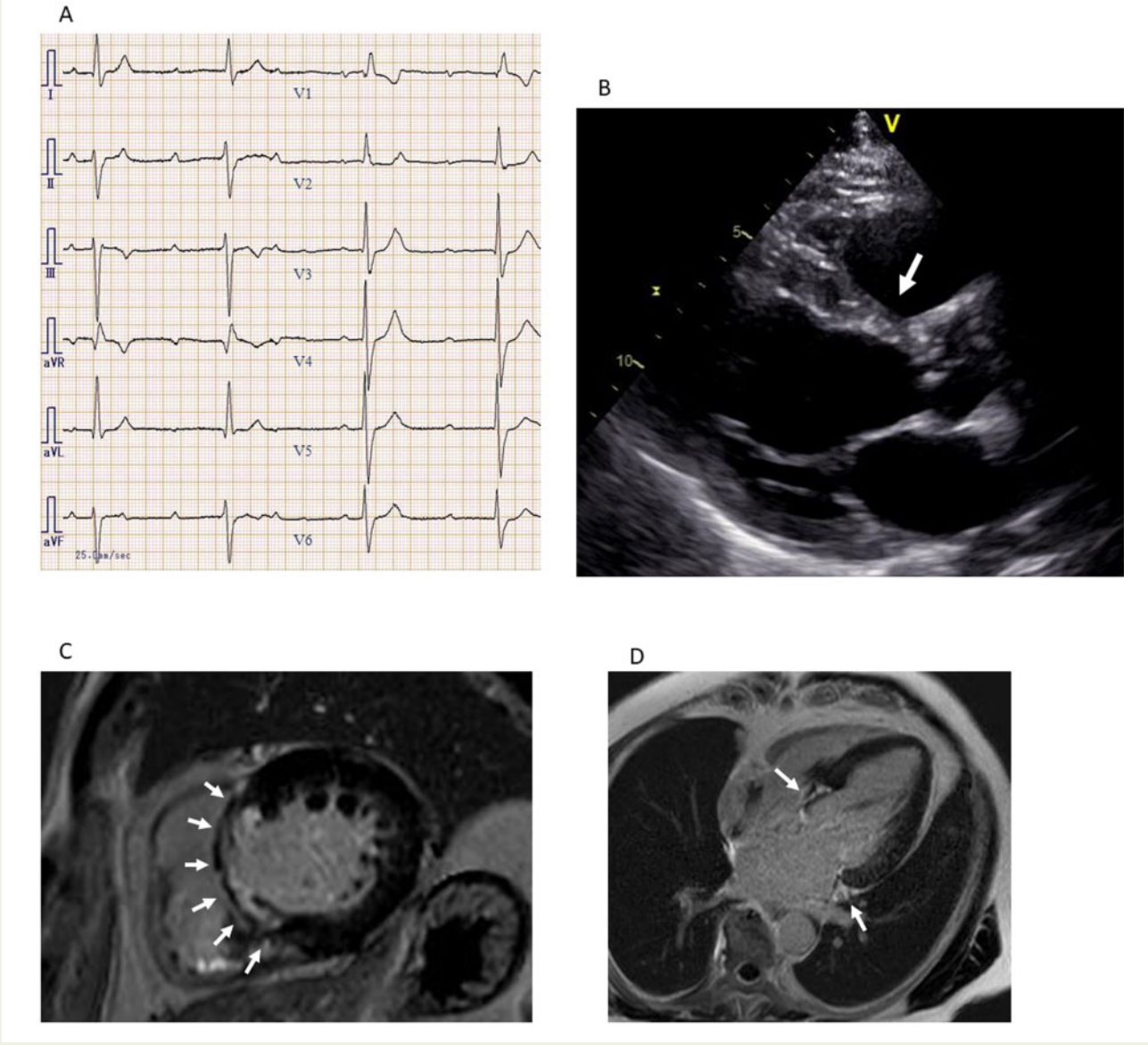


Figure 1 Imaging findings at the first admission. (*A*) Complete atrioventricular block on electrocardiography. (*B*) Basal thinning of interventricular septum on echocardiography. (*C* and *D*) Late gadolinium enhancement of basal interventricular septum and lateral wall of the left ventricle on cardiac magnetic resonance imaging.

Discussion

We report a case with CS showing deteriorating cardiac function and newly developed focal uptake in myocardium and hilar lymph nodes on FDG-PET/CT before surgery for gastric cancer. After the gastric surgery and initiation of corticosteroid, LV contraction improved and the uptake in both myocardium and hilar lymph nodes disappeared. To our knowledge, this is the first report about a patient who developed abnormal myocardial uptake in FDG-PET/CT after the development of cancer, and was diagnosed to have CS.

Myocardial uptake in ^{18}F-FDG PET imaging reflects active inflammation in sarcoidosis. In current clinical practice, ^{18}F-FDG PET scanning has a pivotal role in the diagnosis, therapeutic evaluation, and determination of prognosis for patients with CS. Although several reports have documented the utility of serial ^{18}F-FDG PET scanning for evaluating the therapeutic response and effect,[7–9] the usefulness of serial ^{18}F-FDG for making the diagnosis of CS remains unknown.[10]

An increased incidence of cancer in patients with sarcoidosis compared with the general population has been suggested by several case reports and series, and some combination of the following mechanisms has been proposed: chronic inflammation, immune dysfunction, shared aetiologic agents, and genetic susceptibility to both cancer and autoimmune diseases. A meta-analysis study

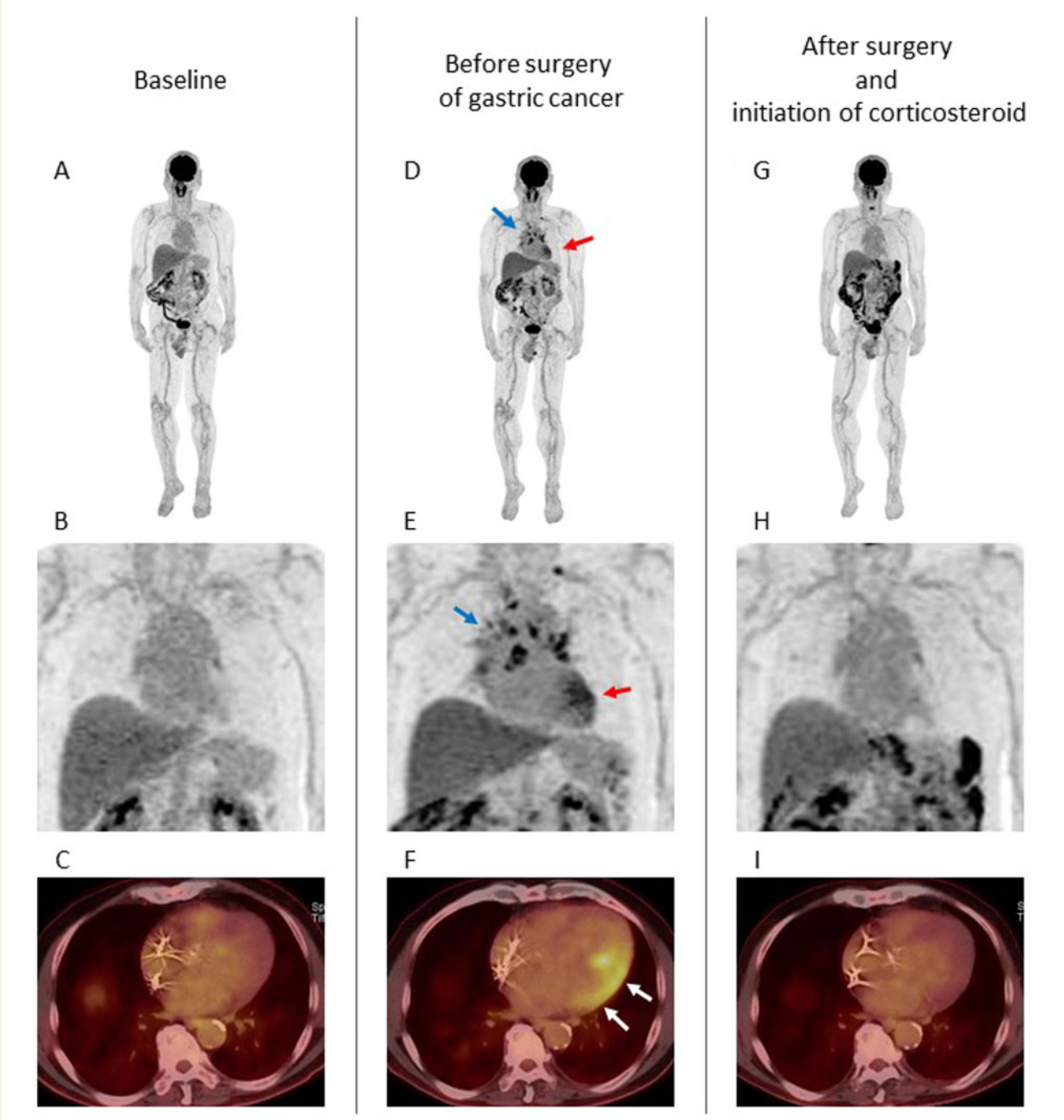
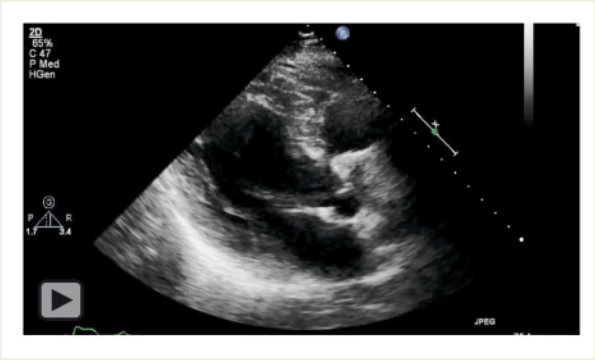


Figure 2 Serial change of ^{18}F-fluorodeoxyglucose positron emission tomography findings. Baseline images showed no ^{18}F-fluorodeoxyglucose uptake including in the heart (*A–C*). However, abnormal focal uptake was noted at the lateral walls of left ventricle (red and white arrow) and hilar lymph nodes (blue arrow) on repeated fluorodeoxyglucose-positron emission tomography/computerized tomography before surgery for gastric cancer (*D–F*). One year after corticosteroid initiation, fluorodeoxyglucose-positron emission tomography/computerized tomography showed no uptake in either myocardium or hilar lymph nodes (*G–I*).

noted the relative risk of developing a malignant tumour in the upper digestive tract in patients with sarcoidosis to be 1.73 (95% confidence interval 1.07–2.79).[6]

In the present case, it is speculated that the first inflammation which left scarred areas showing LGE was already completed before the first FDG-PET/CT. Although the reason for the change in myocardial uptake from negative to positive in FDG-PET/CT is unclear, the development of gastric cancer may be associated with the reactivation of CS. Cardiac re-evaluation in patients with CS may be needed before cancer surgery.



Video 1 Serial change of echocardiography. (*A*) Initial echocardiography showed basal thinning of the interventricular septum, dilatation of left atrium (43 mm), and preserved left ventricular ejection fraction of 59% with normal left ventricular diastolic diameter of 50 mm. (*B*) Repeated echocardiography demonstrated enlargement left ventricle (63mm of left ventricular diastolic diameter) and diffuse systolic dysfunction of left ventricular wall motion (31% of left ventricular ejection fraction). (*C*) Echocardiography at 1 year later of corticosteroid initiation showed recovery of left ventricular function (52% of left ventricular ejection fraction and 49 mm of left ventricular diastolic diameter).

Conclusion

We report a case with CS showing deteriorating cardiac function and new uptake in myocardium and hilar lymph nodes on ^{18}F-FDG PET before surgery for gastric cancer.

Lead author biography

Hideki Kawai graduated from Nagoya University in 2002. His research interest is mainly focused on multimodal cardiac imaging, in particular ischaemic heart disease and cardiomyopathy.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

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