Undiagnosed Cardiac Sarcoidosis Causing Refractory Heart Failure After Acute Myocardial Infarction due to Thromboembolism

Takashi Kai,1 MD, Yoshiyasu Ono,1,2 MD, Shouji Matsushima,1 MD, Keisuke Shinhara,3 MD, Ryosuke Nakashima,1 MD, Takuro Kawahara,1 MD, Masato Katsuki,1 MD, Takeo Fujino,1 MD, Toru Hashimoto,4 MD, Taiki Higo,1 MD and Hiroyuki Tsutsui,1 MD

Summary
A 61-year-old woman suffered chest pain and was admitted to a nearby hospital emergency department. She was diagnosed with acute myocardial infarction probably due to thromboembolism in the left anterior descending coronary artery and aspiration thrombectomy was performed. Afterwards, she developed refractory heart failure with severe global left ventricular dysfunction and was transferred to our hospital. An 18F-FDG-PET/CT scan revealed abnormal 18F-FDG uptake in non-infarcted regions of the left ventricle. Non-caseating granulomas were detected by biopsy from a skin eruption. She was diagnosed with cardiac sarcoidosis. In cases of refractory heart failure which cannot be explained only by myocardial infarction, evaluation of other undiagnosed cardiomyopathies is important for optimal management.

Key words: Coronary thromboembolism

Heart failure (HF) is a common complication of acute myocardial infarction (AMI) even in the coronary revascularization era.1-3) Patients with in-hospital HF after AMI had greater in-hospital and 1-year mortalities than patients without HF;4) Large infarct size, left ventricular (LV) dysfunction, and underlying cardiac diseases are associated with in-hospital HF after AMI.1,4,5) In particular, in cases of refractory HF, underlying cardiac diseases including undiagnosed cardiomyopathies need to be evaluated for optimal management. We report here a patient with refractory HF after AMI due to thromboembolism, in whom cardiac sarcoidosis was diagnosed and treated with a corticosteroid.

Case Report
A 61-year-old woman with no history of hypertension, diabetes mellitus, or cardiovascular disease was admitted to a hospital emergency department due to chest pain. An electrocardiogram (ECG) showed ST segment elevation in precordial leads (Figure 1A) and coronary angiography demonstrated complete occlusion in the left anterior descending coronary artery (Figure 1B) and no apparent atherosclerotic lesions in other coronary arteries. Based on these findings, she was diagnosed as having acute anteroseptal MI due to thromboembolism. Aspiration thrombectomy and stenting were successfully performed (Figure 1B). Her peak creatine kinase (CK) level was 4944 U/L. There were no signs of thrombosis in other arteries and veins. Echocardiographic studies demonstrated severe hypokinesis at the inferior and lateral segments as well as the anteroseptum of the left ventricle, which could not be explained only by anteroseptal MI. She was treated with antiplatelets and diuretics, but not beta-blockers and renin-angiotensin system inhibitors because of low blood pressure. Once discharged, she was readmitted to hospital due to worsening HF 24 days after the onset of AMI and transferred to our hospital.

Her blood pressure was 82/62 mmHg, pulse rate was 106 beats per minute (bpm), and blood oxygen saturation was 91% at ambient air. A holosystolic murmur of Levine 3/6 and the third heart sound at the apex, and inspiratory crackles were audible in the bilateral lungs. Jugular venous distention and moderate pitting edema of the bilateral legs were noted. Chest radiography exhibited cardiac silhouette enlargement, pulmonary congestion, and mild pleural effusion. She was treated with intravenous vasodilators and inotropes and was administered enalapril. An ECG showed poor R progression in precordial leads. Her B-type natriuretic peptide level was 707 pg/mL and the troponin T level was 0.03 ng/mL. Protein C and S activities were normal and anti-phospholipid antibody was negative. An echocardiogram demonstrated LV dilatation with an LV end-diastolic diameter (LVDd) of 61 mm and...
global hypokinesis with an LV ejection fraction of 24%. The basal interventricular septum was as thin as 4 mm and severe mitral regurgitation was detected (Figure 2). There was neither thrombus in the left ventricle and atrium nor an intracardiac shunt. A continuous ECG monitor did not detect atrial fibrillation. The pulmonary capillary wedge pressure (PCWP) was elevated to 24 mmHg and the cardiac index was decreased to 1.9 L/min/m². An endomyocardial biopsy did not show any obvious abnormality. Cardiac magnetic resonance imaging (MRI) demonstrated late gadolinium enhancement (LGE) in the anteroseptal, anterior, inferior, and lateral regions of the LV (Figure 3A). In addition, an ¹⁸F-FDG-PET/CT examination revealed enhanced ¹⁸F-FDG uptake at cervical, axillary, hilar, and mediastinal lymph nodes and the identical sites of LGE in the heart (Figure 3A). Computed tomography (CT) revealed bilateral hilar lymphadenopathy (BHL) (Figure 3B). Non-caseating granulomas were detected by a biopsy of the skin lesion in her left shin (Figure 3C). Her laboratory data showed the angiotensin converting enzyme level was normal (12.6 U/L) but soluble interleukin 2 receptor was increased (554 U/mL). Based on these findings, she was diagnosed as having sarcoidosis involving the heart and skin. An implantable cardioverter-defibrillator (ICD) was implanted for frequent non-sustained ventricular tachycardia. She was administered 30 mg of prednisone per day and then down-titrated by 10 mg every 4 weeks. Sixty days after starting the immunosuppression therapy with prednisolone, the abnormal ¹⁸F-FDG uptake had disappeared (Figure 4) and the troponin T level was de-escalated. She was eventually weaned from intravenous inotropic support and started on carvedilol.

Discussion

We have presented here a rare case of undiagnosed cardiac sarcoidosis causing refractory HF after AMI due to thromboembolism. This case report indicates that, in cases of cardiac dysfunction which cannot be explained only by AMI, the involvement of undiagnosed cardiomyopathies such as cardiac sarcoidosis needs to be evaluated. To the best of our knowledge, this is the first report regarding cardiac sarcoidosis complicated with AMI due to thromboembolism.

The incidence of HF among patients hospitalized for an AMI has been reported to be 25-50%. Patients with in-hospital HF after AMI had a 2- to 6-fold greater in-

Figure 1. A: An electrocardiogram showed ST segment elevation in precordial leads. B: Coronary angiography demonstrated occlusion in the left coronary artery and percutaneous coronary intervention (PCI) was successfully performed.

Figure 2. Transthoracic echocardiography demonstrated LV dilatation, basal septal thinning (white arrows), and severe mitral regurgitation. RV indicates right ventricle; LV, left ventricle; LA, left atrium; and Ao, Aorta.
**Figure 3.** A: Cardiac magnetic resonance imaging (MRI) demonstrated late gadolinium enhancement (LGE) in the anteroseptal, anterior, inferior, and lateral regions of the LV (white arrowheads). An $^{18}$F-FDG-PET/CT examination revealed enhanced $^{18}$F-FDG uptake in the anteroseptal, anterior, inferior, and lateral regions of the LV which was at the same site as LGE. B: Computed tomography (CT) exhibited bilateral hilar lymphadenopathy (BHL) (white arrows). C: The skin lesion on the left shin. Non-caseating granulomas with multinucleated giant cells were detected in a skin biopsy.

**Figure 4.** Follow-up $^{18}$F-FDG-PET/CT scan after induction of prednisolone. $^{18}$F-FDG uptake in the LV walls disappeared. RV indicates right ventricle; RA, right atrium; LV, left ventricle; and LA, left atrium.
hospital mortality and up to a 5-fold increased 1-year mortality compared with patients without HF. The occurrence of in-hospital HF is associated with not only large infarct size but also underlying cardiac diseases. Thus, in addition to early coronary intervention, the accurate evaluation of any underlying cardiac disease is critically important.

Sarcoidosis is a multi-system inflammatory disorder of unknown etiology associated with formation of non-caseating granulomas. Cardiac involvement is relatively rare and reported to occur only in 2-5% of patients with pulmonary/systemic sarcoidosis. Clinical manifestations of cardiac sarcoidosis include complete atrioventricular block, ventricular arrhythmia, and systolic and diastolic LV dysfunction. However, it is difficult to detect cardiac involvement in many cases because of a lack of specific cardiac features and the low sensitivity of myocardial biopsy. Major causes of HF are known to be hypertensive heart disease, ischemic heart disease, valvular heart disease, and cardiomyopathies such as dilated cardiomyopathy in Japan and sarcoidosis is not a frequent cause of HF. This case fell into refractory HF with global LV dysfunction, which could not be explained only by AMI. Since BHL was detected by CT and thinning of the basal IVS was observed by echocardiography, a concealed cardiac disorder such as cardiac sarcoidosis was suspected. Basal IVS thinning, defined as a thickness ≤4 mm and/or a basal IVS/IVS ratio ≤0.6, is an important diagnostic feature of cardiac sarcoidosis. It could be used as a criterion for diagnosing cardiac sarcoidosis with 99.0% specificity and 38.9% sensitivity. In addition, the biopsy from a skin lesion in her left shin revealed non-caseating granulomas. In order to reach a diagnosis of cardiomyopathy, such as sarcoidosis, a thorough physical examination is important.

This case had complete occlusion in the left anterior descending coronary artery and no apparent atherosclerotic lesions in other coronary arteries. Neither thrombi in the left ventricle and atrium nor atrial fibrillation were detected. However, it is possible that cardiac dysfunction or cardiomyopathy existed before the onset of AMI. Thus, intracardiac thrombus as an embolic source was not completely excluded. Furthermore, the association of thromboembolism and sarcoidosis has been recently suggested. It is likely that an increased risk of thromboembolism in patients with sarcoidosis is related to a procoagulative phenotype associated with inflammatory activity. These findings indicate that preexisting cardiomyopathy such as sarcoidosis should be noted as a possible cause of coronary thromboembolism. Patients with AMI due to coronary arterial embolism are known to have a higher risk of cardiovascular events than that due to coronary atherosclerosis. Therefore, anticoagulant therapy is indicated for such patients.

Corticosteroids are particularly effective in reducing inflammation and are the first-line drugs used in treating patients with sarcoidosis. The present patient was initially administered 30 mg of prednisone per day, which was then down-titrated by 10 mg every 4 weeks. After starting prednisone, uptake in 18F-FDG PET disappeared and the troponin T level was decreased, suggesting that prednisone attenuated myocardial inflammation and injury. Afterwards, this patient could be weaned from intravenous inotropic support.

In conclusion, we have described a case of undiagnosed cardiac sarcoidosis complicated with AMI due to coronary artery thromboembolism resulting in advanced HF. In cases of refractory HF which cannot be explained only by AMI, the coincidence of other underlying etiologies including cardiac sarcoidosis needs to be evaluated for optimal management.

Disclosure

Conflicts of interest: None.

References

1. Juilliere Y, Cambou JP, Bataille V, et al. Heart failure in acute myocardial infarction: a comparison between patients with or without heart failure criteria from the FAST-MI registry. Rev Esp Cardiol (Engl Ed) 2012; 65: 326-33.
2. Shah RV, Holmes D, Anderson M, et al. Risk of heart failure complication during hospitalization for acute myocardial infarction in a contemporary population: insights from the National Cardiovascular Data ACTION Registry. Circ Heart Fail 2012; 5: 693-702.
3. Tor diagnosed asabi A, Cleland JG, Khan NK, et al. The timing of development and subsequent clinical course of heart failure after a myocardial infarction. Eur Heart J 2008; 29: 859-70.
4. Hellermann JP, Jacobsen SJ, Gersh BJ, et al. Heart failure after myocardial infarction: a review. Am J Med 2002; 113: 324-30.
5. Stone GW, Dixon SR, Grines CL, et al. Predictors of infarct size after primary coronary angioplasty in acute myocardial infarction from pooled analysis from four contemporary trials. Am J Cardiol 2007; 100: 1370-5.
6. Santoro GM, Carrabba N, Migliorini A, et al. Acute heart failure in patients with acute myocardial infarction treated with primary percutaneous coronary intervention. Eur J Heart Fail 2008; 10: 780-5.
7. Su W, Wang M, Zhu J, et al. Underweight predicts greater risk of cardiac mortality post acute myocardial infarction. Int Heart J 2020; 61: 658-64.
8. Sulo G, Igland J, Voltset SE, et al. Heart failure complicating acute myocardial infarction: Burden and timing of occurrence: A nation-wide analysis including 86 771 patients from the Cardiovascular Disease in Norway (CVDNOR) Project. J Am Heart Assoc 2016; 5: e002667.
9. Baughman RP, Teirstein AS, Judson MA, et al. Clinical characteristics of patients in a case control study of sarcoidosis. Am J Respir Crit Care Med 2001; 164: 1885-9.
10. Tsutsui H, Tsuchihashi-Makaya M, Kinugawa S, et al. Diagnosis and management of cardiac sarcoidosis. Prog Cardiovasc Dis 2010; 52: 336-46.