A case of cardiac sarcoidosis mimicking cardiac amyloidosis on cardiovascular magnetic resonance

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Abstract

A 52-year-old male visited our hospital with abnormal electrocardiogram and exertional fatigue. The electrocardiogram showed first-degree atioventricular block, complete right bundle branch block, and inverted T waves in Leads II, III, aVF, V3, and V4. Echocardiography showed biventricular wall thickening involving granular sparkling of the interventricular septum. Late gadolinium enhancement on cardiovascular magnetic resonance (CMR) was found at the circumferential right ventricular wall and patchy regions of the left ventricle. Although these findings strongly suggested cardiac amyloidosis, he was finally diagnosed with systemic sarcoidosis due to the following. First, endomyocardial biopsy revealed non-caseating epithelioid granuloma with giant cells. Second, 18F-fluorodeoxyglucose positron emission tomography showed uptake in bilateral hilar lymph nodes, para-aortic lymph nodes, and the biventricular wall of the heart. Although echocardiography and CMR are very useful tools for diagnosis of cardiomyopathies, their specificity and accuracy need to be considered.

Keywords Cardiac sarcoidosis; Cardiac amyloidosis; Late gadolinium enhancement; 18F-Fluorodeoxyglucose positron emission tomography; Endomyocardial biopsy

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Introduction

Cardiovascular magnetic resonance (CMR) is a useful diagnostic tool for cardiomyopathies.1 It is well known that cardiac amyloidosis presents a characteristic pattern as global subendocardial late gadolinium enhancement (LGE) on CMR,2 as well as on echocardiographic findings.3 In cardiac sarcoidosis (CS), the LGE distribution on CMR shows a wide variety of types such as nodular, circumferential, subepicardial, and subendocardial types.4,5 The differential diagnosis between cardiac amyloidosis and sarcoidosis is critical because it leads to different treatments and prognoses.

We experienced an unusual case of CS mimicking cardiac amyloidosis on echocardiography and magnetic resonance imaging findings, which was finally diagnosed by endomyocardial biopsy and 18F-fluorodeoxyglucose positron emission tomography (FDG-PET).

Case report

A 52-year-old male came to our hospital with exertional fatigue. One year ago, he underwent radiofrequency catheter ablation at another hospital for frequent monofocal premature ventricular contractions originating from the right ventricular (RV) moderator band near the apex. Pre-operational echocardiogram showed first-degree atrioventricular block and inverted T waves in Leads II, III, aVF, V3, and V4. At the first visit to our hospital, complete right bundle branch block and inverted T waves in Leads II, III, aVF, V3, and V4 were also recorded (Figure 1). On physical examinations, he had no leg oedemas, lymphadenopathies, or exanthemas. Chest X-ray did not show any pulmonary congestion, cardiomegaly, or bilateral hilar lymphadenopathy. With regard to laboratory data, serum creatinine level, BNP level, and Troponin I level were elevated (1.27 mg/dL, 154.2 pg/mL, and 0.131 ng/mL, respectively). However, serum angiotensin-converting enzyme level and

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soluble interleukin 2 receptor were not elevated (8.6 U/L and 116 U/mL, respectively). Echocardiography showed biventricular wall thickening with granular sparkling echogenicity of the interventricular septum (Figure 2). On echocardiographic assessment, enlarged RV (RV diastolic area 34 cm²/m² and RV systolic area 28 cm²/m²), decreased RV fractional area change (18%), and diffusely reduced left ventricular (LV) ejection fraction (48%) with normal LV dimension (in diastole 49 mm and in systole 38 mm) were also recorded. His Doppler cardiac index was significantly decreased (1.42 L/min/m²). CMR also demonstrated diffuse biventricular wall thickenings, and LGE was shown in both ventricles with high signal under T2-weighted image (Figure 3). Coronary artery disease was excluded from coronary computed tomography angiography. Although these findings strongly suggested cardiac amyloidosis, he was finally diagnosed with CS by FDG-PET (Figure 4), showing invasive uptake in the free wall of the RV and the anteroseptal wall of the LV, and endomyocardial biopsy.
Figure 3  Cardiovascular magnetic resonance images. On cine images, diffuse biventricular wall thickenings are shown. Late gadolinium enhancement is present in multiple locations, including both ventricles. On the T2-weighted image (Pre), a clear bright signal in the right ventricle (RV) and the anteroseptal wall of the left ventricle (LV) is noted, but after steroid treatment (Post), these lesions are not well delineated.

Figure 4  $^{18}$F-Fluorodeoxyglucose positron emission tomography imaging. (A) On planar imaging, distinct and focal uptake of fluorodeoxyglucose (FDG) is shown in the bilateral hilar lymph nodes of the lung and the heart. (B) On a transverse image, intense uptake of FDG is shown in the right ventricle and anteroseptal wall of the left ventricle. (C) On a sagittal image, intense uptake of FDG is shown in the right ventricle and anteroseptal wall of the left ventricle and hilar lymph nodes. The regions of high FDG uptake show signal enhancement by T2-weighted cardiovascular magnetic resonance.
(Figure 5), showing non-caseating epithelioid granuloma with giant cells. The patient was treated with methyl prednisolone pulse therapy (1000 mg/day) for 3 days, followed by oral prednisolone (30 mg/day). The dosage of prednisolone was gradually reduced. During hospitalization, sustained ventricular tachycardia (VT) originating from the RV lateral and inferior walls was frequently observed. VT still persisted in spite of radiofrequency ablation and administration of beta-adrenergic receptor blocker (bisoprolol fumarate 1.25 mg/day) and Class III anti-arrhythmic agent (sotalol hydrochloride 80 mg/day). However, after 3 months of steroid therapy, his cardiac function has significantly improved (LV ejection fraction 70%, RV fractional area change 40%, and Doppler cardiac index 2.34 L/min/m²). Although his cardiac function improved, an implantable cardioverter defibrillator was implanted considering patient's age and preference. The patient has been followed at an outpatient clinic for a year. He experienced no worsening of cardiac function, heart failure, and VT thereafter.

Discussion

This patient provided two important clinical suggestions. First of all, CS can present with biventricular wall thickening involving a granular sparkling appearance of the interventricular septum. Although it is well known that this ventricular wall thickening with granular sparkling pattern of the septum on echocardiography is characteristic of infiltrative cardiomyopathy such as cardiac amyloidosis, septal thickening in CS is quite rare. In CS, echocardiographic characteristics vary according to the disease activity and may reveal wall thickening due to inflammation of granulomatous lesions and thinning due to fibrous scar formation. Furthermore, this case also showed a global high signal intensity in the RV and the septum and anterior region of the LV on T2-weighted images, which correspond to the myocardial uptake regions on FDG-PET indicating granulomatous infiltration.

Compared with that in pre-steroid condition, improved T2-weighted high signal intensity was observed after steroid therapy (Figure 3). This T2-weighted high signal intensity should be considered as a sign of cardiac inflammation and oedema in ongoing CS.

Second, CS can show global LGE in both ventricles on CMR. In our patient, LGE was observed over a wide range of the RV and in patchy and transmural regions of the LV, mimicking cardiac amyloidosis. In cardiac amyloidosis, accumulated abnormal proteins expand more widely in the interstitial space, resulting in several different patterns of LGE on CMR such as entire subendocardial circumference, focal intramural, and subepicardial patterns in both ventricles. On the other hand, it is well documented that LGE in CS is patchy and typically involves the basal septum and lateral LV walls, but rarely in the free wall of the RV. Yared et al. reported a case of CS imitating arrhythmogenic RV

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Figure 5: Histopathological pictures of a cardiac biopsied specimen from the right ventricle. Non-caseating epithelioid granuloma with giant cell and inflammatory cell infiltration is observed. Lower magnification (A) and higher magnification (B).
dysplasia suspected by echocardiography, in which LGE was shown in the portion of the RV free wall and the subepicardial portion of the LV. On FDG-PET, intense uptake was observed in the RV and patchy in the LV, suggesting that these findings were similar to our case.

Recently, hybrid imaging of FDG-PET and CMR has been applied for non-invasive imaging of cardiac diseases. In particular, cardiac positron emission tomography–magnetic resonance imaging is reported to be clinically feasible for the detection of cardiac inflammation such as active CS. A combination of positron emission tomography and CMR may be more desirable in non-invasive imaging for CS to differentiate it from other types of cardiac hypertrophy.

In conclusion, CS can present as biventricular wall thickening involving granular sparkling of the interventricular septum and also shows a wide range of transmural and patchy LGE on CMR mimicking cardiac amyloidosis. Although CMR is a useful diagnostic tool, its interpretation needs to be considered.

Conflict of interest
None declared.

References

1. Bluemke DA. MRI of nonischemic cardiomyopathy. Am J Roentgenol 2010; 195: 935–940.
2. Maceira AM, Joshi J, Prasad SK, Moon JC, Persugni E, Harding I, Sheppard MN, Poole-Wilson FA, Hawkins PN, Pennell DJ. Cardiovascular magnetic resonance in cardiac amyloidosis. Circulation 2005; 111: 186–193.
3. Koyama J, Ikeda S, Ikeda U. Echocardiographic assessment of the cardiac amyloidoses. Circ J 2015; 79: 721–734.
4. Smedema JP, Snoep G, van Kroonenhurgh MP, van Geuns RJ, Dassen WR, Gorgels AP, Crijns HJ. Evaluation of the accuracy of gadolinium-enhanced cardiovascular magnetic resonance in the diagnosis of cardiac sarcoidosis. J Am Coll Cardiol 2005; 45: 1683–1690.
5. Watanabe E, Kimura F, Nakajima T, Hiroe M, Kasai Y, Nagata M, Kawana M, Hagiwara N. Late gadolinium enhancement in cardiac sarcoidosis: characteristic magnetic resonance findings and relationship with left ventricular function. J Thorac Imaging 2013; 28: 60–66.
6. Okabe T, Yakushiji T, Hiroe M, Oyama Y, Iigawa W, Ono M, Kido T, Ebara S, Yamashita K, Yamamoto MH, Saito S, Hoshimoto K, Kisaki A, Isomura N, Araki H, Ochiai M. Steroid pulse therapy was effective for cardiac sarcoidosis with ventricular tachycardia and systolic dysfunction. ESC Heart Fail 2016; 3: 288–292.
7. Yazaki Y, Isobe M, Hayasaka M, Tamaki M, Fujii T, Sekiguchi M. Cardiac sarcoidosis mimicking a hypertrophic cardiomyopathy: clinical utility of radionuclide imaging for differential diagnosis. Jpn Circ J 1998; 62: 465–468.
8. Matsumori A, Hara M, Nagai S, Izumi T, Ohashi N, Ono K, Sasayama S. Hypertrophic cardiomyopathy as a manifestation of cardiac sarcoidosis. Jpn Circ J 2000; 64: 679–683.
9. Vignaux O, Dhote R, Duboc D, Blanche P, Devaux JY, Weber S, Legmann P. Detection of myocardial involvement in patients with sarcoidosis applying T2-weighted, contrast-enhanced, and cine magnetic resonance imaging: initial results of a prospective study. J Comput Assist Tomogr 2002; 26: 762–767.
10. Syed IS, Glockner JF, Feng D, Araoz PA, Martinez MW, Edwards WD, Gertz MA, Dispenzieri A, Oh JK, Bellavia D, Tajik AJ, Grogan M. Role of cardiac magnetic resonance imaging in the detection of cardiac amyloidosis. JACC Cardiovascular Imaging 2010; 3: 155–164.
11. Vogelstein B, Mahnoldt H, Deluigi CC, Yilmaz A, Kupetz EM, Greulich S, Kingel K, Kandolf R, Sechtem U. Cardiovascular magnetic resonance in clinically suspected cardiac amyloidosis: noninvasive imaging compared to endomyocardial biopsy. J Am Coll Cardiol 2008; 51: 1022–1030.
12. Yared K, Johri AM, Soni AV, Johnson M, Alkassat T, Cury RC, Jung H, Mamuya W. Cardiac sarcoidosis imitating arrhythmogenic right ventricular dysplasia. Circulation 2008; 118: e113–e115.
13. Rischpler C, Nekolla SG, Dregely I, Schweiger M. Hybrid PET/MR imaging of the heart: potential, initial experiences, and future prospects. J Nucl Med 2013; 54: 402–415.
14. White JA, Rajchl M, Butler J, Thompson RT, Prato FS, Wisenberg G. Active cardiac sarcoidosis: first clinical experience of simultaneous positron emission tomography–magnetic resonance imaging for the diagnosis of cardiac disease. Circulation 2013; 127: e639–e641.
15. Dweck MR, Abgral R, Trivieri MG, Robson PM, Karakatsanis N, Mani V, Palmisano A, Miller MA, Lala A, Chang HL, Sanz J, Contreras J, Narula J, Fuster V, Padilla M, Fayad ZA, Kocacic JC. Hybrid magnetic resonance imaging and positron emission tomography with fluorodeoxyglucose to diagnose active cardiac sarcoidosis. JACC Cardiovascular Imaging 2018; 1: 94–107.