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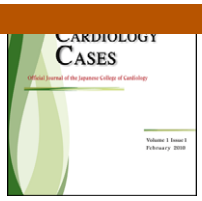

Case report

A case of cardiac sarcoidosis masquerading as arrhythmogenic right ventricular cardiomyopathy awaiting heart transplant

Sahika Hisaoka (MD)[a], Tomoko Sugiyama-Kato (MD, PhD)[a,b,*], Toshiharu Iwamura (MD)[a], Hideharu Okamatsu (MD)[a], Tsukasa Kamakura (MD)[a], Hajime Sato (MD)[a], Takeshi Nakatani (MD, PhD)[b], Kazuhiko Hashimura (MD)[a], Masafumi Kitakaze (MD, PhD, FJCC)[a], Hatsue Ishibashi-Ueda (MD, PhD)[c], Toshiaki Shishido (MD, PhD)[d], Kazuo Komamura (MD, PhD, FJCC)[a,b]

[a] *Department of Cardiovascular Medicine, National Cardiovascular Center, Osaka, Japan*
[b] *Department of Organ Transplantation, National Cardiovascular Center, Osaka, Japan*
[c] *Department of Pathology, National Cardiovascular Center, Osaka, Japan*
[d] *Department of Cardiovascular Dynamics, National Cardiovascular Center, Osaka, Japan*

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Summary We report a case of 45-year-old man, who was diagnosed with arrhythmogenic right ventricular cardiomyopathy (ARVC) and presented with right ventricular (RV) enlargement with a global decrease in RV contractility accompanied by impairment of left ventricular function. He was placed on the heart transplant waiting list. Endomyocardial biopsy from RV septal wall did not show any evidence of sarcoidosis or inflammatory change. Four years after he was put on the heart transplant waiting list, a computed tomography chest scan for the purpose of anatomical evaluation for coronary sinus prior to biventricular pacing lead implantation incidentally showed bilateral hilar lymphadenopathy, which suggested the possibility of sarcoidosis. Biopsy of the inguinal lymph node pathologically was consistent with sarcoidosis. The 2[^{18}F]fluoro-2-deoxy-D-glucose positron emission tomography scanning (FDG-PET) demonstrated intense uptake in the myocardium, and the patient was finally diagnosed as having cardiac sarcoidosis. After steroid treatment, the abnormal FDG-PET uptake disappeared. The patient therefore represented a case of cardiac

* Corresponding author at: Department of Cardiovascular Medicine and Organ Transplantation, National Cardiovascular Center, 5-7-1 Fujishiro-dai, Suita, Osaka 565-8565, Japan. Tel.: +81 6 6833 5012; fax: +81 6 6872 8160.
E-mail address: rinnko@sannet.ne.jp (T. Sugiyama-Kato).

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sarcoidosis masquerading as ARVC. It should be recognized that RV involvement is one of the manifestations in cardiac sarcoidosis.

Case report

A 45-year-old man without significant past medical history was admitted to hospital 6 years ago due to exertional dyspnea. Two-dimensional transthoracic echocardiography demonstrated dilated left ventricle (LV) with decreased contraction and concentric hypertrophy. Coronary angiography was normal, and a left ventriculogram showed diffuse hypokinesis. The endomyocardial biopsy obtained from right ventricular septal wall showed severe fibrosis and sporadic hypertrophied myocytes without any inflammatory changes. The LV ejection fraction was 7% at that time, and he was diagnosed with the dilated phase of hypertrophic cardiomyopathy at this point, and has since been undergoing β-blocker (carvedilol) therapy.

However, his heart failure symptoms of New York Heart Association class II to III had not been improved in spite of β-blocker therapy, therefore, he was transferred to our hospital for heart transplant evaluation 2 years after the initial episode of admission due to heart failure. His physical examination showed hepatomegaly with a small amount of ascites. Two-dimensional transthoracic echocardiography revealed significant right ventricle (RV) enlargement with a markedly global decrease in RV contractility accompanied by impairment of dilated LV contraction and severe tricuspid regurgitation (Fig. 1). Gadolinium-enhanced cardiovascular magnetic resonance imaging (MRI) revealed late enhancement in biventricles (Fig. 2). The 24-h Holter electrocardiogram monitoring showed non-sustained ventricular tachycardia with left bundle branch block morphology and more than 1000 polymorphic premature ventricular beats. He was diagnosed with possible arrhythmogenic right ventricular cardiomyopathy (ARVC) on the basis of these findings. Since then, he has been on the heart transplant waiting list.

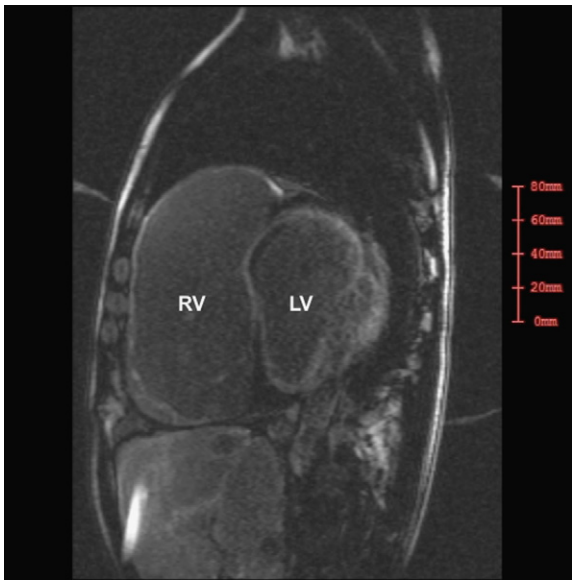

Figure 2 Delayed gadolinium-enhanced MRI demonstrating delayed enhancement of biventricles and significant right ventricular enlargement. LV, left ventricle; RV, right ventricle.

Four years later, antiarrhythmic therapy (amiodarone) was initiated due to recurrence of non-sustained ventricular tachycardia, however, despite amiodarone administration he was readmitted because of exacerbation of chronic heart failure, with a demonstration of atrial flutter with 1:1 atrio-ventricular conduction. The chest X-ray, 12-lead

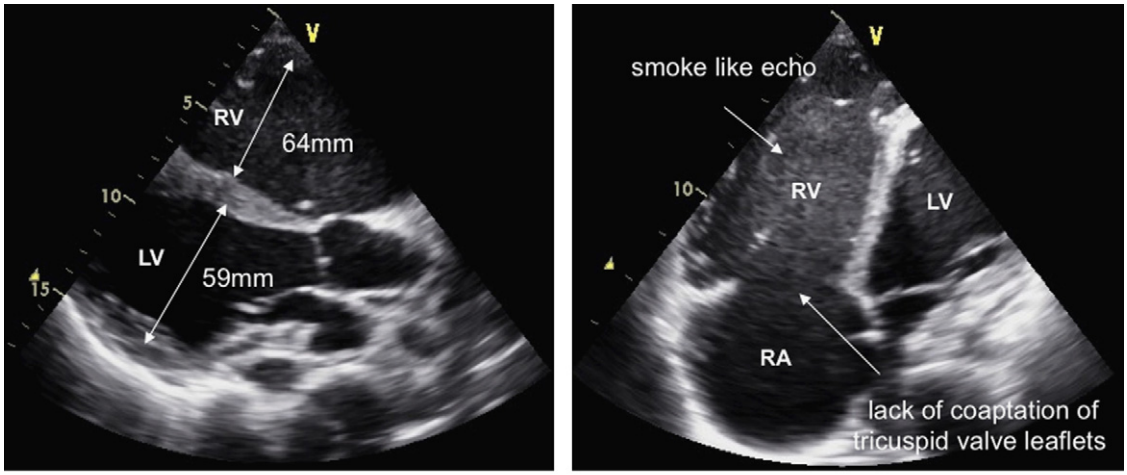

Figure 1 Two-dimensional transthoracic echocardiography showing significant biventricular enlargement. LV, left ventricle; RV, right ventricle; RA, right atrium.

Table 1 Laboratory examination on the latest admission.

Laboratory parameter	Results of examination	Normal range
Hematological examination of peripheral blood		
WBC (/μL)	3.20×10^3	$4.40–9.00 \times 10^3$
RBC (/μL)	4.44×10^6	$4.20–5.50 \times 10^6$
Hg (g/dL)	14.8	13.5–18.0
Ht (%)	43.5	36.0–54.0
Plat (/μL)	122×10^3	$150–350 \times 10^3$
Biochemical examination of serum		
TP (g/dL)	60	6.7–8.3
Alb (g/dL)	3.2	4.0–5.0
Na (mEq/L)	141	138–146
K (mEq/L)	3.6	3.6–4.9
Cl (mEq/L)	108	99–109
CA (mEq/L)	9.1	8.7–10.3
T-Bil (mg/dL)	1.5	0.3–1.2
D-Bil (mg/dL)	0.7	0.0–0.4
AST (U/L)	29	13–33
ALT (U/L)	21	8–42
LDH (U/L)	184	119–229
ALP (U/L)	504	115–359
γGTP (U/L)	329	1–47
CK (U/L)	53	62–287
BUN (mg/dL)	19	8.0–22.0
Cre (mg/dL)	0.97	0.60–1.10
UA (mg/L)	5.1	3.6–7.0
FBG (mg/dL)	77	80–112
HbA1c (%)	5.9	4.3–5.8
TC (mg/dL)	130	128–219
TG (mg/dL)	55	30–149
CRP (mg/dL)	0.08	0.0–0.3
BNP (pg/mL)	825.8	<20
Lysozyme (μg/mL)	12.6	4.2–11.5
ACE (IU/L)	13.4	7.7–29.4

WBC: white blood cell count; RBC: red blood cell count; Hb: hemoglobin; Hct: hematocrit; Plat: platelet count; TP: total protein; Alb: albumin; Na: sodium; K: potassium; Cl: chloride; CA: calcium; T-Bil: total bilirubin: D-Bil: direct bilirubin; AST: aspartate aminotransferase; ALT: alanine aminotransferase; LDH: lactate dehydrogenase; ALP: alkaline phosphatase; γGTP: gamma-glutamyltransferase; CK: creatine phosphokinase; BUN: blood urea nitrogen; Cre: creatinine; UA: uric acid; FBG: fasting blood glucose; HbA1c: hemoglobin A1c; TC: total cholesterol; TG: triglyceride; CRP: C-reactive protein; BNP: brain natriuretic peptide; ACE: angiotensin-converting enzyme.

electrocardiogram just after admission demonstrating atrial flutter with 2:1 atrio-ventricular conduction, and 12-lead electrocardiogram after cardioversion are shown in Fig. 3, and the laboratory examination results on admission are described in Table 1.

A cardiac resynchronization plus defibrillator was then implanted. Before the leads for resynchronization therapy were implanted, a computed tomography scan of the chest was performed with the aim of identifying the coronary sinus. The computed tomography scan showed bilateral hilar lymphadenopathy (Fig. 4(a)) suggesting the possibility of sarcoidosis. Gallium-67 scintigraphy was then obtained to evaluate the activity and to confirm a suspicion of sarcoidosis, which showed abnormal uptake in the bilateral hilar lymph nodes (Fig. 4(b)). Because the patient was on the waiting list for heart transplant, the diagnosis of sarcoidosis was essential for considering a future immunosuppressant protocol after transplantation. Therefore, in addition to the diagnostic finding of imaging, histological definitive diagnosis was essential for this patient. Therefore, a biopsy of the inguinal lymph node was performed, which revealed numerous noncaseating epithelioid granulomas with multinuclear giant cells consistent with sarcoidosis (Fig. 4(c)). The 2-[^{18}F]fluoro-2-deoxy-D-glucose positron emission tomography scanning (FDG-PET) demonstrated intense uptake in the myocardium (Fig. 4(d-I)), and the patient was finally diagnosed with cardiac sarcoidosis. Although mediastinal lymphadenopathy is an important and useful finding to diagnose cardiac sarcoidosis [1], mediastinal lymphadenopathy was detected neither by FDG-PET nor by Gallium-67 scintigraphy in this patient. He started to be treated with steroids for active cardiac sarcoidosis. After 1 month of steroid administration, the abnormal uptake detected by FDG-PET disappeared (Fig. 4(d-I) and (d-II)). The frequency of arrhythmia decreased after steroid therapy, however, his cardiac function did not improve and he remains on the heart transplant waiting list.

Discussion

We experienced a patient, who was initially diagnosed with dilated phase of hypertrophic cardiomyopathy and then diagnosed with ARVC on account of echocardiographic findings of remarkable RV enlargement and decreased contraction. However, finally he was confirmed to have cardiac sarcoidosis. The diagnosis of cardiac sarcoidosis was finally made on the basis of the pathological findings of the inguinal lymph node and active uptake of the heart detected by FDG-PET. In this case, the abnormal uptake detected by FDG-PET was diminished after adequate therapy such as steroid administration for sarcoidosis. FDG-PET scanning is a useful tool not only for diagnosing cardiac sarcoidosis, but also evaluating effectiveness of treatment [2–4].

The echocardiographic manifestations of presumed cardiac sarcoidosis are thinning of the basal septum, as a well-known feature, regional wall motion abnormalities, pericardial effusion, and LV chamber dilatation with decreased systolic function. However, these representative features are not always seen in patients with cardiac sarcoidosis. Moreover, a definitive histological diagnosis of cardiac sarcoidosis is extremely difficult, because the granulomas of sarcoidosis are locally found within the myocardium and an endomyocardial biopsy may not prove the diagnosis [5].

Cardiac sarcoidosis mimicking ARVC is extremely rare, although several authors have reported cardiac sarcoidosis involving mainly RV or biventricles [6,7] such as seen in this patient. ARVC would be a suspected diagnosis for a patient who has ventricular arrhythmias and generalized dilatation or localized abnormalities of RV in the presence of preserved LV size and function. ARVC is a heart muscle disease affecting RV, rarely involving LV, and is pathologically characterized by fibro-fatty replacement of the myocardium [8].

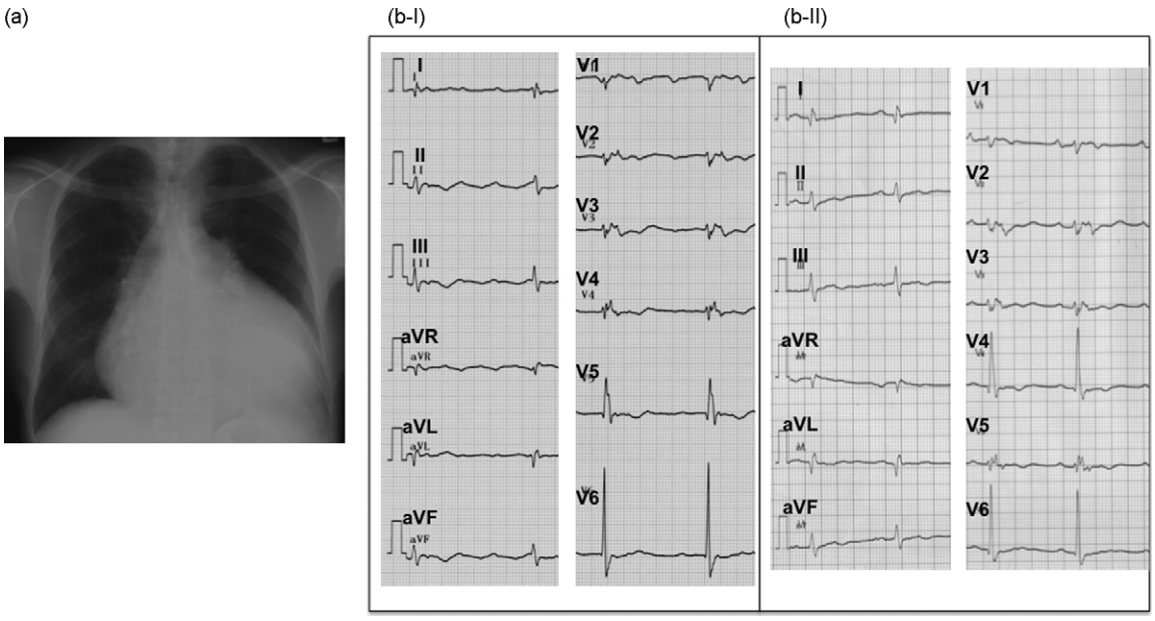

Figure 3 (a) Chest X-ray showing marked cardiomegaly with cardio-thoracic ratio of 81%. (b-I) Twelve-lead electrocardiogram showing atrial flutter with 2:1 atrio-ventricular conduction, low voltage in V1—4. (b-II) Twelve-lead electrocardiogram showing sinus rhythm after cardioversion.

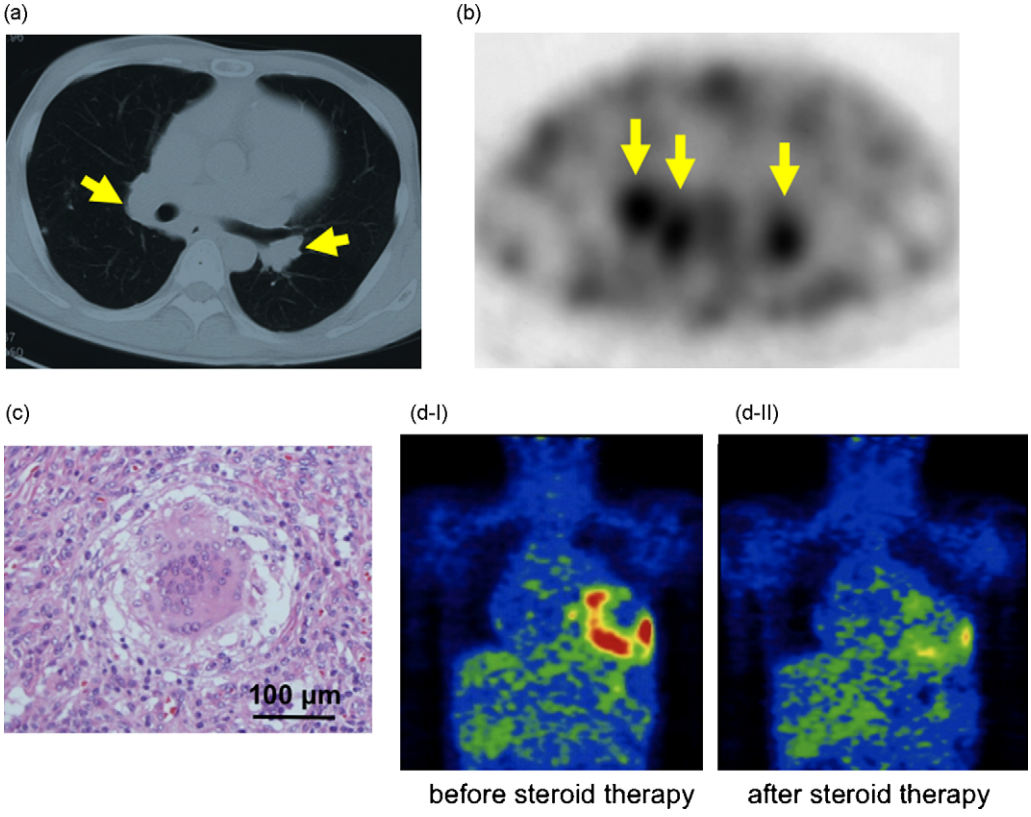

Figure 4 (a) Computed tomography scan of the chest. The arrows indicate marked bilateral hilar lymphadenopathy. (b) Gallium-67 scintigraphy of the chest. The arrows indicate abnormal uptake in the bilateral hilar lymph nodes. (c) Photomicrograph of the inguinal lymph node biopsy showing noncaseating epithelioid granuloma with multinuclear giant cells (hematoxylin and eosin stained histological sections at 400×). (d-I) The 2-[^{18}F]fluoro-2-deoxy-D-glucose positron emission tomography scan demonstrating intense uptake in the myocardium before steroid therapy. (d-II) The scan obtained after steroid therapy, which showed disappearance of abnormal uptake.

Initially, the patient in this report was diagnosed with dilated phase of hypertrophic cardiomyopathy, and then diagnosed as ARVC with LV involvement. Sen-Chowdhry et al. [9] demonstrated that late enhancement of gadolinium-enhanced cardiovascular MRI is suggestive of LV involvement in ARVC, and 84% of patients diagnosed with ARVC have LV involvement. The patient in this report also had late enhancement in biventricles on gadolinium-enhanced cardiovascular MRI, which was interpreted as supporting evidence for diagnosing this patient as having ARVC at this point. Several previous papers reported that cardiac sarcoidosis in its early stage mimics hypertrophic cardiomyopathy [10]. Due to the relatively well-preserved wall thickness despite of severe LV dysfunction, the patient was initially diagnosed as having dilated phase of hypertrophic cardiomyopathy. However, we might have been able to suspect cardiac sarcoidosis at this point in hindsight. LV concentric hypertrophy initially shown in this patient would be a sign of early stage of cardiac sarcoidosis.

We emphasize the need to consider cardiac sarcoidosis in the differential diagnosis of patients who present with structural abnormalities of RV and who are suspected of having ARVC. In addition, it should be recognized that RV involvement is one of the manifestations of cardiac sarcoidosis.

Conflicts of interest

This study did not receive financial support and the authors declare no conflicts of interest.

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