Acta Med. Okayama, 2021
Vol. 75, No. 4, pp. 517–521

Acta Medica Okayama
http://escholarship.lib.okayama-u.ac.jp/amo/

Case Report

Arrhythmogenic Right Ventricular Cardiomyopathy Diagnosed during Hospitalization for Cardiac Arrest

Masahiko Ochi[a], Atsuyoshi Iida[b]*, Yuka Takahashi[c], Masamichi Tanaka[a], Hironori Saito[a], Hiromichi Naito[d], Takeshi Mikane[b], and Soichiro Fuke[a]

Departments of [a]Cardiology, [b]Emergency Medicine, Japan Red Cross Okayama Hospital, Okayama 700-8607, Japan, [c]Division of Pathology and Clinical Laboratories, National Cancer Center Hospital, Tokyo 104-0045, Japan, [d]Department of Emergency, Critical Care, and Disaster Medicine, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama 700-8558, Japan

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a genetically mediated cardiomyopathy characterized by progressive myocardial loss of the right ventricle and its replacement by fibrofatty tissue, causing dyskinesia, aneurysm, and/or arrhythmia. The prevalence of ARVC is estimated to be 1 in 2,000-5,000, with the condition accounting for up to 20% of sudden cardiac deaths in individuals < 35 years old. This report describes the case of 61-year-old Japanese who was diagnosed with ARVC after cardiac arrest (CA) and successful resuscitation. After the sudden CA, the restoration of spontaneous circulation was achieved with appropriate resuscitation, followed by the introduction of target temperature management in the intensive care unit. He was diagnosed with ARVC based on angiography and histology results. An ICD (implantable cardioverter-defibrillator) was implanted, and he was discharged without neurological sequelae 1 month post-CA. ARVC is an important cause of sudden CA, and successfully resuscitated patients with right ventricular dilation should undergo testing to rule out ARVC.

Key words: inverted T-wave, right ventricular dilatation, sudden cardiac arrest, sudden cardiac death

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is an inherited myocardial disease characterized by fibrofatty degeneration and aneurysmal enlargement of the right ventricle (RV). This condition is associated with exercise-mediated ventricular tachycardia and is one of the recognized causes of sudden cardiac death. Sudden cardiac arrest (CA) is one of the major causes of death worldwide. The diagnosis and prevention of CAs is a major challenge. Bystander-witnessed CA accounts for an estimated 19,000 cases in Japan. The reported 1-month survival rate of sudden CA is 12.2%, and the survival rate without neurological sequelae is 7.9% [1]. ARVC is estimated to have a prevalence of 1 in 5,000 people and to account for up to 20% of sudden cardiac deaths in the population of individuals < 35 years of age [2]. ARVC was first reported over 30 years ago, but despite its clinical importance as a cause of sudden death, it is still under-recognized. This report describes the case of a middle-aged man who recovered from a CA without neurological sequelae and was diagnosed with ARVC.

Case Report

A 61-year-old Japanese man presented with palpitations and edema of the lower limbs. The electrocardiogram (ECG) showed rhythms suggestive of atrial fibrillation, and echocardiography revealed severe mitral

Received October 1, 2020; accepted January 21, 2020.
*Corresponding author. Phone : +81-86-222-8811; Fax : +81-86-222-8841
E-mail : pp7h4al1@okayama-u.ac.jp (A, Iida)

Conflict of Interest Disclosures: No potential conflict of interest relevant to this article was reported.

regurgitation and a left ventricular ejection fraction (LVEF) of 16%. The right atrium (RA) and right ventricle (RV) were also dilated without aneurysmal change, *i.e.*, the RV outflow tract (prox.) was 39 mm, the basal RV diameter was 39 mm, and the mid-RV diameter was 44 mm. The patient underwent ablation therapy and was administered amiodarone 200 mg daily. The dose of amiodarone was gradually reduced to 100 mg after 14 months and was stopped after 20 months. The LVEF gradually improved to 48%.

Six months after the cessation of amiodarone, the patient suddenly experienced a CA while playing golf outdoors. Basic life support was immediately performed by a bystander, and an automated external defibrillator (AED) was applied. The AED monitor showed a wide QRS wave and "R on T" followed by VT, and subsequently AED was performed twice. Restoration of spontaneous circulation (ROSC) was achieved upon the patient's admission to the hospital, and the ECG findings indicated an incomplete right bundle branch block (RBBB), first-degree AV block, and inverted T-waves in leads V4-V6 (Fig. 1).

A two-dimensional echocardiography (2D-echo) examination was performed and revealed dilation of the RV and diffuse hypokinesis of the left ventricle (LV) wall; the LVEF was 45%, and both atria were dilated. No significant regurgitation was observed, and the tricuspid regurgitation pressure gradient (TR-PG) was 15 mmHg (Fig. 2).

The results of coronary angiography were normal, and RV angiography showed ventricular dilatation and regional dyskinesia (Fig. 3). In electrophysiology studies, VTs were reproducibly induced by a program of stimulation of the RV apex or the outflow tract. When pilsicainide was administered, Brugada syndrome, QT prolongation syndrome, and catecholaminergic polymorphic ventricular tachycardia were absent. Cardiac magnetic resonance imaging (MRI) demonstrated typical dilation of the right atrium and ventricle. The ventricular wall was isointense on T1-weighted MRI and hyperintense on T2-weighted MRI. There was no evidence of late gadolinium enhancement. As these results suggested that the patient had ARVC, a right anterior myocardial biopsy was performed, and it revealed that ventricular myocytes were replaced by adipose and fibrous tissues (Fig. 4).

The patient was treated with target temperature management in the ICU, after which full recovery of consciousness was achieved. During his hospital stay, 100 mg of amiodarone was administered daily. The patient was transferred to another hospital for implantable cardioverter-defibrillator (ICD) implantation 12 days after admission, with no neurological sequelae.

Discussion

Despite its importance as a cause of sudden CA, ARVC is not widely known to clinicians. It is mandatory that all patients who are resuscitated following a CA and who have right ventricular dilatation undergo RV angiography and a myocardial biopsy, and their family history should be determined appropriately.

The prevalence of ARVC varies among different ethnicities and is estimated to be between 1 in 2,000 to 1 in 5,000 individuals [3, 4]. Right ventricular dilation and inverted T-waves (V1-V3) are keys to the diagnosis of ARVC. Inverted T-waves reflecting abnormal right ventricular repolarization are seen during the early stages of ARVC.

ARVC was first reported in a case series in 1982 by Marcus *et al.* [5]. It is a cardiomyopathy characterized by right ventricular dilation and dysfunction and ventricular arrhythmias of right ventricular origin. Pathologically, fibrofatty scar tissue progresses mainly from the epicardial side to the endocardial side of the RV, causing thinning and dilatation of the ventricular wall [6]. Fibrofatty scar tissue that replaces normal myocardial tissue delays intraventricular conduction and becomes a substrate for arrhythmia through a macro-reentry mechanism, and this contributes to the development of ventricular arrhythmia, similar to that observed after a myocardial infarction [7].

The diagnosis of ARVC is based on the criteria of the International Task Force for the Clinical Diagnosis of ARVC [8]. The findings in the present case that met the international criteria were as follows: regional RV dyskinesia with a reduced right ventricular ejection fraction detected by echocardiography, MRI, and angiography findings; $<50\%$ residual myocytes estimated by fibrous replacement in RV free-wall myocardial samples; inverted T-waves in the right precordial leads; sustained ventricular tachycardia with a left bundle branch block; and the superior axis pattern.

The estimated mortality rate for ARVC varies among studies and ranges from 0.08% to 3.6% of cases per year [9]. The prognosis of patients with ARVC depends

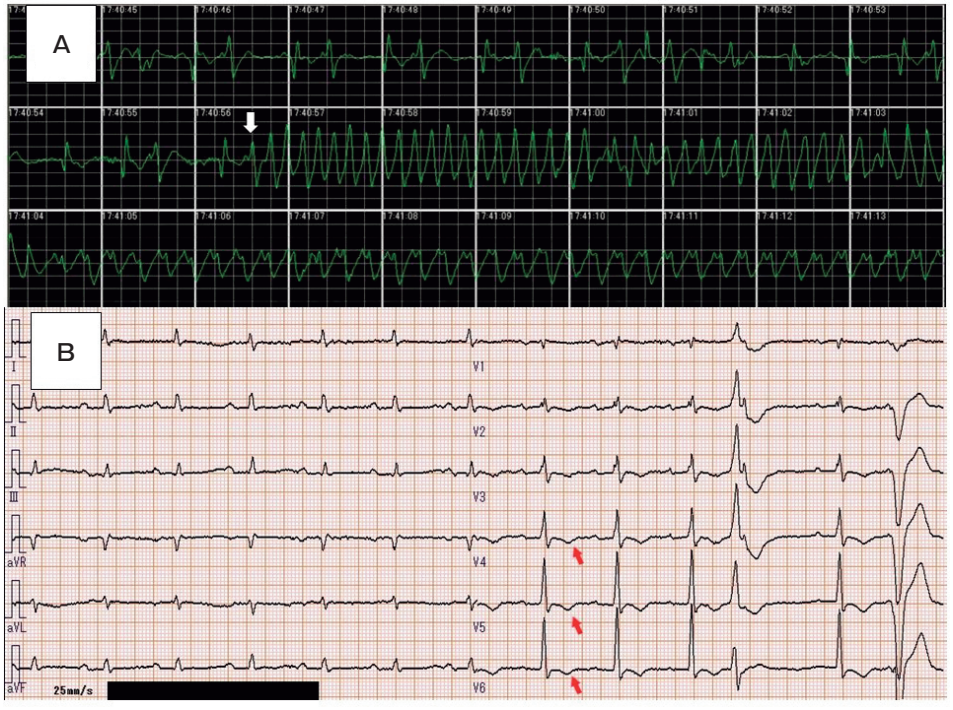

Fig. 1 **A**, "R on T" followed by ventricular tachycardia on the AED monitor at the pre-hospitalization facility (*arrow*); **B**, Post-electrical cardioversion 12-lead electrocardiogram showing complete right bundle branch block, paroxysmal ventricular compression, and T-wave inversion (*arrows*).

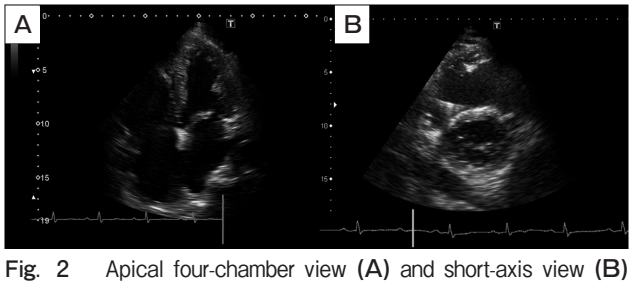

Fig. 2 Apical four-chamber view **(A)** and short-axis view **(B)** showing the dilated right ventricle.

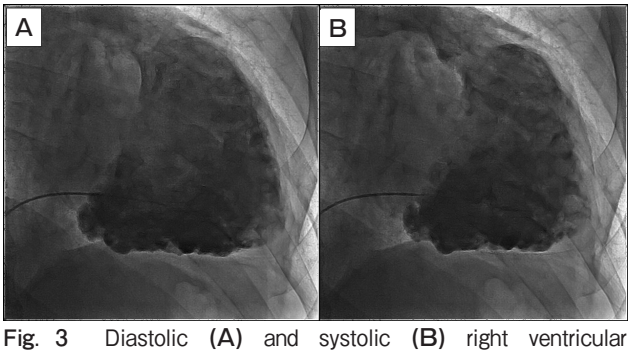

Fig. 3 Diastolic **(A)** and systolic **(B)** right ventricular angiography showing ventricular dilatation and regional dyskinesia.

strongly on the residual cardiac function and the severity of the arrhythmia [9-12]. Recent cohort studies have shown that well-diagnosed and treated patients and their families have good prognoses [13-15]. Since ARVC is a cardiomyopathy resulting from ventricular arrhythmias with impaired cardiac function, the goal of patient management is to alleviate these symptoms, reduce the risk of sudden cardiac death, and improve the quality of life [16]. Ventricular arrhythmias in particular cause sudden cardiac death and thus require strict prevention and management. Sports activities can increase the risk of sudden cardiac death in ARVC patients [6,17], as lethal arrhythmias could develop

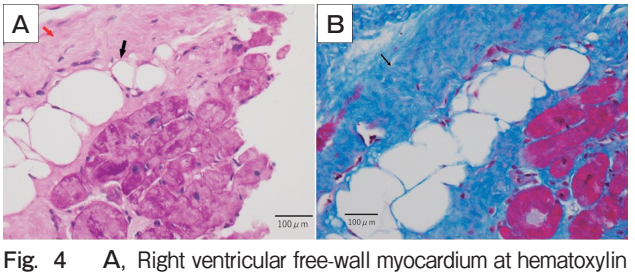

Fig. 4 **A**, Right ventricular free-wall myocardium at hematoxylin and eosin staining shows the fibrous replacement (*red arrow*) and fatty replacement (*black arrow*) of myocyte tissue; **B**, RV free-wall myocardium shows fibrous replacement (*arrow*) (Masson trichrome staining).

during such activities.

This patient was not diagnosed with ARVC when examined at the pre-hospitalization facility. After admission to our hospital, ablation and amiodarone therapy were provided, and the patient's cardiac function then improved. Catheter ablation is sometimes performed for VT associated with ARVC. Nogami *et al.* reported that ablation of the isolated delayed component significantly reduces the recurrence rate of arrhythmias [18]. However, since many VT substrates appear in patients with ARVC due to disease progression, the frequency of arrhythmia recurrence increases over time, and there is no strong evidence that ablation effectively prevents sudden cardiac death [19-23]. In fact, VT can recur several years after ablation, even in the present case.

Amiodarone is used for the treatment of VT. Amiodarone is an effective antiarrhythmic drug that is either prescribed alone or together with a beta-blocker, and the combination provides both the class III antiarrhythmic effects of amiodarone and beta-adrenergic blockade [24-26]. However, long-term treatment with amiodarone is challenging due to its severe cumulative toxic effects, such as pulmonary fibrosis, especially in younger patients. In the present case, amiodarone was discontinued based on the good clinical course, but 6 months later, the patient developed ventricular arrhythmias leading to the CA. This coincided with the time point at which the patient's blood concentration of amiodarone decreased, indicating that amiodarone was effective in suppressing VT in this patient. The patient resumed amiodarone treatment after his admission to the hospital.

The use of an ICD has been effective in ARVC patients who have episodes of lethal arrhythmia. Randomized controlled trials of defibrillation therapy have not yet been conducted; however, observational studies have consistently shown safe and effective results of ICDs [11, 12, 15, 24, 25, 27]. An ICD should be considered essential in ARVC patients who have been successfully resuscitated, as in the present case [28]. The patient underwent ICD transplantation 2 weeks after his resuscitation from lethal arrhythmia and is alive without major adverse events >6 months later.

In conclusion, it is necessary to test for ARVC and perform appropriate interventions in resuscitated patients with right ventricular dilatation.

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