

Arrhythmogenic Right Ventricular Dysplasia / Cardiomyopathy :
A Case Report and Literature Review

Po-Tsang Chen, Ta-Chun Hong, Charles Jia-Yin Hou,
Yu-San Chou, and Cheng-Ho Tsai

Cardiology Division, Department of Internal Medicine,
Mackay Memorial Hospital, Taipei, Taiwan

Abstract

Arrhythmogenic right ventricular dysplasia/cardiomyopathy (ARVD/C) is a rare cardiomyopathy with a familial predilection. It is characterized pathologically by progressive fibrofatty replacement of the myocardium, primarily of the right ventricular free wall. Clinically, it presents with life-threatening malignant ventricular arrhythmias which may lead to sudden death, most often in young people and athletes. ARVD/C is difficult to diagnose, although standardized diagnostic criteria have been proposed, based on the presence of major and minor criteria encompassing electrocardiographic, arrhythmic, morphofunctional, histopathologic, and genetic factors. The therapeutic options at present are focused on the prevention of life-threatening cardiac arrhythmia, by using antiarrhythmic drugs, catheter ablation, and/or an implantable cardioverter defibrillator. We describe a young patient with ARVD/C in sinus rhythm but with frequent ventricular ectopy who also had spontaneous echo contrast in the right atrium and right ventricle. The diagnosis was made on the basis of electrocardiography and imaging studies. Further investigation of this entity is needed to determine the best therapeutic approach for reducing the risk of lethal ventricular arrhythmias as well as thromboembolic complications. (J Intern Med Taiwan 2003; 14: 124-129)

Key Words : ARVD/C; Ventricular arrhythmia; Sudden death; Magnetic resonance imaging of heart; Anticoagulation

Introduction

Although hypertrophic obstructive cardiomyopathy remains the most common cause of sudden cardiac death in young people, rare causes such as arrhythmogenic right

ventricular dysplasia/cardiomyopathy (ARVD/C) are now being increasingly recognized in such cases. Recent reports have advanced our understanding of the clinical presentation, gene-tic inheritance, pathogenesis, diagnosis, and treatment of ARVD/C. We present a 34-year-old man recently diagnosed with this disorder and review the literature.

Case Report

In November 1998, a 31-year-old man undergoing a periodic health exam was found to have cardiomegaly. His history was negative for cardiac symptoms except for one brief presyncopal spell lasting a few seconds while playing basketball as an adolescent. He had continued to engage in vigorous activity after that without any discomfort. His older brother had died suddenly at the age of 31, but no autopsy had been done. The patient denied use of tobacco or alcohol abuse. His preliminary physical examination was unremarkable. The electrocardiogram showed a normal sinus rhythm, right axis deviation, inverted T waves in the inferior (II, III, aVF) and precordial (V1 to V6) leads, and epsilon wave in

V1 lead. There was one premature ventricular complex with a superior axis and right-bundle-branch block morphology. Echocardiography disclosed right atrial enlargement, right ventricular enlargement (29mm in diameter), and severe tricuspid valvular regurgitation but no structural abnormality of the tricuspid valve. The pulmonary artery pressure was normal.

Although further investigation was contemplated, the patient did not return for follow-up until December, 2002. At that time, he complained of episodes of chest discomfort for half a year. He had atypical chest pain in the left precordium apparently unrelated to exertion. The duration of the pain varied from minutes to a few hours, and it usually subsided spontaneously. On physical examination, his blood pressure was within normal limits and his heart rate and rhythm were normal. The jugular veins were not engorged, and there was no hepatosplenomegaly or ankle edema. The chest X-ray showed marked cardiomegaly. On electrocardiography, he had normal

sinus rhythm, right axis deviation, inverted T waves in the inferior (II, III, aVF) and precordial (V1 to V6) leads ,and epsilon waves in V1 to V6 (Figure 1) .

Frequent, isolated, polymorphic premature ventricular beats (1440/24hours) and supraventricular premature beats (1902/24hours) were documented on Holter monitoring. Transthoracic and transesophageal echocardiography both disclosed global dilatation and severe hypokinesia of the right ventricle, a markedly dilated right atrium, and striking spontaneous echo contrast without thrombus in the right atrium and ventricle (Figures 2 and 3). There was mild tricuspid regurgitation without significant pulmonary hypertension. There was no evidence of other

identifiable cardiac disease (e.g., Ebstein's anomaly, atrial septal defect, patent foramen ovale) or pulmonary disease. Magnetic resonance imaging of the heart demonstrated fibrofatty replacement of the free wall and subtricuspid region of the right ventricle (Figure 4). There were anterior focal bulging of the right ventricular outflow tract (Figure 5) and right heart morphologic and functional alterations similar to those seen on echocardiography (Figure 6). ARVD/C was diagnosed according to the International Society and Federation of Cardiology criteria 1. He had two major criteria: 1) severe dilation of the right ventricle with reduction of the right ventricular ejection fraction, and 2) epsilon waves in the right precordial leads; and two minor criteria: 1) inverted T waves in the right precordial leads in the absence of right bundle branch block, and 2) frequent ventricular extrasystoles (> 1000/24h). We recommended admission for an electrophysiologic study in order to plan a treatment strategy. The natural history of ARVD/C and its major risks, including malignant ventricular arrhythmias and sudden death, were explained to the patient. However, he refused further investigation. We therefore treated him empirically with amiodarone, hoping to prevent malignant ventricular arrhythmia, and warfarin, to reduce the risk of thromboembolic events.

Discussion

ARVD/C is a myocardial disease primarily affecting the free wall of the right ventricle (RV) and rarely the left ventricle. It is characterized histologically by the gradual replacement of myocardium by fibrofatty tissue 2-7. ARVD/C is an important cause of sudden death in individuals under 30 years of age, and has been found in up to 20% of cases of sudden death in young people 2,5,7,8. There is a familial predilection of the disease, which is typically inherited as an autosomal dominant trait with variable penetrance and incomplete expression 2-7. In addition to the inheritance pattern, there is evidence that other mechanisms may be involved in the fibrofatty replacement, such as dysontogenesis, degeneration, infection or inflammation, apoptosis, or myocyte transdifferentiation 2,4,5,7. However, there is as yet no definitive understanding of the pathogenesis of ARVD/C.

An expert consensus group proposed diagnostic criteria for ARVD/C in 1994, based on the presence of major and minor criteria encompassing electrocardiographic, arrhythmic, morphologic, functional, histopathologic, and genetic features 1. Although these guidelines represent a useful clinical approach to ARVD/C , optimal assessment of diagnostic criteria requires prospective evaluation from large patient population 5,6.

A definite diagnosis of ARVD/C requires the histologic finding of fibrofatty replacement of the right ventricular free wall. However, diagnosis by endomyocardial biopsy is difficult because the RV wall involvement is usually segmental early in the

disease, and the interventricular septum, the area usually biopsied, is rarely involved 2,5,6,7.

The imaging modalities used to evaluate the RV include conventional angiography, echocardiography, radionuclide angiography, ultrafast computed tomography, and magnetic resonance imaging (MRI) 2,3,5-7. The latter is potentially a very useful test because fat has a high signal intensity on T1-weighted images, so whether it is focal or diffuse, it can be distinguished from cardiac muscle 7. Heart MRI can also depict both functional and structural abnormalities of the heart and even quantify systolic and diastolic dysfunction of the RV 2-7. However, there are some limitations to MRI. The RV free wall is so thin that quantification of wall thickness is unreliable. Also, recent studies have demonstrated that more than 50% of normal elderly people have significant fatty infiltration of the RV 8. Thus, although MRI may have a role in the diagnosis of ARVD/C, its sensitivity and specificity still need to be defined by further studies 5-7. It is important to consider the entire clinical context, including symptoms, family history, etc, in addition to MRI findings. While positive MRI findings may be considered a major criterion for ARVD/C, other criteria are still required to make the diagnosis 3,4,7.

One of the most common and catastrophic manifestations of ARVD/C is a malignant ventricular arrhythmia of RV origin, resulting in sudden cardiac death. Although prevention of arrhythmic sudden death is the first objective of treatment, management of patients with ARVD/C must be individualized and based on local experience because, at present, there are still no precise guidelines to determine which patients need treatment and what therapy is the best 4-6.

Therapeutic options include pharmacologic (beta blocker or antiarrhythmic agents) and non- pharmacologic treatment (catheter ablation, implantable cardioverter defibrillator, or heart transplantation). However, further studies are needed to define the relative effectiveness of the various modalities in reducing mortality.

There are rare case reports of spontaneous echo contrast or even thrombus formation of the right heart in advanced cases of ARVD/C 10-12. Our patient had spontaneous echo contrast in his right atrium and ventricle, which we attributed to blood stasis secondary to the severe dilatation of the right atrium and marked systolic dysfunction of the RV. Until we have better experimental evidence addressing this issue, the decision as to whether and when to use anticoagulation will need to be based on assessment of individual patients.

Conclusion

While our understanding of ARVD/C is increasing, there is much that still needs to be clarified in terms of diagnosis and management. Given its significant role in sudden cardiac death, it is an entity that clinicians must be alert for.

References

1. Mckenna WJ, Thiene G, Nava A, et al. Diagnosis of arrhythmogenic right ventricular dysplasia/cardiomyopathy: task force of the working group myocardial and pericardial disease of the European Society of Cardiology and of the Scientific Council on Cardiomyopathies of the International Society and Federation of Cardiology. *Br Heart J* 1994; 71: 215-8.
2. Gemayel C, Pelliccia A, Thompson P. Arrhythmogenic right ventricular cardiomyopathy. *J Am Coll Cardiol* 2001; 38: 1773-81.
3. Corrado D, Basso C, Thiene G. Arrhythmogenic right ventricular cardiomyopathy: diagnosis, prognosis, and treatment. *Heart* 2000; 83: 599-5.
4. Corrado D, Buja G, Basso C, Thiene G. Clinical diagnosis and management strategies in arrhythmogenic right ventricular cardiomyopathy. *J Electrocardiol* 2000; 33: 49-55.
5. Fontaine G, Gallais Y, Fornes P, Hebert J-L, Frank R. Arrhythmogenic right ventricular dysplasia/cardiomyopathy. *Anesthesiology* 2001; 95: 250.
6. Naccarella F, Naccarelli G, Fattori R, et al. Arrhythmogenic right ventricular dysplasia / cardiomyopathy: current opinions on diagnostic and therapeutic aspects. *Curr Opin Cardiol* 2001; 16: 8-16.
7. HWM Kayser, EEvd Wall, et al. Diagnosis of arrhythmogenic right ventricular dysplasia: a review. *Radiographics* 2002; 22: 639-50.
8. Thiene G, Nava A, Corrado D, Rossi L, Pennelli N. Right ventricular cardiomyopathy and sudden death in young people
N Engl J Med 1998; 318: 129-33.
9. Burke A, Farb A, Tashko G, Virmani R. Arrhythmogenic right ventricular cardiomyopathy and fatty replacement of the right ventricular myocardium: are they different diseases? *Circulation* 1998; 97: 1571-80.
10. Bilge M, Eryonucu B, Guler N, et al. A case of arrhythmogenic right ventricular cardiomyopathy in sinus rhythm associated with thrombus in the right atrium. *J Am Soc Echocardiogr* 2000; 13: 154-6.
11. Christine H, Attenhofer J, Thomas B, et al. Extensive thrombus formation in the right ventricle due to a rare combination of arrhythmogenic right ventricular cardiomyopathy and heterozygous prothrombin gene mutation G20210A. *Cardio* 2000; 93: 127-30.
12. Jaroslaw K, Zdzislawa K-J, Andrzej W. Atrial epicardial pacing with long stimulus to P wave interval in a patient with arrhythmogenic right ventricular dysplasia complicated by right atrial thrombus. *PACE* 1999; 22: 1111-3.

心律不整性右心室發育不全 / 心肌病變：
一病例報告及文獻回顧

陳柏蒼 洪大川 侯嘉殷 周友三 蔡正河

台北市馬偕紀念醫院 心臟內科

摘 要

心律不整性右心室發育不全/心肌病變是種罕見，具遺傳傾向的心肌病變。其病理特徵為右心室心肌逐漸被纖維或脂肪組織取代。臨床上多以惡性心室性心律不整及猝死為主要表徵，且好發於年輕人及運動選手。診斷標準雖已訂立，包括心電圖的特徵、心室性心律不整、右心室結構功能及組織病理上的異常、和家族病史，但此病迄今仍難以診斷。治療著重於預防惡性心室性心律不整及猝死，包括心律不整藥物，電氣生理燒灼術，和置放心臟去顫器/電擊器。本篇病例報告描述一年輕病患臨床特徵及診斷根據。未來有賴於找出減低惡性心室性心律不整和血栓栓塞形成的最佳治療方法。

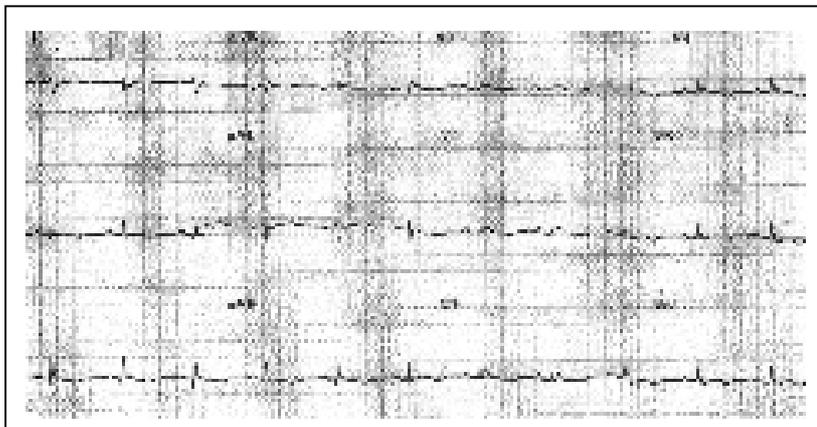


Fig.1. The electrocardiogram shows a normal sinus rhythm, right axis deviation, inverted T waves in the inferior (II, III, aVF) and precordial (V1 to V6) leads, and epsilon waves in V1 to V6, a major criterion for the diagnosis of ARVD/C.

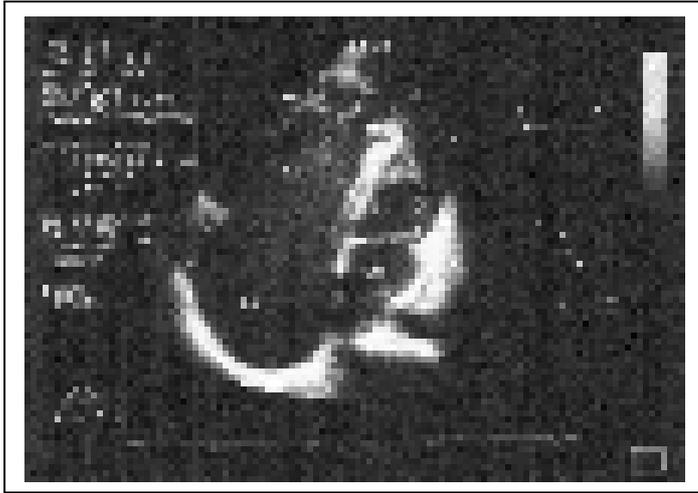


Fig.2. Transthoracic echocardiography, 4-chamber view, showing a severely dilated right atrium and ventricle and spontaneous echo contrast in both chambers. LA, Left atrium; RA, right atrium; LV, left ventricle; RV, right ventricle.

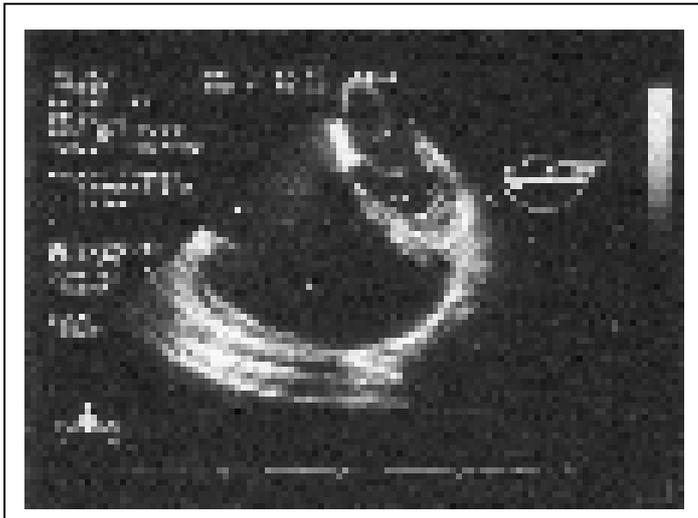


Fig.3. Transesophageal echocardiography, 4-chamber view showing a severely dilated right atrium and ventricle and spontaneous echo contrast in both chambers. LA, Left atrium; RA, right atrium; LV, left ventricle; RV, right ventricle.

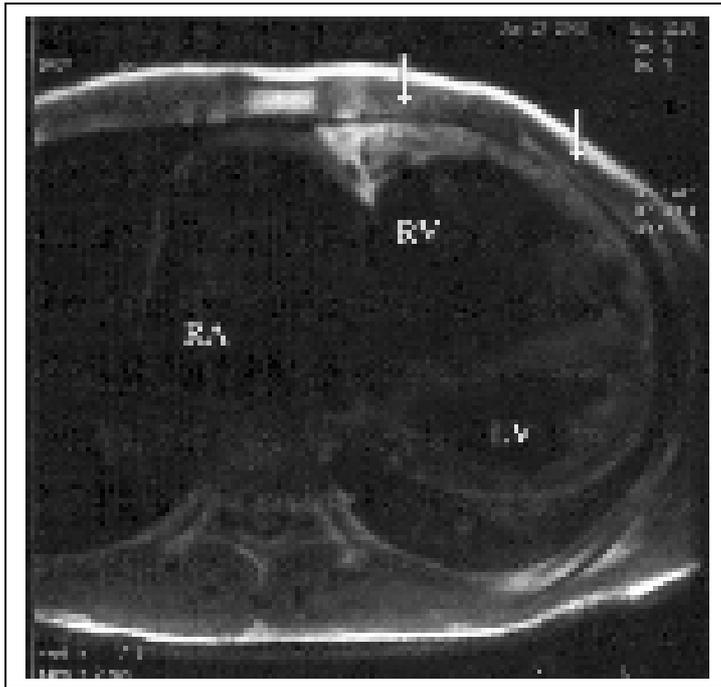


Fig.4. Axial T1-weighted black blood spin-echo image of heart MRI in the transverse plane showing the characteristic high signal intensity of fat in the free wall and subtricuspid region of the right ventricle (arrow), with the severely dilated right atrium. RA, right atrium; LV, left ventricle; RV, right ventricle.

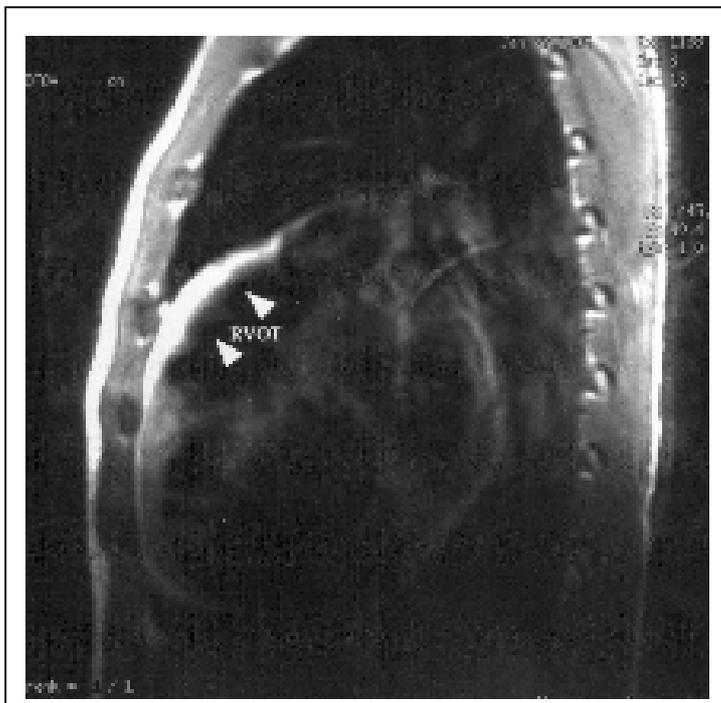
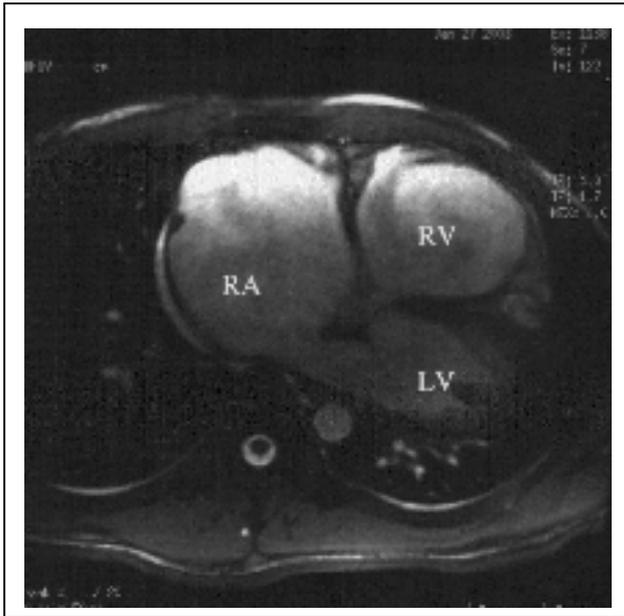
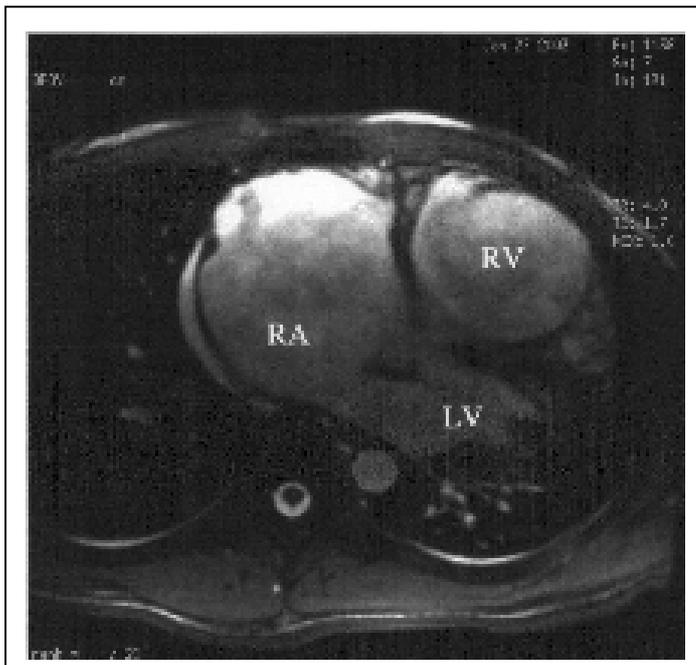


Fig.5. Axial T1-weighted black blood spin-echo image of heart MRI in the sagittal plane showing anterior focal bulging (arrowheads) of the right ventricular outflow tract (RVOT).



(A)



(B)

Fig.6. Axial balanced cine fast-field-echo images of heart MRI showing severe hypokinesia to akinesia of the right ventricle (RV); (A) end-diastolic, and (B) end-systolic phases of the RV chamber. RA, right atrium; LV, left ventricle; RV, right ventricle.