

Familial form of arrhythmogenic right ventricular dysplasia presenting with recurrent ventricular tachycardia

NS Mok, HH Tsang, PO Lee, LS Ho, MT Chan, YC Choi

We report on a 48-year-old man who presented with recurrent sustained monomorphic ventricular tachycardia, which resulted in syncope on one occasion. Subsequent investigation confirmed the diagnosis of arrhythmogenic right ventricular dysplasia. Familial screening for the disease was conducted using 12-lead electrocardiography, signal-averaged electrocardiography, and magnetic resonance imaging. Two of the four relatives who were screened showed evidence of the disease, thus confirming the familial form of arrhythmogenic right ventricular dysplasia in the patient. He underwent a subpectoral implantation of an implantable cardioverter defibrillator in view of the malignant nature of the ventricular tachycardia and his intolerance to drug treatment.

HKMJ 1999;5:402-5

Key words: Arrhythmia/etiology; Heart ventricle/abnormalities; Magnetic resonance imaging; Myocardial diseases/diagnosis; Tachycardia, ventricular

Introduction

Arrhythmogenic right ventricular dysplasia (ARVD) is a heart muscle disorder that is characterised pathologically by the partial or total replacement of the right ventricular wall by fibrofatty tissue.¹ It is increasingly being recognised as a cause of malignant ventricular tachyarrhythmia and sudden cardiac death. The cause of ARVD is unknown, but the existence of a familial form of the disease suggests that ARVD has a genetic basis.² We report on a patient with ARVD who presented with recurrent sustained monomorphic ventricular tachycardia (VT). Familial screening using 12-lead electrocardiography (ECG), signal-averaged ECG (SAECG), and magnetic resonance imaging (MRI) suggested that two other members of the patient's family had ARVD, thus confirming the familial form of the disease in this patient.

Case report

A 48-year-old man presented to the Princess Margaret Hospital in October 1996 after a sudden collapse and loss of consciousness without any preceding chest pain or warning symptom. Ventricular tachycardia was diagnosed in the Accident and Emergency Department and was successfully treated by performing a 200-J electrical cardioversion. Post-cardioversion ECG demonstrated a deep T-wave inversion in leads V₁ to V₃. The level of the patient's cardiac enzymes were elevated (peak creatine kinase 264 U/L [normal range, 42-245 U/L]; creatine kinase isoenzymes, MB fraction, 9%). Intravenous lignocaine infusion was given for 1 day. There was no recurrence of VT during his stay in hospital. The working diagnosis was VT secondary to a possibly acute non-Q wave myocardial infarction. The patient claimed to have good past health and no history of angina pectoris. He also had no family history of coronary artery disease or sudden death.

The patient subsequently underwent cardiac catheterisation, which revealed a 70% stenosis in his mid-left anterior descending artery. The ventriculogram showed good global left ventricular function and normal regional wall motion. Percutaneous transluminal coronary angioplasty and stenting to the mid-left anterior descending artery were performed in December

Princess Margaret Hospital, 2-10 Princess Margaret Hospital Road, Laichikok, Kowloon, Hong Kong:
NS Mok, MRCP, FHKAM (Medicine)
HH Tsang, MRCP, FHKAM (Medicine)
YC Choi, FRCP, FHKAM (Medicine)
Department of Radiology
PO Lee, FRCP, FHKAM (Radiology)
Department of Surgery
LS Ho, FRCS, FHKAM (Surgery)
MT Chan, FRCS, FCSHK

Correspondence to: Dr NS Mok

1996. He remained asymptomatic until the last few months of 1997, when he had three episodes of rapid palpitation accompanied by dizziness. In January 1998, he was readmitted to the Princess Margaret Hospital because of palpitation, which was documented to be a sustained monomorphic VT and which was terminated by giving an intravenous lignocaine injection. Echocardiography revealed a dilated and hypokinetic right ventricle. Time-domain analysis of the SAECG showed the presence of a late ventricular potential.

A second cardiac catheterisation showed a 30% in-stent stenosis in the patient's mid-left anterior descending artery and good left ventricular function but a grossly dilated and hypokinetic right ventricle with regional dyskinesia. Electrophysiological examination showed inducible sustained monomorphic VT of a left bundle branch block (LBBB) configuration. The VT was accompanied by hypotension without syncope and was terminable by administering overdrive ventricular pacing. Magnetic resonance imaging of the heart revealed a dilated right ventricle, and thinning and focal excavation of the right ventricular wall (Fig 1). The diagnosis of VT secondary to ARVD was established. The patient received sotalol and underwent a subpectoral implantation of an implantable cardioverter defibrillator (ICD) via a transvenous approach (Fig 2) in view of the malignant nature of the VT and his intolerance to sotalol. Two months post-implantation, the ICD recorded two episodes of VT, which were successfully terminated by anti-tachycardia pacing that was delivered by the ICD.

Because ARVD may run in families, three of the patient's first-degree relatives, who were living in Hong Kong, and his sister's daughter who had complained of occasional palpitation for few years, were examined using 12-lead ECG, SAECG, and MRI. Two

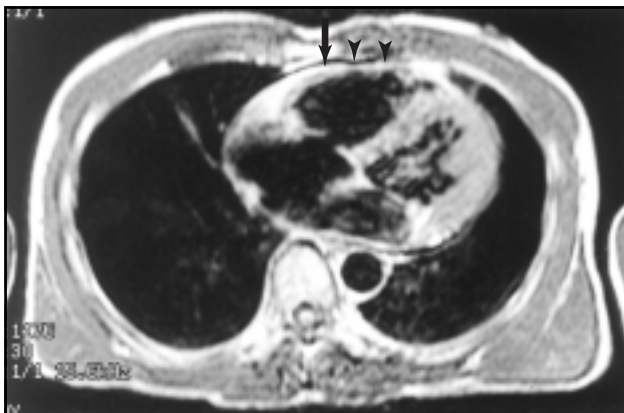


Fig 1. Magnetic resonance axial spin-echo T1-weighted image showing the diffuse thinning of the right ventricular anterior wall (arrow) and focal excavations (arrowheads)

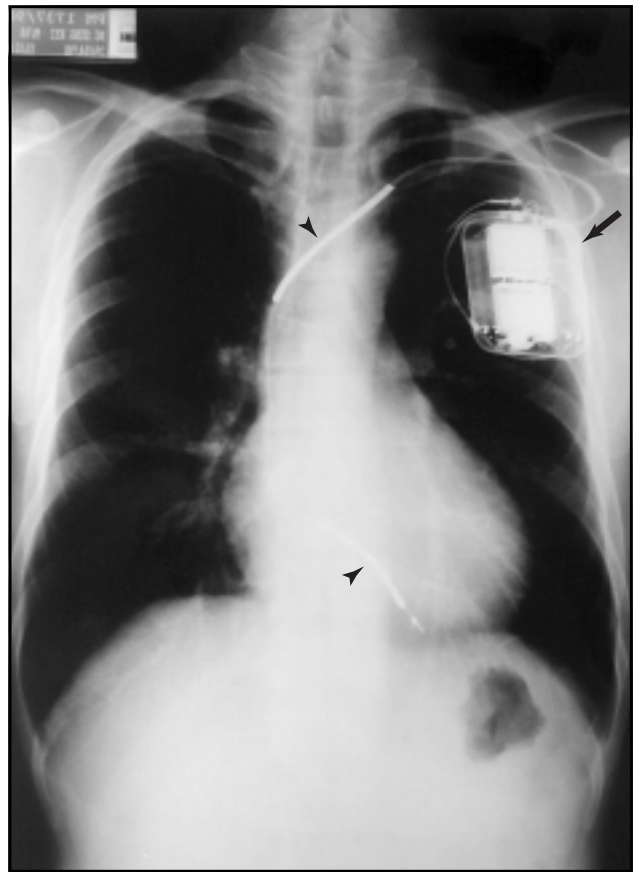


Fig 2. Chest X-ray showing the unipolar single-lead transvenous defibrillation system

The pulse generator (arrow) is the cathode of the implantable cardioverter defibrillator, and the coil electrodes (arrowheads) in the superior vena cava and the right ventricular apex are the anodes

of the four relatives screened were found to have late ventricular potentials in their SAECG scans and features of ARVD in their MRI scans. Holter monitoring of the affected subjects, however, revealed only infrequent ventricular extrasystoles but no sustained ventricular tachyarrhythmias. They received no medical treatment for their ventricular ectopy.

Discussion

Arrhythmogenic right ventricular dysplasia was first described in 1977³ and is increasingly being recognised as a clinical entity worldwide. Cardiac arrhythmias are the hallmark of the clinical presentation of ARVD; the arrhythmias range from isolated ventricular extrasystoles through VT to ventricular fibrillation. The disease may be familial,^{1,2,4} and its incidence is unknown but is probably higher than originally thought.⁵

Because ARVD is a relatively rare disease, an accurate diagnosis requires a high index of suspicion. The presence of ARVD should be suspected in a patient who has ventricular arrhythmias or syncope,

but who has no apparent heart disease. The suspicion of ARVD should be greater if the patient is a male, if the ventricular arrhythmias have an LBBB configuration (which reflects their right ventricular origin), or if there is a family history of sudden cardiac death at a young age. We have recently reported on two middle-aged adult males with ARVD who presented with sudden cardiac arrest due to ventricular fibrillation.⁶ One patient survived whereas the other died.

The patient in this case initially presented with syncope due to VT that had an LBBB configuration. The correct diagnosis was not reached earlier, however, because of coexisting coronary artery disease; suspected non-Q wave myocardial infarction was wrongly attributed as the cause of the VT. Following the percutaneous transluminal coronary angioplasty, no further investigations were initiated until the patient presented again with recurrent VT. In retrospect, the diagnosis of non-Q wave myocardial infarction could not be established confidently, based only on the findings of a slightly elevated creatine kinase level after cardioversion and a persistent T-wave inversion on precordial leads in the absence of any chest pain. When evaluating patients with monomorphic VT, physicians should therefore be aware that significant angiographic coronary stenosis may not be the cause of arrhythmia. Accordingly, all potential arrhythmogenic substrates should be investigated, even after coronary revascularisation has been performed.

A definitive diagnosis of ARVD is based on the histological demonstration, at either autopsy or surgery, of the transmural replacement of the right ventricular myocardium by fibrofatty tissue.⁷ In most patients, however, it is not possible to assess the transmural myocardium, and the diagnosis of ARVD relies on the results of various invasive and non-invasive investigations, which can demonstrate structural, functional, and electrophysiological abnormalities. The diagnosis can be confirmed if the criteria published by the 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 can be met.⁸

The patient in this case demonstrated the classical features of ARVD, such as T-wave inversion in precordial leads V_1 to V_3 on the 12-lead ECG scan; a late ventricular potential on the SAECG scan; inducible VT with an LBBB configuration during the electrophysiological study; and a dilated and hypokinetic right ventricle on the echocardiogram and angiogram.

Magnetic resonance imaging using conventional T1-weighted spin-echo sequences has recently been shown to accurately differentiate high-signal intensity fat from other medium-intensity tissues such as myocardium⁹ and is thus a useful non-invasive method in diagnosing ARVD. The non-invasive nature of MRI also makes it a convenient screening tool to detect the disease in family members who may be at risk of sudden death, and to follow the progress of the disease. In this patient, MRI revealed a grossly dilated right ventricle, and diffuse thinning and focal excavation of the right ventricular anterior wall, which is a typical feature of ARVD.

Familial forms of ARVD have been reported since 1982.¹ The estimated prevalence of ARVD in affected families is approximately 30%,⁸ although one study has shown a 100% familial prevalence.⁴ An autosomal dominant transmission that has variable penetrance and clinical expression has been suggested.¹⁰ Familial screening for ARVD is an important part of the investigations of any patient with confirmed ARVD. To screen the relatives of this patient, 12-lead ECG, SAECG, and MRI were used. The SAECG scans of two of the screened relatives showed a late ventricular potential. This feature is frequently found in the scans of ARVD patients: one study showed that 16% of individuals from affected families had late ventricular potentials, compared with only 3% of a control group.⁴ The MRI scans of both relatives in this case also showed features of ARVD—namely, intramural fatty infiltration of the right ventricular wall and/or diffuse wall thinning of the right ventricle. This finding strongly suggested that the two relatives had ARVD and confirmed the familial form of the disease in the patient. To the best of our knowledge, this is the first case report of a familial form of ARVD in the Hong Kong Chinese population. The optimal management of ARVD in family members has not been established. Because the two family members in this case were asymptomatic and because Holter monitoring did not show significant ventricular arrhythmia, anti-arrhythmic drug therapy was not initiated.

Drug treatment used to be the first and most frequently given therapy to treat arrhythmias of ARVD. However, some large trials that have compared the implantation of an ICD with the most effective anti-arrhythmic drugs to treat haemodynamically significant ventricular tachyarrhythmias showed that performing the implantation is the better treatment.¹⁰⁻¹³ During the past decade, the implantation of an ICD has become the most important non-pharmacological form of treatment of ventricular tachyarrhythmia. The

ICD is an implantable device that can accurately detect and terminate VT or ventricular fibrillation by administering anti-tachycardia pacing, cardioversion, or defibrillation. Data from a study of 18 patients with ARVD who received such an implant have suggested that this treatment can safely and effectively terminate recurrent arrhythmias and may thus improve the long-term prognosis in a high-risk subgroup of these patients.¹⁴

Recently, the Antiarrhythmics versus Implantable Defibrillators study¹¹ has shown that defibrillator implantation is superior to amiodarone and sotalol in prolonging survival in patients who have VT that results in syncope or cardiac arrest. In addition, spontaneous VT with or without haemodynamic compromise is now regarded (with good supporting data) as a Class I indication for defibrillator implantation by the American College of Cardiology and the American Heart Association.¹⁵ The ICD that was implanted in this patient (Fig 2) was a single-lead defibrillation system. The defibrillator was implanted via a transvenous approach, which is associated with a much lower surgical mortality and morbidity than is the traditional epicardial approach, which requires thoracotomy.¹⁶

In conclusion, a high index of suspicion is needed to diagnosis ARVD. Magnetic resonance imaging of the heart, by virtue of its ability to differentiate fat from muscle, is a useful diagnostic tool; familial screening is an important part of the investigation. The implantation of an ICD can improve prognosis in high-risk subgroups of patients with ARVD.

References

- Marcus FI, Fontaine GH, Guiraudon G, et al. Right ventricular dysplasia: a report of 24 adult cases. *Circulation* 1982;65:384-98.
- Laurent M, Descaves C, Biron Y, Deplace C, Almange C, Daubert JC. Familial form of arrhythmogenic right ventricular dysplasia. *Am Heart J* 1987;113:827-9.
- Fontaine G, Guiraudon G, Frank, et al. Stimulation studies and epicardial mapping in ventricular tachycardia; study of mechanisms and selection for surgery. In: Kulbertus HE, editor. *Reentrant arrhythmias*. Lancaster: MTP Publishing; 1977:334-50.
- Hermida JS, Minassian A, Jarry G, et al. Familial incidence of late ventricular potentials and electrocardiographic abnormalities in arrhythmogenic right ventricular dysplasia. *Am J Cardiol* 1997;79:1375-80.
- Thiene G, Nava A, Corrado D, Rossi L, Pennelli N. Right ventricular cardiomyopathy and sudden death in young people. *N Engl J Med* 1988;318:129-33.
- Mok NS, Lee PO, Lee KC, et al. 2 cases of arrhythmogenic right ventricular dysplasia presenting with sudden cardiac death. *J HK Coll Cardiol* 1997;5:133-9.
- Lobo FV, Heggveit HA, Butany J, Silver MD, Edwards JE. Right ventricular dysplasia: morphological findings in 13 cases. *Can J Cardiol* 1992;8:261-8.
- 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.
- Blake LM, Scheinman MM, Higgins CB. MR features of arrhythmogenic right ventricular dysplasia. *AJR Am J Roentgenol* 1994;162:809-12.
- Nava A, Thiene G, Canciani B, et al. Familial occurrence of right ventricular dysplasia: a study involving nine families. *J Am Coll Cardiol* 1988;12:122-8.
- The Antiarrhythmics versus Implantable Defibrillators (AVID) Investigators. A comparison of antiarrhythmic-drug therapy with implantable defibrillators in patients resuscitated from near-fatal ventricular arrhythmias. *N Engl J Med* 1997;337:1576-83.
- Kuck K. Heart failure and arrhythmia. *Cardiac Arrest Study Hamburg (CASH)*. American College of Cardiology. News Online; 31 March 1998. Website: <http://www.acc.org>
- Connolly S. Heart failure and arrhythmia. Results from the Canadian Implantable Defibrillator Study (CIDS). American College of Cardiology. News Online; 31 March 31 1998. Website: <http://www.acc.org>
- Breithardt G, Wichter T, Haverkamp W, et al. Implantable cardioverter defibrillator therapy in patients with arrhythmogenic right ventricular cardiomyopathy, long QT syndrome, or no structural heart disease. *Am Heart J* 1994;127:1151-8.
- Gregoratos G, Cheitlin MD, Conill A, et al. ACC/AHA guidelines for implantation of cardiac pacemakers and antiarrhythmia devices: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Pacemaker Implantation). *J Am Coll Cardiol* 1998;31:1175-209.
- Raitt HR, Bardy GH. Advances in implantable cardioverter defibrillator therapy. *Curr Opin Cardiol* 1994;9:23-9.