Arrhythmogenic right ventricular dysplasia. An illustrated review highlighting developments in the diagnosis and management of this potentially fatal condition

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Abstract

Arrhythmogenic right ventricular dysplasia is an inherited, progressive condition. Characterised by fatty infiltration of the right ventricle, it frequently results in life threatening cardiac arrhythmias, and is one of the important causes of sudden cardiac death in the young. There are characteristic electrocardiographic and echocardiographic features that all physicians need to be aware of if we are to reduce these occurrences of premature death. Diagnosis with magnetic resonance imaging is discussed along with current treatment options.

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Arrhythmogenic right ventricular dysplasia (ARVD) is an important cause of sudden death in young people. Awareness of the condition is essential so that it may be recognised as soon as possible. This may avoid postmortem diagnosis and allow prompt screening of relatives. The prevalence of this condition is one in 5000 and in 30%–40% of patients it is inherited as an autosomal dominant trait, with incomplete penetrance and variable expression.^{1–4} Four loci have been mapped, but no gene has been identified as yet.⁵ Clinical descriptions of ARVD first appeared in 1961,⁶ but it was not until 1978 that it was first given this title.⁷

Presentation

Individuals, more often male, may present between the ages of 7–40 years with the youngest recorded case being 4 years. Eighty per cent of patients are detected before their 40th birthday.^{8–9} The classic presentation is with symptomatic sustained ventricular tachycardia, the electrocardiogram (ECG) showing a left bundle branch block pattern. Less common presentations are as a supraventricular tachycardia, multiple ventricular ectopics,^{7–10–11} or merely cardiomegaly on chest radiography.⁹

Typical symptoms are fatigue on minimal exertion and syncope; this reflects the high incidence of the arrhythmia during exercise. Unfortunately a proportion will also present as sudden cardiac death.^{8–12}

Thiene *et al* discovered that postmortem examination showed evidence of ARVD in 20% of sudden deaths in people under the age of 35.¹³

Aetiology and pathology

ARVD is characterised by the deposition of adipose tissue and the development of fibrosis within the right ventricular myocardium¹⁴ a feature rarely found in the left ventricle.^{15–18} Typically this process will commence in the epicardium and progress towards the endocardium.

The aetiology is unknown but Thiene *et al* have suggested that an inflammatory or autoimmune process may be involved.¹⁹

Case report

In 1978 a 25 year old male athlete was investigated for epilepsy having lost consciousness while running. The exercise itself was not thought to be influential, as he regularly ran in excess of five miles daily. There was a history of palpitation while running but investigations were all normal.

Four years later he presented with extreme nausea and malaise during exercise. An ECG recorded during one of these episodes was consistent with atrial tachycardia. Investigations including echocardiography, radionuclide angiography, and cardiac catheterisation were normal. During electrophysiological studies only a self terminating atrial tachycardia occurred. The patient was discharged with no treatment. He remained under regular review. Of importance, however, was his 12 lead ECG in sinus rhythm that showed inverted T waves in the precordial leads (fig 1).

Ten years later he was admitted with a symptomatic broad complex tachycardia that required DC cardioversion. Again all of the above investigations were normal apart from his ECG and electrophysiological studies, which this time demonstrated easily induced ventricular tachycardia with the focus in the right ventricle. Over the next few years a variety of medications were used until amiodarone was found to be the best compromise between arrhythmia control and intolerable drug side effects.

In 1985 the diagnosis of ARVD was made supported by radionuclide angiography demonstrating a dilated akinetic right ventricle with an ejection fraction of 15% and electrophysiological studies showing easily inducible sustained ventricular tachycardia. The ventricular tachycardia showed typical left bundle branch block morphology with left axis deviation (fig 2).

In 1994 the patient's younger brother aged 37 years lost consciousness during a karate les-

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Figure 1 ECG in sinus rhythm showing inverted T waves in the precordial leads.

Figure 2 Ventricular tachycardia showing typical left bundle branch block morphology with left axis deviation.

son. His 12 lead ECG showed inverted T waves in the precordial leads and multiple ventricular ectopics. Echocardiography and radionuclide angiography supported the diagnosis of ARVD. Electrophysiological studies including a ventricular tachycardia stimulation test was normal. Three years later he died suddenly while sitting at home. Postmortem examination confirmed abnormalities consistent with ARVD. The patient's daughter has been screened. Her ECG and echocardiogram are also consistent with ARVD.

After being asymptomatic for 12 years the patient then suffered increasingly frequent and prolonged ventricular tachycardia induced by exertion. This was reliably induced on the treadmill. Additional medical treatment (β -blockers) induced Mobitz type II heart block. Therefore, taking these factors and his brother's history into account, a dual chamber pacing rate responsive automatic cardioverter defibrillator was implanted.

Despite the introduction of a small amount of β -blocker he continued to experience frequent episodes of ventricular tachycardia,

which the device detected and treated appropriately. He was intolerant of higher doses of β -blocker. Therefore, a radiofrequency catheter ablation was carried out to one of two ventricular tachycardia foci in the right ventricle. Although initially successful at controlling the slowest foci of ventricular tachycardia, he has experienced a recurrence of symptoms, although these are tolerably well controlled with the combination of amiodarone and a tiny dose of β -blockade.

To date this latest treatment has provided good symptomatic relief but our knowledge of the disease tells us that this history is probably not yet complete.

Detection

ELECTROCARDIOGRAM

The important features on a standard 12 lead ECG are T wave inversion in the precordial leads (which may of course be a normal variant) and prolongation of the QT interval greater than 110 ms (see box 1). The latter is 100% specific but only seen in a third of patients.^{20 21} The cause of this QT interval

Box 1: ECG features of ARVD

- T wave inversion in the precordial leads.
- QT interval greater than 110 ms.
- Ventricular ectopics in excess of 1000 per day.
- Ventricular tachycardia which has a left bundle branch block pattern.

increase is thought to be delayed right ventricular activation, which produces a small irregularity after the QRS complex called an epsilon wave which is rarely seen on a standard ECG can be detected in about a third of patients using signal averaged techniques.²² Ventricular ectopics, although not abnormal in themselves, tend to occur in excess of 1000 per day.²³

Exercise testing can often provoke the arrhythmia resulting in ventricular tachycardia which has a left bundle branch block pattern.²⁴

ECHOCARDIOGRAPHY

Features associated with ARVD are shown in box 2.^{10 25 26} In addition calculations of the ratio of right and left ventricular end diastolic diameters appear to give values of sensitivity of 86% and specificity of 93%.^{27 28}

ENDOCARDIAL BIOPSY

Although the histological abnormalities are predominantly in the right ventricular free wall, biopsies are frequently taken from the septal area to reduce the risk of perforation.²⁹ This obviously reduces the chances of obtaining affected tissue and it must be remembered that a negative biopsy specimen does not exclude the condition.

MAGNETIC RESONANCE IMAGING (MRI) AND RIGHT VENTRICULAR ANGIOGRAPHY

Until recently right ventricular angiography was considered to be the optimal imaging modality for detecting ARVD. However, with cardiac gating and better resolution MRI may well begin to supersede this investigation. Typical features include isolated areas of dyskinesia, transverse hypertrophic trabeculae separated by deep fissures, and an increase in end diastolic volume.³⁰⁻³²

MRI has the ability not only to describe right ventricular morphology but also to highlight areas of myocardial fat distribution.^{33 34} Midiri *et al* have discovered that these areas of adipose tissue within the myocardium correspond with the focus of the arrhythmias.³⁵ McKenna *et al* have defined criteria to aid in the diagnosis of ARVD.³⁶

Treatment**DRUGS**

Amiodarone and β -blockers can both be effective, in addition there appears to be a synergistic affect when they are used together. However, sotalol has been shown by Wichter *et al* to be the most reliable treatment.³⁷

Box 2: Echocardiography features of ARVD

- Right ventricular dilation.
- Bulging of right ventricle during diastole.
- Dyskinesia of inferobasal free wall during systole.
- Dyskinesia of the apex.
- Exaggerated trabecular pattern within right ventricle.
- Structural abnormalities of the moderator band.

Unfortunately ARVD is a progressive disorder and patients often become resistant to one or more medications requiring more invasive intervention.

IMPLANTABLE DEFIBRILLATORS

Implantable defibrillators are now effective treatment for ventricular cardiac arrhythmias.³⁸ As illustrated in our case report ARVD frequently becomes resistant to drug treatment and therefore use of implantable defibrillators in this condition seems appropriate. However, it is important to achieve relatively reliable control of the arrhythmias before implantation as this avoids repeated shocks being delivered by the device, which can be very distressing for the patient.

RADIOFREQUENCY CATHETER ABLATION

Advances in cardiac electrophysiology have enabled cardiologists to map and ablate the focus of the arrhythmias with success rates of up to 70%. In addition, patients in whom the procedure is unsuccessful in itself often find that drug therapy is subsequently more effective. As the disease progresses patients run a high risk of developing a second focus.^{39 40}

SURGERY

Surgical total or partial isolation of the right ventricular free wall appears to have had some success. Even if ventricular tachycardia does occur in the right ventricle it is unable to propagate into the left side. The major postoperative complication is right ventricular failure and long term data on these patients are not yet available.^{41 42} Cardiac transplantation is also a recognised treatment for this condition but carries with it a significant amount of mortality and morbidity and is therefore seen as a last resort.⁴³

Conclusion

ARVD is an important cause of sudden death in young people. The case described here spans the time period during which ARVD was being defined and the delay in diagnosis reflects this. With our current knowledge it is clear that the patient was demonstrating classical symptoms and signs from the outset. The death of his brother and birth of his daughter who also has the classical ECG appearances of ARVD, highlight the genetic importance of the condition.

Our case illustrates how the disease can progress and become unstable, thus requiring a flexible approach to treatment.

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