Ventricular fibrillation without apparent heart disease: Description of six cases

Since 1977, six patients (five males and one female), aged 14 to 35 years, resuscitated from ventricular fibrillation, were referred to our department for detailed evaluation, after exclusion of major cardiac pathologic conditions. Four patients had a family history of heart disease. Basic ECGs showed sinus rhythm in all of them. PR interval was prolonged in one. Two patients had complete and one had incomplete right bundle branch block. One patient had inverted T waves in V1-2 and late potentials. Three had an upsloping ST-T segment elevation in V1-2. The cardio thoracic index was less than 0.5 in five and 0.50 in one. In one of the five patients studied, the clinical episode of ventricular fibrillation was reproduced by stimulation of the right ventricular outflow tract during electrophysiologic study. Results of cross-sectional echocardiography and angiography showed predominantly structural and wall motion abnormalities of the right ventricle in five patients and slight wall motion abnormalities of the left ventricle in two. Two patients also had mitral and tricuspid valve prolapse. Coronary arteries were normal in all five patients examined. Results of endomyocardial biopsy showed no abnormalities in one patient, fibrosis in two, and fibrolipomatosis in one. Two patients died during follow-up: autopsy was performed in one and results showed right ventricular cardiomyopathy. Thus in five of these selected patients with apparent idiopathic ventricular fibrillation, some abnormalities, predominantly of the right ventricle, were documented only after detailed investigation; however, clinical history and some nonspecific ECG abnormalities were factors in the diagnostic procedure. (AM HEART J 1989; 118:1203.)

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Aborted sudden death resulting from ventricular fibrillation is uncommon in young patients. A wide spectrum of well-known cardiovascular anomalies has been described in patients resuscitated from this event.1-3 In some patients with normal heart size and physical tolerance, as well as normal or nonspecific ECG features, the arrhythmia is considered "idiopathic,"4,5,6 because results of cardiac evaluation in these patients do not indicate structural heart disease.

With the development of new diagnostic procedures and techniques, new forms of cardiac disease are being recognized, and this often promotes a retrospective study of previous patients along with a re-view of the clinical profile and investigative features. For this reason we have carefully reevaluated six pa-

METHODS

Since 1977, six young patients who were electrically resuscitated after ventricular fibrillation have been referred to our department for detailed evaluation after results of noninvasive studies had excluded common cardiac causes for the fibrillation. The data presented in this article are not completely uniform because the study is partially retrospective. In some patients reevaluation was performed in light of further study experiences; in particular, after patient 4 died suddenly of a new episode of ventricular fibrillation, it was discovered that he had had right ventricular cardiomyopathy that had not been recognized previously, despite retrospective echocardiography evidence.

We reviewed the clinical examination findings, chest x-rays, standard and 24-hour continuous ECG recordings, and results of exercise stress tests (bicycle ergometer) and cross-sectional echocardiography (Tables I to III) of all six patients. Electrophysiologic study was performed in patients 1, 2, 3, 4, and 6. Patients 1, 2, 4, 5, and 6 underwent left ventricular and coronary angiography; in patients 1, 2, 5, and 6 right ventricular angiography was also performed.
Asymptomatic MPVCs Sudden death (VF)

None after VF PVCs

Table II. Premature ventricular contractions (MPVCs) and nonsustained ventricular tachycardia (NSVT) in six patients. PVCs, premature ventricular contractions. CTI, cardiothoracic index; Tneg and ST refer to inverted T waves and ST segments, respectively.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age (yr)</th>
<th>Circumstance</th>
<th>Preexisting symptoms</th>
<th>Documented arrhythmias</th>
<th>Follow-up (yr)</th>
<th>Evolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>35</td>
<td>Rest</td>
<td>None</td>
<td>None</td>
<td>2</td>
<td>Sudden death</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>14</td>
<td>Cycling</td>
<td>Palpitations/syncope</td>
<td>None</td>
<td>11</td>
<td>MPVCs, NSVT</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>31</td>
<td>Rest</td>
<td>None</td>
<td>None</td>
<td>2</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>24</td>
<td>Rest</td>
<td>None</td>
<td>None</td>
<td>6</td>
<td>Sudden death (VF)</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>17</td>
<td>Mental stress</td>
<td>Palpitations</td>
<td>MPVCs</td>
<td>1</td>
<td>PVCs</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>18</td>
<td>Soccer</td>
<td>None</td>
<td>None</td>
<td>2</td>
<td>PVCs</td>
</tr>
</tbody>
</table>

Age refers to first occurrence of ventricular fibrillation (VF), documented arrhythmias are those detected (at basic evaluation during routine screening) before episode of VF, MPVCs, or NSVT, nonsustained ventricular tachycardia; PVCs, premature ventricular contractions.

Table II. Detailed ECG data and cardiothoracic index from six patients. CTI, cardiothoracic index; T neg and ST refer to inverted T waves and ST segments, respectively.

<table>
<thead>
<tr>
<th>Patient</th>
<th>CTI</th>
<th>PR</th>
<th>QRS</th>
<th>aQRS</th>
<th>Tneg</th>
<th>QTc</th>
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<tbody>
<tr>
<td>1</td>
<td>0.48</td>
<td>180</td>
<td>150</td>
<td>+110</td>
<td>V42</td>
<td>V24</td>
</tr>
<tr>
<td>2</td>
<td>0.45</td>
<td>140</td>
<td>90</td>
<td>+75</td>
<td>V6</td>
<td>—</td>
</tr>
<tr>
<td>3</td>
<td>0.45</td>
<td>240</td>
<td>110</td>
<td>+60</td>
<td>V2</td>
<td>V13</td>
</tr>
<tr>
<td>4</td>
<td>0.50</td>
<td>140</td>
<td>130</td>
<td>-40</td>
<td>V6</td>
<td>V23</td>
</tr>
<tr>
<td>5</td>
<td>0.45</td>
<td>140</td>
<td>90</td>
<td>-45</td>
<td>V1.3</td>
<td>—</td>
</tr>
<tr>
<td>6</td>
<td>0.45</td>
<td>140</td>
<td>90</td>
<td>+60</td>
<td>V46</td>
<td>—</td>
</tr>
</tbody>
</table>

Electrophysiologic study. Real-time recordings were obtained by means of an ink-jet recorder (Mingograph, Siemens Elema AB, Solna, Sweden) with a high-pass filter of 50 to 70 Hz for the intracavitary ECGs at a paper speed of 100 mm/sec. Basic conduction intervals (PA, AH, and HV) were measured. The right ventricular endocardium was accurately mapped to detect late fractionated QRS potentials and to investigate the origin of the tachycardia. Stimulation was performed with a custom-designed, multiprogrammable stimulator (PPS 500, M.E.D.I.CO., Italy) that had a constant-current source and a rectangular impulse of 1 msec duration delivered at twice the diastolic threshold.

The following protocol was then followed to precipitate ventricular arrhythmias and to evaluate the entire conduction system: (1) Atrial and ventricular pacing (S1-S1) at progressively shorter cycles; (2) premature atrial and ventricular stimulation during sinus rhythm (the entire cycle was scanned to the point of atrial and ventricular refractoriness); (3) premature atrial and ventricular pacing (S2) during atrial and ventricular pacing with a drive cycle length (S1-S1) of 500 and 700 msec; (4) double ventricular stimuli (S2-S3) at progressively shorter coupling intervals during ventricular pacing.

Cross-sectional echocardiography. Images obtained in multiple standard views were evaluated by two observers for the presence of regional wall motion and/or structural abnormalities of the right and left ventricles. Right ventricular volume (corrected with a regression equation according to age and body surface area) was calculated by an area-length method derived from orthogonal planes (apical four-chamber and long-axis views). A modified Simpson’s rule was used to calculate left ventricular volumes from the parasternal short-axis and apical two-chamber views. The infundibular diameter was determined from the parasternal short-axis view of the aortic root. The right ventricular outflow tract was also measured from this view as the maximum dimension between the anterior aortic wall and the right ventricular free-wall endocardium.

Hemodynamic study. This included left and right ventricular angiography, coronary arteriography, and pressure recording in the various cavities. Angiocardiography of the right ventricle was performed in the posteroanterior, lateral, and long-axis (oblique right and left anterior) projections to better define the infundibulum (its diameter was calculated from the lateral projection) and posterobasal wall. Angiocardiography of the left ventricle was carried out in the 30-degree left anterior oblique and right anterior oblique projections. Right ventricular volumes were calculated by means of biplane angiocardiography in the an-
RESULTS

reported technique. Nine patients were considered symptomatic because of ventricular dyskinesia, diastolic bulging, fissuring of the cardiac borders, altered echogenicity and nodulation of the moderator band, disarrangement of the trabecular framework, and persistence of dye.

Right ventricular endomyocardial biopsy. This was performed in three patients through the right femoral vein. Four to six tissue specimens (1 to 3 mm each) were fixed in formalin, mounted in paraffin wax, serially cut into 7 mm thick sections, and stained with hematoxylin-eosin and azan-Mallory stains.

Postmortem study. In patient 4 this included histologic investigation of the conduction system by means of a previously reported technique.

Table III. Investigational data derived from ultrasonic, hemodynamic, and histologic study

<table>
<thead>
<tr>
<th>Patient</th>
<th>RVEDV (cc/m2)</th>
<th>RVEF (%)</th>
<th>LVEDV (cc/m2)</th>
<th>LVEF (%)</th>
<th>RVWMA</th>
<th>LWVMA</th>
<th>RVOT (mm)</th>
<th>MVP</th>
<th>TVP</th>
<th>HBE</th>
<th>Histology</th>
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<tr>
<td>1</td>
<td>103</td>
<td>44</td>
<td>68</td>
<td>67</td>
<td>+++</td>
<td>0</td>
<td>45</td>
<td>+</td>
<td>+</td>
<td>VF</td>
<td>F++</td>
</tr>
<tr>
<td>2</td>
<td>124</td>
<td>60</td>
<td>96</td>
<td>61</td>
<td>+++</td>
<td>+</td>
<td>35</td>
<td>+</td>
<td>+</td>
<td>NSVT</td>
<td>F++A+</td>
</tr>
<tr>
<td>3</td>
<td>(94)</td>
<td>(52)</td>
<td>(62)</td>
<td>(63)</td>
<td>++</td>
<td>0</td>
<td>45</td>
<td>0</td>
<td>0</td>
<td>PRR</td>
<td>ND</td>
</tr>
<tr>
<td>4</td>
<td>(105)</td>
<td>(48)</td>
<td>70</td>
<td>60</td>
<td>+++</td>
<td>0</td>
<td>45</td>
<td>0</td>
<td>0</td>
<td>SRR</td>
<td>F+++ A+</td>
</tr>
<tr>
<td>5</td>
<td>110</td>
<td>42</td>
<td>79</td>
<td>62</td>
<td>+++</td>
<td>+</td>
<td>45</td>
<td>0</td>
<td>0</td>
<td>ND</td>
<td>ND</td>
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<tr>
<td>6</td>
<td>76</td>
<td>67</td>
<td>80</td>
<td>84</td>
<td>0</td>
<td>0</td>
<td>25</td>
<td>0</td>
<td>0</td>
<td>SRR</td>
<td>0</td>
</tr>
</tbody>
</table>

RVEDV, right ventricular diastolic volume (indexed), RVEF, right ventricular ejection fraction, LVEDV, left ventricular diastolic volume (indexed), LVEF, left ventricular ejection fraction, RVWMA, right ventricular wall motion abnormalities, LVWMA, left ventricular wall motion abnormalities, RVOT, right ventricular outflow tract (refers to maximum calculated diameter at echocardiography in parasternal short-axis view, normal value, 25 ± 4 mm), MVP, mitral valve prolapse, TVP, tricuspid valve prolapse

Data in parentheses and regarding volumes were derived only from cross-sectional echocardiography. Normal values for right ventricle in our laboratories are 79 ± 3 m/m2 for angiography and 58 ± 6 m/m2 for echocardiography, RVEF = 65 ± 7.4% for angiography and 61 ± 5.4% for echocardiography, HBE. His bundle ECG, during this procedure ventricular fibrillation (VF), nonsustained ventricular tachycardia (NSVT), single or repetitive responses (SR, RR) were induced by different techniques. Histology refers to autopsy data in patient 4 and right ventricular endomyocardial biopsy in patients 1, 2, and 6, F, fibrosis, A, adiposis. O, no abnormalities detected, ND, not done.
branch block. Inverted t waves in the precordial leads in the absence of bundle branch block were variably present (Table II and Fig. 1); patients 1, 3, and 4 had an upsloping ST segment (so-called "early repolarization"), and patient 5 had low-voltage late QRS potentials in V1-a. In patient 6 t wave abnormalities were detected only during hospitalization (he had thoracic trauma as a result of cardiac massage) and disappeared during follow-up. ST segment elevation (early repolarization) was detected in patients 1, 3, and 4.

Electrophysiologic study. Ventricular fibrillation was induced in patient 1 during programmed ventricular stimulation by double (S2-S3) extrastimuli at infundibular levels (Fig. 2). In patient 2 nonsustained polymorphic ventricular tachycardia was induced by the same technique. In patients 3, 4, and 6 only isolated or paired repetitive responses were induced (Table III).

Cross-sectional, hemodynamic, and angiographic examination. Ali except patient 6 had one or more structural and/or wall motion abnormalities of the right ventricle (Table III). Mild hypokinesia of the left lateral wall was detected in patients 2 and 5 but was not associated with increased volume. Coronary arteries, pressure data, and cardiac indexes were normal in the five patients examined. Mitral and tricuspid valve prolapse was present in patients 1 and 2. At the initial evaluation, structural heart disease had been excluded in patients 2, 3, 4, and 5, because attention was focused on the left ventricle and coronary arteries; the abnormalities detected at the right ventricle by cross-sectional echocardiography (in patients 2, 3, and 4) and angiography (in patient 5) during the initial evaluation were not considered specific for cardiovascular disease.

Histologic examination. Results of endomyocardial biopsies performed in patients 1 and 2 showed mild-to-moderate fibrosis and fibrolipomatosis (Table III and Fig. 3). No abnormalities were detected in patient 6. Results of postmortem examination of patient 4 showed a heart weighing 350 gm and a normal left ventricle and coronary arteries. The right ventricle was enlarged with marked dilation of the pulmo-
nary infundibulum; significant fibrous adipose replacement of the free wall and the moderator band was present. Results of histologic examination of the specialized atrioventricular junction by serial sections showed remarkable fibrosis of the bifurcating bundle and proximal bundle branches.

DISCUSSION
Ventricular fibrillation and sudden death can occur in young patients with coronary, congenital, or acquired heart disease, preexcitation syndrome, cardiomyopathy (particularly hypertrophic), myocarditis, or prolonged QT syndrome.1-3 In a few patients
these events are considered "idiopathic," because they occur in the absence of recognizable heart disease. Different study protocols have been pro-posed to examine the structural basis of lethal arrhythmias in these patients as new medical information and techniques become available. Attention has been focused most often on the study of the left ventricle, the coronary arteries, and the electrical mechanisms of the arrhythmias. The right ventricle has been somewhat underestimated as a possible substrate of these events, and little is known about the clinical and investigative features of the localized pathologic conditions that may affect it.

Right ventricular cardiomyopathy, particularly when it is initially seen as a localized, concealed form, has recently been recognized as an important cause of sudden death in apparently healthy young people and has been detected in a considerable number of patients examined in our area. Sudden death and ventricular fibrillation in patients with this pathologic condition, however, have occasionally been described by others, and in most instances the structural abnormalities of the right ventricle were not recognized during life. In light of these findings, as with patient 4 in whom right ventricular cardiomyopathy was discovered at postmortem examination after recurrent ventricular fibrillation, we are studying or reevaluating our patients with apparently idiopathic ventricular arrhythmias. Special attention is being given to clinical history, namely, familial occurrence and previous palpitations, to apparently nonspecific ECG patterns, and to QRS morphology during fibrillation. Invasive and noninvasive studies are focused not only on the left but particularly the right ventricle.

Five of our six patients who had been resuscitated from an apparently idiopathic ventricular fibrillation, had symptoms, familial involvement, and ECG patterns (right bundle branch block, early repolarization, inverted t waves, late QRS potentials) that initially had not received much attention. In four of these patients it was initially thought that a primary electrical disease was the cause, because no recognizable major left-heart disease or coronary pathologic condition was detectable.

In particular we underestimated the ECG features (excluding the ECG of patient 3) that are not extremely rare in young healthy individuals; we did not think that they could be related to some pathologic condition of the right ventricle and this structure was not studied very carefully. After reevaluation and in some instances repeated investigation, a predominant structural and/or wall motion abnormality of the right ventricle, consistent with concealed forms of right ventricular cardiomyopathy, was recognized. In patient 6 no abnormalities were detected; however, we believe that this normal finding may be revised during follow-up as further experience is accumulated and new investigative techniques are developed.

During electrophysiologic study, a major electrical instability was induced in only two patients, and the electrical mechanism was not clearly understood. This lack of inducibility has been reported previously and the findings have been revised.

The diagnosis was formulated from results of cross-sectional echocardiography and right ventricular angiography and was substantiated by histologic findings when available. Mild left ventricular involvement (in patients 2 and 5) and mitral and tricuspid valve prolapse (in patients 1 and 2) were associated anomalies that did not exclude the former diagnosis; these findings, however, may concur in the genesis of the arrhythmia. Patient 4, who died of a new documented episode of ventricular fibrillation, had an intraventricular conduction defect on the ECG, and results of histologic examination showed an association between right ventricular cardiomyopathy and fibrosis of the bundle branches.

Our results confirm that electrical heart disease may often be associated with a pathologic substrate which, in this select group, involved predominantly the right ventricle. We do not know the real prevalence of right ventricular structural heart disease in young patients affected by apparently idiopathic ventricular arrhythmias, and we also do not know if we are always dealing with the same pathologic condition, but we believe that concealed forms of this disease state are more frequent than is generally thought. Much attention must be focused on patients with apparently idiopathic life-threatening events; both ventricles must be studied in detail, and particular consideration must be given to "minor" clinical and ECG features.

Two late deaths occurred in this series, and both subjects were probably not receiving therapy; patient 4 was not treated because of an apparently normal heart and no residual arrhythmia, and patient 1 had spontaneously interrupted the prescribed therapy. This recurrence of ventricular fibrillation confirms previous reports and stresses the importance of both early diagnosis and prophylactic therapy.

REFERENCES