Inflammatory Left Ventricular Microaneurysms as a Cause of Apparently Idiopathic Ventricular Tachyarrhythmias

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Background—We sought to investigate the arrhythmogenic role, incidence, treatment, and prognosis of inflammatory left ventricular (LV) microaneurysms in patients with apparently idiopathic ventricular tachyarrhythmias.

Methods and Results—We studied 156 consecutive patients (71 men, 85 women; mean age, 44.1 ± 11.8 years) with severe ventricular arrhythmias and normal 2D echo cardiac parameters by coronary and ventricular angiography, biventricular endomyocardial biopsy, and electrophysiological study. Polymerase chain reaction was used to detect genomic sequences of enterovirus, adenovirus, Epstein Barr virus, cytomegalovirus, herpes simplex viruses, influenza A and B viruses, and hepatitis C virus in frozen endomyocardial samples. Of these patients, 15 (9.6%) showed angiographic evidence of single or multiple LV microaneurysms. All 15 patients had recurrent episodes of ventricular tachycardia with right bundle-branch block morphology, and the arrhythmias originated within or close to the aneurysms in those patients (n = 6) undergoing ventricular mapping. A lymphocytic myocarditis was observed in LV biopsies of all patients and in the right ventricles of 3 patients. Polymerase chain reaction analysis was performed in 12 and viral genomes were found in 5 (42%): hepatitis C virus in 2, enterovirus in 2, and influenza virus A in 1. The patients were treated with antiarrhythmics, and cardiac function was preserved for the next 47 ± 39.5 months of follow-up. No major clinical event was registered, and arrhythmias were successfully treated by antiarrhythmics.

Conclusions—Inflammatory LV microaneurysms, often of viral origin, are a consistent cause of apparently idiopathic ventricular arrhythmias. Their prognosis so far has been benign, and aggressive therapeutic strategies have been unnecessary. (Circulation. 2001;104:168-173.)

Key Words: tachyarrhythmias ■ aneurysm ■ myocarditis

Severe ventricular arrhythmias may occur in patients with apparently normal hearts.1 They may be associated with inflammatory left ventricular (LV) aneurysms of small dimension.2 However, at present, no data on a consistent number of patients about the incidence, treatment, and prognosis of this entity are available in the literature.

In this article, we report on 15 patients with inflammatory LV microaneurysms causing severe ventricular arrhythmias in apparently normal heart. Histology and polymerase chain reaction (PCR) analysis for the most common cardiotropic viruses have been performed on biventricular endomyocardial biopsies obtained from the areas close to the aneurysms. Clinical and angiographic results at an intermediate-term observation are also reported.

Methods

In our institution, from January 1988 to January 2000, 156 consecutive patients (71 men, 85 women; mean age, 44.1 ± 11.8 years) with severe ventricular arrhythmias and normal 2D echo cardiac dimension and function (LV ejection fraction [EF] ≥ 0.50) were studied by coronary and ventricular angiography, biventricular endomyocardial biopsy, and electrophysiological study according to the American College of Cardiology/American Heart Association (class I indication). Of these, 15 patients (9.6%; 7 men, 8 women; mean age, 37.6 ± 16.4 years) showed angiographic evidence of single or multiple small aneurysms that were not visible at echo.

Characteristics of Patient Population

All 15 patients were admitted because of sustained (patients 1, 3, 5, 7, 11, and 13) or nonsustained ventricular tachycardia, with right bundle-branch block (RBBB) morphology (Figure 1). Five patients (patients 1, 7, 8, 11, and 12) had a history of a flulike syndrome within 3 weeks of the onset of symptoms. None had a family history of cardiomyopathy or sudden death. Physical examination and chest x-ray were normal in all patients.

Clinical Investigations

Cardiac studies included both noninvasive (resting ECG, QRS signal–averaged ECG, Holter monitoring, exercise stress testing, 2D Doppler echocardiography) and invasive (cardiac catheterization, biplane left and right ventriculography, coronary angiography with ergonovine stress test, biventricular endomyocardial biopsy, and electrophysiological study with biventricular mapping in the 6 patients with sustained ventricular tachycardia) exams. All invasive cardiac exams were performed after informed consent was given and were approved by the ethics committee of our institution.

Endomyocardial biopsies (3 to 4 per ventricular chamber) were performed by a Bipal (Cordis) biotome approached by a 7F (501 to
613 and 501 to 613A) long sheet in the septal-apical region of the right ventricle and in different segments of the LV. LV specimens were marked as close to (A) or far from LV aneurysms (B –2 cm above, C =2 cm below, D = ~4 cm from the aneurysm). The regional candidates for biopsy were identified on an x-ray view with flashing of contrast medium. Two to three samples were immediately frozen in OCT compound with isopentane cooled in liquid nitrogen and stored at −80°C. The remaining specimens were fixed in 10% buffered formalin and embedded in paraffin wax. Blood samples were collected at the time of cardiac catheterization and stored at −80°C.

The 6 patients with sustained ventricular tachycardia underwent electrophysiological study as previously described. The study was performed the same way in the patients on the same antiarrhythmic drug (propafenone 600 mg in patients 3 through 7, amiodarone 800 mg in patients 1 through 5, and sotalol 240 mg in patients 11 and 13) that resolved the arrhythmia. Biventricular mapping during sinus rhythm and, in inducible patients, during ventricular tachycardia was performed. Areas of local activation that either were preceded by or were coincident with the onset of the abnormal QRS complexes were considered the origin of the arrhythmia.

**Serological Studies**

All patients underwent routine laboratory tests, serological tests for the most common cardiotropic viruses, and immunological studies.

**Histological and Immunohistochemical Analyses**

Four to six endomyocardial samples from each patient were processed for histological and immunohistochemical studies. For histology, 5-μm-thick sections were cut and stained with hematoxylin

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**TABLE 1. PCR Analysis With Presynthesized Oligonucleotide Primers**

<table>
<thead>
<tr>
<th>Virus</th>
<th>Primer Sequence (Upstream/Downstream)</th>
<th>PCR Product Size, bp</th>
<th>Annealing Temperature, °C</th>
<th>Annealing Time, s</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>3GPDH</td>
<td>5'-AGTGAAGGTCGAGTCAACG-3’</td>
<td>234</td>
<td>50</td>
<td>45</td>
<td>6</td>
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<tr>
<td></td>
<td>5'-GCTCTGGAAAAGTGGATGG-3’</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>β-globine</td>
<td>5'-GGAATAAGACCAATAGGACG-3’</td>
<td>269</td>
<td>44</td>
<td>60</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>5'-ACACAAGTGGTTGACTAGC-3’</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HCV</td>
<td>5'-GCCATGCGTTAGTATGAGT-3’ (outer)</td>
<td>256</td>
<td>60</td>
<td>40</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>5'-CACGGTCTACGAAGACCTCCC-3’</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>5'-GTGACGCTCCAGGACC-3’ (inner)</td>
<td>210</td>
<td>45</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Enterovirus</td>
<td>5'-CCGAGTATGCAATCCCA-3’</td>
<td>180</td>
<td>50</td>
<td>50</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>5'-GCGGCTAACCTAATGC-3’</td>
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<tr>
<td>Cytomegalovirus</td>
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<td>257</td>
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<tr>
<td></td>
<td>5'-CGTCTACCCCCCGGAGTAA-3’</td>
<td></td>
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<tr>
<td>Influenza A</td>
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<td>190</td>
<td>50</td>
<td>50</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>5'-CCCATTCTCATTACTGCTT-3’</td>
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<td></td>
</tr>
<tr>
<td>Influenza B</td>
<td>5'-ATGGAATCTGAGTTCTCTAAC-3’</td>
<td>241</td>
<td>56</td>
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<tr>
<td></td>
<td>5'-GTGACCATGAGTAGAAGCT-3’</td>
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<td></td>
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<tr>
<td>Adenovirus</td>
<td>5'-GCCGAGTGCTTTACATGCAAC-3’</td>
<td>308</td>
<td>56</td>
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<td>11</td>
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<tr>
<td></td>
<td>5'-CAGCCACGCCGGATGTC-3’</td>
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<tr>
<td>HSV</td>
<td>5'-AGAGGCGCGCAAGGTGCT-3’</td>
<td>229 (HSV1)</td>
<td>56</td>
<td>45</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>5'-TGAGGCGATGACATGCTG-3’</td>
<td>241 (HSV2)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>EBV</td>
<td>5'-GTGACCATGAGTAGAAGCT-3’</td>
<td>268</td>
<td>52</td>
<td>45</td>
<td>13</td>
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</tbody>
</table>

HSV indicates herpes simplex virus; EBV, Epstein Barr virus.
and eosin. Miller’s elastic van Gieson’s, and Masson’s trichrome stain and examined by light microscopy. The Dallas criteria were used for histological diagnosis of myocarditis. In all samples, immunohistochemistry for the characterization of inflammatory infiltrate was carried out by use of the following antibodies (all Dako): CD45 (1:20), CD43 (1:40), CD45RO (1:100), CD20 (1:100), CD68 (1:50), CD4 (1:100), and CD8 (1:100). After deparaffinization, the sections were incubated with the monoclonal antibody for 1 hour at room temperature and were then incubated with biotinylated antimusm agents immunoglobulins (Dako EnVision peroxidase mouse) for 30 minutes. Enzyme activity was detected with diaminobenzidine (0.5 mg/mL) with 0.05% NiCl in 50 mmol/L Tris buffer, pH 7.5, and sections were counterstained with Mayer’s hematoxylin.

Molecular Analysis
Two frozen myocardial specimens from each patient were used for molecular analysis in 12 of 15 patients. In the other 3 patients, frozen biopsies were not available. Ventricular myocardial biopsies, obtained at the time of cardiac surgery from 5 age-matched patients with chronic stable angina, no evidence of systemic infection, and no histological evidence of myocarditis, were used as control tissues for PCR analysis.

Total RNA and genomic/viral DNA were extracted simultaneously from patients and control subjects by use of a modification of the RNAzol method. The oligonucleotides used to ascertain the quality of extracted RNA or DNA were complementary to the mRNA 3GPDH and β-globin gene, respectively. Eight primers pairs that had previously designed to detect cardiotropic viruses were used (Table 1). A nested PCR for the highly conserved 5’ noncoding of hepatitis C virus (HCV) was performed for detection of this virus. The positive and negative strands of viral RNA (HCV and enterovirus) were detected by reverse transcription (RT) of RNA samples in the presence of only 1 oligonucleotide primer (either sense or antisense). The DNA obtained in this RT reaction was therefore complementary to 1 of the virus RNA strands and could be amplified by PCR with both oligonucleotide primers.

Total extracted RNA was reverse transcribed in a total volume of 20 μL containing the following components: 50 mmol/L Tris-HCl (pH 8.3), 70 mmol/L KCl, 3 mmol/L MgCl2, 10 mmol/L dithiothreitol, 0.5 mmol/L dNTPs, 25 U human placental ribonuclease inhibitor, antisense primer (0.1 nmol), and 200 U Moloney murine leukemia virus. The reaction was carried out at 37°C for 1 hour.

The PCR was performed on 20 μL of RT reaction in a total volume of 100 μL. The following were used: 10 mmol/L Tris-HCl (pH 8.3), 50 mmol/L KCl, 1.5 mmol/L MgCl2, and 0.2 mmol/L dNTPs sense and antisense primers (0.1 μmol each). Tag gold polymerase (Perkin-Elmer) was added after an initial 10 minutes of incubation at 95°C. Thirty to 35 rounds of amplification were performed under the following conditions: denaturation for 1.5 minutes at 94°C and template extension for 3 minutes at 72°C. The annealing time and temperature are reported in Table 1. For nested PCR of HCV, a second amplification of the first PCR was performed by the addition of 5 μL to a reaction mixture but with 1 μmol/L of the inner primers.

To avoid false-negative results by contamination, the preventive measures of Kwook and Higuchi were followed, and negative controls (ie, no template) were included in all experiments. For each assay, known positive controls (infected viral cells) were also added.

The reaction products were electrophoresed on a 3% NuSieve/1% Seakem TM agarose gel (FMC Bio Products Rockland) stained with ethidium bromide and visualized by ultraviolet transillumination. All viral PCR-positive samples were required to have duplicate results. In the presence of positivity for a viral genome, a stored blood sample was also analyzed the same way for the presence of the viral agent.

The purified PCR products were sequenced directly on an automated ABI model 323 A sequencer as previously described. Sequence comparison was performed by a BLAST search of GenBank databases.

Figure 2. Systolic LV angiography (right anterior oblique view) from patient 3 showing apical LV microaneurysm (arrow).

Follow-Up
All patients were followed up at 4-week to 6-month intervals. At each visit, they underwent physical examination, ECG, 2D echocardiography, and Holter monitoring. At 6 and 12 months, the patients underwent cardiac catheterization with left ventriculography to ascertain the persistence of LV aneurysms. Cardiac MRI was also performed and compared with the angiographic findings to test the ability to detect LV aneurysms.

Statistical Analysis
All values are expressed as mean±SD.

Results
Clinical Study
All patients were in sinus rhythm, and resting ECG showed repolarization abnormalities and intraventricular conduction defects as the most frequent alterations. Late potentials, investigated with signal-averaged ECG, were negative in all cases. On admission, Holter monitoring revealed frequent ventricular ectopic beats with some couples and triplets, phases of bigeminy/trigeminy, and runs of nonsustained ventricular tachycardia in all patients and failed to show transient ST–T–segment ischemic changes.

An ergometric test, performed with the Bruce protocol on specific antiarrhythmic regimen, failed to show signs and symptoms of myocardial ischemia in all patients. No repetitive ventricular ectopic beats appeared during the test. Echocardiography showed normal atrial and ventricular dimension (LV end-diastolic diameter, 47±4.3 mm; left atrium, 0.31±2.5 mm), normal thickness of cardiac walls with regular borders, and normal global LV contractility (LVEF, 58.6±3.5). No segmental wall motion or valvular abnormalities were detected. MRI failed to detect the presence of an LV aneurysm in most patients and was positive only in patients 9 and 13, who had multiple aneurysms.

Cardiac catheterization showed normal pulmonary and LV end-diastolic pressure. Biplane LV angiography revealed normal LV contractility with the unpredictable presence of single (Figure 2) or multiple (Figure 3) small aneurysms with different localization (Table 2). LV aneurysm was defined as an akinetic or dyskinetic well-defined wall bulge persisting during both systole and diastole. Aneurysms size was
1.3±2.4 mm in length and 6.1±3.6 mm in width as measured with cardiac angiography measurement system (quantitative coronary angiography, MEDIS, NL). Right ventricular angiography was normal in all patients. Coronary angiography showed normal epicardial coronary arteries and the absence of vasospasm after ergonovine administration. At electrophysiological study, programmed ventricular stimulation induced rapid monomorphic sustained ventricular tachycardia with RBBB morphology in patients 1 and 5 without hemodynamic deterioration. Patients 3 and 7, treated with propafenone, and patients 11 and 13, treated with sotalol, were no longer inducible. Ventricular mapping showed the arrhythmia originating within or close to the aneurysm in all 6 of these patients.

**Histology and Immunohistochemistry**
Diffuse inflammatory lymphomononuclear infiltrates represented mainly by activated T lymphocytes (CD45RO+) (Figure 4), associated with focal necrosis of adjacent myocytes, were observed in all patients meeting the Dallas criteria for myocarditis. Interstitial and focal replacement fibrosis was commonly identified by Masson’s trichrome and Miller’s elastic van Gieson’s staining. In only 3 patients (patients 1, 2, and 6), right ventricular endomyocardial biopsy showed histological changes consistent with the diagnosis of myocarditis, whereas all LV specimens suggested that entity. Moreover, in the specimens obtained in the region closest to the aneurysm, the myocarditic process was more prominent and severe, being associated with

**TABLE 2. Characteristics of 15 Patients With Ventricular Arrhythmias and Inflammatory LV Aneurysms**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age, y</th>
<th>Sex</th>
<th>Ventricular Arrhythmia</th>
<th>Clinical Presentation</th>
<th>Resting ECG</th>
<th>LVEF, %</th>
<th>Aneurysm Location</th>
<th>Histology</th>
<th>PCR</th>
<th>Treatment at Discharge, mg/d</th>
<th>Follow-Up, mo</th>
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<tbody>
<tr>
<td>1</td>
<td>62</td>
<td>M</td>
<td>sVT</td>
<td>Palpitation</td>
<td>Normal</td>
<td>57</td>
<td>A</td>
<td>M</td>
<td>InfAV</td>
<td>Amiod 400 + Metop 100</td>
<td>56</td>
</tr>
<tr>
<td>2</td>
<td>49</td>
<td>F</td>
<td>nsVT</td>
<td>Palpitation</td>
<td>Normal</td>
<td>53</td>
<td>PB</td>
<td>M</td>
<td>EV</td>
<td>Sotalol 240</td>
<td>20</td>
</tr>
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<td>3</td>
<td>15</td>
<td>M</td>
<td>sVT</td>
<td>Palpitation</td>
<td>LAH</td>
<td>66</td>
<td>A</td>
<td>M</td>
<td>No</td>
<td>Propafenone 600</td>
<td>125</td>
</tr>
<tr>
<td>4</td>
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<td>F</td>
<td>nsVT</td>
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<td>Normal</td>
<td>62</td>
<td>PB</td>
<td>M</td>
<td>Neg</td>
<td>Sotalol 240</td>
<td>70</td>
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<tr>
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<td>sVT</td>
<td>Palpitation</td>
<td>Normal</td>
<td>60</td>
<td>A, PB</td>
<td>M</td>
<td>Neg</td>
<td>Amiod 400 + Metop 100</td>
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<td>Palpitation</td>
<td>LAH</td>
<td>60</td>
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<td>M</td>
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<td>sVT</td>
<td>Syncope</td>
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<td>M</td>
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<td>EV</td>
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<td>RBBB + LAH</td>
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<td>HCV</td>
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<td>M</td>
<td>Neg</td>
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<td>M</td>
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<td>Sotalol 240</td>
<td>12</td>
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</table>

VT indicates ventricular tachycardia; s, sustained; A, apical; M, myocarditis; InfAV, influenza A virus; Amiod, amiodarone; Metop, metoprolol; ns, nonsustained; PB, posterobasal; EV, enterovirus; LAH, left anterior hemiblock; Neg, negative; AL, anterolateral; VRA, ventricular repolarization abnormalities; and AVBI, first-degree AV block.

*LV angiography in right anterior oblique (RAO) view.*
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intense myocytolysis (Figure 4) and large areas of fibrosis (Figure 5). There were no signs of ischemic damage. Sixty-two arterioles were examined from right ventricular and LV specimens (2 to 6 per patient); no arteriole showed evidence of inflammatory damage, lumen narrowing, or occlusion. The endocardium was normal in all patients.

Serology
Serologic tests for cardiotropic viruses were positive in 6 patients. In particular, patients 2 and 8 were positive for coxsackievirus B3 at a dilution of 1:64, patient 1 was positive for influenza virus A at a dilution of 1:128, and patients 9 and 13 were positive for IgG anti-HCV. HCV genotype of both patients was 1b. Immunological studies were positive in patient 6, showing positivity for antinuclear antibodies (titer ≥1/80).

Molecular Studies
In all patients, the presence of sufficient target nucleic acid was confirmed by amplification of β-globin for DNA and 3GPDH for RNA. Viral genomes in the myocardium were detected in 5 of 12 patients (42%): 2 patients (33.3%; patients 2 and 8) were positive for both positive and negative strands of enterovirus genome, 2 patients (33.3%; patients 9 and 13) were positive for both positive and negative strands of HCV RNA, and 1 patient (16.6%; patient 1) was positive for influenza A virus (Figure 6). None of the 5 controls was positive for any virus. Sequencing analysis of enterovirus PCR amplimers showed a high homology with coxsackievirus B3 (AF 198383). Sequencing analysis of the influenza A–positive patient was not performed because of insufficient PCR product amplifier. Positive and negative strands of HCV RNA were also present in the serum of the 2 infected patients, whereas neither enterovirus nor influenza A virus was detected in blood samples of patients 2, 8, and 1.

Treatment
At repeated electrophysiological study, induction of sustained ventricular tachycardia was prevented in patients 1 and 5 with the addition of metoprolol. These patients were discharged with amiodarone (400 mg/d tapered to 200 mg/d after 2 weeks) and metoprolol (100 mg/d). The other 4 noninducible patients were discharged with propafenone 600 mg/d (2 patients) and sotalol 240 mg/d (2 patients). Patients with nonsustained ventricular tachycardia were treated with sotalol (80 mg TID) and metoprolol 200 mg/d (Table 2).

Follow-Up
During the follow-up (mean, 47±39.5 months; range, 10 to 125 months), no death, cardiac arrest, aneurysm rupture, or thromboembolic phenomena were registered. No patient showed significant pharmacological side effects, and no dilatation or impairment of LV function was observed. The arrhythmias were controlled by antiarrhythmic drugs because sequential Holter recording failed to show the presence of repetitive ventricular ectopic beats and no need for an implantable cardioverter-defibrillator emerged during the study. At control angiography, LV aneurysms persisted unchanged, and none required surgical resection.

Discussion
Apparently idiopathic ventricular arrhythmias can be caused by several heterogeneous entities, including genetically determined disorders, focal active myocarditis, concealed arrhythmogenic right ventricular cardiomyopathy, mitral valve prolapse, and LV false tendons.17 This article has described severe ventricular arrhythmias with RBBB morphology caused by localized inflammatory of LV microaneurysms. In all our patients, 2D echocardiography, performed by 2 independent expert operators, failed to show abnormalities of cardiac morphology and function. Unexpectedly, single or multiple LV aneurysms were revealed by LV angiography, and the source of the electrical instability was identified within or close to them in 40% of patients. Interestingly, in most patients, even cardiac MRI was unable to reveal abnormalities in segmental LV motion, suggesting that LV microaneurysms can be missed unless an invasive study is performed.

Inflammatory Origin of LV Aneurysms
The inflammatory origin of LV aneurysms has been supported by the morphological characteristics of the aneurysms

Figure 5. Histology from patient 13 showing foci of active myocardiitis (arrows) with extensive areas of fibrous replacement (F). Stained with hematoxylin and eosin; magnification ×100.

Figure 6. RT-PCR analysis of enterovirus (180 bp) and influenza A virus (190 bp) and nested RT-PCR of HCV (210 bp) in myocardium of patients with LV microaneurysms. Products were detected by ethidium bromide staining of 3% agarose gel. M indicates DNA molecular weight marker VIII; lane 1, enterovirus-positive control (infected cells); lane 2, endomyocardial biopsy of patient 2; lane 3, enterovirus-negative control (uninfected cells); lane 4, HCV-positive control (liver biopsy of patient with chronic active hepatitis); lane 5, endomyocardial biopsy of patient 9; lane 6, negative control (no template); lane 7, influenza A virus–positive control (infected cells); lane 8, endomyocardial biopsy of patient 1; and lane 9, influenza virus–negative control (uninfected cells).
(small size, fairly localized, sometimes multiple), usual young age of patients, absence of a history of ischemic heart disease, normal coronary arteriogram, and histological findings indicating a lymphocytic myocarditis. The histological diagnosis has been provided by applying the Dallas criteria on biventricular endomyocardial biopsy and confirmed by immunohistochemical staining. Interestingly, in only 3 of our 15 patients (20%), right ventricular biopsy showed histological changes consistent with a myocarditic process, whereas all LV specimens suggested that entity. In addition, among LV biopsies, those taken from the areas closest to the aneurysm showed the most severe inflammatory changes. The low concordance between LV and right ventricular histological findings indicates that in most cases cardiac inflammation was localized only in the LV and, inside that, particularly in specific myocardial segments. These observations suggest that in selected patients with severe clinical manifestations and localized abnormalities of the LV wall, an LV endomyocardial biopsy is useful for a correct diagnosis.

Molecular analysis, performed on frozen endomyocardial tissue in 12 of our 15 patients, showed the presence of a viral infection in 5 patients. In particular, HCV was identified in 2 patients, influenza A virus in 1, and enterovirus in 2. Enteroviruses are considered the most common pathogens responsible for viral myocarditis, and experimental studies demonstrate that coxsackievirus B myocarditis may cause ventricular aneurysms manifesting with ventricular arrhythmias. Recently, even HCV has been associated with both myocarditis and cardiac arrhythmias, whereas ventricular arrhythmias are often associated with influenza syndrome. Our study demonstrated that cardiac aneurysm formation might concur to electrical instability even in these 2 last categories of patients.

**Pathogenesis of Inflammatory Microaneurysms**

The mechanism of inflammatory aneurysm formation is, at the moment, unclear. In experimental models, cellular infiltration and tranmsural destruction of myocardial fibers seem to be the most likely cause. In our patients, localized intense myocarditis has been observed in biopsies taken from the areas close to the aneurysms, suggesting a similar pattern of myocardial damage. Nevertheless, an inflammatory lesion with occlusion of intramural vessels cannot be completely ruled out, even though no such finding (vasculitis) has been observed in 62 arterioles examined.

**LV Aneurysm as a Cause of Ventricular Arrhythmias**

Severe ventricular arrhythmias are frequently associated with the evidence of LV aneurysm, usually as a consequence of a previous myocardial infarction with systolic bulging of the scarred myocardium. Ventricular tachyarrhythmias have also been described in association with congenital, cardiomyopathic, inflammatory, and idiopathic LV aneurysm. In the present study, the origin of sustained RBBB ventricular tachycardia from inflammatory LV aneurysms has been demonstrated in 6 patients by biventricular mapping. The presence of inflammatory infiltrate with intense myocytolysis and large areas of fibrosis may be considered the pathogenetic substrate of ventricular arrhythmias in inflammatory LV microaneurysms.

In conclusion, inflammatory LV microaneurysms, often of viral origin, may be the cause of ventricular arrhythmias in patients with apparently normal hearts. Their prognosis so far is benign, and major therapeutic strategies seem unnecessary.

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**References**

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