Idiopathic restrictive cardiomyopathy

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ABSTRACT This report details the clinical, hemodynamic, and morphologic data from four patients 59 to 77 years old (mean 66) with a primary restrictive cardiomyopathy. All patients had symptoms of congestive heart failure, jugular venous distention, and murmurs of mitral and tricuspid regurgitation. Four patients required pacemakers, three for the brady-tachy syndrome and one for complete heart block. Chest X-ray demonstrated cardiomegaly in all four patients and pulmonary congestion and/or pleural effusions in three. Echocardiographic examination documented left atrial enlargement in all patients, along with normal left ventricular internal dimensions. Global left ventricular systolic function was normal in all, and left and right ventricular filling pressures were elevated and similar in three. A dip and plateau pattern was present in the pressure tracings of two of three patients. Unlike previous reports of restrictive cardiomyopathy, in our four patients there was no specific morphologic cause noted at necropsy. Pathologic evaluation demonstrated biventricular dilatation in all patients, with thrombi present in the atrial appendages in three. Normal ventricular cavity size and mild right ventricular hypertrophy were present in all patients and mild-to-moderate left ventricular hypertrophy was present in two. There were no significant pericardial, endocardial, or valvular abnormalities and no infiltrative myocardial disorders were present. Light and electron microscopic studies demonstrated only interstitial fibrosis of the myocardium. A restrictive hemodynamic profile may be observed in the absence of specific infiltrative disorders and affected patients may exhibit a prolonged clinical course of 4 to 14 years (mean 9). However, in these patients congestive heart failure responded poorly to medical therapy or surgical correction of valvular regurgitation, which is common in this disorder.


RESTRICTIVE CARDIOMYOPATHY is a form of myocardial disease with a clinical and hemodynamic profile very similar to and frequently indistinguishable from that of constrictive pericardial disease. Clinical evidence of systemic venous congestion is frequently associated with hemodynamic evidence of elevated left and right heart filling pressures, including a "dias-tolic dip and plateau" configuration of ventricular pressure curves (square root sign).

Although the atria are frequently dilated, the ventricular cavities are usually normal in size and systolic performance as judged by ejection fraction is often well maintained. The pathologic basis for most cases of restrictive cardiomyopathy includes infiltrative disorders such as amyloidosis, hemochromatosis, glycogen storage disease, mucopolysaccharidoses, endomyocardial fibrosis with or without eosinophilia, endocardial fibroelastosis, sarcoïdosis, and collagen-vascular diseases like scleroderma.

In this report we describe the clinical, hemodynamic, and morphologic data from four patients who presented with restrictive cardiomyopathy that was not associated with the usual pathologic entities responsible for this clinical-hemodynamic syndrome.

Patients and methods

The salient clinical characteristics of the four patients included in this report are summarized in table 1.

Clinical presentation (table 1). All four patients presented with symptoms of biventricular failure, i.e., dyspnea, pedal edema, and/or ascites that had been present for 4 to 8 years (mean duration 5 years).

Antedating the onset of symptoms of congestive heart failure, complete heart block was noted in patient No. 1 14 years earlier and atrial arrhythmias were noted in patient No. 2 13 years earlier. One patient (No. 3) had a history of an isolated syncopal episode and two other patients (Nos. 2 and 4) had palpitations.

Physical findings included those of jugular venous distention (in all patients), peripheral edema, ascites, and murmurs of mitral and tricuspid regurgitation.

Electrocardiographic findings. All four patients had atrial fibrillation. One patient demonstrated paroxysms of supraventricular tachycardia and atrial fibrillation (No. 2). One patient also had complete heart block (No. 1). All patients required a permanent pacemaker, one for complete heart block and three
present in three patients and pleural effusions were documented in three. No pericardial calcifications were evident on lateral chest x-rays in any patient.

**Echocardiographic findings.** M mode and two-dimensional echocardiograms were available for three patients (Nos. 1 to 3). All patients had left atrial enlargement (7.2, 6.3, and 5.2 cm respectively). No patient had left ventricular dilatation. The left ventricular end-diastolic dimensions ranged from 4.0 to 4.2 cm. Borderline left ventricular hypertrophy (wall thickness 1.2 to 1.3 cm) was present in the ventricular septum and posterior free wall in two patients and in the posterior free wall in one patient. The mitral valve "E" point-septal separation was normal, as was the mitral valve diastolic (E-F) slope. Two-dimensional echocardiography demonstrated right atrial enlargement and confirmed M mode echocardiographic findings of right ventricular enlargement (>2.7 cm) in two patients. The three patients studied who had a rhythm originating from right ventricular pacing were found to have reduced interventricular septal motion. The clinical findings of tricuspid regurgitation were confirmed in each patient by results of two-dimensional echocardiographic contrast studies.10

**Hemodynamic and angiographic findings (table 2).** Complete left and right heart catheterizations were performed in three patients. Hemodynamic findings included elevated left ventricular filling pressures (determined directly as left ventricular end-diastolic pressure) as well as elevated right ventricular end-diastolic pressure in all. A prominent early diastolic dip and middle-to-late diastolic plateau was noted in the ventricular pressure tracings of two patients.

Left ventricular contrast angiography was performed in three patients and revealed 1+ to 2+ mitral regurgitation in all. The left ventricular ejection fraction (determined by contrast angiography in three and radionuclide ventriculography in one) was 0.50 or greater in all patients. The analysis of regional left ventricular wall motion revealed posterobasal hypokinesis in one and normal contraction in three patients.

Right ventricular contrast angiography was performed in three patients. The degree of tricuspid regurgitation ranged from mild (1+/4+) to severe (4+/4+).

In all patients, coronary arteries were normal.

**TABLE 2**

Hemodynamic values

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>CI (l/min/m²)</th>
<th>SAP (mm Hg)</th>
<th>LVSP/LVEDP (mm Hg)</th>
<th>PCWP or LAP (mm Hg)</th>
<th>RVSP/RVEDP (mm Hg)</th>
<th>Mean RAP (mm Hg)</th>
<th>Mean LVEDP (mm Hg)</th>
<th>Mean LV (mm Hg)</th>
<th>Dip and plateau (%)</th>
<th>LV EF</th>
<th>RV EF</th>
<th>LV gram</th>
<th>RV gram</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.4</td>
<td>100/60</td>
<td>100/17</td>
<td>22</td>
<td>45/17</td>
<td>16</td>
<td>+</td>
<td>0.50</td>
<td>1+ MR</td>
<td>4+ TR</td>
<td>Postbasal hyperkinesis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1.6</td>
<td>110/70</td>
<td>110/24</td>
<td>24</td>
<td>40/18</td>
<td>18</td>
<td>+</td>
<td>0.60</td>
<td>1-2+ MR</td>
<td>1+ TR</td>
<td>Normal ( TR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>—</td>
<td>170/90</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>+</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>4(a)</td>
<td>2.88</td>
<td>108/60</td>
<td>112/22</td>
<td>23</td>
<td>30/2</td>
<td>7</td>
<td>—</td>
<td>0.82</td>
<td>1-2+ MR</td>
<td>Trace MR</td>
<td>2+ TR</td>
<td>Right ventricular wall motion</td>
<td></td>
</tr>
<tr>
<td>4(b)</td>
<td>1.85</td>
<td>115/60</td>
<td>115/22</td>
<td>22</td>
<td>42/15</td>
<td>22</td>
<td>—</td>
<td>0.78</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

4(a) is before mitral valve replacement, 4(b) after mitral valve replacement (8 months after 4a).

CI = cardiac index; EDP = end-diastolic pressure; EF = ejection fraction; LAP = left atrial pressure; LV = left ventricular; LV gram = left ventriculogram; MR = mitral regurgitation; PCWP = pulmonary capillary wedge pressure; RAP = right atrial pressure; RV gram = right ventriculogram; RV = right ventricular; SAP = systemic arterial pressure; SP = systolic pressure; TR = tricuspid regurgitation.

*Evaluated by radionuclide angiography and two-dimensional echocardiography.

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**TABLE 1**

Clinical data

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>NYHA class</th>
<th>Duration of cardiac symptoms</th>
<th>Duration of congestive heart failure</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>66</td>
<td>F</td>
<td>IV</td>
<td>168+</td>
<td>36</td>
<td>Digitalis, diuretics, vasodilators, ventricular pacemaker</td>
</tr>
<tr>
<td>2</td>
<td>77</td>
<td>M</td>
<td>IV</td>
<td>156</td>
<td>96</td>
<td>Digitalis, diuretics, vasodilators, AV sequential pacemaker</td>
</tr>
<tr>
<td>3</td>
<td>63</td>
<td>F</td>
<td>III</td>
<td>48</td>
<td>48</td>
<td>Digitalis, diuretics, vasodilators, ventricular pacemaker</td>
</tr>
<tr>
<td>4</td>
<td>59</td>
<td>F</td>
<td>IV</td>
<td>60</td>
<td>60</td>
<td>MVR, re-op, TVR, digitalis, diuretics, ventricular pacemaker</td>
</tr>
</tbody>
</table>

MVR = mitral valve replacement; TVR = tricuspid valve replacement; NYHA = New York Heart Association; AV = atrioventricular.

*Complete heart block developed 14 years before death.

†Atrial arrhythmias 13 years before death.

for the brady-tachy syndrome. No patient demonstrated bundle branch block or a pattern of myocardial infarction.

**Chest x-ray.** The roentgenographic findings demonstrated an enlarged cardiac silhouette with cardiothoracic ratio greater than 0.50 in all cases. Pulmonary vascular redistribution was
Clinical course and follow-up (table 1). Congestive heart failure was treated with diuretics, digitalis, and vasodilatory therapy. Two patients underwent an open thoracotomy for pericardial and/or myocardial biopsy and one underwent the procedure for mitral and tricuspid valve replacement. Two patients died from intractable heart failure, one died from pericardial tamponade after diagnostic thoracotomy, and one patient died suddenly at home. The average duration of cardiac symptoms before death was 9 years (range 4 to 14 years). The mean survival after the onset of congestive heart failure was 5 years (range 3 to 8 years).

Pathologic study

Gross findings (figure 1). All patients were studied by necropsy. The heart weights were mildly to moderately increased at 487 ± 97.5 g (range 380 to 680). In each of the four patients gross inspection of the pericardium showed that it was normal except for minor focal fibrous epicardial adhesions secondary to prior surgical exploration. Marked biatrial dilatation was found in all patients (figure 1) and thrombi were present in one or both atrial appendages in three. The atrioventricular and semilunar valves were structurally normal at necropsy. However, in patient No. 1, one chorda tendinea adjacent to a pacemaker lead was ruptured. The annuli of the tricuspid and mitral valve were mildly dilated. The tricuspid valve annuli measured 12.2 ± 0.8 cm (range 12 to 14, normal = 11 to 13)11 and the mitral annuli 11.3 ± 0.2 cm (range 11 to 11.5, normal = 9 to 11.11) Ventricular cavity size was normal in three patients and biventricular dilatation was present in patient No. 4, who had undergone mitral valve replacement 24 months and tricuspid valve replacement 12 months before death. Right ventricular wall thickness was increased (>0.3 cm), measuring 0.5 cm in all patients, and increased left ventricular wall thickness (>1.5 cm) was present in two. Concentric left ventricular hypertrophy was present in patient No. 4 (ventricular septal and free wall thicknesses were 2.0 cm) and increased left ventricular posterior wall thickness (1.7 cm) was observed in patient No. 2. There were no patients with asymmetric septal hypertrophy. The endocardium had patchy fibrosis in the right and left ventricular outflow tract in one patient but was normal in the other three. Gross and microscopic examination of the major epicardial coronary arteries demonstrated only minimal (less than 25%) or mild (less than 50%) cross-sectional area luminal narrowing by atherosclerosis in the four patients.

Microscopic findings. In all four patients the pericardium was normal. The myocardium stained with hematoxylin and eosin, congo red, and trichrome stains showed only interstitial fibrosis that ranged from very mild to severe (figure 1, C) and involved both ventricles to a similar degree. In patient No. 2 there was more myocardial fibrosis in the atria than in the ventricles. In no case was there evidence of myofiber disarray, nor was there evidence of amyloid deposits or inflammatory cells. Electron microscopic studies were performed in two patients (Nos. 1 and 2). In each case the light microscopic findings were confirmed. In ad-

FIGURE 1. Opened heart from patient 1. a. Note the markedly dilated right atrium (RA) and much smaller right ventricle (RV). The indwelling pacing catheter has been encapsulated (arrow) within the RA. Organizing thrombus (T) is present in the atrial appendage. b. The opened left side of the heart showing marked left atrial (LA) enlargement with a relatively normal-sized left ventricle (LV). Note the normal circumflex coronary artery (arrow). c. A histologic section from the left ventricle demonstrates the mild fibrosis noted in this section from patient 1.
dition, non-specific degenerative changes of myocardial fibers were noted in all cases. The conduction system was studied in three patients and in each mild-to-moderate fibrosis was present in the sinoatrial and atrioventricular nodes. The patient with complete heart block (No. 1) had extensive fibrosis in the bundle of His, whereas patient No. 2 had only mild and No. 3 no abnormal fibrosis in the bundle of His.

Discussion

Major findings. In this report we have described four patients with a clinical syndrome characterized by pulmonary and systemic venous congestion, varying degrees of atrioventricular valvular regurgitation, atrial arrhythmias, atrioventricular conduction abnormalities, markedly dilated atria, normal left ventricular global systolic function, lack of left ventricular dilatation, elevated left and right ventricular filling pressures (in three, with equalization in two and a dip and plateau in two), and absence of significant coronary artery disease as well as pericardial disease. Interstitial fibrosis was the primary histopathologic finding in the myocardium. These clinicopathologic and hemodynamic findings are consistent with an idiopathic restrictive cardiomyopathy.1, 2

Previous reports of restrictive cardiomyopathy have indicated that it usually results from a specific pathologic disorder involving the heart, namely amyloidosis, hemochromatosis, glycogen storage disease, mucopolysaccharidosis, sarcoidosis, collagen-vascular disease, endocardial fibroelastosis, endomyocardial fibrosis, or neoplastic infiltration.1, 8, 11 Restrictive cardiomyopathy without a specific pathologic basis has not been well characterized. In a clinical study Benotti et al. reported nine patients with a restrictive hemodynamic profile without a specific pathologic basis. In four patients, however, associated diseases were present (chronic obstructive lung disease, hypertrophic cardiomyopathy, and von Recklinghausen’s disease) and may have produced the syndrome.12 Case reports by Arbustini et al.13 and Dubost et al.14 describe three additional patients with a restrictive hemodynamic profile and histologic evidence (from myocardial biopsy) of myofiber disarray. However, in the clinical reports of Benotti,12 Arbustini,13 and Dubost14 and their colleagues, complete morphologic data on patients were not available. In addition to the documentation of the absence of infiltrative and endocardial disorders in our patients, there was no evidence of associated conditions such as right ventricular infarction15 or hypertrophic cardiomyopathy,1, 12, 16 which may produce a hemodynamic profile simulating constrictive pericarditis or restrictive cardiomyopathy. The four patients presented are unusual in that they demonstrate the classical clinical and hemodynamic findings of restrictive heart disease in the absence of a morphologic cause. We believe that these cases represent a clinicopathologic entity that is best labeled idiopathic restrictive cardiomyopathy. We have also seen two additional patients who did not undergo autopsies but in whom there were similar clinical and hemodynamic findings, normal pericardium, and no specific findings on endomyocardial biopsy.

Clinical implications. Our study emphasizes that a restrictive hemodynamic profile may occur in the absence of specific infiltrative disorders and that affected patients may exhibit a protracted clinical course, as indicated by the long-standing nature of the symptoms in our patients. Furthermore, constrictive pericarditis may be simulated. Diagnostic exploratory thoracotomy resulted in a worsening of clinical condition in two patients and occurrence of death shortly after thoracotomy in one patient. In our patients with idiopathic restrictive cardiomyopathy, congestive heart failure responded poorly to medical therapy as well as to surgical correction of valvular regurgitation, which is commonly associated with this entity.

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References

Idiopathic restrictive cardiomyopathy.
R J Siegel, P K Shah and M C Fishbein

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