Dilated phase of hypertrophic cardiomyopathy caused by Fabry disease with atrial flutter and ventricular tachycardia

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Summary We describe a case of a 60-year-old male with dilated phase of hypertrophic cardiomyopathy caused by Fabry disease. He was diagnosed to have a cardiac variant of Fabry disease by an enzyme assay and a right ventricular endomyocardial biopsy which revealed specific features of this disease and cardiac involvement was the sole manifestation. He has developed dilated cardiomyopathy with sustained atrial flutter and frequent non-sustained ventricular tachycardia requiring isthmus ablation and cardiac resynchronization therapy with defibrillator.

Introduction

Fabry disease is an X-linked recessive glycosphingolipid storage disorder caused by a deficiency of the lysosomal enzyme α-galactosidase A [1]. Left ventricular (LV) hypertrophy is a most common cardiac manifestation in Fabry disease [2,3]. And it is recognized that Fabry disease patients are known to have systolic and diastolic dysfunction, and supraventricular and ventricular arrhythmia [4–6]. To date, the optimal therapies for Fabry disease with congestive heart failure and arrhythmia have not been well described.

Case report

A 60-year-old male patient presented with dyspnea and palpitation on mild effort in December...
Figure 1  (A) Twelve-lead ECG recorded in 1995, this shows signs of left ventricular hypertrophy and ST segment depression with negative T wave (I, aVL, V4-6).  (B) Twelve-lead ECG recorded in December 2007 shows typical atrial flutter and 2:1 to 4:1 atrio-ventricular conduction with left bundle branch block (QRS = 160 ms).  (C) Sinus rhythm was maintained after the ablation for atrial flutter (QRS = 160 ms).  (D) ECG of bi-ventricular pacing shows the narrowing of QRS duration (130 ms).

Table 1  Time course of electrocardiography and echocardiography findings.

<table>
<thead>
<tr>
<th>Date of examination</th>
<th>May, 1995’</th>
<th>January 4, 2008’</th>
<th>January 30, 2008’</th>
<th>February 8, 2008’</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rhythm</td>
<td>Sinus</td>
<td>AFL</td>
<td>Sinus</td>
<td>Paced</td>
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<tr>
<td>Heart rate (bpm)</td>
<td>70</td>
<td>125</td>
<td>71</td>
<td>75</td>
</tr>
<tr>
<td>QRS duration (ms)</td>
<td>100</td>
<td>160</td>
<td>160</td>
<td>130</td>
</tr>
<tr>
<td>LVDD (mm)</td>
<td>48</td>
<td>57</td>
<td>59</td>
<td>55</td>
</tr>
<tr>
<td>LVDS (mm)</td>
<td>32</td>
<td>54</td>
<td>55</td>
<td>48</td>
</tr>
<tr>
<td>%FS (%)</td>
<td>33</td>
<td>4.7</td>
<td>7</td>
<td>12</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>/</td>
<td>17</td>
<td>24</td>
<td>36</td>
</tr>
<tr>
<td>LAD (mm)</td>
<td>38</td>
<td>45</td>
<td>39</td>
<td>39</td>
</tr>
<tr>
<td>IVST (mm)</td>
<td>17</td>
<td>17</td>
<td>18</td>
<td>16</td>
</tr>
<tr>
<td>PWT (mm)</td>
<td>13</td>
<td>16</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>E (cm/s)</td>
<td>37</td>
<td>115</td>
<td>80</td>
<td>42</td>
</tr>
<tr>
<td>A (cm/s)</td>
<td>64</td>
<td>/</td>
<td>39</td>
<td>87</td>
</tr>
<tr>
<td>E/A</td>
<td>0.6</td>
<td>/</td>
<td>2.1</td>
<td>0.5</td>
</tr>
<tr>
<td>Deceleration time (ms)</td>
<td>260</td>
<td>108</td>
<td>126</td>
<td>148</td>
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</table>

AFL, atrial flutter; FS, fractional shortening; IVST, interventricular septal wall thickness; LAD, left atrial dimension; LVDD, left ventricular end-diastolic dimension; LVDS, left ventricular end-systolic dimension; LVEF, left ventricular ejection fraction; PWT, posterior wall thickness.
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2007. The blood pressure was 116/98 mm Hg. Chest X-ray revealed enlargement of the heart (cardio-thoracic ratio = 62%). A 12-lead electrocardiogram (ECG) showed atrial flutter (mean ventricular rate, 115 bpm, Fig. 1B). Oral drug therapy was initiated for rate control and anti-coagulation in an outpatient clinic.

Twelve years before presentation (May 1995), he had received a diagnosis of hypertrophic non-obstructive cardiomyopathy. ECG showed signs of LV hypertrophy with normal QRS duration (Fig. 1A). Echocardiography showed eccentric LV hypertrophy with normal LV systolic function (Table 1). He had been treated with atenolol and imidapril for 2 years. Subsequently, he had discontinued medical treatment because he had no symptoms. There was no family history of hypertrophic cardiomyopathy or Fabry disease or sudden cardiac death (<50 years old).

At the beginning of January 2008, however, he felt severe dyspnea at rest, and was admitted to our hospital. Heart rate was 117 bpm and chest X-ray showed severe congestion of bilateral lung and pleural effusion. Echocardiography showed diffuse cardiac hypertrophy with LV ejection fraction (LVEF) of 17% (Table 1), and plasma brain natriuretic peptide (BNP) level was 1239 pg/ml.

Coronary angiography revealed normal coronary artery, while left ventriculography revealed severe LV dilatation and systolic dysfunction (LV end-diastolic volume index = 147 ml/m², LV end-systolic volume index = 123 ml/m², LVEF = 16%). Right ventricular endomyocardial biopsy was performed. This revealed central vacuolar degeneration of myocytes with concentric lamellar structure ‘zebra bodies,’ which are specific features of Fabry disease (Fig. 2). Leukocyte α-galactosidase A activity was measured and was below normal range (7.4 Agal U, cut off <17.0 in male). Cardiac magnetic resonance imaging showed hypertrophy of both ventricles. Late-enhanced signals after gadolinium infusion were observed (Fig. 3). The serum creatinine level was 0.9 mg/dl and total of urine peptide levels was <10 mg/(dl day). Since he did not present non-cardiac signs of Fabry disease such as cutaneous, renal, or gastrointestinal involvement, he was diagnosed with a cardiac variant of Fabry disease.

Atrial flutter was confirmed as typical atrial flutter by electroanatomical mapping and entrainment mapping. Subsequently, atrial flutter was terminated by linear ablation between inferior vena cava and tricuspid annulus, and bi-directional isthmus block was successfully verified.

Twelve-lead ECG revealed sinus rhythm and persistent left bundle branch block (QRS duration = 160 ms, Fig. 1C). ECG monitor recording revealed frequent episodes of non-sustained ventricular tachycardia (heart rate was 150 bpm and maximum duration was 13 s).

Although LVEF improved to 24%, transmitral Doppler flow revealed restrictive pattern indicating severe diastolic dysfunction (Table 1). Analyzing the LV dyssynchrony using tissue Doppler imaging (TDI), the difference in the time to peak systolic velocity of 4 LV basal segments [7] (septal, lateral, inferior, anterior) was 172 ms.

Cardiac resynchronization therapy with defibrillator (CRTD) was implanted with standard methods (Fig. 1D). After CRTD implantation, LVEF improved to 36% by decreasing the mechanical dyssynchrony.
Figure 3  (A) Cardiac magnetic resonance imaging shows hypertrophy of both ventricles. (B) Late-enhanced signals after gadolinium infusion is observed at the endocardial lesion (white arrow 1) and papillary muscle (white arrow 2) and mid-layer of interventricular septal wall (white arrow 3).

Plasma BNP level decreased to 532 pg/ml after CRTD implantation. Subsequently, oral carvedilol therapy, which had been intolerable before CRTD implantation due to hypotension and general fatigue, was successfully initiated. After the initiation of carvedilol, plasma BNP level further decreased to 325 pg/ml at the time of discharge. 6 min walk distance increased from 372 m to 506 m. The patient’s NYHA functional status improved from class IV to class I, and he was able to perform activities involving moderate effort without any cardiac symptoms.

He has been planned to be treated with enzyme replacement therapy since several studies have reported safety and efficacy of this approach [8,9].

Discussion

Several studies have identified Fabry disease as a relatively frequent cause of unexplained LV hypertrophy [10—12]. Fabry disease is associated with substantial risk for atrial fibrillation in middle-aged and elderly patients [5]. As reports of atrial flutter in Fabry disease are very rare, frequency and optimal treatment of atrial flutter remain unclear. Furthermore, it is recognized that Fabry disease patients are known to have ventricular tachycardia and occasionally suffer sudden cardiac death [4—6,13]. Since sudden cardiac death can be the first manifestation of Fabry disease, careful risk stratification is required.

To date, descriptions of CRT implantation for cardiac Fabry have been limited [4,5]. In patients with cardiac Fabry disease, LV end-diastolic dimension is increased and %fractional shortening is decreased during follow up [4]. In addition, an increase in QRS duration is seen [4], although prevalence of cardiac Fabry disease with left bundle branch block is not particularly common [5]. Of note, CRT can also improve diastolic function [14,15] and diastolic function is deteriorated even in the early phase of Fabry disease [16,17]. Consequently, cardiac Fabry disease with both systolic and diastolic dysfunction can be a candidate for CRT.

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References

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