Combined Vasodepressive and Cardioinhibitory Syncope in a Patient with Hypertrophic Cardiomyopathy

Ying-Hsiang Lee, Jui-Peng Tsai, Hung-I Yeh, Kuang Te Wang, Charles Jia-Yin Hou and Cheng-Ho Tsai

Syncope occurring in patients with hypertrophic cardiomyopathy (HCM) can be triggered by several mechanisms, among which autonomic dysfunction is often ignored. A 58-year-old woman was transferred to our hospital after resuscitation with epinephrine. She had had several episodes of unexplained syncope before. Her medical history included hypertension, obstructive HCM, and old ischemic stroke. Subsequent tests to explore the underlying cause of syncope, including coronary angiography, echocardiography, electrophysiologic study, and tilt table test, were inconclusive. An episode of near-syncope, associated with spontaneous lowering of blood pressure and then slowing of heart rate, was finally recorded and it was diagnosed as vagally mediated syncope related to autonomic dysfunction. After a pacemaker was implanted with special feature of rate drop response (RDR), the patient rarely had syncope in the following 12 months.

Key Words: Syncope • Autonomic dysfunction • Hypertrophic cardiomyopathy • Pacemaker • Rate drop response

INTRODUCTION

Altered autonomic cardiac control-related exercise hypotension is common in HCM. It presents with blunted blood pressure response with or without bradycardia.1 The pathophysiologic mechanism is similar to that of vasovagal syncope, and it can be treated effectively with several pharmacologic agents used for vasovagal syncope.2 The most popular diagnostic tool is the upright tilt table test, which shows abnormal vasodilatation in HCM. However, the disorder is still a diagnosis of exclusion most of the time, and relies on detailed history, physical examination plus serial images and/or tests. We report a lady with obstructive HCM and syncope, which was not related to exercise provocation and was successfully managed by permanent pacemaker with RDR.

CASE REPORT

A 58-year-old woman lost consciousness with no detectable pulse and was immediately given 1 mg of epinephrine intravenously by a local medical doctor. She was clear on arrival at the emergency room 20 minutes later; her heart rate was 111/min and blood pressure 219/119 mmHg. The electrocardiogram showed left ventricular hypertrophy, with ST-segment depression and T-wave inversion in the inferior leads and lateral leads (Figure 1). The cardiac enzymes were elevated (troponin-I 1.4 ng/mL, upper normal limit 1.0 ng/ml; CK/CKMB 522/24 U/L, upper normal limit 174/9.5 U/L). Other biochemistry and blood tests were within normal limits. The emergency coronary angiography was normal, with TIMI-3 flow.
The patient had had stage 1 hypertension 6 years before and mild left side weakness for more than 6 years. Transthoracic echocardiography (TTE) 6 years previous showed obstructive HCM, but the ventricular hypertrophy and outflow obstruction improved substantially after treatment with aspirin, β-blockade and verapamil (Table 1). Valsartan/hydrochlorothiazide was added one year before this event due to higher blood pressure.

The patient had many similar episodes of syncope and near-syncope for more than 6 years, which started before all medical therapies. They were usually self-limited and preceded by prodrome of malaise and breathlessness, which continued for a while after recovery from syncope. All episodes were not associated with specific triggering events, and cardiac enzymes checked in some of the attacks were all normal prior to this admission. Extensive studies, including serial carotid duplex and Holter monitoring, were inconclusive except for old lacunar infarcts in the right putamen and thalamus on the brain computed tomography (CT), which was re-confirmed by electroencephalography (EEG). Off-drug electrophysiologic studies showed normal sinus node recovery time, atroventricular node conduction and no inducible tachyarrhythmia on isoproterenol 1 μg/minute. Postural orthostatic tachycardia syndrome was observed by upright tilt table test; however, it could not have con-

### Table 1. Echocardiographic findings

<table>
<thead>
<tr>
<th>Date</th>
<th>Jun. 21, 1997</th>
<th>Jan. 17, 2000</th>
<th>Sep. 27, 2005</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVS*</td>
<td>19 mm</td>
<td>16 mm</td>
<td>13 mm</td>
</tr>
<tr>
<td>LVPW†</td>
<td>14.2 mm</td>
<td>12 mm</td>
<td>12 mm</td>
</tr>
<tr>
<td>IVS/LVPW</td>
<td>&gt; 1.3</td>
<td>&lt; 1.3</td>
<td></td>
</tr>
<tr>
<td>LVOT PG‡</td>
<td>49 mmHg</td>
<td>41.7 mmHg</td>
<td>31 mmHg</td>
</tr>
<tr>
<td>LVEDV§</td>
<td>97.8 mL</td>
<td>108 mL</td>
<td>123 mL</td>
</tr>
<tr>
<td>LVEF</td>
<td></td>
<td></td>
<td>68.9%</td>
</tr>
<tr>
<td>SAM¶</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

*A IVS = interventricular septum, †LVPW = left ventricular posterior wall, ‡LVOT PG = left ventricular outflow tract pressure gradient, §LVEDV = left ventricular end-diastolic volume, ||LVEF = left ventricular ejection fraction, ¶SAM = systolic anterior motion.*
tributed to all the patient’s resting episodes.

During admission in ICU, the patient frequently complained of dyspnea and malaise, which was associated with unexplained hypotension and variable bradycardia. An episode of junctional rhythm with ventricular asystole lasting even for 2.96 seconds was noted. It always spontaneously resolved and was too rapid to understand the relationship between the symptoms and vital signs. We therefore applied continuous arterial blood pressure plus electrocardiographic monitoring and successfully recorded a course of attack (Figure 2). Initially, the patient experienced breathlessness and malaise in a peaceful supine position without triggering events. Blood pressure and heart rate dropped sequentially thereafter. Vital signs returned to normal spontaneously but there were still residual symptoms lasting for minutes. The tracing was compatible with cardioinhibitory vagally mediated reflex. The similar attacks occurred 5 more times even days after discontinuing β-blockade and all the other hypotensive agents. In two such episodes, the bradycardia was reversed by 1 mg of intravenous atropine.

Owing to the bradycardia and vagally mediated syncope, the patient received a permanent pacemaker backup with DDI mode and RDR (Medtronic Kappa KDR903; settings: both drop rate/size = 60 ppm/25 bpm, intervention rate/duration = 100 ppm/2 min, detection window = 15 min), designed for neurocardiogenic syncope, which would initiate pacing at 100 ppm for 2 minutes when detecting rate reduction of more than 25 bpm and below 60 bpm in two consecutive beats within 15 minutes of detection window. During the following 12 months, the frequency of syncope was effectively decreased from 5-6 times per month to only once in 12 months. Although the patient still experienced vagally mediated “prodrome” frequently, the duration was shortened with attenuation of post-attack residual symptoms. The patient was satis-

![Figure 2. The first strip showed baseline BP 123/61 mmHg and HR 58/min. The second strip showed unexpected drop of BP, with nadir of 79/48 mmHg (arrows). HR slightly rose to 69/min (15%) in the following four minutes. The third strip showed HR finally dropped, with junctional bradycardia during the eighth minute. (BP: blood pressure, HR: heart rate).](image-url)
fied at the improvement in quality of life.

DISCUSSION

Syncope is a common problem seen in patients with HCM visiting the emergency department. The underlying mechanisms are diverse. It may even evolve to sudden cardiac death, usually due to tachyarrhythmia, bradyarrhythmia, myocardial ischemia, outflow tract obstruction, and/or diastolic dysfunction. Therefore, accurate diagnosis is necessary to guide the treatment. However, the interval of recurrence ranges from minutes to years, making the diagnosis difficult. Among unexplained syncope, neurally mediated syncope, including vasovagal syncope (also named as neurocardiogenic syncope), accounts for 50-66% of incidence in general population. This type of syncope is attributed to the dysfunction of the autonomic nervous system to regulate the heart rate and blood pressure. Up to one third of patients with HCM have altered autonomic control that either blunts the increase of blood pressure or induces inappropriate vasodilatation during exercise. It hypothetically results from the activation of left ventricular mechanoreceptors or local wall strain with reduced cardiopulmonary baroreflex sensitivity. Vagal action is thus introduced via brain stem and sometimes leads to bradycardia and/or syncope. The paradoxically abnormal vasodilatation can result in collapse without impaired cardiac output or dysrhythmia, not always related to left ventricular outflow obstruction. Therefore, exercise hypotension with variable bradycardia is one of the characteristics of dysautonomia in HCM, similar to vasovagal reflex. The diagnosis of syncope is usually a disease of exclusion. Drug effects, arrhythmias, structural heart diseases, organic brain lesion and seizure must be ruled out. The history, physical examination, and specific tests also play important roles. A history of obstructive HCM is traditionally characterized by a triggering event such as exercise, myocardial ischemia or any events leading to dynamic increase of left ventricular outflow pressure gradient. In vagally mediated syncope, the patients typically have a prodrome and “residual” symptoms before and after syncope that helps to distinguish it from arrhythmic syncope. Further differentiation of carotid sinus hypersensitivity can be made by carotid massage. Orthostatic hypotension must be preceded by upright position clinically, not defined only by any tests. Upright tilt table test is a convenient tool to reassure and differentiate altered autonomic hypotension, including vasovagal syncope, orthostatic hypotension and inappropriate hypotension in HCM. But its negative predictive value was only 43%.

In our patient with obstructive HCM and unexplained syncope, serial examinations including brain CT and EEG, and carotid artery duplex made organic brain disorders least likely. Normal coronary angiography may exclude the possibility of acute ischemia as the cause of recurrent syncope, in particular if there has been no elevation of cardiac enzymes in the last few years. While ventricular tachycardia cannot be absolutely ruled out by negative electrophysiologic studies, it is rare in this condition. Although TTE showed left ventricular outflow tract obstruction (resting left ventricular outflow tract pressure gradient, 31 mmHg), there was no SAM. Dynamic change of pressure gradient should be evaluated by exercise test, but the patient could not perform the test due to sequela of old cerebral infarct. However, it could be grossly excluded by events neither associated with exercise nor tachycardia via history. Vagally mediated syncope is the most likely etiology in prevalence, either dysautonomia in HCM or vasovagal reaction in general population. However, it is difficult to diagnose definitely in the absence of physical and emotional triggering events. Postural orthostatic tachycardia syndrome noted by upright tilt test could not have contributed to all the resting supine episodes in this case but it was suggestive of altered autonomic function. As another clue of autonomic dysfunction, heart rate variability before pacing was lacking in this case. Eventually, continuous arterial blood pressure plus electrocardiographic monitoring simply and cost-effectively led us to our diagnosis.

Because abnormal vasodilatation with bradycardia in HCM is similar to the mechanism of vasovagal reflex, Thaman et al. effectively treated it with medications which were used for vasovagal syncope. Our patient basically had high blood pressure (180/100 mmHg) and low heart rate (60/min), which excluded the use of these drugs. Her previous long-term administration of β-blocker also suggested further dose titration useless, and α-agonist was not appropriate to stage 2 hypertension. Her increasing frequency of syncope complicated by non-occlusive myocardial damage discouraged us to treat con-
servatively. Fortunately, documented vagally mediated syncope with junctional bradycardia and the near-three seconds of ventricular asystole permitted us to try pacemaker backup (class II indication in vasovagal treatment) with RDR. Although RDR is considered a second-line treatment for cardioinhibitory vasovagal syncope in improving quality of life, it has not been applied for HCM-related dysautonomic syncope. Our patient may be the first case of HCM paced with RDR to overcome vagally mediated syncope. The benefit of such a treatment to quality of life in our patient was apparent.

CONCLUSION

In patients with HCM related cardioinhibitory syncope, pacemaker with RDR may be helpful to improve quality of life.

REFERENCES

肥厚型心肌病變患者合併有血管張力失調型及心臟抑制型昏厥

李應湘1 蔡瑞鵬2 葉宏一1 王光德2 侯嘉殷1 蔡正河1
台北市 馬偕紀念醫院 內科部 心臟内科1
台東縣 馬偕紀念醫院台東分院 心臟内科2

肥厚型心肌病變患者可經由數種機轉導致昏厥，自律神經失調是其中較少被報導的一種。本文報告一名五十八歲女性罹患高血壓、阻塞性肥厚型心肌病變及陳舊性中風。她經歷數次昏厥但原因不明。在某次發作時，診所醫師投予腎上腺素治療並轉至本院。一連串的檢查包括冠狀動脈攝影、心臟超音波、心臟電氣生理檢查及傾斜床檢查等皆無法找出病因。最後經由連續性血壓暨心律監視器紀錄了一次自發性低血壓伴隨心率下降，讓我們得以診斷為自律神經失調引起的迷走神經相關性昏厥 (vagally mediated syncope)。經心臟節律器施予心率下降反應 (rate drop response) 治療，患者再接下來十二個月得到明顯改善。

關鍵詞：昏厥、自律神經失調、肥厚型心肌病變、心臟節律器、心率下降反應。