Case Report

Recurrent syncope in two patients with a sigmoid-shaped interventricular septum and no left ventricular hypertrophy

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Abstract

Sigmoid-shaped interventricular septum (SIS) is not uncommon in elderly patients and is considered a normal part of the aging process. However, several patients have been reported to have clinical symptoms due to the narrowing of the left ventricular outflow tract (LVOT). Two patients with SIS presented with recurrent episodes of syncope after drinking or taking sublingual nitroglycerin (NG). In both patients, a head-up tilt test involving provoked with alcohol, NG, or isoproterenol induced the vasovagal reflex along with an increase in the pressure gradient between the apex and LVOT. The patients experienced no further episodes of syncope after initiating bisoprolol treatment. In patients with SIS, induction of the vasovagal reflex via an increase in left ventricular (LV) pressure due to LVOT obstruction concomitant with increased LV construction is a potentially important cause of syncope, which may be effectively prevented by beta-blockers.

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1. Introduction

A sigmoid-shaped interventricular septum (SIS) is generally considered a normal part of the aging process and of little clinical significance. However, certain patients with SIS may experience clinical symptoms such as dyspnea upon effort and syncope. In patients with hypertrophic obstructive cardiomyopathy (HOCM), narrowing of the left ventricular outflow tract (LVOT) generates a left ventricular (LV) pressure gradient, resulting in reduced cardiac output and subsequent syncope. In these patients, the vasovagal reflex, i.e., the Bezold-Jarisch reflex [1], could play an important role in the occurrence of syncope. By contrast, the mechanisms of syncope in patients with SIS without left ventricular hypertrophy (LVH) [2–4] have yet to be fully elucidated. Here, we report two patients with SIS who presented with recurrent syncope. We were successful in clarifying the mechanisms of syncope and effects of beta-blockers in these cases.

2. Case 1

An 81-year-old man with no history of heart disease was admitted to our hospital for the treatment of recurrent episodes of syncope after drinking. He experienced the first episode at age 75. On admission, his blood pressure (BP) was 144/81 mmHg and the heart rate (HR) was 56 beats/min. Physical examination was otherwise unremarkable except for a grade 2/6 systolic ejection murmur at the apex area. Routine blood tests were unremarkable. A chest X-ray revealed a cardiothoracic ratio of 51%. An 12-lead electrocardiogram revealed normal sinus rhythm and left axis deviation without LVH, ST segment depression, and T-wave inversion.

Two-dimensional transthoracic echocardiography (2DE) revealed an SIS protruding into the LV (Fig. 1A) and normal systolic function (ejection fraction, 77%). LVH was not evident (interventricular septum/posterior wall = 8/8 mm). Color Doppler echocardiography revealed turbulent systolic flow at the LVOT with a pressure gradient of 8 mmHg, determined by continuous-wave Doppler (Fig. 1B). The reliability of the Doppler measurement of the pressure gradient at the LVOT was validated by a board-certified fellow of the Japan Society of Ultrasonics in Medicine (JSUM). M-mode echocardiography demonstrated systolic anterior movement of the mitral chordae tendineae. To investigate the cause of syncope after drinking, a head-up tilt test (HUT) was performed with 25 g of alcohol loading. At 16 min of a
60-degree HUT, the LVOT pressure gradient increased from 8 to 176 mmHg, and M-mode echocardiography demonstrated mid-systolic hemiclosure of the aortic valve (Fig. 1C). At 18 min of the head-up tilt test, blood pressure (BP) and heart rate (HR) decreased, and the patient experienced presyncopal symptoms.

3. Case 2

A 66-year-old man presented with recurrent syncope after drinking. On admission, his BP and HR were 123/82 mmHg and 65 beats/min, respectively. Physical examination was unremarkable except for a grade 2/6 systolic ejection murmur at the fourth intercostal space on the left sternal border. An electrocardiogram revealed sinus rhythm (62 beats/min) and left axis deviation without LVH and ST-T changes. His chest X-ray was normal, and 2DE showed SIS with normal systolic function (ejection fraction, 74%). LVH was not evident (interventricular septum/posterior wall = 6/6 mm). Color Doppler echocardiography revealed...
turbulent systolic flow at the LVOT with a peak pressure gradient of 8 mmHg, determined by continuous-wave Doppler. M-mode echocardiography demonstrated systolic anterior movement of the mitral chordae tendineae.

After excluding other possible causes of syncope with non-invasive tests, HUT was performed (Fig. 2). No symptoms occurred, and both BP and HR were not significantly decreased during the baseline tilt (60°) or during HUT+NG. However, presyncopal symptoms developed in association with abrupt hypotension and bradycardia at 2.5 min of HUT with an isoproterenol infusion (0.015 μg/kg/min). A Task Force Monitor™ (CN Systems, Graz, Austria) revealed that at the time of presyncope, total peripheral vascular resistance (TPR) decreased (Fig. 2) and high-frequency power increased (Fig. 3). Therefore, a diagnosis of vasovagal reflex was made based on the HUT with an isoproterenol infusion. An isoproterenol provocation test was also performed in the supine position. At 1 min and 46 s after initiating the isoproterenol infusion (0.02 μg/kg/min), hypotension and sinus bradycardia were induced along with ventricular escape beats and presyncopal symptoms (Fig. 4). At that time, the peak pressure gradient at the LVOT was increased from 8 to 59 mmHg with a decrease in TPR. We started the patient on bisoprolol (2.5 mg/day), and his syncopal episodes have not recurred since.

4. Discussion

SIS is a morphological characteristic of the basal interventricular septum that protrudes into the LV cavity. This cardiac malformation has generally been considered a natural part of aging without pathophysiological or clinical significance [5,6]. However, several studies demonstrated that SIS could be

![Fig. 3. Analysis of heart rate variability during the head-up tilt test in Case 2. During head-up tilt test after nitroglycerine (NG) intake, the power of the high-frequency component (HF, 0.15–0.4 Hz) decreased. However, it increased during the head-up tilt test with isoproterenol (ISP) infusion (arrow).](image)

![Fig. 4. Changes in blood pressure and the pressure gradient of the left ventricular outflow tract in the supine position in Case 2. At 1 min and 46 s after the start of isoproterenol infusion (0.02 μg/kg/min), sinus bradycardia with a ventricular escape rhythm and hypotension developed acutely and the patient experienced presyncopal symptoms. The peak pressure gradient (ΔPG) at the left ventricular outflow tract increased from 8 to 59 mmHg. BP = blood pressure, HR = heart rate, TPR = total peripheral resistance.](image)
associated with clinical symptoms such as dyspnea on effort and syncope, as seen in patients with HOCM. Syncope in patients with SIS might be attributable to an increase in the LVOT pressure gradient, particularly when vasodilators or inotropic drugs are administered [2,4]. In patients with SIS, recurrent syncope and dyspnea on effort are caused by a decrease in cardiac output through LVOT obstruction, as in patients with HOCM [7]. Class Ia antiarrhythmic drugs such as cibenzoline as well as β-blockers have been effective in treating these symptoms [2–4,8]. However, in patients with SIS, vasovagal reflex could be an important cause of syncope. In Case 1, a decrease in cardiac venous return caused by the vasodilatory effects of alcohol or NG reduced cardiac output, thereby enhancing sympathetic nerve activity. These changes also increased LV contraction and LV pressure due to LVOT obstruction. An increase in LV pressure concomitant with increased LV contraction can induce vasovagal reflex via activation of the LV mechanoreceptor [9]. In Case 2, presyncopal symptoms with hypotension and bradycardia developed during HUT with an isoproterenol infusion (Fig. 3). A decrease in cardiac venous return caused by a 60-degree HUT reduced LV volume, resulting in increased sympathetic nerve activity. Isoproterenol further enhanced LV contraction and LVOT obstruction, and vasovagal reflex was similarly induced via activation of the LV mechanoreceptor as in Case 1. Because high-frequency power was increased at the time of presyncope in Case 2, isoproterenol induced not only LVOT obstruction but also vasovagal reflex, resulting in hypotension and bradycardia.

The narrowing of the LVOT along with an increase in the left ventricular pressure gradient might be related to clinical symptoms in patients with SIS, as seen in HOCM patients. It is well known that the negative inotropic action of β-blockers decreases the LVOT pressure gradient and can prevent syncope in patients with HOCM. However, the efficacy of β-blockers for the prevention of syncope has not been fully clarified in patients with SIS. The administration of cibenzoline in addition to atenolol was recently reported to decrease the LV pressure gradient, thereby relieving clinical symptoms in patients with SIS [3]. In the present study, we showed that the vasovagal reflex played a major role in the induction of syncope. We further showed that bisoprolol could prevent syncope by decreasing the LV pressure gradient in two patients with SIS. Unfortunately, we did not test the effects of cibenzoline in our patients.

Conflict of interest

None.

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