【 CASE REPORT 】

Total Clinical Course and Autopsy Findings of Left Ventricular Outflow Tract Obstruction Due to Sigmoid Septum: Histologically Proven Isolated Basal Septal Hypertrophy

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Abstract:

We herein report the total course and autopsy findings of a woman who complained of chest discomfort and had plasma B-type natriuretic peptide 43 pg/mL and left ventricular outflow tract obstruction (with a resting pressure gradient of 181 mmHg) due to sigmoid septum at 73 years of age. Betaxolol and verapamil decreased her pressure gradient to 14 mmHg, but the pressure gradient (101 mmHg) again worsened. The betaxolol dose was increased and cibenzoline was added, resulting in a pressure gradient ≤21 mmHg. An autopsy was performed after death from a urinary tract infection at 80 years of age. The absence of any disarray of cardiac myocytes was confirmed.

Key words: sigmoid septum, autopsy finding, left ventricular outflow tract obstruction

Introduction

Several terms have been used to describe basal septal bulge in older adults, including sigmoid septum, isolated basal septal hypertrophy, discrete upper septal hypertrophy, and sigmoid-shaped interventricular septum. Recent reports (1-3) showed that medical therapy with beta-blockers or cibenzoline was effective in resolving left ventricular outflow tract obstruction (LVOTO) caused by sigmoid septum. Based on echocardiography, however, it may be difficult to determine whether basal septal bulge with LVOTO indicates hypertrophic cardiomyopathy (HCM) or the more benign sigmoid septum, namely isolated basal septal hypertrophy. This is the first report of a histologically proven sigmoid septum-induced LVOTO that was relieved by medical treatments including beta-blockers, verapamil, and cibenzoline.

Case Report

We herein report the case of a 73-year-old woman with a history of essential hypertension, cerebral infarction, and Parkinsonism. The patient measured 146 cm in height and weighed 42 kg. Her blood pressure was 124/76 mmHg, and her heart rate was 84 beats/min.

Hypertension was first diagnosed at 50 years of age, and antihypertensive medications were initiated. At 64 years of age, echocardiography showed no abnormality. At 71 years of age, echocardiography showed no left ventricular (LV) hypertrophy (LVH) and an LV outflow tract (LVOT) velocity of 1.9 m/s. At 73 years of age, she had chest discomfort, but her electrocardiogram was nearly normal. By echocardiography, hypertrophy was sharply confined to the basal septum just below the aortic valve (basal septal bulge). The
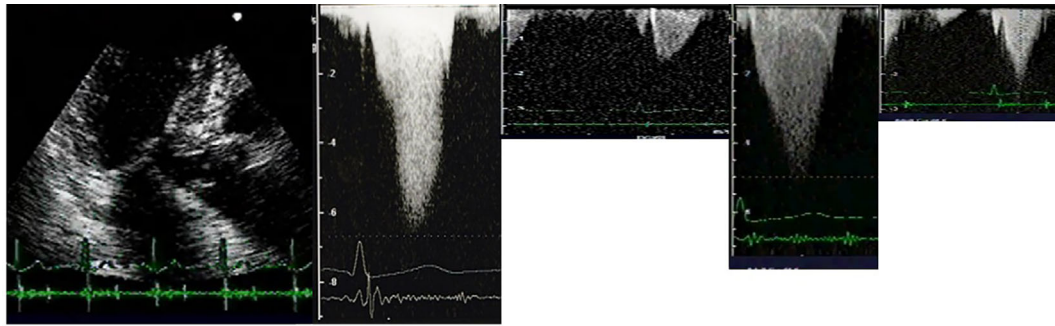
Age (years)	73	74	75	77
Rest LVOT velocity (m/s)	6.7	1.8	5.0	2.3
Rest LVOT pressure gradient (mmHg)	181	14	101	21

Figure 1. An echocardiographic image (apical 3 chamber view) and changes in Doppler imaging with age, showing a resting LVOT pressure gradient. Hypertrophy measuring 15 mm confined to the basal septum just below the aortic valve (basal septal bulge), SAM of the mitral valve, and an increased late systolic velocity peak (at 73 and 75 years of age) were observed. The LVOT pressure gradient was estimated by the simplified Bernoulli equation. Four images were adjusted to the same velocity scale. LVOT: left ventricular outflow tract, SAM: systolic anterior motion
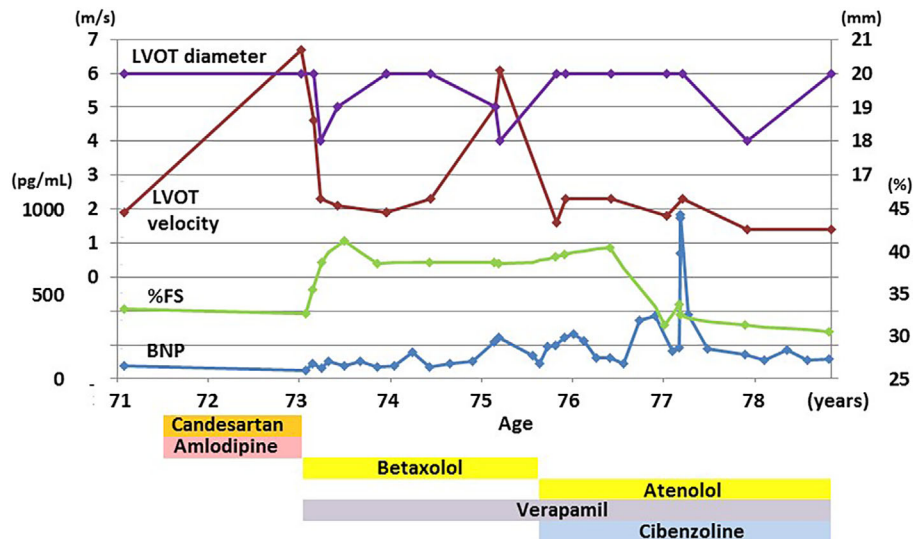

Figure 2. Changes in the echocardiogram measurements (LVOT diameter at diastole, LVOT velocity, and %FS), BNP, and medical treatments with age. The narrowing of the LVOT diameter with the occurrence of an increased LVOT velocity was observed at 73 and 75 years of age. LVOT: left ventricular outflow tract, %FS: percent fractional shortening, BNP: B-type natriuretic peptide

aorto-septal angle was 105°, and systolic anterior motion (SAM) of the mitral valve, severe mitral regurgitation and LVOTO, with a peak gradient of 181 mmHg at rest were observed (Fig. 1, 2). The LV end-diastolic dimension was 35 mm and the left atrial dimension was 40 mm. The diastolic thickness of the ventricular septum and the posterior LV wall were both 8 mm. The percent fractional shortening (%FS) was 33%, and the early to atrial transmitral peak velocity ratio was 0.67. Her plasma B-type natriuretic peptide (BNP) concentration was 43 pg/mL.

Since the SAM in our patient was very similar to that of individuals with HCM, we considered conventional treatment options for hypertrophic obstructive cardiomyopathy (HOCM) for our patient. Medication for hypertension with 8 mg candesartan daily and 5 mg amlodipine daily was discontinued, and 5 mg betaxolol daily and 80 mg verapamil daily were started (Fig. 2). She reported a marked symptomatic improvement after starting these treatments.

At 74 years of age, betaxolol and verapamil decreased her pressure gradient to 14 mmHg (Fig. 1, 2). At 75 years of age, a worsening of LVOTO with a peak gradient of 101 mmHg at rest over time following an initial response to a beta-blocker and verapamil was observed (Fig. 1, 2). At the same time, a narrowing of the LVOT diameter at diastole (18 mm) was also found (Fig. 2). Coronary angiography showed no significant coronary artery stenosis. The be-
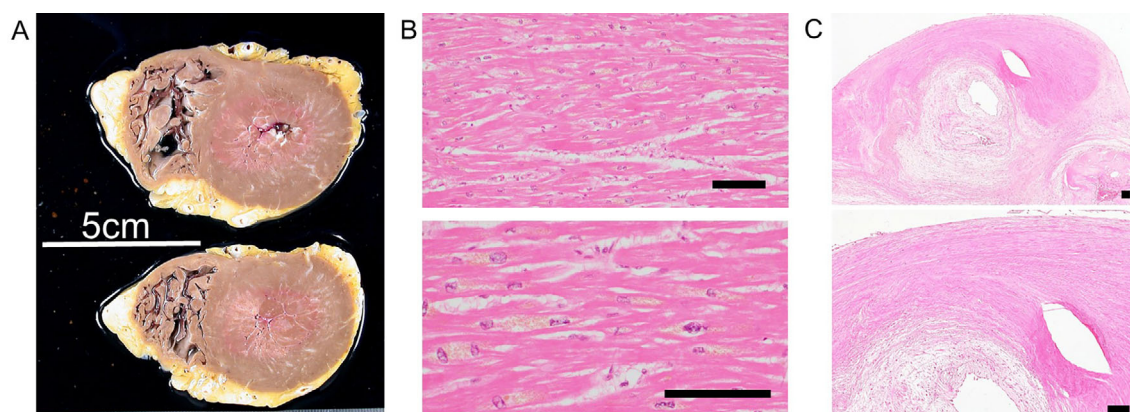
Figure 3. Autopsy specimens. (A) Sequential autopsy myocardium specimens. There were no findings of asymmetric septal hypertrophy. (B) Tissue preparations show cardiac myocytes without disarray [Hematoxylin and Eosin (H&E) staining; bars: 100 μm]. (C) The aortic surface of the anterior mitral valve cusp which showed macroscopic thickening. Histology showed superficial dense collagenous and elastic thickening of the endocardium which is characteristic of friction lesions as the result of repeated systolic contact between the free edge of the cusp and the septum (H&E staining; bars: 100 μm).

Table. Literature Review for Baseline Characteristics, Including BNP Levels, in Patients with Left Ventricular Outflow Tract Obstruction Due to Sigmoid Septum.

Reference	Age	Sex	Rest LVOT PG (mmHg)	BNP (pg/mL)	LVH	Histology
[2] (n=2)	64	M	136	17	(-)	ND
	78	M	83	27	(-)	ND
[7]	74	F	100	85	(-)	Myectomy, disarray (±)
[12] (n=3)	71±7	U	76±42	282±173	(-)	ND
[1]	83	F	122	455	(+)	ND
Present case	73	F	181	43	(-)	Autopsy, disarray (-)

BNP: B-type natriuretic peptide, F: female, LVH: left ventricular hypertrophy, LVOT: left ventricular outflow tract, M: male, ND: not done, PG: pressure gradient, U: unknown

taxolol dosage was increased up to 10 mg daily, resulting in a pressure gradient of 13 mmHg. However, because dobutamine stress echocardiography of 20 μg/kg/min showed LVOTO with a peak gradient of 108 mmHg, 300 mg cibenzoline daily was added. At that time, betaxolol was changed to 100 mg atenolol daily by the attending physician. Thereafter, her resting pressure gradient was less than or equal to 21 mmHg (Fig. 1, 2).

An autopsy was performed after she died at 80 years of age due to a urinary tract infection and sepsis. The weight of her heart was within the normal range at 315 g (4). As shown in Fig. 3, there were no findings of asymmetric septal hypertrophy. Histologic evidence of myofiber disarray was not present in any transverse sections of her heart. Although no remarkable macroscopic abnormality was found in her chordae tendineae and papillary muscles, her anterior mitral valve cusp showed moderate macroscopic thickening. As shown in Fig. 3, the aortic surface of her anterior mitral cusp had the microscopic features of an endocardial friction lesion due to systolic contact between the cusp and septum, namely SAM.

Discussion

To the best of our knowledge, this is the first report of a histologically proven sigmoid septum (isolated basal septal hypertrophy)-induced LVOTO that could be successfully relieved by medical treatments. In clinical practice, when a basal septal bulge is associated with SAM and LVOTO, a diagnosis of HCM is often made. However, McLeod et al. (5) found that HCM with the sigmoid-shaped septum exhibited the mildest degrees of disarray. Belenkie et al. (6) reported that an autopsy performed in one patient with localized septal hypertrophy and without SAM showed no fiber disarray. In addition, according to Fujita et al. (7), a specimen of the resected septum in sigmoid septum with LVOTO showed only slight myocardial disarray, which was not compatible with HCM. In the present case, HCM was completely ruled out as a cause of basal septal bulge based on the autopsy findings.

The Table reviews the literature for baseline characteristics, including BNP levels, in patients with LVOTO due to sigmoid septum. In four out of eight patients, including the

present case, the BNP levels were <100 pg/mL. Sigmoid septum is generally considered to be an incidental finding associated with older age and hypertension (4). The plasma BNP levels were 27±17 pg/mL in hypertensive patients (8). In addition, the plasma BNP levels were <100 pg/mL in 83% of hypertensive patients (9). On the other hand, Nishigaki et al. (10) reported the mean plasma BNP levels in patients with HOCM to be 397±168 pg/mL and BNP levels were greater than 200 pg/mL in 87% of the patients with HOCM. Hamada et al. (11) showed the mean plasma BNP concentration in patients with HOCM to be 431±296 pg/mL. Therefore, the plasma BNP levels <100 pg/mL might be used to distinguish patients with sigmoid septum with LVOTO from those with HOCM. However, as shown in Table, when the BNP is >100 pg/mL (1, 12), it may be difficult to determine on the basis of the BNP level whether basal septal bulge with LVOTO indicates HCM or sigmoid septum.

In patients with sigmoid septum, SAM and LVOTO may develop due to hypercontraction of the left ventricle, which may be attenuated by medications with negative ionotropic effects (2, 3). However, in patients with LVOTO without typical HCM, the mean %FS at post-treatment, including beta-blockers, declined by 5.45%, but this decrease failed to reach statistical significance (3). Additionally, %FS remained unchanged after the chronic use of cibenzoline in patients with HOCM (13). Recently, Uematsu et al. (14) found that the non-HCM patients with sigmoid septum showed SAM not only under hyperkinetic conditions, but also under resting conditions (mean LV ejection fraction 57%). As shown in Figs. 2 and 3, in the present case without LV hypercontraction (%FS 33%), SAM of the anterior mitral leaflet was apparently responsible for LVOTO. In addition, an enlargement of the narrowed LVOT diameter seems to be important for attenuating the LVOT velocity by medical therapy. Indeed, the LVOT diameter at diastole was smaller (p<0.001) in the latent LVOTO (+) group than the latent LVOTO (-) group in non-LVH patients with malignancy (15). Therefore, LVOT narrowing by sigmoid septum seems to be the primary mechanism responsible for SAM and LVOTO in the present case. In addition, age-related anatomical changes, such as a shorter end-systolic mitral leaflet tethering distance in the sigmoid septum, may predispose the occurrence of SAM (16), although no remarkable macroscopic abnormality was found in the mitral apparatus of our case.

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