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Citation	Journal of Cardiology Cases. 26(1); 66-69
Issue Date	2022-07
Version of Record	2022-06-30
Type	Journal Article
Textversion	Author
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DOI	10.1016/j.jccase.2022.02.010

Okada, N., Shibata, A., Tanihata, A., Kitada, R., Ehara, S., & Izumiya, Y. (2022). A case of hypertrophic cardiomyopathy with right ventricular outflow tract and left midventricular obstruction. *Journal of Cardiology Cases*. 26, 66–69. https://doi.org/10.1016/j.jccase.2022.02.010

A case of hypertrophic cardiomyopathy with right ventricular outflow tract and left midventricular obstruction

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Keywords: hypertrophic cardiomyopathy, midventricular obstruction, right ventricular outflow tract obstruction

Total word count: 1,322 words (excluding title page, abstract, references, figures and tables)

Declarations of interest: none

Abstract

We describe a case of a 59-year-old woman with hypertrophic cardiomyopathy who remained right ventricular outflow tract obstruction after the pressure gradient in the left midventricle was resolved by a drug with a negative inotropic effect. The patient was diagnosed with hypertrophic cardiomyopathy 30 years ago and was only on low-dose beta-blocker therapy. She presented at our hospital with suspected exacerbation of heart failure because of the development and exacerbation of dyspnea and chest tightness. Transthoracic echocardiography showed an accelerated blood flow of 3 m/s in the middle of the left ventricle; thus, she was started on *cibenzoline*, a drug with a negative inotropic effect. After admission, intracardiac pressure measurement showed no pressure gradient in the left chamber. However, there was a pressure gradient of 18 mmHg between the apex of the right ventricle and the right ventricular outflow tract, and right ventricular outflow tract obstruction was confirmed on cardiac magnetic resonance imaging. We decided to reinforce the negative inotropic effect by adding *bisoprolol*, and the subjective symptoms and auscultatory systolic murmur were eliminated 2 months later.

Learning objective

Hypertrophy of the right ventricular myocardium can occur in patients with hypertrophic cardiomyopathy (HCM). However, right ventricular outflow tract obstruction remains a rare finding in patients with HCM, despite the presence of morphological abnormalities such as right ventricular hypertrophy. In patients with HCM, obstruction of the right ventricle should be considered if the symptoms and auscultatory findings do not match the left ventricular imaging findings.

Introduction

Hypertrophic cardiomyopathy (HCM) is a hereditary disease characterized by primary hypertrophy of the left and/or right ventricular myocardium and decreased left ventricular diastolic function due to cardiac hypertrophy. Obstructive HCM is defined as a peak instantaneous gradient of ≥ 30 mmHg at rest in the left ventricular outflow tract (LVOT) or the left ventricle. Luminal stenosis in the midventricle is termed midventricular obstruction (MVO) and is reported to account for about 10% of Japanese HCM cases [1]. Although less attention has been paid to the right ventricle than the left in patients with HCM, hypertrophy of the right ventricular myocardium may also occur. Right ventricular hypertrophy with a maximum wall thickness of 8 mm or more is reportedly observed in 33% of patients with HCM [2]. However, despite the known presence of right ventricular hypertrophy in patients with HCM, right ventricular outflow tract obstruction (RVOTO) remains a rare finding. We herein report a case of a patient with HCM in whom RVOTO manifested after MVO was resolved by a drug with a negative inotropic effect.

Case report

A 59-year-old woman receiving pharmacological treatment for HCM that had been diagnosed 30 years previously was referred to our department for investigation of dyspnea. Thirty years earlier, she had presented to hospital with dyspnea, underwent a myocardial biopsy, and was diagnosed with HCM. However, she had since changed hospitals and continued to take only a small dose of a beta-blocker. She presented to a primary care physician owing to the recurrence and exacerbation of dyspnea plus chest tightness during exertion, and was referred to our hospital. She was started on

cibenzoline (150 mg/day) because transthoracic echocardiography showed an accelerated blood flow of 2 m/s in the LVOT and 3 m/s in the left midventricle (Fig. 1). However, the dyspnea on exertion did not improve, so she was admitted to hospital for further investigation.

On admission to our hospital, the patient had a heart rate of 75 bpm and blood pressure of 131/85 mmHg. Chest auscultation revealed a grade 3/6 harsh midsystolic murmur that was loudest at the second intercostal space on the left sternal border. Pulmonary auscultation was normal. Chest radiography showed cardiac enlargement without pulmonary congestion. Electrocardiography showed left axis deviation, left ventricular high potential, and a deep S wave of V5–6. Cardiac magnetic resonance imaging showed asymmetric left ventricular thickening of the anterior wall, septum, and inferior wall, and MVO. In addition, there was late gadolinium enhancement at the ventricular junction of the anterior and inferior walls, and non-contrast T1 mapping revealed an extension at the same site. Coronary angiography showed no significant stenosis. Left and right ventriculography revealed no obvious stenosis in the left midventricle, but a narrowed area in the right ventricular outflow tract (RVOT) (Fig.2). Intracardiac pressure measurements showed a left ventricular apical pressure of 139/21 mmHg, left midventricular distal pressure of 148/21 mmHg, left midventricular proximal pressure of 147/19 mmHg, and LVOT pressure of 138/20 mmHg. No clear pressure gradient was observed in the left chamber. However, the pressure at the apex of the right ventricle was 43/7 mmHg, while the pressure at the RVOT was 25/6 mmHg, resulting in an 18-mmHg pressure gradient between the apex of the right ventricle and the RVOT (Fig. 3). RVOTO was also confirmed on sagittal cross-sectional cardiac magnetic resonance imaging (Fig. 4).

The cardiopulmonary exercise test showed no increase in the end-tidal carbon dioxide concentration after the start of exercise, suggesting that the exercise may not have caused the expected increase in pulmonary blood flow; this was thought to be one of the causes of the awareness of dyspnea on exertion. However, it is unclear whether this is due to RVOTO or to the severe diastolic dysfunction associated with HCM.

Because the pressure gradient of the RVOT was about 18 mmHg and we judged that the patient had no surgical indication, we decided to reinforce the treatment with negative inotropic drugs. After 2 months of oral *cibenzoline* (150 mg/day) and *bisoprolol* (2.5 mg/day), the subjective symptoms and auscultatory systolic murmur had been eliminated. The symptom-free ambulatory blood pressure was 124/70 mmHg, and there was no negative chronotropic effect. Although we considered confirming the success of the treatment by performing dobutamine stress echocardiography, a screening computed tomography scan revealed pancreatic head carcinoma and we decided to prioritize the treatment of the carcinoma.

Discussion

We present a patient with HCM with MVO and RVOTO. The prevalence of right ventricular involvement in HCM is unknown. A previous study of 46 patients with HCM detected right ventricular hypertrophy of > 8 mm in 15 (33%) patients, and right ventricular hypertrophy of > 10 mm in four (9%) [2]. In another study of 73 patients with HCM, 33% demonstrated mild (5–8 mm) right ventricular hypertrophy, while 10% showed moderate (9–12 mm) right ventricular hypertrophy [3]. Thus, mild right ventricular hypertrophy may be relatively common. However, despite the known presence of right ventricular involvement in patients with HCM, RVOTO remains a rare

finding. Although a small study reported that RVOTO is found in nearly 10% of patients with HCM [4], there have been no previous reports of RVOTO remained after MVO was resolved by a drug with a negative inotropic effect, as in the present case.

Although there is no standard definition of RVOTO, the condition has been defined as a pressure gradient of 16 mmHg or more [4]. In the present case, the pressure gradient of the RVOT was 18 mmHg, which is considered mild RVOTO but may require intervention. The mechanism of RVOTO is thought to be primary invasion due to hypertrophy of myocardial cells in the right ventricle or secondary invasion due to septal hypertrophy bulging to the right ventricular side [5]. Patients with right ventricular hypertrophy and RVOTO have more severe symptoms than those with RVOTO without right ventricular hypertrophy [4]. One study reported that right ventricular hypertrophy correlates with the NYHA classification and risk score of sudden death and is independently associated with ventricular arrhythmia [6]. In addition, patients with severe right ventricular hypertrophy associated with RVOTO reportedly have a poor clinical prognosis and multiple gene mutations [7].

The optimal therapy for patients with HCM and significant right ventricular involvement is unknown. The treatment method for RVOTO is basically surgical removal of hypertrophied muscle bundles, which provides relief from symptoms such as dyspnea and fatigue. In some cases, right ventricular outflow stent placement and ablation to the conus branch of the right coronary artery may be effective [8, 9]. The site at which drugs exert a negative inotropic effect has not been identified. While these medications reduce the right intraventricular gradient and diminish symptoms in some patients, other patients are non-responders [5]. In the present case, it was difficult to visualize the RVOT by transthoracic echocardiography, so it was not possible to fully

evaluate the effect of the drug therapy. However, the drug therapy seemed to have an effect clinically, as the symptoms were alleviated and the systolic murmur was no longer audible. Percutaneous transluminal septal myocardial ablation or ablation to the conus branch is indicated for patients who are unresponsive to drug therapy and have a resting left ventricular pressure gradient of ≥ 30 mmHg [9]. RVOT stenosis due to right ventricular hypertrophy is considered likely to become severe over time. Therefore, it is important to consider the timing of surgical intervention.

Conclusion

In the present case, *cibenzoline* improved the pressure gradient in the left midventricle at rest, but a pressure gradient remained in the RVOT. If patients with HCM have persistent dyspnea on exertion despite drug therapy, the possibility of RVOTO should be investigated.

Financial support

This report received no specific grant from any funding agency, commercial, or not-for-profit entity.

Ethical standards

The patient provided informed consent for publication.

Conflict of interest

The authors have no conflicts of interest to disclose.

Acknowledgments

We thank Kelly Zammit, BVSc, from Edanz (https://jp.edanz.com/ac) for editing a draft of this manuscript.

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Figure Legends

Figure 1. Transthoracic echocardiography.

(A, B) B shows the flow velocity of the red arrow in A. The left ventricular outflow tract has an accelerated blood flow of 2 m/s, and the pressure difference is about 16 mmHg.

(C, D) D shows the flow velocity of the red arrow in C. The left midventricle has an accelerated blood flow of 3 m/s, and the pressure difference is about 36 mmHg.

Figure 2. Left and right ventriculography. A. Diastolic of the left ventricle; B. Systolic of the left ventricle; C. Diastolic of the right ventricle; D. Systolic of the right ventricle.

Figure 3. Intracardiac pressure measurement of the right heart system. A. Right atrium; B. Right ventricular apex; C. Right ventricular outflow tract; D. Pulmonary artery. The pressure gradient between the apex of the right ventricle and the right ventricular outflow tract is 18 mmHg.

Figure 4. Right ventricular outflow tract obstruction confirmed on a sagittal cardiac magnetic resonance imaging. LA = left atrium; LV = left ventricle; RV = right ventricle; PA = pulmonary artery.

Figure 1

Fig. 1

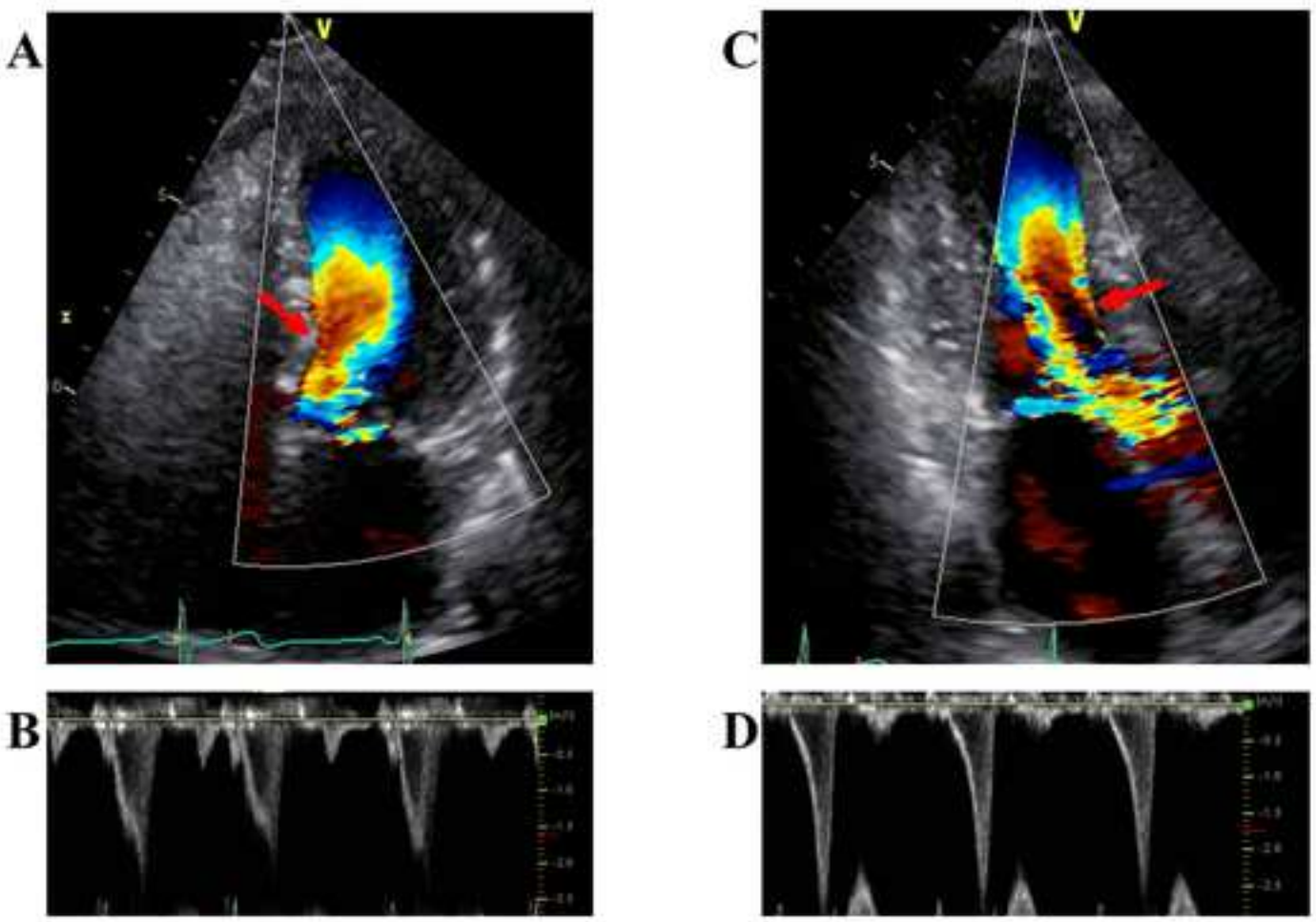

Figure 2

Fig. 2

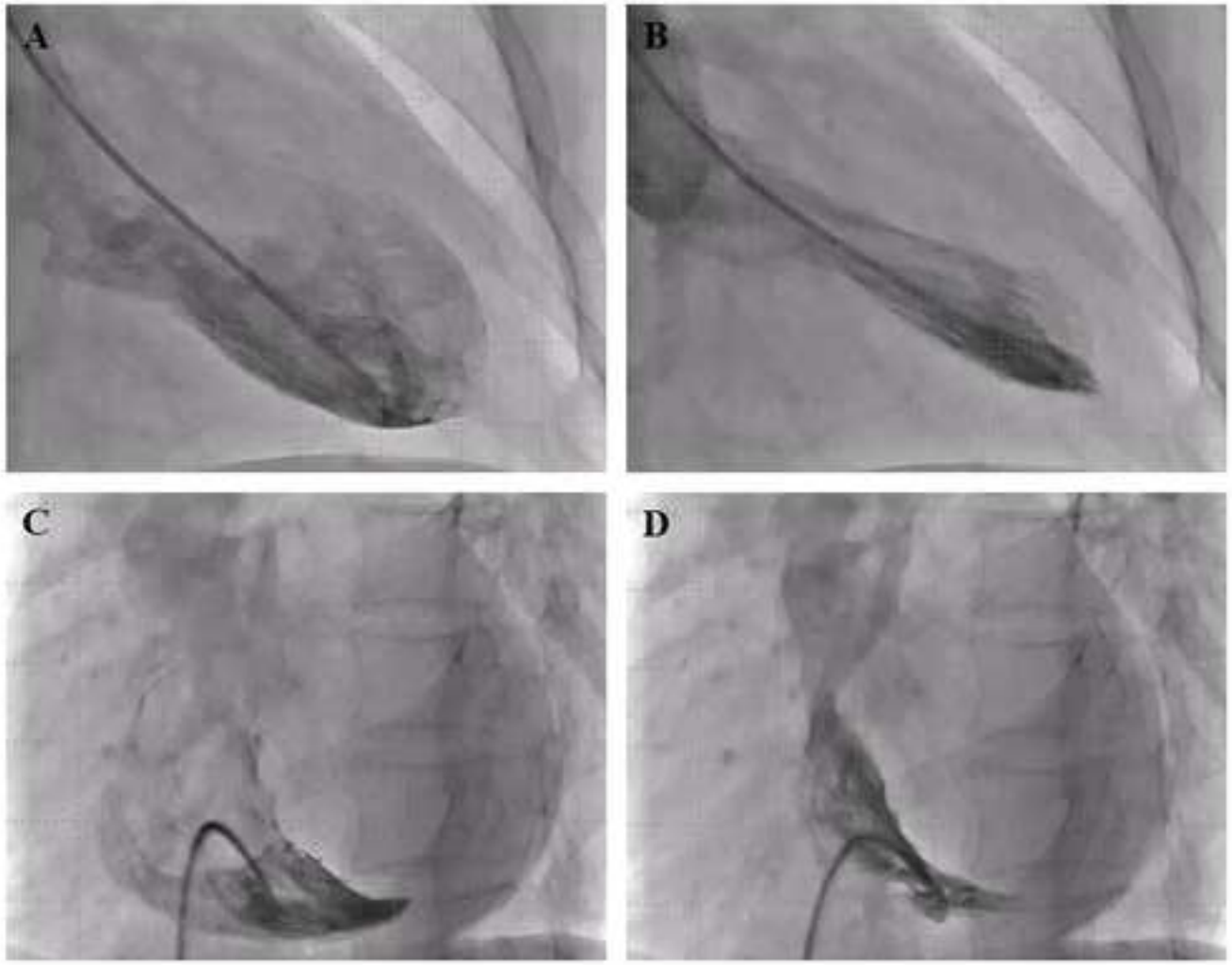

Figure 3

Fig. 3

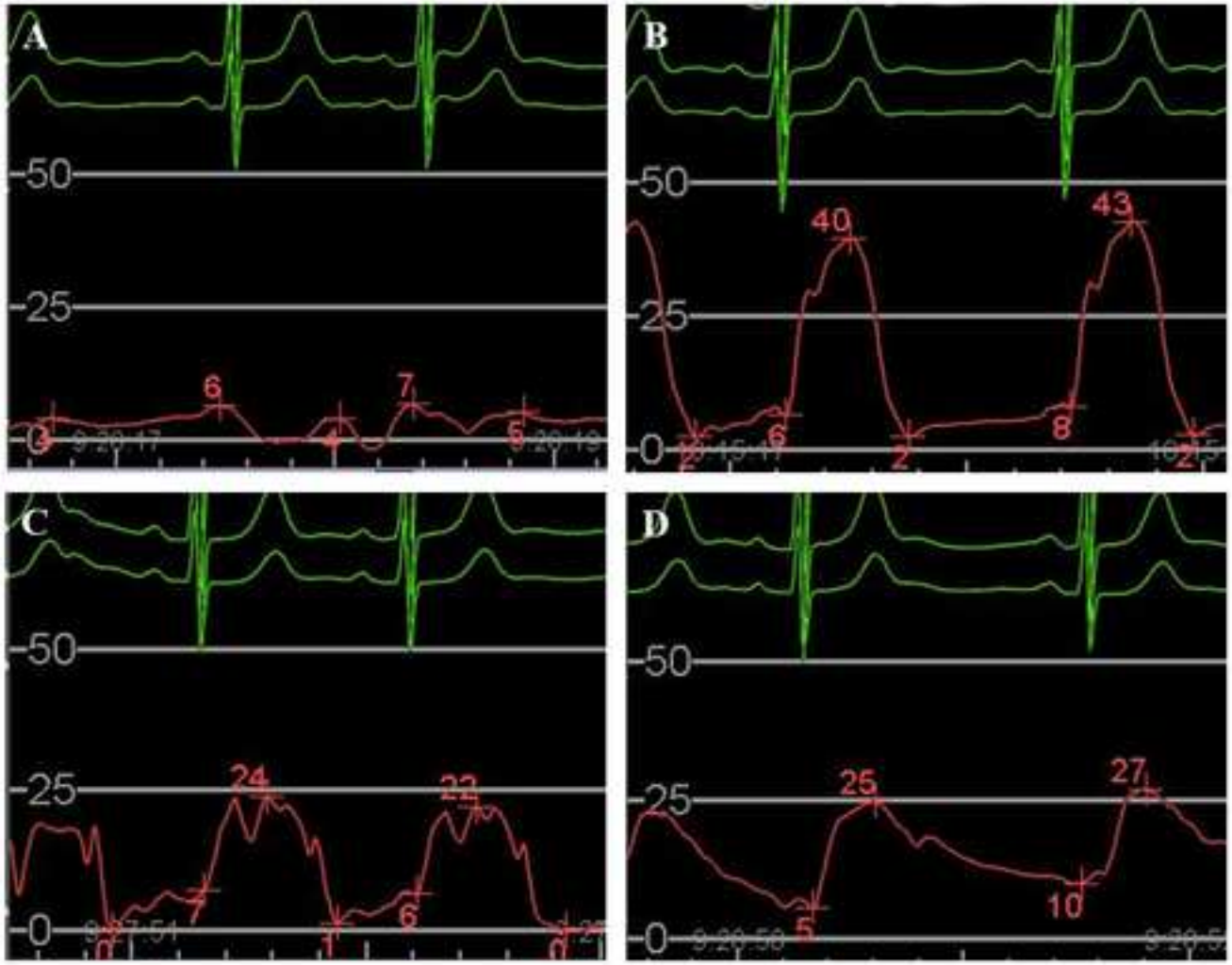

Figure 4

Fig. 4