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CASE REPORT

ADVANCED

CLINICAL CASE

Recurrent Takotsubo Cardiomyopathy in a Patient With Hypertrophic Cardiomyopathy Leading to Cardiogenic Shock Requiring VA-ECMO

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ABSTRACT

Providing hemodynamic support for patients with hypertrophic cardiomyopathy and cardiogenic shock can be challenging because inotropic medications worsen intraventricular obstruction, and the effect of appropriate mechanical support remains undefined. We report a patient with hypertrophic cardiomyopathy in shock because of takotsubo cardiomyopathy requiring venoarterial extracorporeal membrane oxygenation and septal reduction for full recovery. (**Level of Difficulty: Advanced.**) (J Am Coll Cardiol Case Rep 2020;2:1014–8) © 2020 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A 68-year-old woman with a history of hypertension and takotsubo cardiomyopathy (9 years prior, recovered) presented with back pain, nausea, and diaphoresis. Her admission electrocardiogram demonstrated a previously known left bundle branch block, and her initial serum troponin T level was elevated at 0.46 ng/ml. She underwent coronary angiography, which demonstrated no obstructive coronary artery disease. Left ventriculography demonstrated apical ballooning with hyperdynamic basal contractility consistent with recurrent takotsubo cardiomyopathy. By catheter assessment, she was found to have an intraventricular gradient of 46 mm Hg at rest. Subsequently, she developed hypotension and signs of shock.

LEARNING OBJECTIVES

- To discuss the differential diagnosis of shock in patients with HCM and takotsubo cardiomyopathy.
- To discuss options for management of cardiogenic shock in patients with HCM and potential consequences.

MEDICAL HISTORY

The patient's medical history included hypertension and an episode of takotsubo cardiomyopathy 9 years prior, which was attributed to multiple stressors including the death of a parent.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of shock developing in a patient with an intraventricular gradient (suggesting

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hypertrophic cardiomyopathy [HCM] physiology), coincident apical dyskinesis, and left ventricular (LV) systolic dysfunction may include low cardiac output due to LV pump failure and/or severe left ventricular outflow tract (LVOT) obstruction. The observation of apical ballooning raises the possibility that hypotension and shock are due primarily to pump failure, as has been observed in up to 20% of patients with takotsubo cardiomyopathy (1). The presence of a systolic murmur and a systolic intraventricular gradient at cardiac catheterization suggest LVOT obstruction may contribute significantly to hypotension and shock.

INVESTIGATIONS

Transthoracic echocardiography showed severe LV dysfunction with apical ballooning and an estimated LV ejection fraction of 30%. There was also hyperdynamic contraction of the basal segments, systolic anterior motion (SAM) of the anterior mitral valve leaflet, and suggestion of a late-peaking gradient in the LVOT of 25 to 35 mm Hg (Video 1).

Although prior echocardiography performed 13 months prior to the patient's presentation was reported as demonstrating concentric LV hypertrophy, review of the images revealed asymmetrical septal hypertrophy with a septal wall thickness of 1.9 cm and a posterior wall thickness of 1.0 cm, SAM of the mitral valve, and a late-peaking dynamic LVOT gradient of 16 mm Hg at rest that increased to 45 mm Hg with Valsalva maneuver (**Figure 1**, Video 1). These echocardiographic characteristics are consistent with a diagnosis of obstructive HCM.

ABBREVIATIONS AND ACRONYMS

HCM = hypertrophic cardiomyopathy

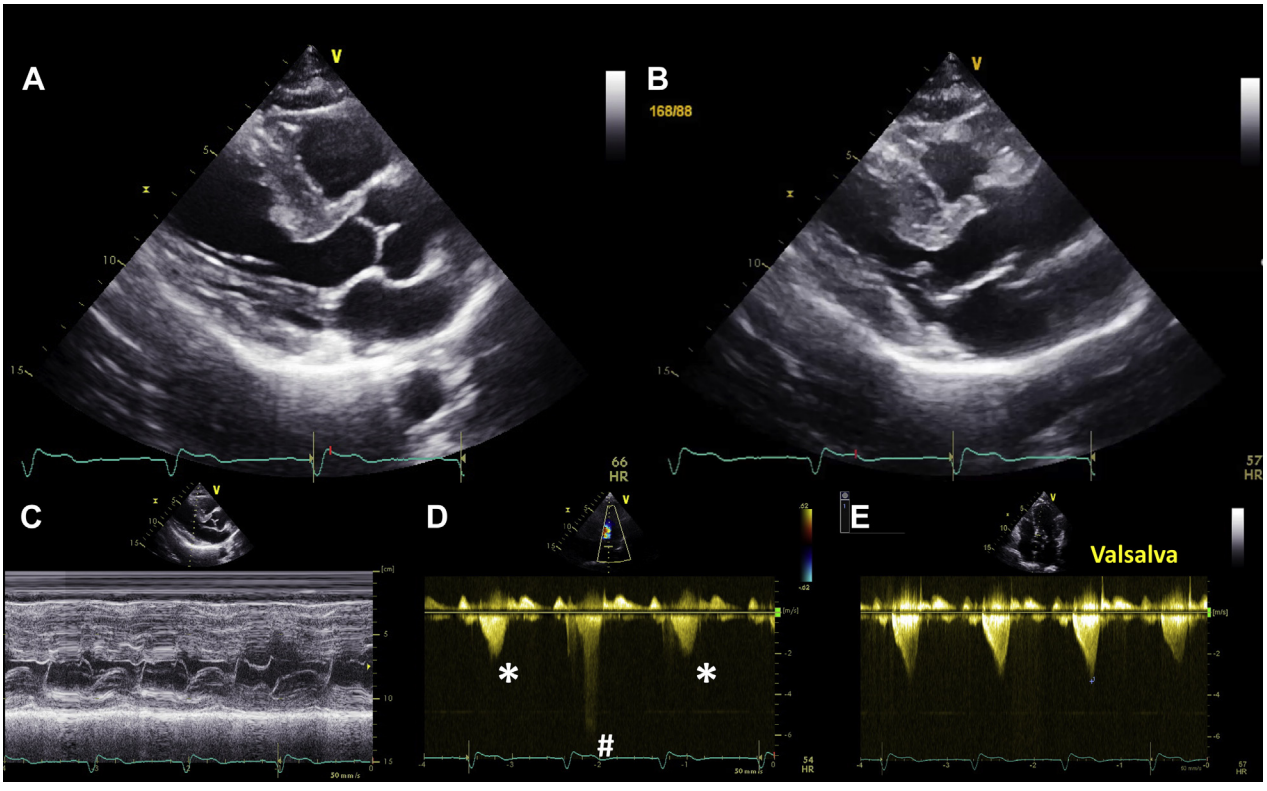
LV = left ventricular

LVOT = left ventricular outflow tract

SAM = systolic anterior motion

VA-ECMO = venoarterial extracorporeal membrane oxygenation

FIGURE 1 Transthoracic Echocardiography 13 Months Prior to Current Presentation



Parasternal long-axis in end-diastole **(A)** revealing asymmetrical septal hypertrophy (septal wall 1.9 cm vs. posterior wall 1.0 cm) and in systole **(B)** revealing systolic anterior motion (SAM) of the mitral valve (MV). M-mode imaging through the MV **(C)** also demonstrating SAM of the MV. Continuous-wave Doppler **(D)** revealed an intraventricular gradient of 16 mm Hg (* = gradient, # = mitral regurgitation). Pulsed-wave Doppler confirmed that the gradient was localized to the left ventricular outflow tract (not shown). The gradient increased to 45 mm Hg with Valsalva maneuver **(E)**.

TABLE 1 Effects of Various Vasoactive Medications and Mechanical Support Devices in HCM

Therapy	Effect on Inotropy	Effect on Afterload	Potential Effect on LVOT Obstruction in HCM
Dobutamine	↑↑	↓↓	↑↑
Norepinephrine	↑	↑↑	↔/↑
Epinephrine	↑↑	↑↑	↑
Phenylephrine	↔	↑	↔/↓
IABP	↔/↑	↓↓	↑
Impella	↔/↑	↔	↔/↑
VA-ECMO	↔	↑↑	↓ (presuming adequate preload)

HCM = hypertrophic cardiomyopathy; IABP = intra-aortic balloon pump; LVOT = left ventricular outflow tract; VA-ECMO = venoarterial extracorporeal membrane oxygenation.

MANAGEMENT

Some options beneficial for the management of cardiogenic shock in patients with normal or dilated hearts may carry hazard for those with HCM (Table 1). Inotropic and vasopressor medications increase myocardial contractility and may aggravate dynamic LVOT obstruction, if present, while agents known to reduce myocardial contractility and LVOT obstruction, such as beta-adrenergic blockers, that may be beneficial for HCM may also reduce cardiac output and worsen hypotension and shock for a patient with acute LV systolic dysfunction. Mechanical circulatory support options that cause ventricular unloading, such as intra-aortic balloon pump counterpulsation or the Impella percutaneous LV assist device (Abiomed, Danvers, Massachusetts), may reduce load on the failing left ventricle and augment cardiac output; however, they may aggravate dynamic LVOT obstruction.

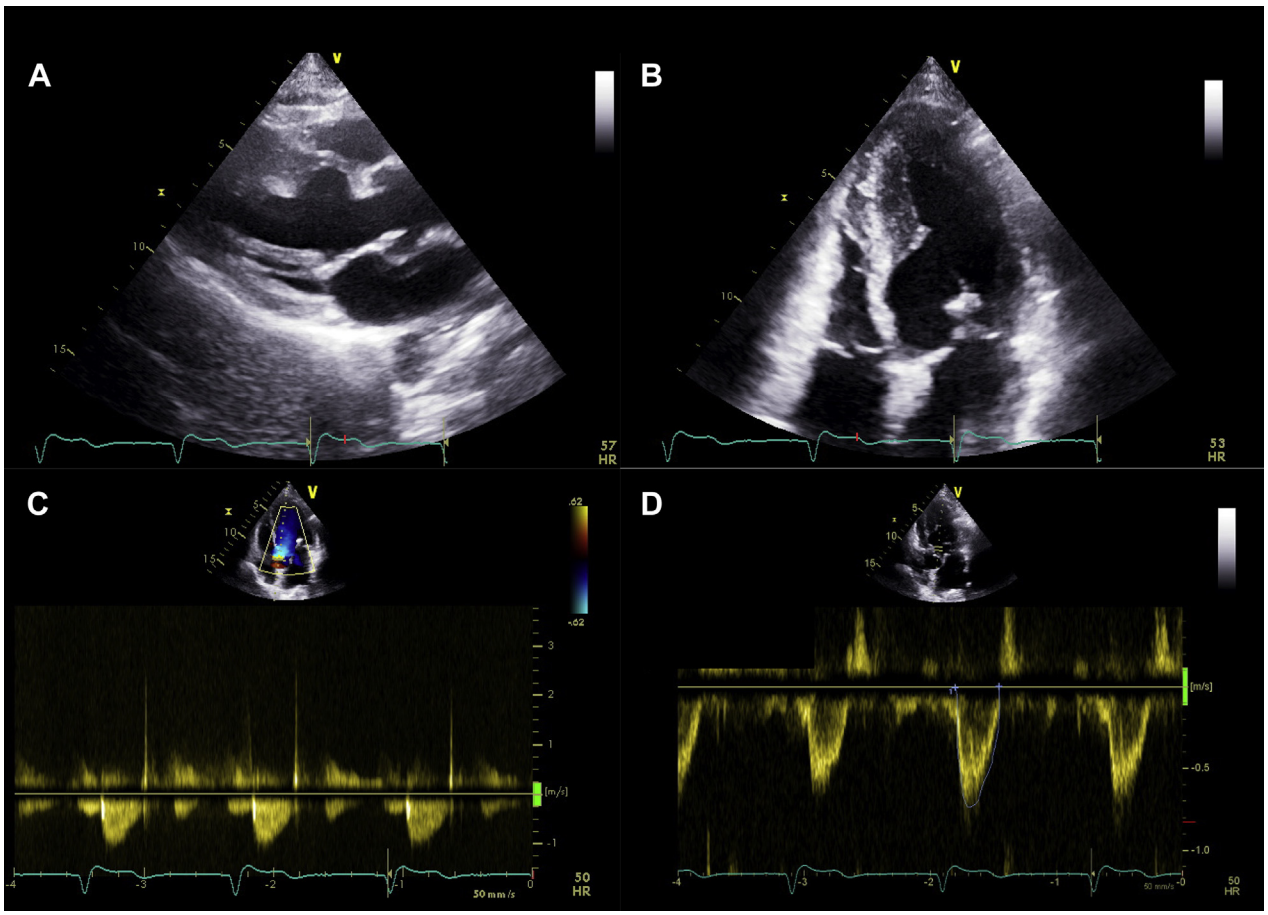
In this patient, intravenous vasoactive medications, including dobutamine and dopamine, were initiated without improvement in her hemodynamic status. As epinephrine and, to a lesser degree, norepinephrine can stimulate cardiac beta-sympathetic receptors that increase myocardial contractility, these agents were avoided, as use in patients with obstructive physiology has the potential to precipitate worsening cardiogenic shock. Despite placement of an intra-aortic balloon pump and subsequent placement of an Impella CP catheter, the patient's shock continued to worsen. She then required cannulation for venoarterial extracorporeal membrane oxygenation (VA-ECMO) support. Over the next few days, this patient improved clinically on VA-ECMO support such that the Impella CP catheter was removed; however, with evident SAM of the mitral valve and significant LVOT obstruction, she was refractory to weaning from VA-ECMO support. After multiple heart team discussions, the patient underwent a minimally invasive extended septal myectomy and subsequent VA-ECMO decannulation.

TABLE 2 Summary of Published Cases and Management of Takotsubo Cardiomyopathy Complicated by Shock in Patients With HCM

First Author (Year) (Ref. #)	Journal	Information
Modi et al. (2011) (2)	*International Journal of Cardiology*	A 54-year-old woman with quadriplegia from advanced motor neuron disease presented with chest pain and hypotension, with ECG illustrating T-wave inversions and positive cardiac biomarkers. Echocardiography illustrated asymmetric septal hypertrophy (19 mm), SAM, and apical ballooning. Coronary angiography illustrated no obstructive coronary artery disease but a did demonstrate a mid-LAD muscle bridge. Intervention: NE, DBA, and IABP Vital status: death 3 days after presentation
Nalluri et al. (2017) (3)	*Cardiovascular Imaging Case Reports*	An 81-year-old woman with known obstructive HCM presented with chest pain and dyspnea; takotsubo cardiomyopathy was subsequently diagnosed during cardiac catheterization. The patient developed cardiogenic shock post-procedure necessitating phenylephrine infusions. Intervention: phenylephrine for shock, then medical therapy Vital status: discharged home 3 days after presentation
Arakawa et al. (2018) (4)	*Internal Medicine*	A 62-year-old woman with a family history of obstructive HCM presented with chest pain and developed cardiogenic shock treated by norepinephrine infusion. Cardiac catheterization diagnosed takotsubo cardiomyopathy with a 50 mm Hg LVOT gradient. Echocardiography showed septal thickness of 12 mm, but RV biopsy illustrated myocyte disarray consistent with HCM. Intervention: intravenous vasoactive medications, then medical therapy Vital status: discharged home
Sossalla et al. (2019) (5)	*Circulation: Cardiovascular Interventions*	A 78-year-old woman with known obstructive HCM and prior alcohol septal ablation was found to have a recurrence of a LVOT gradient. She then presented with dyspnea and catheterization diagnosed takotsubo cardiomyopathy. Because of cardiogenic shock, the patient was transferred and placed on VA-ECMO. Intervention: repeat alcohol septal ablation Vital status: discharged to rehabilitation

DBA = dobutamine; ECG = electrocardiography; LAD = left anterior descending coronary artery; NE = norepinephrine; RV = right ventricular; SAM = systolic anterior motion; other abbreviations as in Table 1.

FIGURE 2 **Transthoracic Echocardiography 3 Months After Current Presentation**



Parasternal long-axis **(A)** and apical four-chamber **(B)** illustrating evidence of the extended septal myectomy and absence of systolic anterior motion. Continuous-wave Doppler **(C)** and pulsed-wave Doppler **(D)** demonstrating no dynamic left ventricular outflow tract obstruction. Note that in addition to being lower velocity, the profiles are now early peaking, not late peaking.

DISCUSSION

Managing a patient such as this, with apical ballooning, cardiogenic shock, coexistent LVOT obstruction due to basal asymmetrical septal hypertrophy and SAM, can be complex and challenging, as conventional therapeutic interventions for the failing heart with systolic dysfunction may aggravate the LVOT obstruction. Although inotropic and vasoactive medications may increase cardiac contractility, mechanical circulatory support can have varying effects on ventricular loading conditions. As a result, in obstructive HCM, increasing inotropy and/or decreasing pre-load or afterload can worsen LVOT obstruction. Therefore, for patients with obstructive HCM, many conventional therapies beneficial for other patients in cardiogenic shock can worsen LVOT obstruction and thereby worsen the severity of cardiogenic shock, complicating the management of these patients.

There are only 4 other reported cases of patients with HCM presenting with takotsubo cardiomyopathy who developed cardiogenic shock (**Table 2**) (2–5). To the best of our knowledge, the first such case was reported in 2011 (2), and we report only the second published case of a patient requiring the use of VA-ECMO. Both the previous case and our case illustrate the difficulty of liberating a patient from VA-ECMO support in the recovery phase because of ongoing low output of the left ventricle and insufficient LV filling from reduced pre-load (5). Our case is unique in that our patient was treated by a minimally

invasive extended septal myectomy in order to subsequently liberate from VA-ECMO support.

This case highlights several teaching points. First, it illustrates the importance of reviewing prior imaging when confronted with a discordant clinical picture and/or findings that suggest additional diagnoses. In this case, the cardiac catheterization suggested the diagnosis of HCM in addition to recurrent takotsubo cardiomyopathy. Reviewing this patient's echocardiogram led to confirmation of the diagnosis of HCM and the realization that septal reduction therapy was an important consideration to improve her hemodynamic status.

Second, it is important to be aware of underlying HCM and the degree of dynamic LVOT obstruction when considering advanced mechanical support in cardiogenic shock, as the choice of mechanical support device could lead to worsening LVOT obstruction. Given the risks of unloading a heart with associated LVOT obstruction, the preferred mechanical support in patients with HCM may be VA-ECMO, contingent on maintaining adequate pre-load to prevent worsening LVOT obstruction.

Last, once a diagnosis of HCM is made, it is important to communicate to the patient that lifelong follow-up is needed and that there are important implications for family members (i.e., clinical screening for HCM).

FOLLOW-UP

The patient did well post-operatively, as all vasoactive medications were weaned off and she was discharged to a rehabilitation facility on post-operative day 12. The patient did not require a pacemaker post-operatively and was discharged on metoprolol. Despite being counseled that HCM was a genetic disease, she was not interested in obtaining genetic testing during the time of her diagnosis. Histological examination of the myectomy specimen did not demonstrate any evidence of a storage or infiltrative cardiomyopathy. Three months after discharge, echocardiography revealed a thinned basal septum at the site of the extended septal myectomy, no dynamic LVOT obstruction, and fully recovered LV systolic function (**Figure 2**, Video 1).

CONCLUSIONS

We report the case of a patient with HCM who presented in cardiogenic shock due to recurrent takotsubo cardiomyopathy, needing mechanical circulatory support, and requiring an extended septal myectomy to be liberated from VA-ECMO. Positive inotropic medications and the use of certain temporary mechanical circulatory support devices can worsen LVOT obstruction in these patients, posing challenges to appropriate management. In select patients, VA-ECMO with careful attention to pre-load may be the preferred option for circulatory support when indicated for patients with HCM in cardiogenic shock. There are currently limited data on the recurrence risk for episodes of takotsubo cardiomyopathy after septal reduction therapy. However, if this patient were to again develop takotsubo cardiomyopathy, she would theoretically be at a lower risk for hemodynamic decompensation as a result of her obstructive physiology being surgically alleviated.

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REFERENCES

1. Sharkey SW, Pink VR, Lesser JR, Garberich RF, Maron MS, Maron BJ. Clinical profile of patients with high-risk tako-tsubo cardiomyopathy. Am J Cardiol 2015;116:765–72.

2. Modi S, Ramsdale D. Tako-tsubo, hypertrophic obstructive cardiomyopathy & muscle bridging—separate disease entities or a single condition? Int J Cardiol 2011;147:133–4.

3. Nalluri N, Asti D, Anugu VR, Ibrahim U, Lafferty JC, Olkovsky Y. Cardiogenic shock secondary to takotsubo cardiomyopathy in a patient with preexisting hypertrophic obstructive cardiomyopathy. CASE (Phila) 2017;2:78–81.

4. Arakawa K, Gondo T, Matsushita K, Himeno H, Kimura K, Tamura K. Takotsubo cardiomyopathy in a patient with previously undiagnosed hypertrophic cardiomyopathy with latent obstruction. Intern Med 2018;57:2969–73.

5. Sossalla S, Meindl C, Fischer M, Lubnow M, Müller T, Maier LS. Bail-out alcohol septal ablation for hypertrophic obstructive cardiomyopathy in a patient with takotsubo cardiomyopathy-induced cardiogenic shock. Circ Cardiovasc Interv 2019;12:e007425.

KEY WORDS acute heart failure, cardiac assist devices, cardiomyopathy

APPENDIX For a supplemental video, please see the online version of this paper.