CLINICAL PROBLEM-SOLVING

A Change of Heart

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In this Journal *feature, information about a real patient is presented in stages (boldface type)
to an expert clinician, who responds to the information, sharing his or her reasoning with
the reader (regular type). The authors' commentary follows.*

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A 57-year-old teacher with a history of hypertension presented to an urgent care center with nonradiating chest pressure and light-headedness. The chest pressure had begun soon after she arrived at work that morning, when she was physically threatened by a parent of one of her fifth-grade students. Her symptoms improved with rest immediately after the event but then worsened by the end of the day. When she returned home, her husband took her blood pressure and noted systolic values ranging from 80 to 90 mm Hg, with a heart rate of approximately 110 beats per minute. Her symptoms and blood pressure did not improve by drinking fluids, which prompted her visit to the center.

Chest pressure may suggest any of several disease processes, ranging from benign conditions to life-threatening emergencies. In the presence of hypotension, the initial evaluation must focus on ruling out the latter, which include an acute coronary syndrome, aortic dissection, pulmonary embolism, esophageal rupture, and tension pneumothorax. Additional cardiac disorders such as myocarditis or pericarditis are also consistent with this patient's presentation. Noncardiac disorders that can cause chest pressure include gastroesophageal reflux disease, peptic ulcer disease, costochondritis, herpes zoster infection, pleuritis, and panic attack; however, none of these would be expected to cause hypotension.

The patient had a history of well-controlled hypertension but no other medical problems. Her only medication was lisinopril, 5 mg daily. There was no family history of early coronary artery disease or sudden cardiac death. She had smoked approximately five cigarettes daily for 30 years, rarely drank alcohol, and reported no illicit-drug use.

On initial evaluation, the patient reported slight chest pressure but was not in acute distress. She was afebrile. Her blood pressure was 83/50 mm Hg, her heart rate was 110 beats per minute, and her respiratory rate was 14 breaths per minute. Pulse oximetry revealed an oxygen saturation of 99% while she was breathing 2 liters of oxygen through a nasal cannula. Her neck was supple, and jugular venous pressure was not elevated. Auscultation of the chest revealed a loud, crescendo systolic murmur, best heard at the right upper sternal border, but her lungs were clear. The abdominal examination was unremarkable. Her lower extremities were warm, with symmetric distal pulses, and showed no edema. The remainder of the physical examination was normal.

This patient's hypotension and tachycardia are worrisome. They suggest the early stage of shock and thus warrant urgent diagnostic testing and management, particu-

larly in a patient with chest pressure. Her hypertension and history of smoking increase the likelihood of an acute coronary syndrome and aortic dissection. The loud crescendo systolic murmur may be related to a chronic condition, such as a bicuspid aortic valve with stenosis, hypertrophic obstructive cardiomyopathy, or pulmonic-valve stenosis. A new murmur may herald a mechanical complication of myocardial infarction, such as ventricular septal rupture or papillary-muscle rupture, causing acute mitral regurgitation.
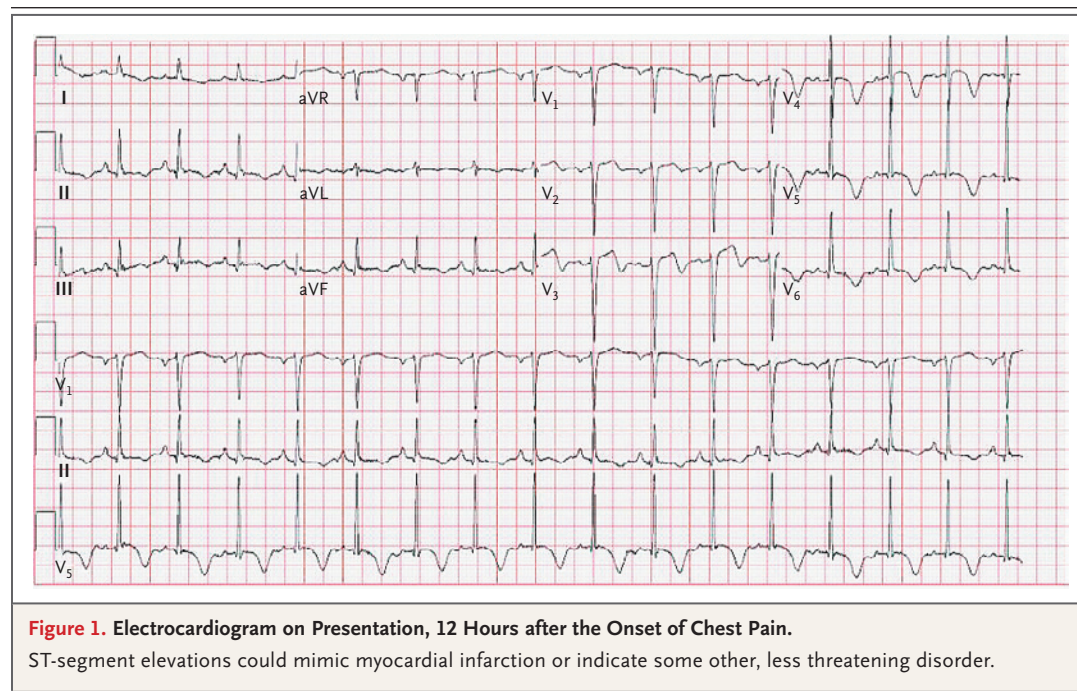
One can quickly rule out some of these conditions by obtaining an electrocardiogram. Additional studies that should be performed include chest radiography, measurements of cardiac biomarkers, and transthoracic echocardiography, although this last option may not be available at an urgent care facility.

A 12-lead electrocardiogram, obtained approximately 12 hours after the onset of the chest pressure, revealed normal sinus rhythm; ST-segment elevations of 1 to 2 mm in leads V_2 to V_4, with a biphasic T wave in V_3; and deep, symmetric T-wave inversions in leads V_4 to V_6 (Fig. 1). Laboratory studies, including measurements of cardiac biomarkers, were ordered. Chest radiography showed a normal mediastinum, small bilateral pleural effusions, and Kerley's B lines, findings that were compatible with mild interstitial pulmonary edema (Fig. 2).

The electrocardiographic findings are consistent with an acute myocardial infarction, but other conditions that are associated with ST-segment elevation and may thus mimic myocardial infarction must also be considered. Left ventricular hypertrophy with a repolarization abnormality, the most common of such conditions, is not typically manifested as symmetric T-wave inversions in the precordial leads, and the ST-segment elevations are usually less than 1 mm in women and are concave rather than convex. In acute pericarditis, ST-segment elevations are diffuse, not localized. Apical ballooning syndrome, an acute cardiomyopathy with reversible left ventricular dysfunction, may also cause ST-segment elevation and diffuse T-wave inversions. The syndrome is frequently precipitated by a stressful event, which is consistent with this patient's presentation.

The patient was given aspirin, 325 mg orally, and a 4000-unit bolus of intravenous heparin followed by continuous infusion. Preparations were made for emergency transfer to a hospital where a percutaneous coronary intervention could be carried out.
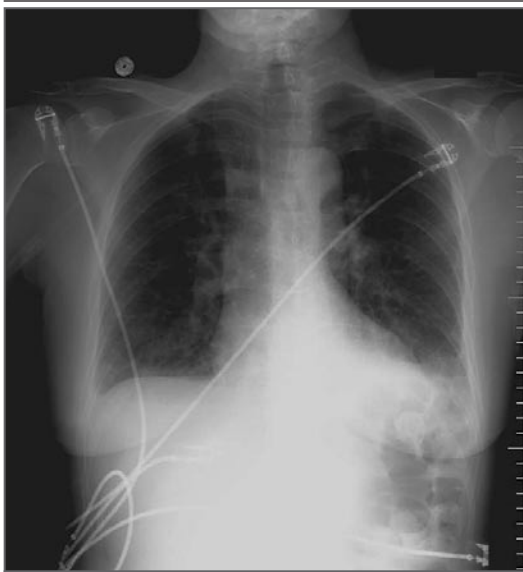

Figure 1. Electrocardiogram on Presentation, 12 Hours after the Onset of Chest Pain.
ST-segment elevations could mimic myocardial infarction or indicate some other, less threatening disorder.

Figure 2. Chest Radiograph on Admission.

The film shows small bilateral effusions and Kerley's B lines. (Note that gray vertical lines are artifactual.)

Because of the patient's low blood pressure, tachycardia, and congestive heart failure, primary percutaneous coronary intervention would be preferable to fibrinolytic therapy. Thus, preparation for transfer to a hospital with this capability would be ideal, but some form of reperfusion therapy is still urgently required. Aggressive fluid administration should be avoided, given the evidence of pulmonary edema on chest radiography. Dopamine could be considered for the low blood pressure. I would not recommend beta-blockers or nitroglycerin at this time, given the hypotension.

On the patient's arrival at the hospital, her chest pressure had improved but was not completely resolved. Her blood pressure was 82/61 mm Hg, with a heart rate of 97 beats per minute. The laboratory results obtained from the urgent care facility were as follows: the hemoglobin level was 11.1 g per deciliter, the platelet count was 190,000 per cubic millimeter, the white-cell count was 10,300 per cubic millimeter, the serum creatinine level was 0.7 mg per deciliter (62 μmol per liter), the blood urea nitrogen level was 17 mg per deciliter (6.1 mmol per liter), the blood glucose level was 106 mg per deciliter (5.9 mmol per liter), the creatine kinase level was 135 IU per liter (normal range, 26 to 180), the creatine kinase MB isoenzyme level was 14.1 ng per milliliter (normal range, 0 to 4.9), and the serum troponin I level was 4.23 ng

per milliliter (normal value, <0.30). A repeat electrocardiogram showed persistent ST-segment elevation and T-wave inversions.

Mildly elevated cardiac biomarkers confirm myocardial injury but are inconsistent with 12 hours of complete coronary-artery occlusion. These levels are somewhat unexpected and suggest either spontaneous, intermittent coronary reperfusion throughout the day or other cardiovascular conditions, such as myocarditis, pericarditis, or pulmonary embolism. Although it is possible that the cardiac biomarkers have already peaked and are now declining, the time course and electrocardiographic findings are not consistent with this explanation. An echocardiogram might identify regional wall-motion abnormalities, a valve disorder, pericardial effusion, mechanical complications of acute myocardial infarction (as noted above), or even proximal aortic disease. Yet the most likely cause of ST-segment elevation and elevated cardiac biomarkers in this setting remains acute myocardial infarction. Left heart catheterization with coronary angiography is warranted without further delay.

Coronary angiography, performed on an emergency basis, revealed minimal luminal irregularities with no evidence of plaque rupture or thrombus (Fig. 3). Left heart catheterization revealed a left ventricular end-diastolic pressure of 30 mm Hg (normal range, 5 to 15) and a left ventricular systolic pressure of 123 mm Hg. However, a gradient of 49 mm Hg was noted between the aortic and left ventricular systolic pressures (Fig. 4). Further evaluation of this gradient revealed its location to be subvalvular. Left ventriculography showed severe distal anterolateral, apical, and diaphragmatic dyskinesis with hypercontractile basal segments. Moderate mitral regurgitation was noted, and the overall estimated ejection fraction was 35% (Fig. 5).

Taken together, these findings are consistent with apical ballooning syndrome, a condition often precipitated by emotional stress and characterized by sudden changes in left ventricular systolic wall motion in the absence of angiographically significant coronary artery disease. The left ventriculogram shows the characteristic wall-motion abnormalities, with akinesis of the middle and apical segments and preservation of basal function. These abnormalities extend beyond the distribution of any single coronary artery, making it less likely

that an occlusive thrombus has spontaneously dissolved or that intermittent vasospasm has occurred. This is a critical observation, given that apical ballooning syndrome is a diagnosis of exclusion.

Although uncommon, dynamic obstruction within the left ventricular outflow tract, as noted in this patient, is possible with apical ballooning syndrome and is believed to be caused by compensatory hyperkinesis of the basal segments. As in hypertrophic cardiomyopathy, dynamic outflow tract obstruction can be made worse by low filling pressures or decreased afterload. The degree of mitral regurgitation in this patient is also impressive. This results from acceleration of blood through the dynamic obstruction, leading to a Venturi effect, with the anterior mitral leaflet being sucked into the left ventricular outflow tract. The appearance of the aortic valve on the ventriculogram and careful evaluation of the intraventricular pressure tracings rule out aortic-valve stenosis.

We now have an explanation for the hypotension. It is due to poor left ventricular systolic function, as well as dynamic obstruction of the left ventricular outflow tract. Given these findings, it would be important to avoid systemic vasodilators and inotropic stimulation, which can worsen the outflow tract gradient. Fluids should be cautiously used in this situation, since the patient has elevated left-side filling pressures and evidence of pulmonary edema. If she is symptomatic, a vasopressor such as phenylephrine could be given carefully to increase blood pressure and decrease the outflow tract gradient. Given her low blood pressure, the use of beta-blockers in this setting is controversial. However, beta-blockade may decrease hypercontractility of the base of the left ventricle, thereby decreasing the outflow tract gradient, increasing diastolic filling, and improving systemic blood pressure.

The patient was transferred to the cardiac intensive care unit. Aspirin therapy was continued and treatment with a statin was started. The chest pain resolved overnight, and cardiac biomarker levels decreased from the peak values noted at admission. Her blood pressure and heart rate remained stable. Treatment with metoprolol and lisinopril was initiated on the third hospital day, both at low doses. A transthoracic echocardiogram revealed an ejection fraction of 35%; moderate mitral regurgitation with systolic anterior motion of the leaflet; and mild ventricular systolic dysfunction with akinesis of the apex, mid anterior wall, mid anterosep-
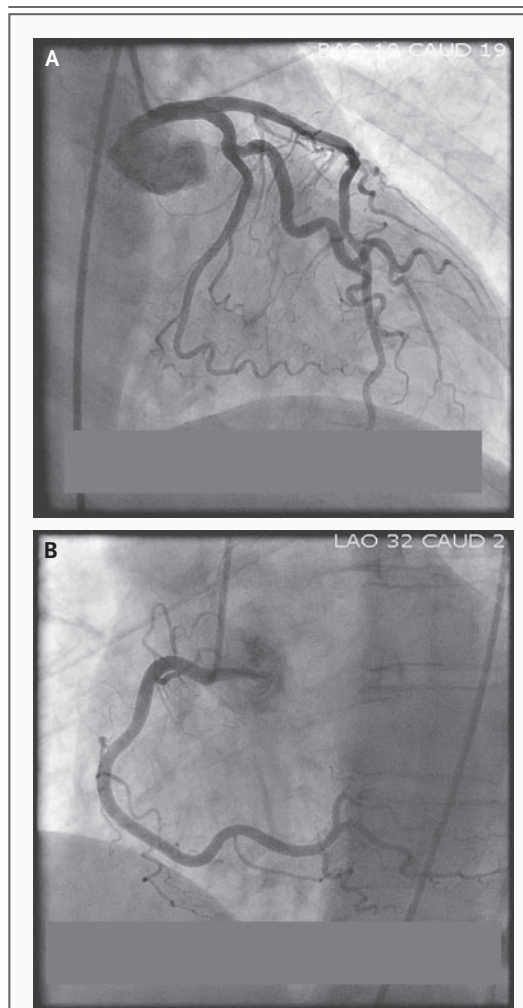

Figure 3. Coronary Angiograms.
The left coronary artery (Panel A) and right coronary artery (Panel B) show no evidence of plaque rupture or thrombus. (Note that gray vertical lines are artifactual.)

tum, mid septum, and mid posterior wall (see Videos 1 and 2, available with the full text of this article at NEJM.org). She was discharged on hospital day 4 on a regimen of aspirin (81 mg daily), lisinopril (5 mg daily), simvastatin (40 mg daily), and extended-release metoprolol (25 mg daily).

Patients with apical ballooning syndrome generally have an excellent prognosis, with full recovery of left ventricular function expected within 4 to 6 weeks. Prescribing statins at discharge may be reasonable, given the other risk factors in this patient, but there are no data to support their use specifically in apical ballooning syndrome. It is also not clear whether an angiotensin-converting–

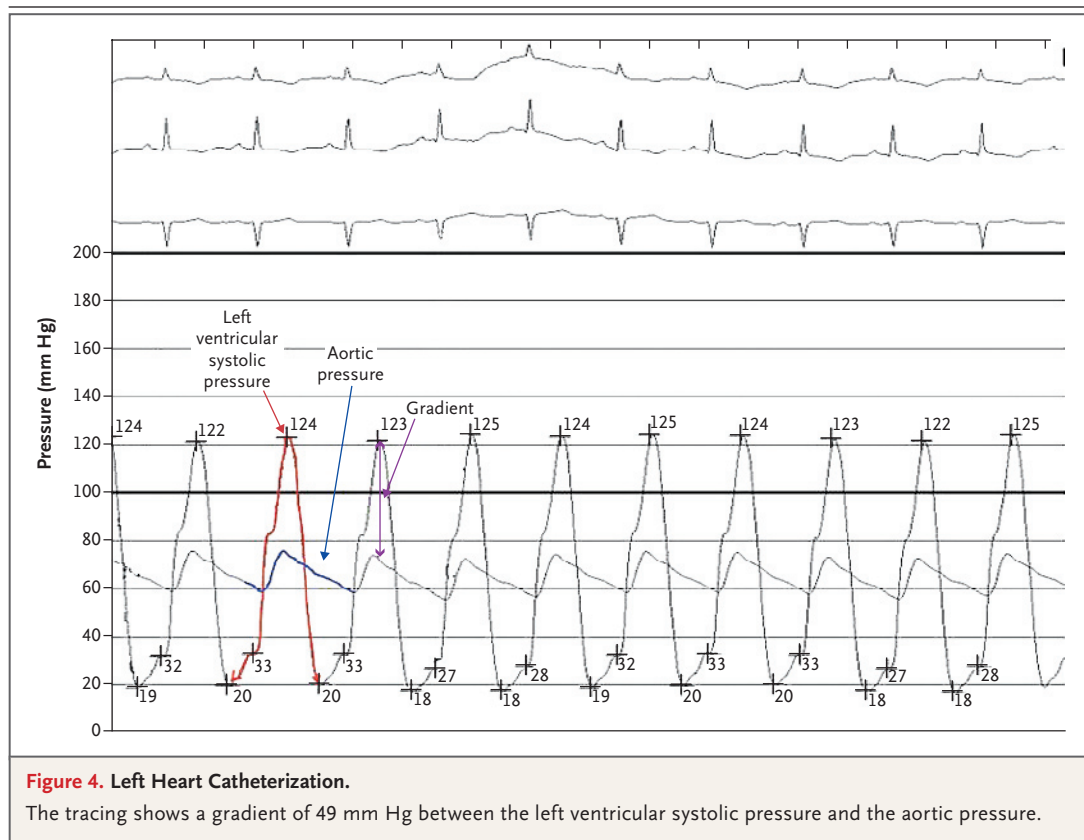*Videos of transthoracic echocardiograms are available at NEJM.org*

Figure 4. Left Heart Catheterization.

The tracing shows a gradient of 49 mm Hg between the left ventricular systolic pressure and the aortic pressure.

enzyme inhibitor provides a benefit in cases of acute remodeling, since the left ventricular systolic dysfunction is believed to be due to myocardial stunning rather than injury.

In theory, long-term beta-blocker therapy for the patient's hypertension may be helpful for suppressing catecholamines during stress, although some clinicians have expressed concern that beta-blockers result in unopposed and high local concentrations of catecholamines at alpha-adrenergic receptors. Some experts recommend that all patients with apical ballooning syndrome be tested for occult pheochromocytoma. Finally, the patient should stop smoking, so I would encourage her to participate in a smoking-cessation program.

The patient was seen in the clinic 1 month after discharge. She had returned to work with no limitations. She had no recurrent chest pain or dyspnea. A repeat echocardiogram showed left ventricular hypertrophy with normal left ventricular function, an estimated ejection fraction of 75% (see Videos 3 and 4), and resolution of the mitral regurgitation. Given her complete recovery, the diagnosis of apical ballooning syndrome was con-firmed. Six months later, the patient continued to do well, with no electrocardiographic abnormalities and no symptoms.

COMMENTARY

Apical ballooning syndrome is an increasingly recognized condition that can closely mimic acute myocardial infarction. Its incidence is estimated to be 1 to 2% in patients who present with a presumed acute myocardial infarction, and it classically affects postmenopausal women in the fifth to seventh decade. As is true for many patients with apical ballooning syndrome, the diagnosis in our patient was confirmed in the cardiac catheterization laboratory. The discussant astutely considered this diagnosis early in the evaluation, in view of the patient's presentation after a stressful event, coupled with the findings on the electrocardiogram and the elevated cardiac biomarkers.

Key features of apical ballooning syndrome are the absence of obstructive coronary artery disease in the setting of characteristic "ballooning" of the left ventricle from severe anteroapical akinesis and

hypercontractility of the basal segments.[1] First described in 1991, it is known by several names, including tako-tsubo cardiomyopathy,[2] stress-induced cardiomyopathy, and the broken-heart syndrome.[1,3] The pathophysiology of apical ballooning syndrome has not been clearly elucidated. Leading hypotheses include transient catecholamine toxicity,[4] aborted ST-elevation myocardial infarction with spontaneous lysis of thrombus, coronary vasospasm, and microcirculatory dysfunction.[4-6] Similar wall-motion abnormalities have been seen in other states of catecholamine excess, such as subarachnoid hemorrhage and pheochromocytoma.[7,8]

Although it is critical to quickly differentiate apical ballooning syndrome from acute myocardial infarction, it can be challenging to do so. There are no electrocardiographic findings that clearly distinguish apical ballooning syndrome from acute myocardial infarction. With apical ballooning syndrome, the elevations in troponin are typically much lower than would be expected on the basis of the wall-motion abnormalities.[9] However, it is difficult to rely on cardiac biomarkers alone, since these are often only modestly elevated during the early stages of an acute myocardial infarction.

Although an emotional trigger is classically present in patients with apical ballooning syndrome, other acute conditions associated with chest pain, such as acute myocardial infarction or aortic dissection, may also be preceded by emotional events.[10] Thus, the diagnosis frequently becomes evident only in the cardiac catheterization laboratory when no angiographically significant coronary artery disease is found.[11] It is generally not advisable to withhold antithrombotic treatments such as heparin and aspirin while the diagnosis remains uncertain, since acute myocardial infarction is much more common. Decisions about fibrinolytic therapy are more complicated, given its associated risk of intracerebral hemorrhage. Whenever feasible, emergency coronary angiography should be performed, as was done in this patient, to assist in clinical decision making.

Heart failure is present in approximately 50% of patients with apical ballooning syndrome, and cardiogenic shock occurs in up to 15%.[12] Approximately 20% of these patients also have a transient systolic murmur associated with subvalvular pressure gradients that can mimic hypertrophic obstructive cardiomyopathy.[13]

In our patient, a pressure gradient of 49 mm Hg was noted between the aortic and left ventricular
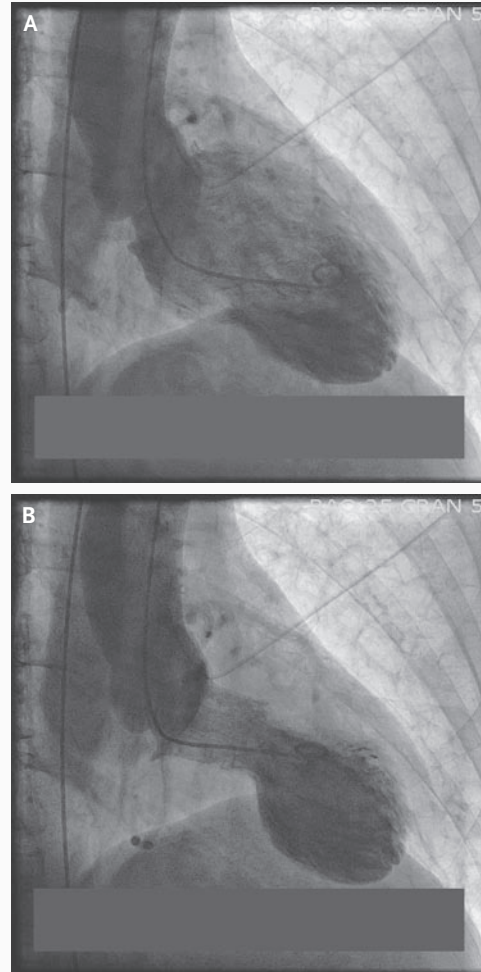
Figure 5. Right Anterior Oblique Left Ventriculogram.
The ventriculographic findings in diastole (Panel A) and systole (Panel B) show severe distal anterolateral, apical, and diaphragmatic dyskinesis. (Note that gray vertical lines are artifactual.)

systolic pressures. In this situation, treatment should focus on ensuring adequate intravascular volume to minimize the outflow tract obstruction. Beta-blockers may also be considered in an attempt to slow the heart rate and increase the diastolic filling time.[1] Although data from clinical trials are scant, some experts suggest treating patients with beta-blockers and angiotensin-converting–enzyme inhibitors until left ventricular systolic function normalizes; it has also been hypothesized that treatment with beta-blockers may reduce the risk of recurrence[1] (which is reported in a case series to be approximately 10%[14]). Inotropic agents should be avoided, since they may exacerbate the outflow tract gradient. Aspirin

should be considered for patients who have co-existing coronary artery disease. Some clinicians recommend anticoagulation with warfarin for several weeks in patients with severe systolic dysfunction in order to prevent left ventricular thrombus formation.[15]

As in most patients with apical ballooning syndrome, this patient's condition improved rapidly with supportive measures. Complete recovery of systolic function is typically observed within 4 to 6 weeks, and the overall prognosis tends to be excellent.

No potential conflict of interest relevant to this article was reported.

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