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INTERMEDIATE

CASE REPORT: CLINICAL CASE

Left Ventricular Cavity Obliteration From Eosinophilic Myocarditis in a Patient With Classic Hodgkin Lymphoma

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ABSTRACT

A 43-year-old female with a history of hypereosinophilia developed acutely decompensated heart failure. Prototypical features of eosinophilic myocarditis, including a distinctive left ventricular mass and severe mitral regurgitation, were identified on a transthoracic echocardiogram. The patient's eosinophilia was subsequently attributed to Hodgkin lymphoma, and chemotherapy resolved her heart failure symptoms. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2020;2:210–5) © 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/).

PRESENTATION

A 43-year-old female patient presented with shortness of breath, hypotension, and tachycardia. She described progressive fatigue in the week leading up to admission and was referred to the emergency department from an outpatient clinic for evaluation of resting hypoxia. The hemodynamics at admission were heart rate 104 beats/min, blood pressure 88/45 mm Hg, respiratory rate 20, and SpO_2 86% on room air (100% when placed on noninvasive pressure ventilation). On examination, the patient had distended neck veins, a fourth heart sound, and mild pitting edema. Chest radiography revealed bilateral pleural effusions, pulmonary edema, and fluid in the minor fissure (**Figure 1**). Notable laboratory studies from admission included an N-terminal pro-B-type natriuretic peptide concentration of 3,771 pg/ml (upper reference limit, 178 pg/ml) and elevated serum lactate concentration of 1.8 mmol/l (upper reference limit, 1.6 mmol/l). An electrocardiogram showed no signs of acute ischemia, and a computed tomography (CT) pulmonary angiogram showed no evidence of a pulmonary embolus.

LEARNING OBJECTIVES

- Develop a differential diagnosis for intracardiac masses, particularly, left ventricular masses.
- Appreciate the cardiac manifestations of a systemic condition such as hypereosinophilia.

The history, examination, and laboratory data all pointed to a diagnosis of heart failure, prompting an urgent transthoracic echocardiogram (characteristic images are highlighted in **Figures 2 and 3**; see also Videos 1, 2, 3, 4, 5, and 6). The echocardiogram revealed an intracardiac mass within the left ventricular cavity, adjacent to the inferior and inferolateral walls, with extension into the posterior mitral valve leaflet. The left ventricular end-diastolic dimension was normal, but the mass obliterated the

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Informed consent was obtained for this case.

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ventricular cavity during systole. In addition, there was moderate left atrial enlargement and severe mitral regurgitation (Figure 4). An echocardiogram performed 6 months earlier showed none of the aforementioned findings were present (Figure 5).

MEDICAL HISTORY. Two years prior to the patient's presentation, she underwent routine testing by her primary care doctor and a complete blood count identified marked hypereosinophilia (9.36 k WBC/mm^3 with 45% eosinophils; upper reference limit, 4.9%). This finding prompted a number of subsequent tests which revealed no evidence of an underlying malignancy or myeloproliferative disorder, so her condition was diagnosed as primary eosinophilia and managed conservatively.

Three months prior to presentation, the patient's leukocytosis and eosinophilia progressed (20.06 WBC/mm^3 with 73% eosinophils). She was referred to a hematologist and was started on imatinib, 400 mg daily. However, she developed profound diarrhea and treatment was stopped within 1 week. Shortly thereafter, the patient developed the symptoms which brought her urgently to the authors' hospital.

DIFFERENTIAL DIAGNOSIS. This report presents the case of a middle-aged female with symptoms of acute left heart failure and evidence of an intracardiac mass on transthoracic echocardiography. The differential diagnosis for intracardiac masses is highlighted in Table 1. The differential of consequence can be narrowed based on the location of the intracardiac mass. In a seminal study by Dujardin et al. (1), among 75 patients undergoing cardiac surgery for mass excision, 8% had a mass located in the left ventricle. Mural thrombus accounted for one-half of all left ventricular masses, whereas lipomas and metastatic disease were the next most common causes.

INVESTIGATIONS. The patient's marked hypereosinophilia and echocardiogram led to a diagnosis of eosinophilic myocarditis (EM). The echocardiogram featured many of the classic features of the thrombotic stage of the disease, including substantial mural thrombus, which was most pronounced in the inferior and inferolateral walls, adjacent to the mitral valve and papillary muscle apparatus. The heart dimensions were also inverted, with a small left ventricular cavity and a large left atrium. Furthermore, the condition often leads to mitral regurgitation, which was observed in this patient (Figure 4) as a consequence of thrombus and, eventually, fibrosis distorting the chordae tendinea, the mitral valve apparatus, and the leaflets themselves (2). The other echocardiographic hallmarks of EM were not appreciated, including the "Merlon sign," defined by basal hypercontractility and apical hypokinesis, and the "square-root sign," which describes septal and posterior wall motion patterns on M-mode slices through the mid-ventricle (3).

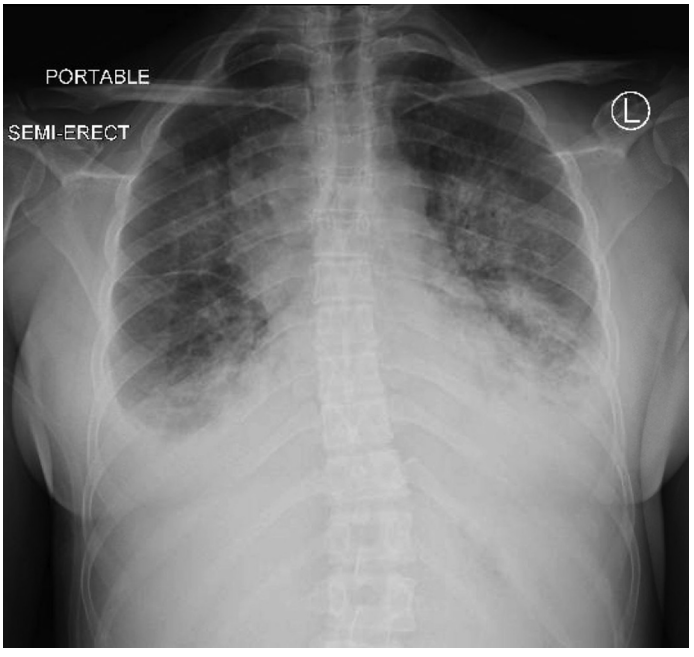
In light of these characteristic findings, advanced imaging such as cardiac magnetic resonance and cardiac biopsy were deferred. The patient ultimately underwent a biopsy of a mediastinal mass, which was detected by cross-sectional imaging on presentation and classic Hodgkin lymphoma (nodular-sclerosing type) was diagnosed. Further evaluation revealed that her disease was restricted to lymph nodes above the diaphragm (Stage II) and that there were no other additional high-risk features.

MANAGEMENT. The patient presented originally in clinical heart failure and required hemodynamic optimization prior to treatment of the underlying lymphoid malignancy. Accordingly, diuresis and anticoagulation were commenced. Once her respiratory status stabilized, chemotherapy with doxorubicin, vinblastine, and dacarbazine (AVD) was administered.

ABBREVIATIONS AND ACRONYMS

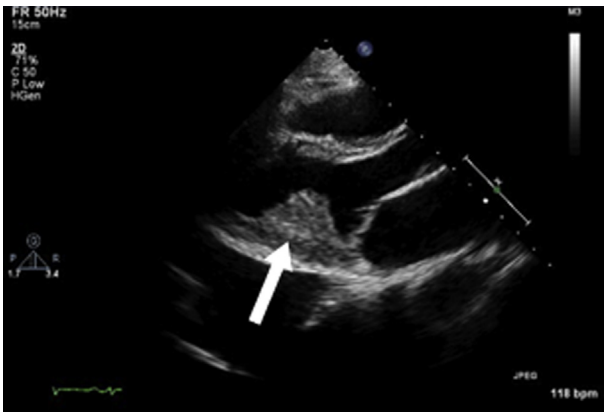
CT = computed tomography
EM = eosinophilic myocarditis
WBC = white blood cell

FIGURE 1 PA Chest Radiograph



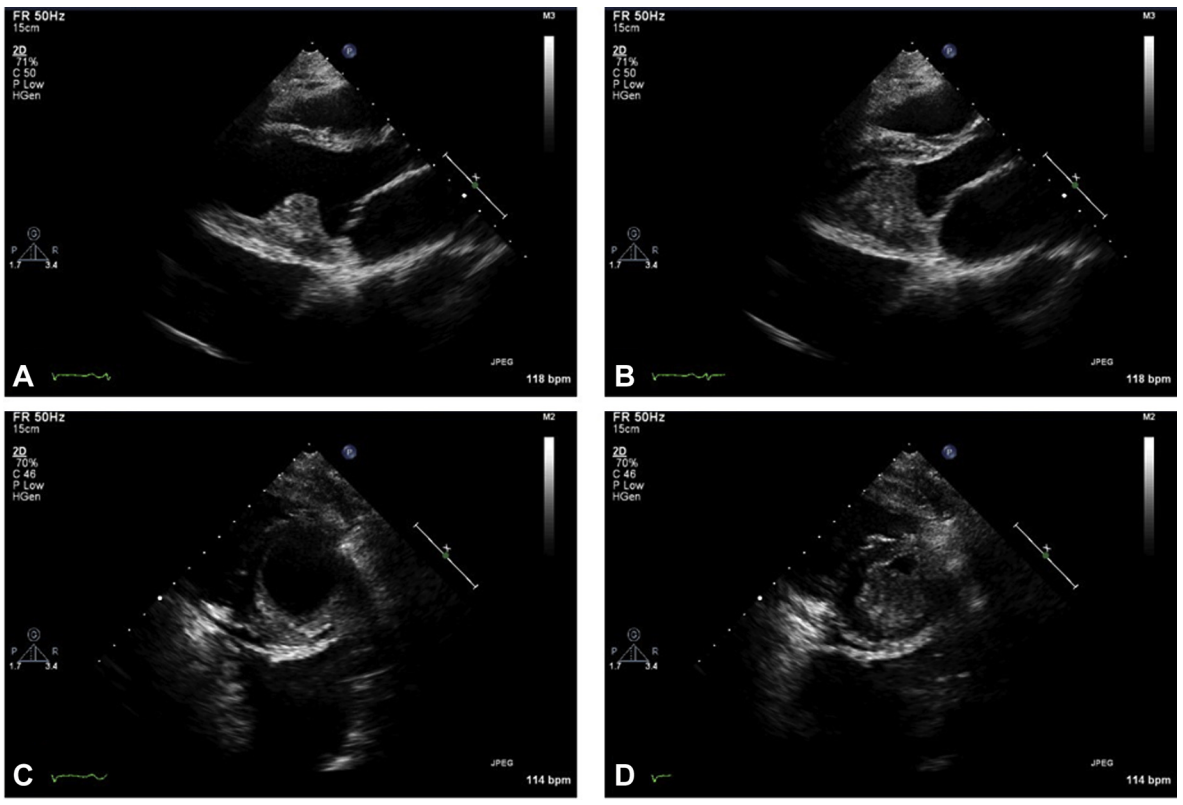
Posteroanterior (PA) chest radiograph demonstrates bilateral pleural effusions and pulmonary vascular congestion.

FIGURE 2 PLAX View Illustrating a Large Mass



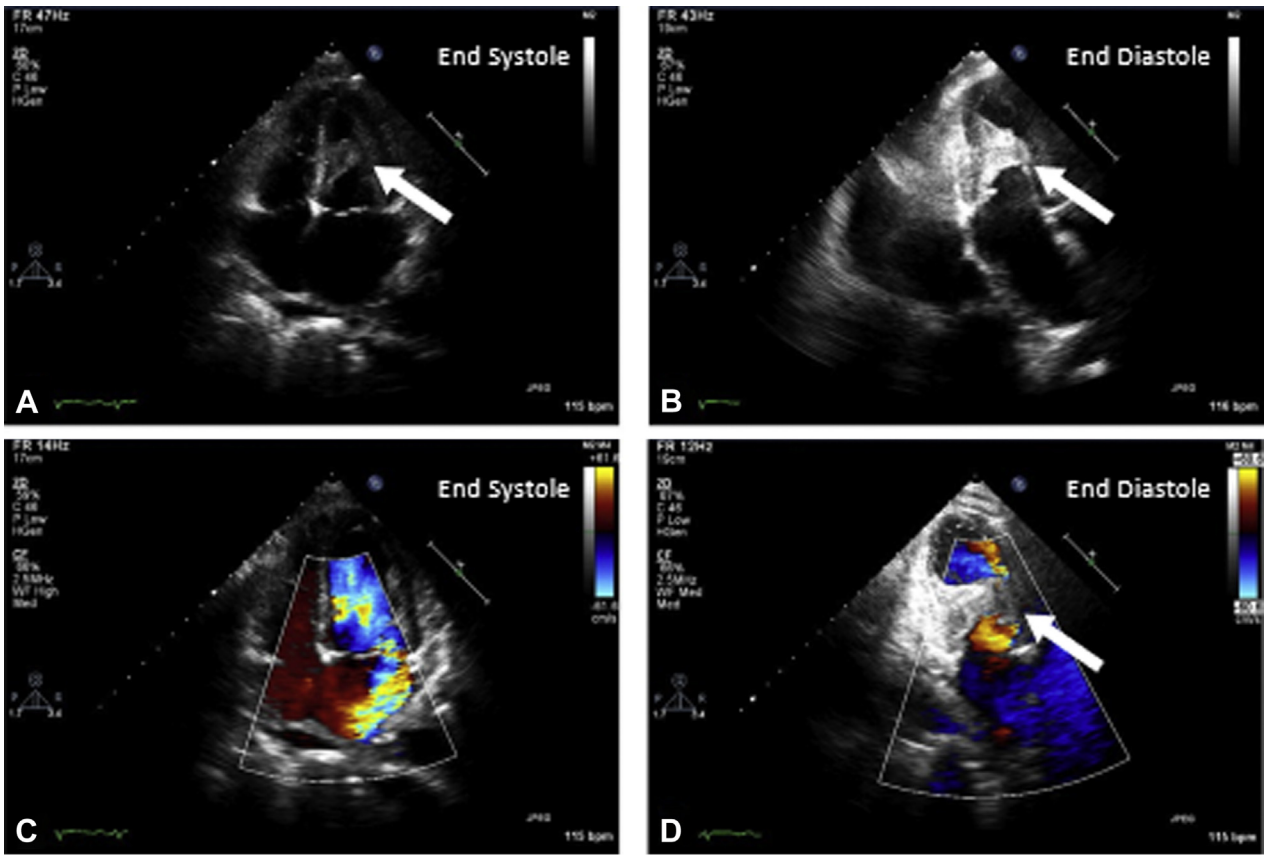
Parasternal long-axis (PLAX) view illustrates a large mass within the left ventricle emanating from the inferolateral wall.

FIGURE 3 Images From Admission Transthoracic Echocardiography



Representative images from admission transthoracic echocardiography: **(A)** PLAX view in diastole. **(B)** PLAX view in systole. **(C)** PSAX view in diastole. **(D)** PSAX view in systole. Abbreviations as in Figures 1 and 2.

FIGURE 4 Color Doppler Images Illustrating Severe Eccentric Mitral Regurgitation



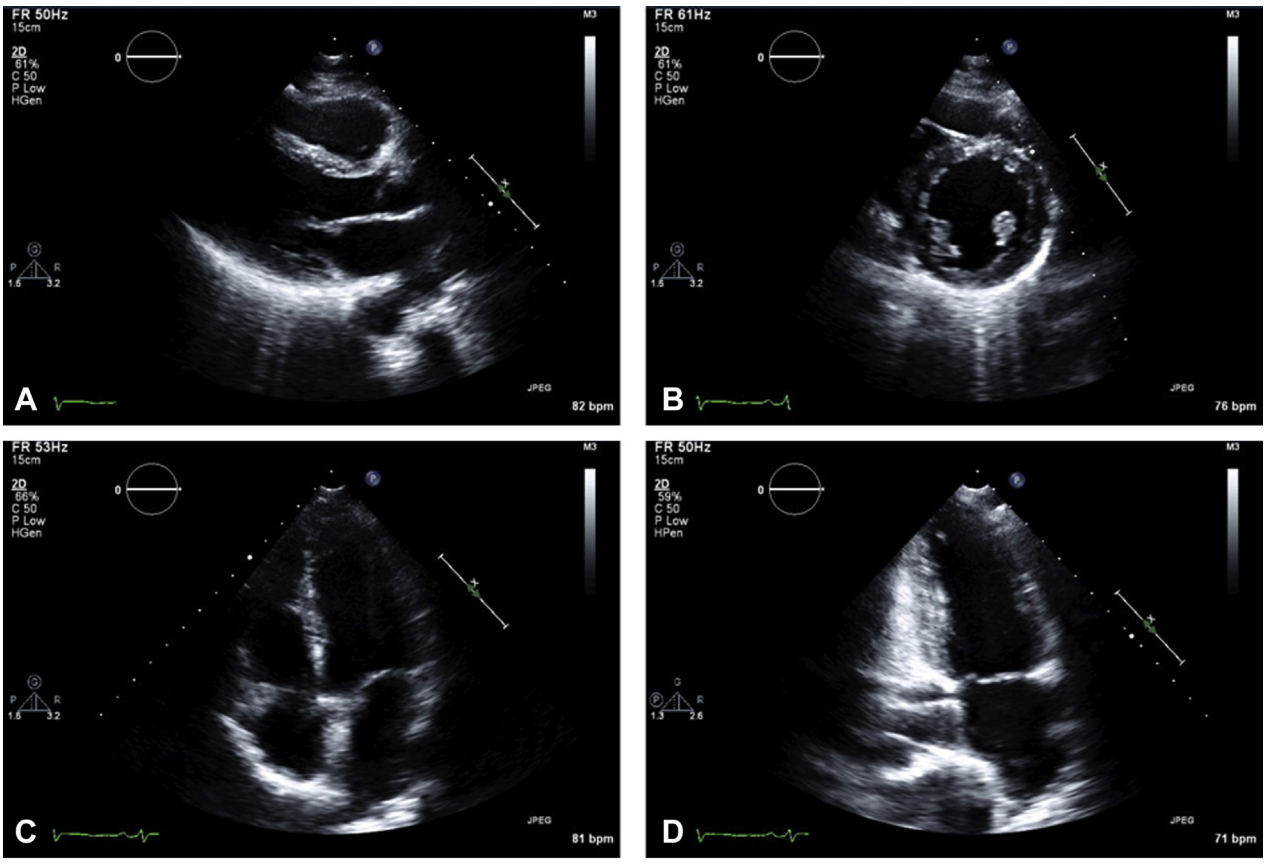
(A) Apical 4-chamber (A4C) view. **(B)** Color Doppler images illustrate severe, eccentric mitral regurgitation. **(C)** Apical 3-chamber (A3C) view. **(D)** Color Doppler images demonstrate flow acceleration and nearly complete obstruction of the left ventricular outflow tract.

DISCUSSION

Hypereosinophilia is defined by an absolute eosinophil count in the peripheral blood >500 cells/mm^3 and may arise in the absence of an underlying cause (i.e., idiopathic hypereosinophilic syndrome) or as a secondary consequence of many different conditions. Parasitic infections, medication side effects (e.g., from antimicrobials, antiretrovirals, medications with sulfa moieties, and non-steroidal anti-inflammatory drugs), autoimmune disorders, and hematologic malignancies, including classical Hodgkin lymphoma, are the most common culprits of secondary hypereosinophilia (4). Eosinophilic tissue infiltration produces the end-organ dysfunction associated with the condition, and cardiac involvement occurs in most cases. Pathophysiology is mediated by degranulation and release of eosinophils' cardiotoxic cellular contents, which activate intracardiac mast cells and lead to inflammation and fibrosis (5).

EM broadly characterizes the multiple cardiac manifestations of hypereosinophilia, which range from endomyocardial fibrosis resulting in a restrictive cardiomyopathy to valvular dysfunction related to Loeffler endocarditis to an eosinophilic coronary arteritis. The condition has 3 distinct phases: 1) an acute inflammatory phase characterized by eosinophilic infiltration; 2) a thrombotic phase where inflammation produces ventricular mural thrombi; and 3) a fibrotic phase where long-standing inflammation leads to a restrictive cardiomyopathy (5). Patients progress through each of these phases at variable paces. Symptoms and clinical presentations depend on the stage of EM. In the acute inflammatory phase, patients develop heart failure symptoms and chest discomfort, which may mimic an acute coronary

FIGURE 5 Representative Images From Transthoracic Echocardiography Performed 6 Months Prior to Admission



(A) PLAX; **(B)** PSAX; **(C)** A4C; **(D)** apical 2-chamber view. Abbreviations as in Figures 1, 2, and 4.

syndrome. In the thrombotic phase, embolic complications predominate. The fibrotic stage is typified by restrictive heart failure physiology and prominent right heart dysfunction.

TABLE 1 Differential Diagnosis of Intracardiac Masses

	Common	Rare
Neoplasm		
Primary	Angiosarcoma Leiomyosarcoma	Lymphoma Fibrous histiosarcoma
Secondary	Breast Lung Renal Melanoma	Thyroid Hepatic Adrenal Genitourinary
Non-neoplasms		
Benign masses	Myxoma Primary fibroelastoma Hamartoma	Lipoma Rhabdomyoma Fibroma
Miscellaneous	Thrombus Vegetation Carcinoid	Calcified amorphous tumor Infiltrative disorders Endocardial disease

Adapted from Bruce (3).

Management hinges on prompt recognition of EM prior to the onset of irreversible fibrosis. Until targeted therapies for the underlying condition can be initiated, patients should be treated with guideline-directed treatments for heart failure. Cardiogenic shock may complicate EM, and case reports describe the use of inotropes and mechanical circulatory support (6). Bradyarrhythmias from varying degrees of atrioventricular block and tachyarrhythmias such as ventricular tachycardia have also been described in the context of EM (7). Anticoagulation for mural thrombi is indicated as well. Once the patient is stabilized hemodynamically, therapy should be targeted at the underlying cause of hypereosinophilia.

FOLLOW-UP. The present patient completed 1 cycle of chemotherapy without incident. Her peripheral blood eosinophil counts normalized immediately (4.20 WBC/mm^3 with 1.4% eosinophils), and a repeat CT scan of her chest showed substantial reduction in

tumor burden. She described no symptoms of heart failure and no longer required diuretics. An echocardiogram repeated 2 months into therapy demonstrated partial regression of the mural thrombus (**Figure 6**, Video 7).

CONCLUSIONS

This report describes a unique case of EM and Loeffler syndrome producing cavity-obliterating left ventricular thrombi and severe mitral regurgitation. The patient's eosinophilia originated from Hodgkin lymphoma, which was promptly treated with chemotherapy, resulting in rapid resolution of her heart failure symptoms.

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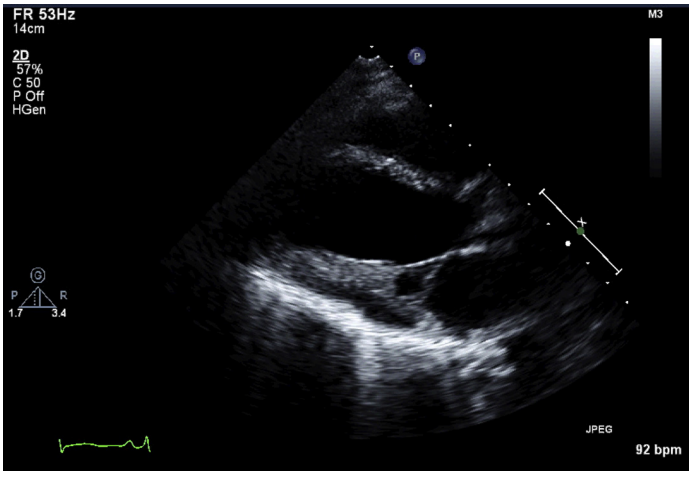
FIGURE 6 Representative PLAX Image From Echocardiography Performed Approximately 2 Months Into Treatment



Note the regression of the mural thrombi compared with those in **Figures 2 and 3**. PLAX = parasternal long axis.

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KEY WORDS diastolic heart failure, restrictive cardiomyopathy, ventricular thrombus

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