

Biventricular Thrombi in Substance-Induced Dilated Cardiomyopathy



Andrew M. Jacobson, MD, and Jason R. Darrah, MD, *La Crosse, Wisconsin*

INTRODUCTION

Intracardiac thrombi have increasingly been noted on cardiac imaging, but only a small number of case reports have included descriptions of biventricular thrombi. Optimal treatment for such clinical situations remains unclear. We present a case report with emphasis on diagnostic imaging techniques and management of biventricular thrombi.

CASE PRESENTATION

A 30-year-old man with a history of polysubstance abuse (intravenous methamphetamine, intranasal cocaine, alcohol) and recent diagnosis of dilated cardiomyopathy (left ventricular ejection fraction 18.7%), presented reporting worsening shortness of breath and flank pain. The patient had been compliant with recently started heart failure medications (metoprolol XL 25 mg/day, spironolactone 12.5 mg/day, lisinopril 5 mg/day, and furosemide 20 mg/day) for the past month. On arrival, he was found to be tachycardic but otherwise clinically stable. Pertinent initial laboratory workup revealed the following findings: troponin I 0.05 ng/mL (normal range, 0.02–0.03 ng/mL), brain natriuretic peptide 1,755.0 pg/mL (normal range, 5.0–100.0 pg/mL), D-dimer 1.44 mg/L fibrinogen-equivalent units (normal range, 0.19–0.50 mg/L fibrinogen-equivalent units), white blood cell count 9.88 K/ μ L (normal range, 3.70–10.40 K/ μ L), eosinophils 0.15 K/ μ L (normal range, 0.00–0.50 K/ μ L), thyroid-stimulating hormone 1.24 μ U/mL (normal range, 0.40–5.50 μ U/mL), and negative human immunodeficiency virus antibodies. Chest radiography revealed an enlarged cardiac silhouette. Electrocardiography revealed sinus tachycardia, a prolonged corrected QT interval, biatrial enlargement, left-axis deviation, previously noted anterior Q waves, and nonspecific inferolateral ST- and T-wave abnormalities (Figure 1).

Computed tomography of the abdomen and pelvis revealed a splenic infarct, bilateral renal infarcts, and possible cardiac thrombi (Figure 2).

Transthoracic echocardiography (TTE) revealed a left ventricular ejection fraction of 10% to 15% and multiple large thrombi within both the left and right ventricles (Figures 3 and 4, Videos 1 and 2). These masses measured as large as 2.5 cm in diameter, located in the apices, and appearing relatively fixed and immobile. Thrombi

VIDEO HIGHLIGHTS

Video 1: TTE, modified apical four-chamber view, revealing large biventricular masses.

Video 2: TTE, modified apical four-chamber view, with focus on the right ventricle, revealing large biventricular masses.

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were a new finding compared with TTE completed 1 month previously.

A heparin drip was started. Cardiac magnetic resonance imaging (cMRI) demonstrated masses in the right and left ventricular apices (Figure 5). The right mass measured 24 \times 17 mm, and the left mass measured 14 \times 19 mm. Following tissue characterization and gadolinium contrast, it was determined that these masses were consistent with thrombi.

It was felt that the likely etiology of the patient's dilated cardiomyopathy was polysubstance abuse leading to the formation of bilateral intracardiac thrombi. The case was discussed with interventional radiology, which believed that the risk for aspiration thrombectomy was too great, citing concern for ventricular wall perforation, damage to valves and chords, and possible embolization. Surgical intervention was discussed, but ultimately it was believed that medical management with anticoagulation should be pursued first. The patient was continued on a heparin drip, and warfarin was initiated. He was continued on a heparin drip for 48 hours after his international normalized ratio (INR) became therapeutic, for a total of 5 days. A hypercoagulable workup did not reveal evidence of a genetic predisposition for thrombophilia. We strongly recommended cessation of alcohol and substance use. He was continued on appropriate heart failure medications with the addition of warfarin, was enrolled in a cardiac rehabilitation program, and discharged home in stable condition. At a follow-up appointment 4 months following discharge, the patient reported mild orthopnea. TTE revealed a left ventricular ejection fraction of 10% and biventricular thrombi that had decreased in size (Figure 6).

The patient was continued on warfarin, and automatic implantable cardioverter-defibrillator placement was discussed but ultimately deferred until the thrombi fully resolve.

From the Department of Medical Education (A.M.J.) and Department of Cardiology (J.R.D.), Gunderson Health System, La Crosse, Wisconsin.

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DISCUSSION

The majority of intracardiac thrombi are detected on TTE, which is low in cost and widely available.¹ Characteristics distinguishing thrombi include (1) a mass with margins distinct from the endocardium; (2) a mass noted throughout the cardiac cycle and visualized in at least two orthogonal views; (3) a mass distinguishable from papillary muscles, chordae, trabeculations, and technical artifacts;

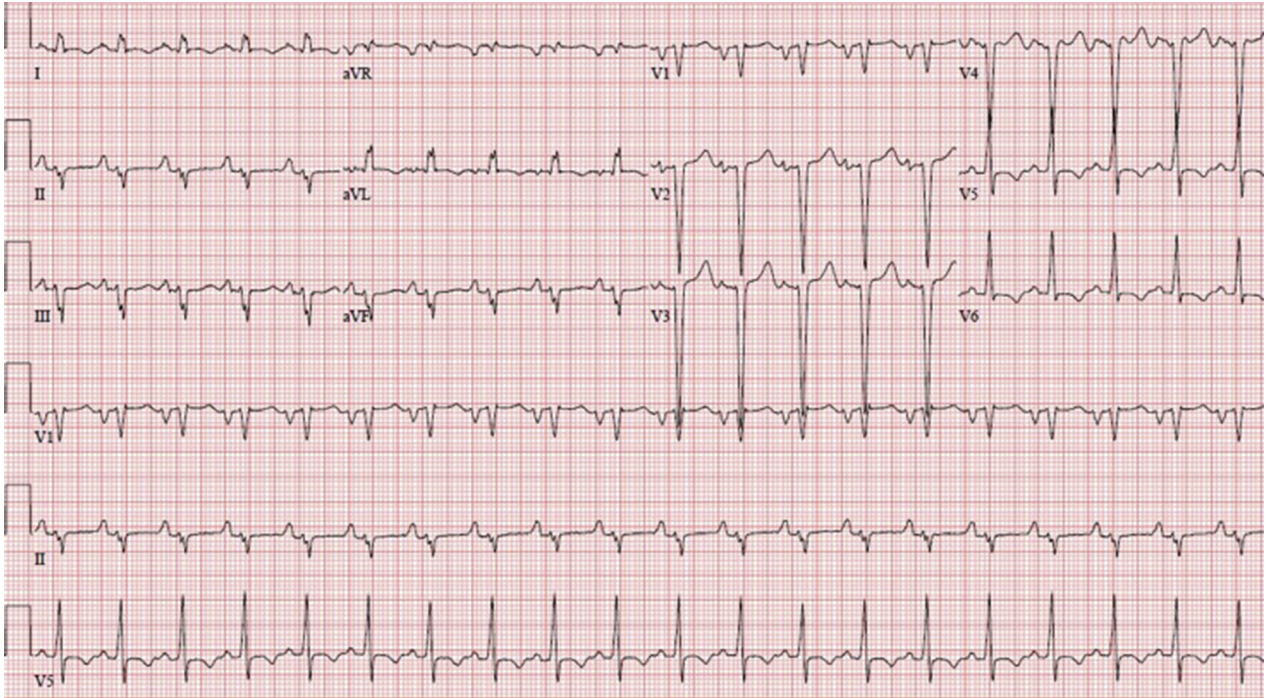


Figure 1 Electrocardiogram revealing sinus tachycardia, previously noted anterior Q waves, and nonspecific inferolateral ST- and T-wave abnormalities.

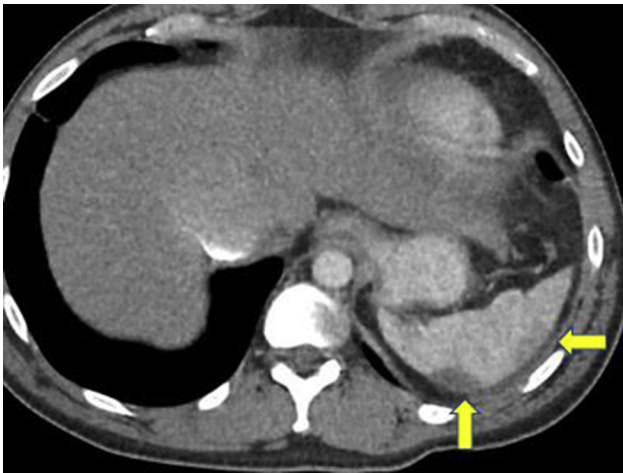


Figure 2 Computed tomography of the abdomen and pelvis, coronal view; *arrows* indicate splenic infarcts.

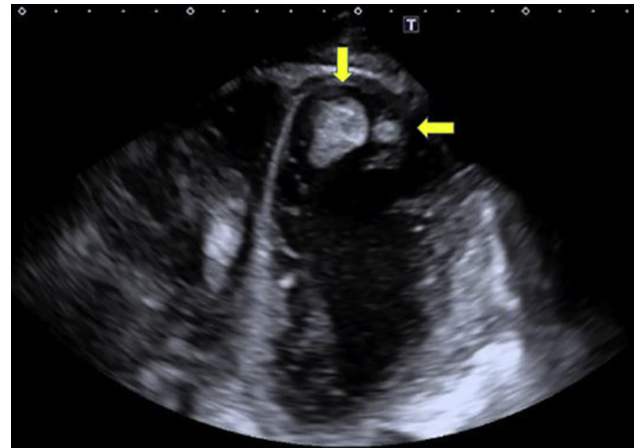


Figure 3 TTE, modified apical four-chamber view, revealing large biventricular masses; *arrows* indicate large thrombi to the left ventricular apex.

(4) characteristics consistent with avascular tissue; and (5) potential regional wall motion abnormality.² The use of contrast can help nearly double the sensitivity of thrombi detection on echocardiography.^{3,4} In one study, the sensitivity of left ventricular thrombi detection with TTE was improved from 35% to 64% with the use of contrast.³

cMRI is another useful tool in the diagnosis of thrombi. In a study comparing the diagnostic capabilities for left ventricular thrombus of TTE, transesophageal echocardiography, and cMRI, cMRI was the most sensitive diagnostic imaging modality. TTE had reported sensitivity of 23%, transesophageal echocardiography 40%, and contrast-enhanced cMRI 88%.⁵ Intracardiac thrombi appear as masses of absent gadolinium uptake, bordered by areas of increased signal intensity.

Gadolinium-based contrast uptake is dependent on the vascularity of the tissue in question. Because thrombi are avascular, they appear black, representing a lack of contrast uptake. Prolonged inversion time can be used for further thrombus characterization by amplifying the thrombus composition (dark, black) surrounded by areas of increased signal intensity (bright, white) representing vascular myocardium (Figure 5). cMRI with gadolinium contrast should be pursued when there remains a question of thrombus on echocardiography or improved thrombi characteristics are required for treatment decision-making.

The differential diagnosis for dilated cardiomyopathy is extensive; examples include idiopathic cardiomyopathy, myocarditis, ischemic heart disease, Chagas's disease, alcohol abuse, and amphetamine

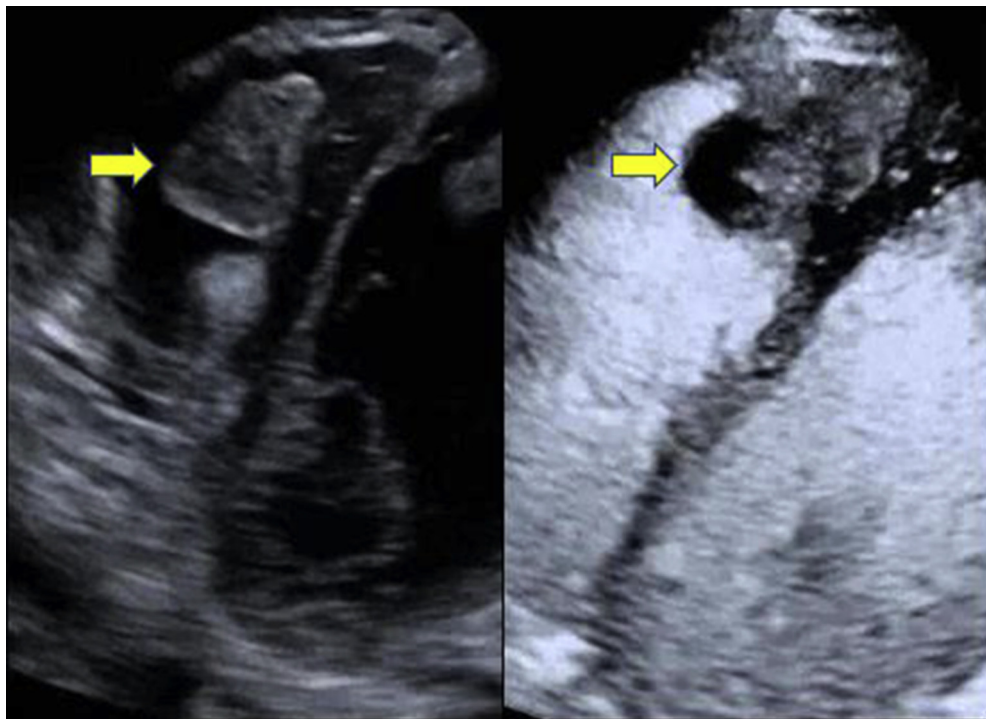


Figure 4 TTE, modified apical four-chamber view; arrows indicate right ventricular thrombi. Contrast enhancement is added to the image on the *right*.

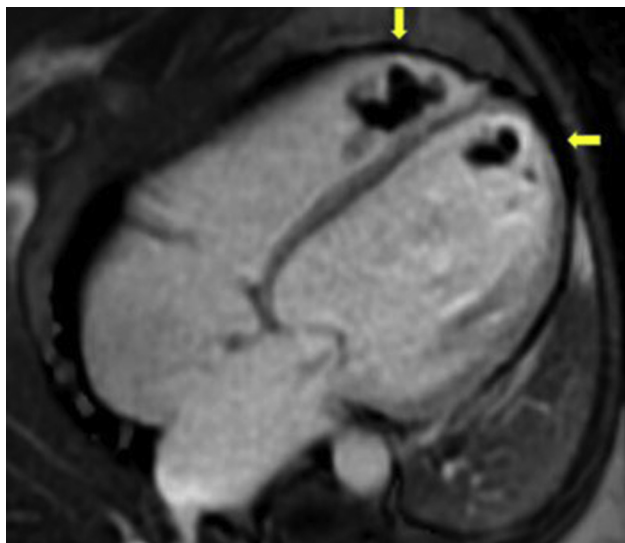


Figure 5 cMRI, four-chamber view, delayed contrast images, prolonged T1 time; arrows indicate masses with characteristics consistent with thrombi.

abuse, among others. With our patient's history of polysubstance abuse, it was speculated that dilated cardiomyopathy was secondary to abuse of alcohol, intranasal cocaine, and intravenous methamphetamine. Continued abuse of amphetamines can lead to cardiac dilation via increased cardiac stress from hypertension, tachycardia, vaso-spasm, and vasoconstriction.

When the etiology of thrombi remains uncertain, a review of familial history of thrombophilic disorders should be investigated, and a hypercoagulable workup should be completed. This often

includes laboratory testing for factor V Leiden gene mutation, prothrombin gene mutation, protein C activity, protein S activity, and antiphospholipid antibody syndrome.^{6,7}

There are several options for the treatment of intracardiac thrombi, such as anticoagulation, thrombolysis, percutaneous retrieval, and surgical intervention.

Warfarin has long been used for the treatment of intracardiac thrombi. In a meta-analysis of seven studies with patients who had documented left ventricular thrombi following anterior myocardial infarction, anticoagulation with warfarin decreased the absolute risk difference of thromboembolism by 33%.⁸ The 2013 American College of Cardiology Foundation/American Heart Association ST-segment elevation myocardial infarction guidelines for subsequent development of left ventricular thrombi include addition of warfarin for ≥ 3 months (when combined with dual-antiplatelet therapy), with a target INR of 2.0 to 2.5.⁹ In contrast, the American Heart Association/American Stroke Association 2014 stroke prevention guidelines target a higher INR of 2.5 (range, 2.0–3.0), following ischemic stroke or transient ischemic attack in the setting of acute myocardial infarction complicated with left ventricular thrombus.¹⁰ Duration of warfarin treatment is currently debated, with some groups recommending 3 months and others continuing treatment until resolution of thrombi as noted on follow-up imaging.^{1,9} As is considered for every case of anticoagulation, medication should be discontinued when the bleeding risk outweighs the benefit of treatment. Follow-up with contrast-enhanced TTE or cMRI within 3 months following treatment initiation is recommended.² If thrombi enlargement is noted on repeat imaging or embolization occurs while a patient is properly anticoagulated, it may be advisable to revisit the idea of surgical or percutaneous intervention.¹¹

In patients believed not to be ideal candidates for warfarin, direct oral anticoagulants have been used in the treatment of cardiac

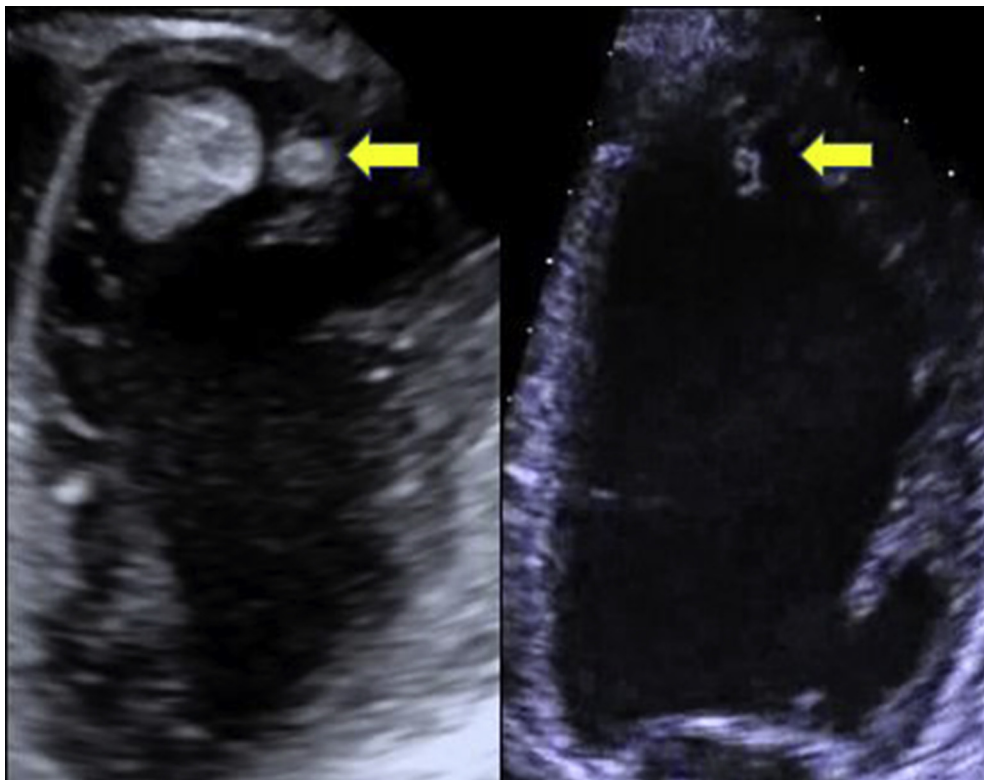


Figure 6 TTE, modified apical four-chamber view, revealing interval decrease in the size of left ventricular thrombi.

thrombi. There have been several publications describing the use of rivaroxaban or apixaban in the successful treatment of left ventricular thrombi.^{1,12-15} Patients falling into this category include those with abnormal liver function, concurrent use of cytochrome P450 inhibitors, histories of liable INRs, and poor follow-up for INR.^{12,13} Although these medications are not recommended as first-line therapy for biventricular thrombi, they do offer an intriguing alternative treatment approach. Further research into the viability of direct oral anticoagulants for the treatment of intracardiac thrombi is ongoing.¹

Catheter-directed thrombolysis, percutaneous aspiration, and surgical retrieval are other useful tools in the treatment of intracardiac thrombi. Often, these treatment options are exercised in patients presenting with symptoms stemming from pulmonary or systemic embolization.¹¹ Thrombi that are mobile, protruding, or with central echolucency have greater propensity to embolize.^{2,6}

CONCLUSION

Because biventricular thrombi remain a rare finding, the ideal treatment modality remains elusive. With review of the limited literature available, anticoagulation with oral vitamin K antagonists is often used successfully. Apixaban, rivaroxaban, and percutaneous and surgical intervention offer treatment options for clinical scenarios for which they are deemed appropriate. As such, treatment plans should be individualized to reflect the patient's comorbidities, risk factors, and thrombi characteristics.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.case.2020.01.007>.

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