

A Case of Bioprosthetic Mitral Valve Dysfunction, Initially Presenting with Valve Thrombosis Followed by Recurrent Thrombosis and Endocarditis



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INTRODUCTION

Bioprosthetic valve thrombosis (BPVT) is a rare entity associated with high morbidity and mortality.^{1,2} BPVT can coexist with other forms of prosthesis dysfunction such as endocarditis or pannus formation³ and has a wide spectrum of clinical presentations. Echocardiography plays a pivotal role in the diagnosis and the differentiation of BPVT from the other forms of valve dysfunction.^{4,5}

We present a case of bioprosthetic mitral valve thrombosis, in a patient with a history of drug abuse, which developed <3 years following original valve implantation. The patient presented with cardiogenic shock and multiorgan failure and was treated with multiple rounds of thrombolysis, with eventual clinical and hemodynamic stabilization and improvement of mitral valve gradients to baseline. Less than 3 months later, the patient was switched from warfarin to a novel anti-coagulant and represented with recurrent valve thrombosis (proven by pathology) and endocarditis of the bioprosthesis requiring surgical valve replacement. Echocardiography played an important role in the diagnosis and guided the management in both presentations.

CASE PRESENTATION

A 57-year-old man with a history of intravenous drug use developed endocarditis 3 years earlier, which was treated with antibiotics and mitral valve replacement using a bioprosthetic valve (27 mm St. Jude's Epic) and concomitant tricuspid valve repair (30 mm Carpentier Edwards annuloplasty ring) due to severe regurgitation from pulmonary hypertension and severe mitral regurgitation.

Three years following surgery he presented with shortness of breath and hemoptysis. On presentation he was afebrile; his blood pressure was 160/90 mm Hg, heart rate was 115 bpm, and oxygen saturation was 86% on room air. He was intubated for hypoxia and developed persistent hypotension requiring vasopressor support. Blood work was significant for leukocytosis, thrombocytopenia, and evidence of organ hypoperfusion (Table 1). Urine toxicology screen was positive for cocaine. Blood cultures were negative.

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Keywords: Bioprosthesis, Thrombosis, Fibrinolysis, Endocarditis, Echocardiography

Conflicts of interest: The authors reported no actual or potential conflicts of interest relative to this document.

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2468-6441

<https://doi.org/10.1016/j.case.2019.05.005>

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Electrocardiogram showed sinus tachycardia with right bundle branch block, and chest imaging revealed bilateral airspace opacities. Swan-Ganz catheter showed elevated wedge pressure (32 mm Hg), pulmonary hypertension (80/47 mm Hg), and low cardiac index (1.6).

Transthoracic echocardiogram (TTE) showed a thickened mitral valve prosthesis with reduced leaflet excursion and suggested significant mitral valve prosthesis stenosis (Videos 1 and 2), of unclear etiology. Bedside transesophageal echocardiogram (TEE) demonstrated mild left and moderate right ventricular dysfunction and severe bioprosthetic mitral valve thrombosis with the thrombus extending onto the lateral wall of the left atrium (Figure 1, Video 3).

Reoperation on the mitral valve was felt to carry a prohibitive risk of mortality. The patient was transfused platelets and was given thrombolysis with tissue plasminogen activator (tPA). After 2 cycles of tPA there was no clinical improvement and repeat echocardiograms showed unchanged mitral valve gradients. After a third cycle of thrombolysis, a TEE showed improvement in the mitral prosthesis thrombus burden (Video 4). At that time, the patient was maintained on a continuous heparin infusion with target anti-Xa 0.4-0.5. A repeat echocardiogram 28 days into hospitalization showed significant improvement in thrombus burden and valve gradients (Figure 2, Videos 5 and 6).

The patient slowly improved, liver and kidney function normalized, and he was transitioned to warfarin with a goal *international normalized ratio* (INR) of 2.5 to 3. Blood cultures remained negative throughout hospitalization. TTE upon discharge showed normalization of left ventricular systolic function and a mildly elevated mean gradient across the mitral bioprosthesis (7 mm Hg), which was similar to the gradient noted after his original surgery (Video 7).

Approximately 3 months following discharge and 2 weeks after warfarin was switched to rivaroxaban due to poor compliance with INR checks, the patient represented with progressive dyspnea on exertion. Upon presentation, he was afebrile; his blood pressure was 90/65 mm Hg, and heart rate was 95 bpm. Pertinent blood work showed anemia, thrombocytopenia, and leukocytosis. The patient denied recurrent drug use and urine toxicology screen was negative.

Repeat echocardiogram showed a large, mobile echodensity on the mitral valve prosthesis, with a 22 mm Hg mean gradient (Figure 3, Videos 8-10). Recurrent thrombosis was felt to be the cause, and he was treated again with tPA infusion. After thrombolysis completion, blood cultures returned positive for methicillin-resistant *Staphylococcus epidermidis*. Antibiotic therapy for prosthetic valve endocarditis was instituted.

Eventually the patient underwent reoperative mitral valve replacement with a 29 mm Carpentier Edwards Mitral MagnaEase bioprosthetic valve. The gram stain and culture of the explanted bioprosthesis were negative, while pathology revealed the presence of thrombus and bacterial colonies, which were consistent with the organism detected in the blood culture. Postoperative TTE showed

VIDEO HIGHLIGHTS

Video 1: Three-chamber apical view on TTE demonstrating well seated but thickened mitral valve bioprosthesis with reduced excursion. Normal mitral valve replacement leaflet excursion is not evident on this limited view.

Video 2: Three-chamber apical view on TTE with color Doppler demonstrating flow acceleration across the mitral valve, narrowed orifice, and turbulent jet in the left ventricle during diastole indicative of mitral valve stenosis and increased gradient across the valve. Mild mitral regurgitation and mild global left ventricular dysfunction are also present.

Video 3: Four-chamber biplane midesophageal view on TEE demonstrating a large amount of thrombus involving the mitral valve bioprosthesis, severely narrowing the mitral valve orifice and causing reduced leaflet excursion. The thrombus is extending into the lateral wall of the left atrium. Severe right ventricular dilation and dysfunction is present. Tricuspid valve annuloplasty ring is also shown.

Video 4: Four-chamber midesophageal view on TEE after three treatments of tPA, demonstrating reduction in thrombus burden and improvement in the mitral bioprosthesis leaflet excursion.

Video 5: Four-chamber midesophageal view on TEE after three treatments of tPA and continuous heparin revealing almost complete resolution of thrombus burden. Mitral leaflets show doming and mildly reduced mobility. Left ventricular systolic function appears normal.

Video 6: Composite video of the mitral valve bioprosthesis in three-dimensional imaging upon initial presentation and after successful thrombolysis. The left panel shows three-dimensional surgeon's view of the mitral valve bioprosthesis demonstrating leaflet thrombosis and reduced excursion. Thrombus adjacent to the valve ring, especially medially, is also suggested. On the right panel three-dimensional surgeon's view of the mitral valve bioprosthesis demonstrating almost complete resolution of the thrombus (possible minimal residual thrombus medially at 4 o'clock) and improvement in leaflet excursion at 28 days into hospital stay after three treatments of tPA and continuous heparin infusion.

Video 7: Parasternal long-axis view on TTE upon first discharge demonstrates a well-seated mitral bioprosthesis with resolution of the thrombus and normal leaflet excursion. Mitral leaflets appear thickened.

Video 8: Zoomed parasternal long-axis view on TTE demonstrates a recurrent, large, mobile echodensity in the orifice of the mitral valve bioprosthesis. There are small mobile components on the left ventricular side of the mass.

Video 9: Midesophageal view of the mitral valve prosthesis on TEE at the time of surgery revealing recurrent mitral valve thrombus with a mobile echodensity prolapsing into the left atrium. The mobile material is multilobulated with new small mobile components on its left atrial side.

Video 10: Composite two-dimensional video of the mitral valve bioprosthesis comparing side by side the first presentation

and the second presentation on TEE. The *left panel* demonstrates a zoomed view of the mitral valve bioprosthesis with significant amount of thrombus causing reduced excursion of the valve and significant stenosis. The *right panel* shows a zoomed view of the mitral bioprosthesis at the second presentation of the patient. The echodense material involving the valve appears more friable and demonstrates mobile components prolapsing into the left atrium, more consistent with endocarditis, differentiating it from the original presentation.

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a well-functioning mitral valve prosthesis (Figure 4). The patient had an uneventful postoperative course and was discharged on warfarin.

DISCUSSION

BPVT is a relatively rare clinical entity, with reported incidence 0.04%-6.2% per year,^{1,2} yet it is still important, as it is associated with high morbidity and mortality. The largest BPVT series to date reported an 11.6% rate of histologically proven thrombosis, among 397 patients who underwent prosthesis explantation.⁶ A recent review reported that only 24% of BPVT cases occurred within the first 3 months.⁷ Mayo Clinic data showed that the peak incidence of BPVT is at 13-24 months following implantation.⁸

Patients with BPVT may have a wide spectrum of clinical presentations. Thrombosis of the valve may be an incidental finding at follow-up imaging with TTE or computed tomography scan.^{3,9} Most patients present clinically with progressive dyspnea and heart failure symptoms or systemic embolization, while patients with severe valve obstruction may present with cardiogenic shock.^{3,9}

The first-line imaging test in suspected BPVT is TTE.^{4,5} The test is useful to identify hemodynamic features suggestive of valve thrombosis (elevated transvalvular gradients); however, morphological features, such as reduced leaflet excursion and the presence of thrombus, may not always be seen.^{4,5} Therefore, after initial screening with TTE, TEE should be performed to better visualize the prosthesis leaflets, evaluate for presence of thrombus, and accurately differentiate it from pannus, vegetation, or valve degeneration.^{4,5} Differentiation of these entities is important, as they are treated in

Table 1 Laboratory data on patient's presentation

	First presentation	Normal values
Hemoglobin, g/dL	16.5	14-17
White blood count	16,500	4,000-10,000
Platelet count	53,000	150,000-350,000
INR	1.1	<1.1
Lactate, mmol/L	2.2	<2
Creatinine, mg/dL	2.2	0.8-1.3
Potassium, meq/L	5.9	3.5-5
AST, units/L	3,125	0-35
ALT, units/L	1,568	0-35
Total bilirubin, mg/dL	1.8	0.3-1.2
BNP, pg/mL	1,200	<100

ALT, alanine aminotransferase; AST, aspartate aminotransferase.

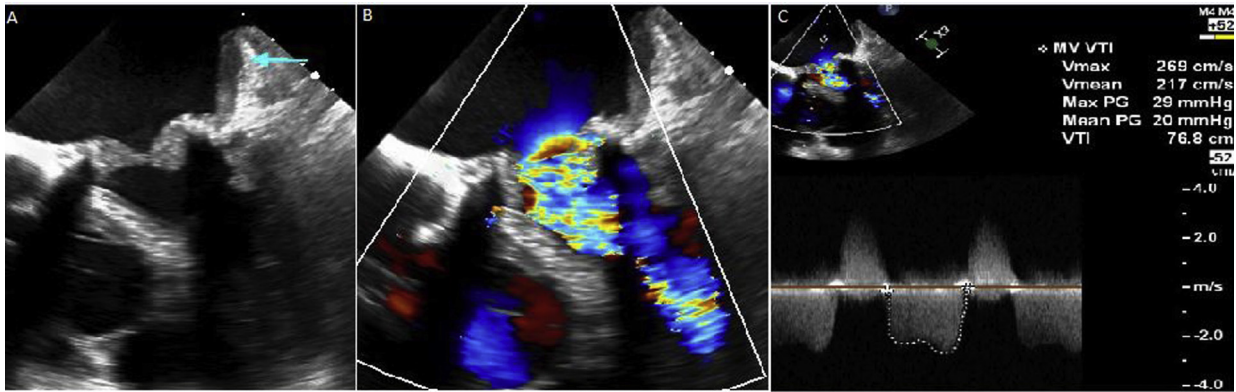


Figure 1 TEE obtained upon initial presentation of the patient. **(A)** Midesophageal four-chamber view demonstrates a thickened mitral valve bioprosthesis with significant thrombus burden and reduced leaflet excursion. The thrombus extends to the lateral wall of the left atrium (*blue arrow*). **(B)** Midesophageal four-chamber view with color Doppler demonstrates significant flow acceleration across the mitral valve during diastole, suggestive of significant mitral valve stenosis. **(C)** Continuous-wave Doppler across the mitral valve in the midesophageal four-chamber window demonstrating peak velocity of 2.69 m/sec and mean gradient of 20 mm Hg across the mitral bioprosthesis, consistent with severe stenosis.

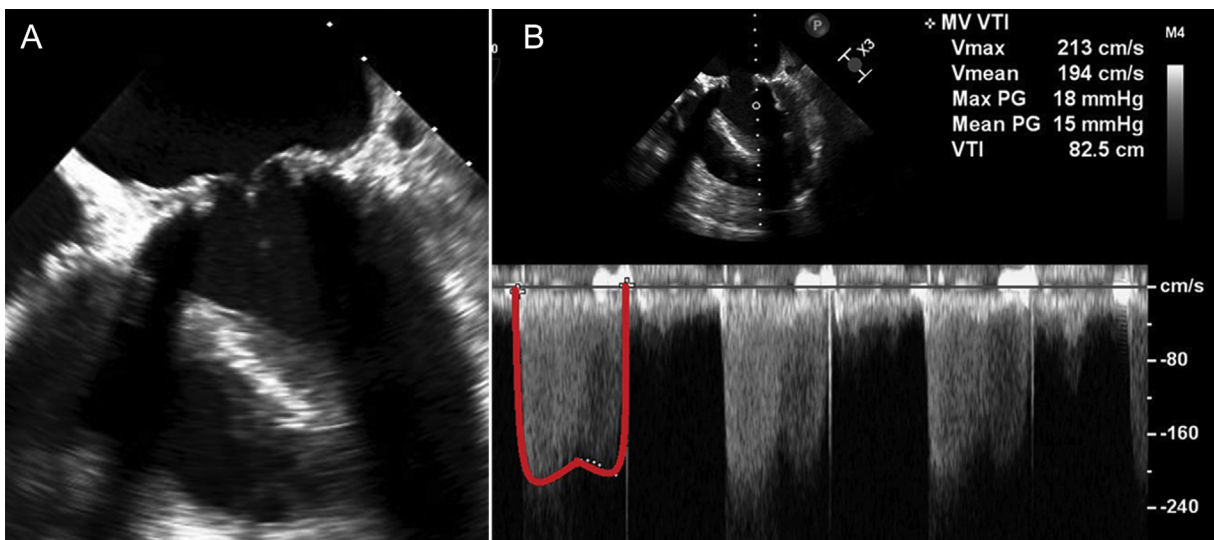


Figure 2 TEE obtained after three rounds of thrombolysis. **(A)** Midesophageal four-chamber view demonstrates almost complete resolution of the thrombus in the mitral bioprosthesis. Minimal amount of thrombus is noted in the ventricular aspect of the posterior mitral leaflet. The left atrial thrombus has resolved. **(B)** Continuous-wave Doppler across the mitral valve in the midesophageal four-chamber window demonstrating improved gradients after three rounds of thrombolysis.

different ways. [Table 2](#) presents clinical and echocardiographic characteristics of the different entities of bioprosthesis dysfunction. Though BPVT typically presents with stenosis, new-onset regurgitation or mixed stenosis-regurgitation can also occur.^{3,5,9,10} In patients with inconclusive TTE and TEE findings, multidetector computed tomography scan can differentiate between thrombus and pannus, based on Hounsfield units.¹¹

The treatment strategy for BPVT depends on clinical presentation, hemodynamic status, valve location, and presence of obstruction.^{3,9,10} In cases of left-sided obstructive thrombi, surgery is the preferred treatment, with fibrinolysis being reserved for patients with poor functional capacity, high surgical risk, or contraindications to surgery.¹² Fibrinolysis can also be considered in patients with good functional capacity and a small thrombus burden, after failure of heparin therapy.¹⁰

For nonobstructive left-sided thrombi that are >5 mm and mobile, surgery can be considered if intravenous heparin fails to resolve the thrombus. For thrombi <5 mm, medical therapy with oral anticoagulation is preferred.¹⁰ In cases of right-sided thrombi that cause obstruction, fibrinolysis is recommended.¹⁰

The optimal duration and intensity of anticoagulation after surgical bioprosthetic valve implantation have never been evaluated in randomized prospective trials, and most of the available evidence stems from large registry studies, with their inherent limitations. On the basis of current evidence, guidelines recommend 3 months of oral vitamin K antagonist therapy, followed by aspirin.¹²

There is no consensus in regards to the type or duration of anticoagulation for patients who present with BPVT.^{10,12} While vitamin K antagonists are the recommended anticoagulation strategy to treat

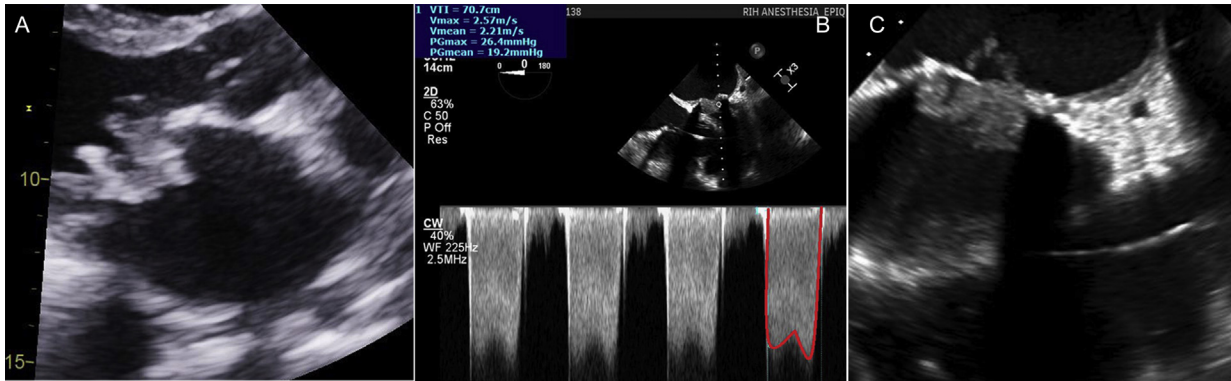


Figure 3 TTE and TEE obtained upon second presentation. **(A)** Transthoracic study: parasternal long-axis view zoomed to the mitral valve demonstrates an echogenic mass attached in the bioprosthesis causing reduced excursion. **(B)** Continuous-wave Doppler across the mitral valve in the midesophageal four-chamber window demonstrating peak velocity of 2.57 m/sec and mean gradient of 19 mm Hg across the mitral bioprosthesis, consistent with recurrent severe stenosis. **(C)** Transesophageal study: midesophageal view at 900 demonstrates a thickened mitral bioprosthesis with recurrent thrombus and friable and mobile components prolapsing to the left atrium consistent with superimposed endocarditis.

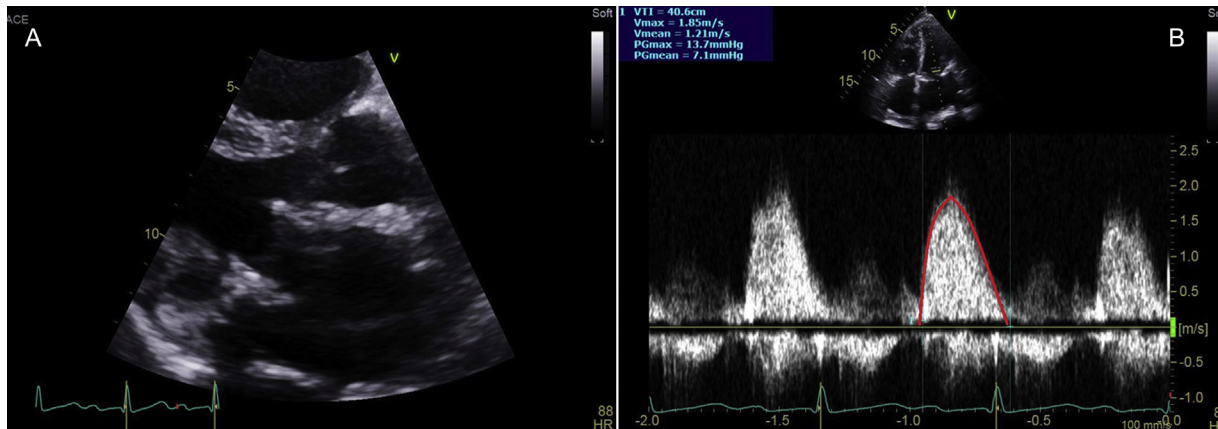


Figure 4 TTE after mitral valve replacement. **(A)** A well-seated bioprosthetic valve in the mitral position with thin leaflets is demonstrated. **(B)** Continuous-wave Doppler across the mitral valve showed a mean gradient of 7 mm Hg.

Table 2 Clinical and echocardiographic characteristics of thrombus, pannus, and vegetation

Thrombus	Pannus	Vegetation
Develops in shorter period after implantation (weeks to months), sudden/acute onset of symptoms.	Develops in longer period (usually years), symptoms are progressive.	May develop early or later after implantation, acute or subclinical symptoms.
Involves a large valve area, higher density, usually located on the atrial side of mitral prostheses, greater leaflet restriction, >50% increase in transvalvular gradient compared with baseline, increased cusp thickness (>2 mm) especially in the downstream aspect of valve, abnormal cusp mobility.	Involves a small valve area, lower density, usually located on the ventricular side of the valve, less leaflet restriction.	Echodense mass attached to the valve, mobile components, friable appearance, can cause leaflet restriction or leaflet destruction.

BPVT, the efficacy and safety of novel anticoagulants are explored in ongoing studies.

We presented a case of mitral bioprosthesis thrombosis, which was treated successfully with fibrinolysis and had recurrence of thrombosis

(proven by pathology) along with endocarditis of the prosthesis, <3 months following successful fibrinolytic therapy. Although we cannot be absolutely sure about the first presentation, since no pathology was acquired, underlying subclinical infection of the valve may

have been present (in light of an elevated white blood cell count and despite negative cultures), with superimposed thrombosis, which was successfully treated with thrombolysis.

CONCLUSION

BPVT occurs within months to years following valve implantation and should be in the differential of patients presenting with heart failure, thromboembolism, or cardiogenic shock. It can coexist with other forms of bioprosthesis dysfunction, such as pannus formation or endocarditis, and it may reoccur after successful treatment with fibrinolysis or anticoagulation. Prospective studies are required to define the appropriate type and duration of anticoagulation following initial surgical implantation and bioprosthesis thrombosis.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.case.2019.05.005>.

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