CLINICAL VIGNETTE

Delayed Reversibility of Late Bioprosthetic Valve Thrombosis

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Case Presentation

A 63-year-old male with a history of human immunodeficiency virus [HIV] and aortic stenosis status post bovine bioprosthetic valve replacement presented with New York Heart Association [NYHA] Class III symptoms and was admitted. Admission vitals were notable for tachycardia of 140 beats/minute. Physical exam revealed an irregularly irregular rhythm with tachycardia on cardiac auscultation, jugular venous pulsation of 8 cm above the sternal angle, and 1+ pitting edema of bilateral lower extremities. He had normal work of breathing, no cutaneous petechiae, and no splinter hemorrhages.

Admission laboratory studies were notable for blood urea nitrogen of 20 mg/dL, creatinine 1.55 mg/dL, brain natriuretic peptide of 380 ng/dL. Arterial blood gas was notable for pH 7.4, pCO2 27 mmHg, pO2 73 mmHg. Urinalysis had 1+ protein. Other studies including white blood cell count, troponin, erythrocyte sedimentation rate and C-reactive protein were within normal limits. Chest radiograph revealed mild pulmonary congestion. Electrocardiogram was notable for an atrial fibrillation with rapid ventricular rate [RVR].

Past medical history includes a 22-year history of human immunodeficiency virus [HIV] on antiretroviral therapy, initially diagnosed when patient presented with opportunistic infections including *Mycobacterium avium* complex, *Pneumocystis jirovecii* pneumonia, cytomegalovirus retinitis, and toxoplasmosis. Four years prior, the patient presented with shortness of breath and was found to have rapid atrial fibrillation and severe aortic stenosis. At that time, cardiac catheterization revealed no coronary artery disease. He subsequently underwent a surgical aortic valve replacement [SAVR] with a Carpentier-Edwards Magna pericardial valve with simultaneous pulmonary vein ablation, after which he took warfarin for three months.

Upon admission, transthoracic echocardiogram [TTE] was notable for severe stenosis of the bioprosthetic valve with peak velocity at 4.27 m/s, peak gradient of 73.1 mmHg, mean gradient of 46.0 mmHg, and aortic valve area of 0.7 cm² (Figure 1).

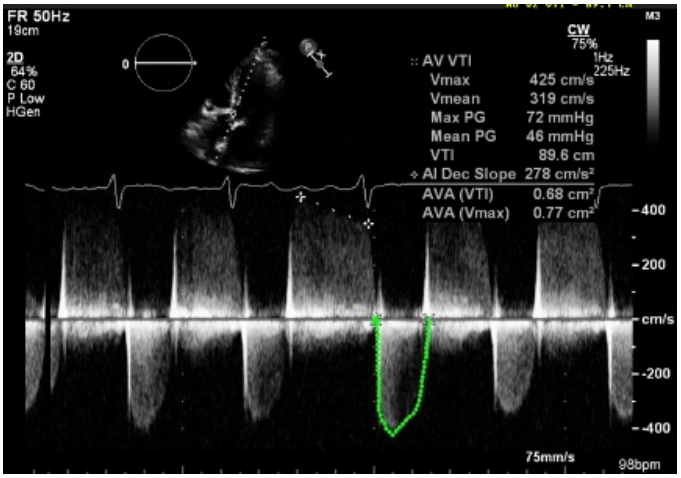

Figure 1. TTE During Presenting Hospitalization: Apical five-chamber view via transthoracic echocardiogram reveals severely elevated pressure gradient and velocity across the valve.

Transesophageal echocardiography [TEE] revealed marked aortic valve thickening and restricted mobility of the leaflets (Figure 2).

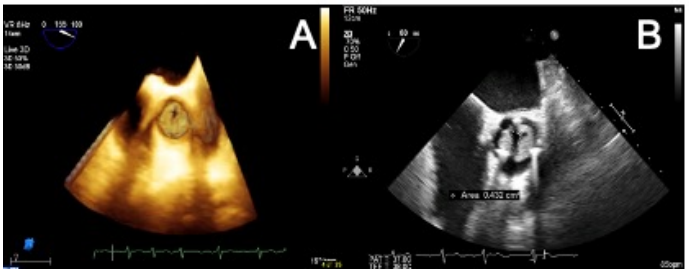

Figure 2. Transesophageal Echocardiography During Presenting Hospitalization: Transesophageal echocardiography reveals A) abnormal cusp motion, marked leaflet thickening, and B) severe stenosis of the bioprosthetic aortic valve.

Bacterial and fungal blood cultures were negative. Polymerase chain reaction for *Bartonella* spp and *Coxiella* spp were negative.

Out of concern that the echocardiographic findings suggested bioprosthetic valve thrombosis [BPVT], and for his CHA_2DS_2-Vasc score of 3, the patient was bridged to warfarin. The patient's RVR was controlled medically and his dyspnea improved to NYHA Class II. Urgent fibrinolysis or re-do surgery was deferred in lieu of outpatient management.

At thirty days following discharge, repeat TTE did not show improvement in pressure gradients or aortic valve area (Figure 3).

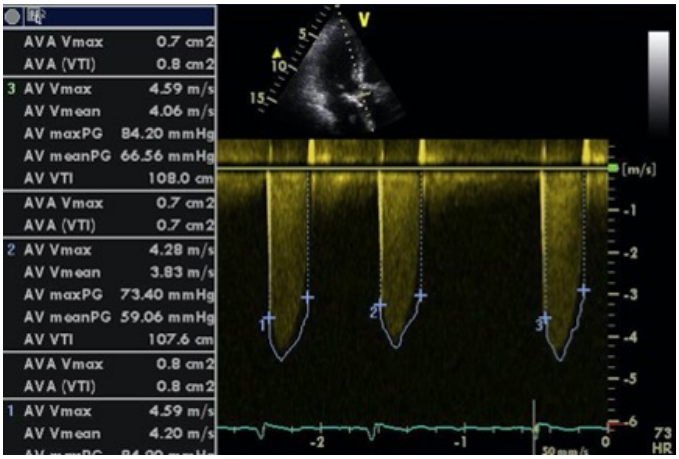

Figure 3. Repeat TTE at One Month of Anticoagulation: Apical five-chamber view reveals no improvement in aortic valve functioning.

The patient continued to report only mild dyspnea with exertion, and declined evaluation for re-do surgical valve repair. At six and sixteen months post-discharge, TTE demonstrated significant improvements including peak aortic velocity of 2.58 m/s and 2.25 m/s, mean pressure gradient of 18.5 mmHg and 9.9 mmHg, and aortic valve area of 1.4 cm^2 and 1.4 cm^2, respectively (Figures 4-5). All hemodynamics are summarized in Table 1.

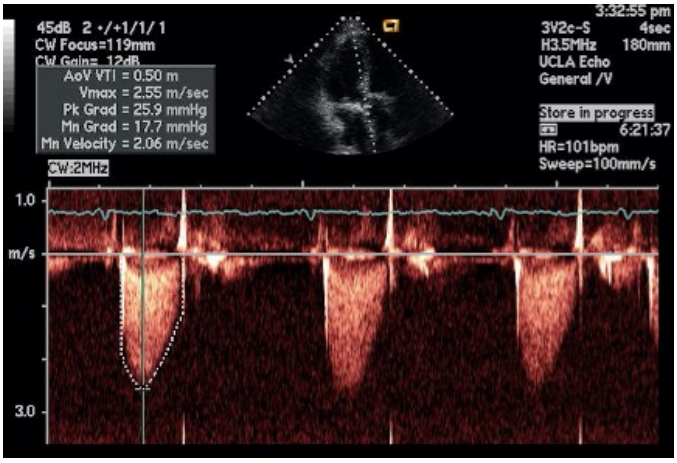

Figure 4: Repeat TTE at Six Months of Anticoagulation: Apical five-chamber view at six months reveals an aortic valve that is less stenotic with improving pressure gradients and velocity.

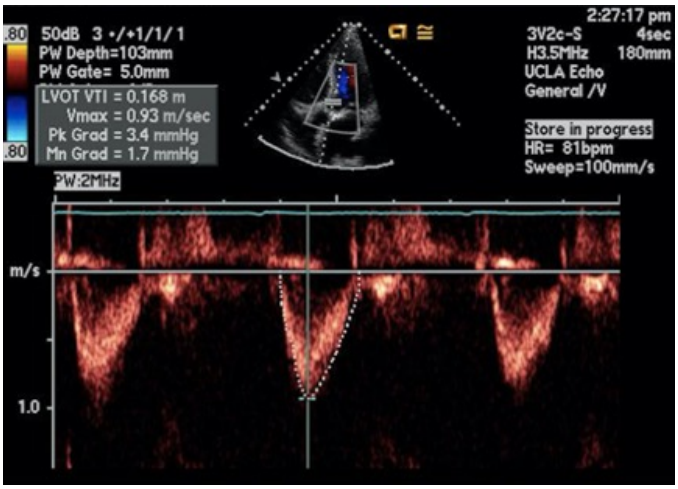

Figure 5: Repeat TTE at Sixteen Months of Anticoagulation: Apical five-chamber view reveals that the aortic valve pressure gradients and calculated valvular area are back to his baseline.

TTE relative to presenting hospitalization (months)	Aortic Valve Mean Pressure Gradient (mmHg)	Aortic Valve Peak Pressure Gradient (mmHg)	Aortic Valve Area (cm^2)	Aortic Valve Peak Velocity (m/sec)
-15 (baseline)	9.5	15.7	1.5	1.98
0 (Presenting hospitalization)	46.0	73.1	0.7	4.27
+ 1	63.0	78.9	0.7	4.44
+ 6	18.5	26.6	1.4	2.58
+ 16	9.9	20.2	1.4	2.25

Table 1: Serial Echocardiographic Measurements of Aortic Valve Pressure Gradients, Velocity, and Area

The patient took warfarin for three years after which he self-discontinued. He repeats TTE every year without evidence of valvular abnormality. He has had no other cardiac-related hospitalizations.

Discussion

This case describes a rare instance of very late BPVT four years after surgical replacement in an HIV+ patient. This case is particularly interesting because the thrombosis did not show improvement after one month of anticoagulation.

Bioprosthetic valves are less thrombogenic than mechanical valves, attributed to antithrombotic endothelium and more natural leaflet hemodynamics.[1] Bioprostheses have been increasingly utilized due to an aging recipient population in whom oral anticoagulation is not as safe.

Recently, there has been increased scrutiny on BPVT out of concern that the incidence is higher than originally understood. Retrospective analyses have estimated the incidence of BPVT between 0.03%-0.74%.[2] The largest related observational study found that up to 180 days post-SAVR, warfarin was associated

with decreased risk of stroke, thromboembolism, and cardiovascular death.[3] Incidence later than this time period has not been well-established, but one retrospective analysis did identify significant rates of occurrence 2-5 years post-operatively.[4] Thus, the American College of Cardiology/ American Heart Association recently extended its recommendation on duration of vitamin K antagonist therapy in bioprosthetic SAVR recipients from 3 to 3-6 months.[5]

TTE and TEE were the cornerstone diagnostic tools in this case. Echocardiographic diagnosis of BPVT and differentiation from pannus or infectious vegetation is difficult. National guidelines suggest that thrombi can be larger with softer sonographic density than pannus.[6] One study identified predictors for BPVT including 50% increase in the transvalvular gradient, abnormal cusp motion, increased cusp thickening, and paroxysmal atrial fibrillation associated with subtherapeutic INR if on warfarin therapy.[7] Notably, cardiac computed tomography was not employed, but may have been a reasonable modality if echocardiographic images were inadequate, as discussed in national guidelines.[8]

Valvular degeneration was felt to be unlikely at only four-years post operation. Suspicion for endocarditis was also low given lack of fever, leukocytosis, and otherwise negative review of systems. Culture-negative endocarditis was considered, but the patient had no abnormal exposures or travel, and was a native of the United States.

It is important to consider other comorbidities in this patient. HIV alone portends a hypercoagulable state,[9] and is an independent predictor of valvular calcification.[10] Further, his proteinuria is associated with hypercoagulability via the loss of antithrombin III. Finally, if he had ongoing, unnoticed atrial fibrillation, this may have increased his risk of valvular thrombosis.

Current guidelines recommend that for patients with BPVT and NYHA III-IV symptoms, evaluation for urgent intervention should be initiated. This patient was less symptomatic and was resistant to intervention. Utilizing shared decision-making, anticoagulation was trialed with close monitoring even after there was no improvement at one month.

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