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INTERMEDIATE

CASE REPORT: CLINICAL CASE

Transcatheter Heart Valve Thrombosis in a Patient With Polycythemia Vera Despite Apixaban Therapy for Atrial Fibrillation

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ABSTRACT

We present a case of transcatheter heart valve thrombosis in a 76-year-old man with paroxysmal atrial fibrillation on therapeutic anticoagulation with apixaban and polycythemia vera. The incidence of transcatheter heart valve thrombosis in patients with atrial fibrillation and on adequate anticoagulation is not well reported. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2021;3:269–72) © 2021 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/).

A 76-year-old White man presented with dyspnea and fatigue of 2 days' duration. Upon presentation, his blood pressure was 100/80 mm Hg, and his heart rate was 85 beats/min. He was afebrile. He had a 1/6 midpeaking systolic ejection murmur at the left upper sternal border with 1+ carotid upstroke. This finding was new from his previous physical examination 3 weeks earlier, when an early peaking systolic murmur and a normal carotid upstroke were noted. No obvious peripheral stigmata of endocarditis were present.

MEDICAL HISTORY

Two months before the index presentation, the patient underwent transcatheter aortic valve replacement (TAVR) with an Edwards Sapien 3 26-mm

LEARNING OBJECTIVES

- To highlight that THV thrombosis is a dreaded complication of TAVR and should be looked for in high-risk patient populations.
- To emphasize that patients with hypercoagulable states are prone to develop thrombosis of the valve despite adequate. anticoagulation and need closer follow-up.
- To identify the presenting features of THV thrombosis, which can range from subclinical to florid heart failure symptoms.
- To highlight that the modality of choice for diagnosis of this complication is CT imaging; however, transesophageal echocardiography may be a valuable alternative without the use of contrast or radiation.

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ABBREVIATIONS AND ACRONYMS

CT = computed tomography

DAPT = dual antiplatelet therapy

TAVR = transcatheter aortic valve replacement

THV = transcatheter heart valve

transcatheter heart valve (THV) (Edwards Lifesciences, Irvine, California). He has paroxysmal atrial fibrillation, is on apixaban 5 mg twice daily, has chronic renal insufficiency, and has JAK2-negative polycythemia vera, treated with bimonthly phlebotomy. There was no history of prior thrombotic events. He had a dental procedure before the index presentation with antibiotic prophylaxis. He was compliant with his medications, and the apixaban was not stopped before the dental procedure.

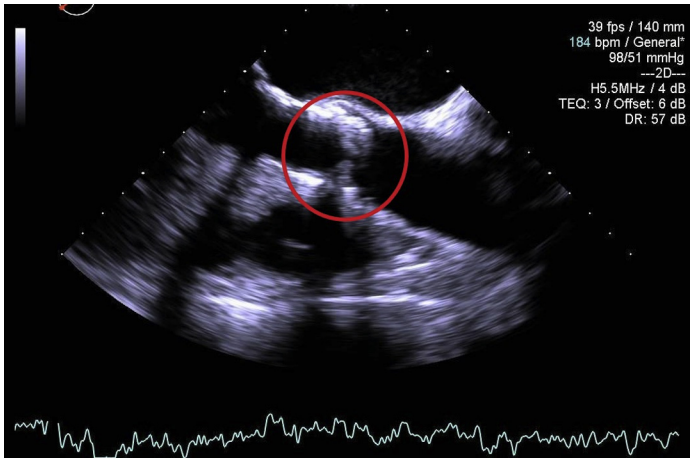
DIFFERENTIAL DIAGNOSIS

Endocarditis, acute exacerbation of congestive heart failure, and THV thrombosis were included in the differential diagnosis.

INVESTIGATIONS

A 12-lead electrocardiogram showed first-degree atrioventricular block. Cardiac troponin I level peaked at 0.352 ng/ml (normal range 0.015 to 0.045 ng/ml); N-terminal pro-brain natriuretic peptide level was 6,445 pg/ml (<450 pg/ml); and there was peripheral blood leukocytosis of 37,000/mm^3 (<25,000/mm^3), hemoglobin level of 12.9 g/dl (13.2 to 17.4 g/dl), red blood cell level of 4.20 m/μl (4.20 to 6.00 m/μl), and platelet count of 181,000/mm^3 (150,000 to 370,000/mm^3). The glomerular filtration rate was 25 ml/min/1.73 m^2 (>90 ml/min/m^2). Repeat transthoracic echocardiogram showed an ejection fraction of 55% with 2+ aortic regurgitation, a peak transaortic gradient of 76 mm Hg, and a mean gradient of 43 mm Hg; there were no vegetations. The valve appeared markedly thickened. There was no major paravalvular leak. Despite the lack of classic vegetation, initial suspicion leaned toward endocarditis, especially given the patient's ongoing use of apixaban. Blood cultures were initially drawn, and results remained negative throughout his hospitalization.

FIGURE 1 Echocardiogram Showing the Longitudinal View of Marked Aortic Valve Leaflet Thickening



MANAGEMENT

The day after initial presentation, the patient developed severe dyspnea and hypotension with a systolic blood pressure of 60 mm Hg. He was transferred to the intensive care unit and initiated on intravenous norepinephrine, noninvasive positive pressure ventilation for respiratory failure, and piperacillin-tazobactam and vancomycin for suspected sepsis. A transesophageal echocardiogram confirmed marked leaflet thickening of the valve leaflets and diminished opening with probable 2+ aortic regurgitation, but no classic vegetation or abscess (**Figures 1 to 3**, Video 1). Apixaban was discontinued in the setting of acute kidney injury, and the patient was initiated on intravenous unfractionated heparin. Because blood culture results were negative, the working diagnosis was THV thrombosis, given the medical history of polycythemia vera. Cardiac surgery was consulted, and the thrombosed aortic valve was urgently explanted. Histopathologic evaluation confirmed valve thrombosis without evidence of endocarditis. There was dramatic post-procedure recovery, and the patient was discharged on post-operative day 7 with long-term warfarin therapy. Outpatient follow-up echocardiography has shown stable tissue aortic valve function with a mean gradient of 11 mm Hg.

DISCUSSION

Clinical or symptomatic leaflet thrombosis after TAVR is rare and typically occurs in 7% of patients with implants, although subclinical THV thrombosis as noted on computed tomography (CT) scanning is increasingly evident and presents with symptoms of heart failure (1). Polycythemia vera is a chronic myeloproliferative disorder characterized by an abnormal increase in red blood cells and is linked to an increased thrombogenic risk. The management of tissue valves in patients with thrombophilic disorders is uncertain. There are no guidelines with regard to the use of antiplatelet versus antithrombotic therapy in this population. The most common symptom of THV thrombosis is progressive dyspnea (3). Embolic

events may also occur. THV thrombosis can be defined as: 1) THV dysfunction secondary to thrombosis, diagnosed based on regression of new-onset heart failure symptoms after initiation of anticoagulation therapy, along with a reduction in the mean gradient on echocardiography; or 2) a mobile mass detected on a THV suspicious for thrombus, irrespective of dysfunction, and in the absence of infection, or by definitive imaging or histopathologic findings (2). The most common findings by echocardiography are an increasing transvalvular gradient, thickened THV leaflets with or without impaired mobility, and visualization of thrombus formation on the valve (2). Transesophageal echocardiogram, although invasive, provides direct visualization of the THV leaflets and can assess leaflet motion and identify abnormal leaflet thickening. Predictors of leaflet thrombosis in TAVR patients include male sex, high body mass index, large sinus of Valsalva, bicuspid aortic valve, large size of THV, valve-in-valve procedure, and lack of anticoagulation (7). Our patient was male and had a hypercoagulable state. CT imaging is the gold standard to assess for THV thrombosis, evaluating for both leaflet thickness and mobility. Hypoattenuated leaflet thickening with reduced leaflet motion is the hallmark of leaflet thrombosis. To definitively exclude subclinical leaflet thrombosis, the scan quality should allow clear visualization of central leaflet coaptation coupled with the absence of hypoattenuation associated with the leaflets (3). Based on current evidence, it is not recommended that routine transesophageal echocardiogram/4-dimensional CT be performed to screen for subclinical leaflet thrombosis; however, it is recommended that the echocardiographic follow-up interval be shortened in cases of subclinical leaflet thrombosis (4). Current American College of Cardiology and American Heart Association guidelines recommend dual antiplatelet therapy (DAPT), typically aspirin and clopidogrel, for 6 months after TAVR, unless the patient has an indication for anticoagulation (5).

There is no clear, optimal antithrombotic strategy for patients with atrial fibrillation who undergo TAVR. Although there is no evidence of benefit of DAPT, most institutions prescribe 1 month of DAPT after TAVR. Oral anticoagulation is now known to prevent bioprosthetic valve thrombosis in TAVR and surgical aortic valve replacement patients; however, the optimal therapy remains unknown. Rosseel et al. (5) suggested in their study on valve thrombosis that such patients should receive oral anticoagulants for 36 months and repeat imaging to document resolution. In the SAVORY (Subclinical Aortic Valve Bioprosthesis Thrombosis Assessed With 4-Dimensional Computed Tomography) registry, which included patients undergoing both TAVR (n = 75) and surgical aortic valve replacement (n = 30),

FIGURE 2 Echocardiogram Showing a Cross-Sectional View of the Thrombosed Aortic Valve

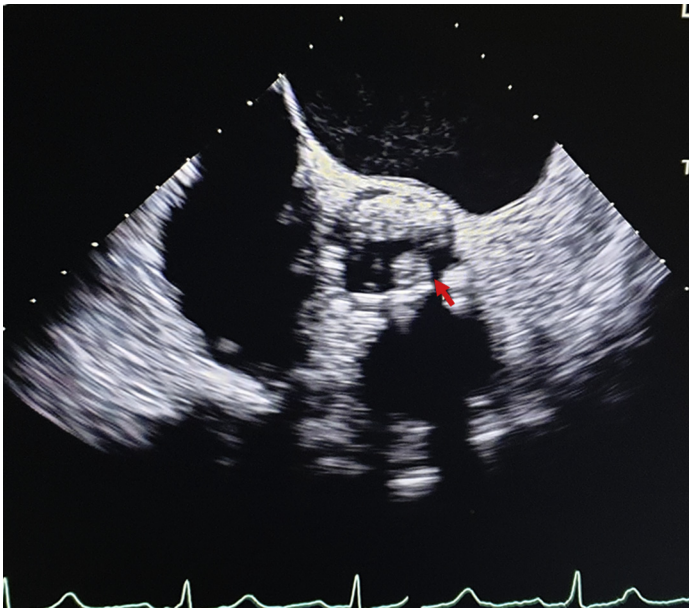
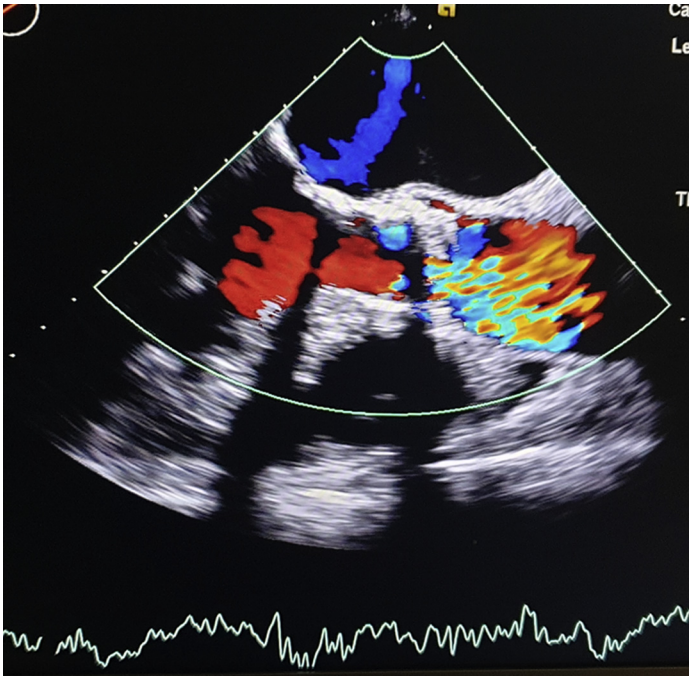


FIGURE 3 Color Doppler Image of the Thrombosed Aortic Valve



Søndergaard et al. (6) established that leaflet thrombosis was less frequently observed in patients using warfarin or novel oral anticoagulants than in those using dual antiplatelet or single antiplatelet therapy (6). However, the GALILEO (Global Study Comparing a Rivaroxaban-based Antithrombotic Strategy to an Antiplatelet-based Strategy After TAVR to Optimize Clinical Outcomes) study demonstrated that the use of oral anticoagulant in patients without an established indication for oral anticoagulation resulted in increased bleeding risk when compared to antiplatelet therapy (8).

FOLLOW-UP

The patient is currently on warfarin, with an international normalized ratio target of 2 to 3. The echocardiogram on follow-up showed an ejection fraction of 60%, and the mean gradient across the aortic valve was 11 mm Hg without any regurgitation.

CONCLUSIONS

Patients with higher predisposition for prosthetic valve thrombosis need closer follow-up post-valve replacement. The formulation of more detailed guidelines with regard to image screening and anticoagulation therapy in this subset of patients should be considered.

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KEY WORDS anticoagulation, antiplatelet, aortic valve, atrial fibrillation, thrombosis

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