Trans-Catheter Aortic Valve Replacement Thrombus in Patient on Xarelto and Aspirin Resolved Three Months After Warfarin

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Abstract

Trans-catheter aortic valve replacement has been gaining ground since it was performed in 2002. Indications for the procedure are also expanding and are expected to include patients with intermediate risk for perioperative mortality. There are no guidelines on the use of anticoagulation in patients who have undergone trans-catheter aortic valve replacement. We present an interesting case of an 82-year-old gentleman with past medical history of paroxysmal atrial fibrillation with a CHA2DS2-V\textsubscript{A}Sc score of 3, coronary artery disease, pernicious anemia, and severe symptomatic aortic stenosis who had trans-catheter aortic valve replacement. He was on Xarelto and aspirin, and still developed thrombus on the aortic valve many months after the procedure. The thrombus resolved after few months of anti-coagulation with Coumadin. This case shows that thrombus on the valve can still occur post-procedure even in patients who are on direct oral anticoagulant and aspirin. This calls into question if there is need to anti-coagulate all patients after TA VR procedure with Coumadin for at least 3 - 6 months. As our knowledge of the post-TA VR complications and outcomes continues to grow, we may be able to answer this question in the future, especially with large scale research studies.

Keywords: TAVR; Aortic prosthetic valve; Thrombosis; Anticoagulation

Introduction

The first trans-catheter aortic valve replacement (TAVR) procedure was performed in 2002 [1]. Since then, it has become the standard of care in prohibitive and high risk patients for surgical aortic valve replacement [2]. Since the first US Food and Drug Administration approval in 2011, over 50,000 patients have undergone TAVR in the United States alone [2]. Although clinical or symptomatic leaflet thrombosis is uncommon, it is a serious adverse event following TAVR with a grave prognosis.

As indications for TAVR is expected to expand in the future to include patients at intermediate and perhaps low risk for perioperative mortality following surgery, an early diagnosis of leaflet thrombosis and treatment with antithrombotic therapy would be critical to optimize clinical outcomes.

It was recorded that most cases appear to occur in the first year following TAVR, and the role of direct oral anticoagulants (DOAC) is being investigated in ongoing trials [3]. Accordingly, there is uncertainty on how to prevent and treat this complication in patients who present after 1 year while on DOAC.

Case Report

Our patient is an 82-year-old gentleman with a past medical history of paroxysmal atrial fibrillation with a CHA2DS2-V\textsubscript{A}Sc score of 3, coronary artery disease, pernicious anemia, and severe symptomatic aortic stenosis. Pre-procedural transthoracic echocardiography (TTE) showed an aortic valve area of 0.67 cm\textsuperscript{2} and preserved left ventricular function. A 29 mm Edwards Sapien III valve was successfully deployed without post dilatation. The post-procedural mean trans-valve gradient was 5 mm Hg, and no significant para-valvular regurgitation was observed by transesophageal echocardiogram (TEE). The patient opted for off-label Xarelto for anticoagulation because he was not doing well on warfarin, with very labile international normalized ratio (INR). A long discussion about the off-label use of Xarelto in the setting of bio-prosthetic aortic valve replacement led to his decision to pursue this along with aspirin for paroxysmal atrial fibrillation, stroke prophylaxis. He was then discharged on Xarelto 20 mg daily and aspirin 81 mg daily. He was otherwise doing well, and without dyspnea or chest tightness. On routine outpatient follow-up, we noted a murmur that was increased in intensity and repeat TTE showed that the gradients had increased to a mean gradient of 24 mm Hg. There was thickening of the aortic valve and thrombosis was concerning and suspected. There was no fever, chills, no
rash, no weight loss, weight gain, or signs of endocarditis or infection, no tooth aches etc. The patient denied any nausea, vomiting, diarrhea. He did undergo TEE which confirmed right coronary cusp thrombus measuring about 1.43 cm by 0.91 cm, which was layered, non-mobile, with normal valve function except for mild restriction leaflets (Fig. 1).

It was decided to admit him for high intensity IV heparin with bridge to warfarin and goal of INR between 2.5 and 3.5. He was discharged from the hospital few days later when his INR reached goal. Repeat TEE 3 months later showed complete resolution of the thrombus and normal valve function (Fig. 2).

Discussion

In a recent large consecutive cohort of 405 patients having TAVR performed with the Edwards balloon-expandable transcatheter heart valve (THV), the thrombus was diagnosed 1 - 3 months after the procedure by multi-detector computed tomography (MDCT) in 7% of the patients [4].

Based on previous studies, it has been noticed that the occurrence of THV thrombosis was associated with large THV size and in cases in which warfarin was not used as an option for antithrombotic agent [4-8]. THV thrombosis is expected to occur in the early period after TAVR and has not previously been reported later than 7 months post-TAVR [4, 9]. This case showed that THV dysfunction or an increase in murmur intensity should evoke prompt investigation for possible thrombus formation.

The predisposing factors for TAVR thrombosis in our case were the presence of paroxysmal atrial fibrillation, the use of Xarelto instead of warfarin and the use of mono antiplatelet therapy.

In a recent meta-analysis that compared aspirin versus aspirin and clopidogrel following TAVR, there was no difference in the 30-day clinical and cerebrovascular adverse event rates; however, a trend toward more bleeding in the aspirin and clopidogrel group was demonstrated, also it was recorded that monotherapy with aspirin was associated with a THV thrombosis risk of 25%, and importantly, all patients who experienced obstructive THV thrombosis received antiplatelet therapy alone [10].

Our patient did not experience any kind of cardiovascular symptoms. The thrombosis was discovered on a regular follow-up at the office with his cardiologist, which stresses the importance of regular long-term follow-up and raises the question of how frequently and for how long should those patients receive echocardiographic assessment of their valves. Based on a study that was done among 460 consecutive patients who underwent TAVR with the Edwards Sapien XT or Sapien 3 (Edwards Lifesciences, Irvine, California), THV thrombosis occurred in 28 of 405 (7%) patients. A total of 23 patients had subclinical THV thrombosis, whereas five (18%) patients experienced clinically overt obstructive THV thrombosis [4].

There are no clear guidelines on how to treat THV thrombus or the choice of anticoagulant for prevention. We and others have observed incidence of THV thrombosis in patients who are not on warfarin, thus indicating that short-term warfarin treatment or even long-term NOAC anticoagulants treatment of THV thrombosis might not be sufficient in patients...
who are prone to developing THV thrombosis [6].

Conclusions

THV thrombosis may develop late after TAVR despite treatment with DOAC and aspirin, and can be reversed with warfarin. As our knowledge of the outcomes post-TAVR continues to increase, this may lead to development of guideline in the future about the use of anticoagulation, especially warfarin, and for how long following the implantation of the valve. Large scale randomized study may be needed in the future to guide the choice of anticoagulant and duration of treatment.

Conflict of Interest

No conflict of interest from any of the authors.

References


