

Apixaban Anticoagulation Failure in Patients with Bio-Prosthetic Aortic Valve with Concomitant Paroxysmal Atrial Fibrillation Presenting as LAD Thrombosis, A Case Report

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Abstract: *One of the significant risk factor for development of a thromboembolic events in patients with bio-prosthetic aortic valve is co-occurrence of paroxysmal atrial fibrillation. Coumadin and New Oral Anti-Coagulants (NOACs) have been used for prevention of these events. Recent studies have shown that NOACs are less potent in preventing these thromboembolic events like stroke and myocardial infarction etc. compared to Coumadin.*

Keywords:

1. Introduction

Valvular atrial fibrillation is frequently associated with repeated thromboembolic events i.e. stroke and Myocardial infarction, especially with the accompaniment of bio-prosthetic aortic valve. Although, Coumadin and new oral anticoagulants (NOACS) have been historically used to prevent thromboembolic events (TE) since years but there is literature which shows that despite use of NOACS for prevention, there is still concrete evidence of development of different thromboembolic events (1). In this case report we are going to introduce an interesting case in which a known case of bio-prosthetic aortic valve with concomitant atrial fibrillation has developed ST segment elevation myocardial infarction (LAD Thrombosis) in spite of being treated with Apixaban (NOAC) for TE prevention.

2. Case Presentation

78 year old female patient with chronic risk factors for cardiovascular disease include systemic hypertension, dyslipidemia, metabolic syndrome, age paroxysmal atrial fibrillation. Previously, she was identified to have severe aortic valvular stenosis with an ascending aortic aneurysm. She subsequently underwent ascending aortic surgery and bio-prosthetic aortic replacement. After uneventful surgery she was started on Apixaban (NOAC) 5 mg once daily, which she tolerated very well. Of note, prior to the surgery, patient had a diagnostic Angiogram, which demonstrated normal flow in left and right coronary arteries.

Patient's clinical picture began evident when she presented to ED with approximately 5 hours history of discomfort between her shoulder blades. The patient was noted with a right bundle branch block and also with EKG deflections in

the lateral leads. Subsequent, EKG demonstrated lateral J-point elevation, which was concave up. Initially troponin was noted to be 0.27 at this time. Given the fact that the patient had atypical symptoms and a normal previous coronary angiogram, there was initial concern for possible aortic dissection given the ascending aortic aneurysm previously repaired. The patient underwent a CAT scan of the chest, which revealed no evidence of dissection, and she was subsequently instituted on heparin therapy by the admitting Internal Medicine Service.

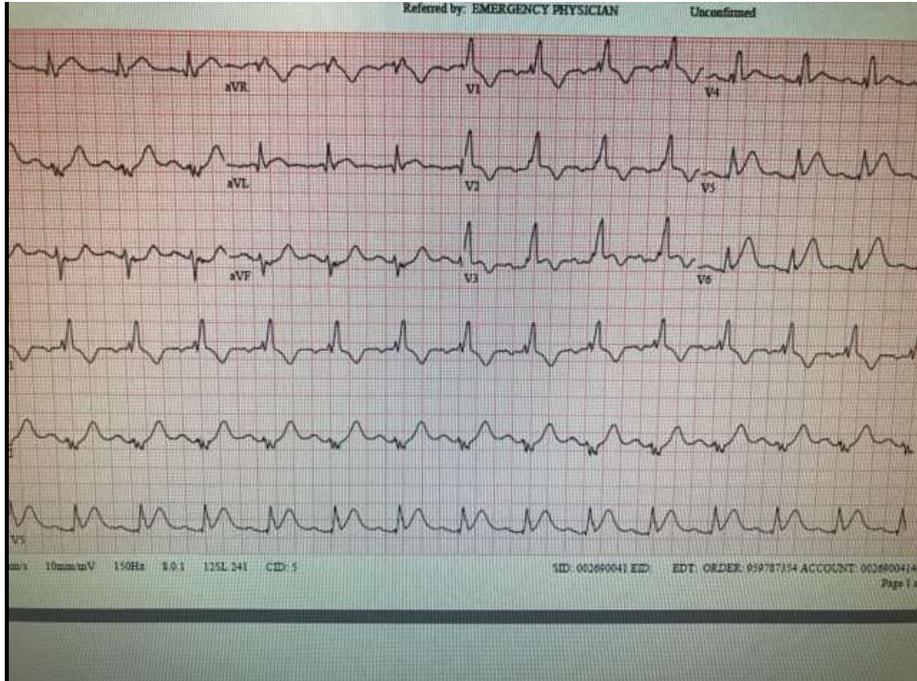
The patient had improvement of her back discomfort with blood pressure control and heparin and patient noted improved back discomfort. Further, ECGs demonstrated improvement in the lateral J-point elevation as well. Bedside echocardiogram demonstrated basal hyperkinesis and anterior apical, infero-apical hypo-kinesis. The patient disclosed at that time that she had a history of recently attending a funeral and there was a strong suspicion for Takotsubo cardiomyopathy given a recent emotional stress and normal angiogram preoperatively prior to aortic valve surgery. Heparin was continued as was the beta-blocker. Later on the patient had complete resolution of her shoulder discomfort and remained uneventful. Very next morning she became hemodynamic unstable and her troponin value continued to rise (despite discordant CPK values) and the patient was referred directly for urgent catheterization. Urgent catheterization at that time demonstrated TIMI grade 3 in all vessels with a subtotal filling defect of the LAD extending into the diagonal. As the patient was shoulder/chest pain free and ST elevation was not noted laterally, P2Y12 inhibitor load was ordered with integrilin bolus to address incomplete filling defects of the LAD and diagonal.

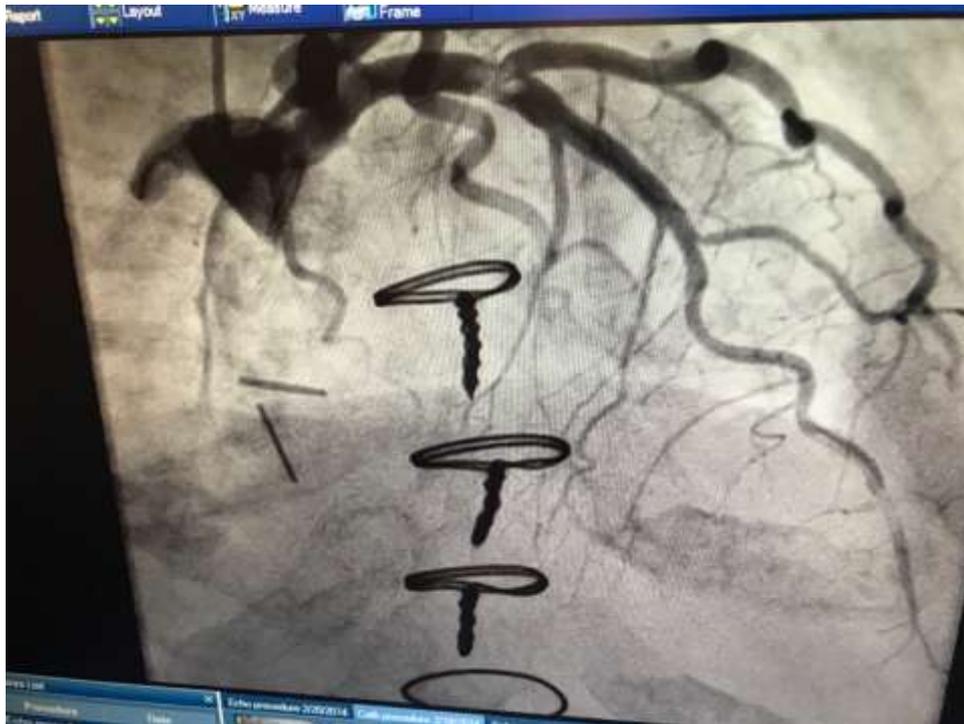
However, she had recurrence of chest pain and hypotension with the concern of Cardiogenic Shock. Percutaneous intervention was recommended because EKG showed recurrence of lateral ST elevation. On catheterization, aspiration of thrombectomy, along with stent placement in proximal portion of LAD was done. Furthermore, after a detailed discussion with cardiology and patient, her Apixaban was stopped and she was placed on Coumadin.

Trans-esophageal echocardiogram was failed to show any residual thrombus. She became hemodynamically stable and discharged home.

Pic 1 Shows the EKG changes.

Pic 2 and 3 shows the LAD thrombosis on Heart Catheterization.





3. Discussion

Patients with prosthetic heart valves including bio-prosthetic valves are at increased risk of thromboembolism especially in the presence of risk factors like age, smoking, hypertension, diabetes, hyperlipidemia, chronic or paroxysmal atrial fibrillation, low ejection fraction and problems with coagulation due to hepatic dysfunction. In bio-prosthetic aortic valve the definitive indications for anticoagulation theory are atrial fibrillation and depression of post-operative bi-ventricular function(2). After 3rd postoperative month ,when endothelium covers all of bio prosthesis there is increased risk of thromboembolism ranging from 0.37% to 6% (3)(4).To decrease this risk of thromboembolism remarkably, a proper anticoagulation therapy should be continued. Cons of using NOACs include no need for laboratory PT and aPTT measurement, fixed dosing, considerable reduced rates of bleeding, as well as fewer drug interactions (5)(6)(7)(8). However the inability of clinicians to check the compliance of the NOACs (Apixaban) and inability to reverse the side effects like bleeding are the limiting factors for their use (11). on the other hand for vitamin K dependent oral anticoagulants can be reversed with antidotes and their compliance can also be monitored with certain tests like INR.

According to our study and study reports we do not recommend use of Non Vitamin K Oral Anticoagulants for anticoagulation of patients with bio-prosthetic aortic valves with concomitant Paroxysmal Atrial fibrillation. However, more studies and clinical trials are needed to show the efficacy and whether Apixaban or any other non-Vitamin K oral anticoagulants can be used for anticoagulation or not (7). Current guidelines according to 2017 American College of Cardiology/American Heart Association AHA/ACC, recommend use of Vitamin K antagonist along with Aspirin(9)(10).

4. Conclusion

We recommend preferring the use of oral vitamin K factor dependent anticoagulants along with aspirin on NOACs for anticoagulation in patients with bio-prosthetic valves with co-existing paroxysmal atrial fibrillation.

5. Financial Disclosures

There is no financial disclosure for any of the authors participating in this study.

6. Abbreviations

NOACs: New oral Anticoagulants, TE: Thromboembolic events, LAD: Left anterior descending coronary artery, EKG: Electrocardiogram, CAT Scan: Computerized tomography, PT: Prothrombin time, aPPT: activated partial thromboplastin time, INR: International normalized ratio,

References

- [1] Bovin A1, Christensen TD, Grove EL. Antithrombotic treatment of patients with valvular atrial fibrillation
- [2] Bodnar AG, HutterAM Jr. Anticoagulation in valvular heart disease preoperatively and postoperativelyBrown ML,
- [3] Park SJ, Sundt TM, Schaff HV (2012) Early thrombosis risk in patients with biological valves in aortic position. J ThoracCardiovascSurg 144(1): 108-111.
- [4] Egbe AC, Pislaru SV, Pellikka PA, Poterucha JT, Schaff HV, et al. (2015) Bioprosthetic Valve Thrombosis Versus Structural Failure: Clinical and Echocardiographic Predictors. J Am CollCardiol 66(21): 2285-2294.
- [5] Fontana P., Goldhaber S. Z., and BounameauxH.. 2014. Direct oral anticoagulants in the treatment and

- long-term prevention of venous thrombo-embolism.
Eur. Heart J. 35:1836–1843.
- [6] Eikelboom JW, Weitz JI: New anticoagulants. *Circulation* 2010, 121(13):1523-1532. 10.1161/CIRCULATIONAHA.109.853119
- [7] Altman R, Vidal HO: Battle of oral anticoagulants in the field of atrial fibrillation scrutinized from a clinical practice (the real world) perspective. *Thromb J* 2011, 9:
- [8] Raghavan N, Frost CE, Yu Z, He K, Zhang H, Humphreys WG, Pinto D, Chen S, Bonacorsi S, Wong PC, Zhang D: Apixaban metabolism and pharmacokinetics after oral administration to humans. *Drug Metab Dispos* 2009, 37(1):74-81. 10.1124/dmd.108.023143
- [9] Guyatt GH, Akl EA, Crowther M, Gutterman DD, Schünemann HJ (2012) for the American College of Chest Physicians Antithrombotic Therapy and Prevention of Thrombosis Panel. Executive Summary: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 141(2_suppl): 7S-47S. doi:10.1378/ chest.1412S3.
- [10] Rick A. Nishimura, Catherine M. Otto, Robert O. Bonow, Blase A. Carabello, John P. Erwin, Lee A. Fleisher, Hani Jneid, Michael J. Mack, Christopher J. McLeod, Patrick T. O’Gara, Vera H. Rigolin, Thoralf M. Sundt, Annemarie Thompson AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease. *Journal of the American College of Cardiology* Jul 2017, 70 (2) 252-289; DOI: 10.1016/j.jacc.2017.03.011
- [11] Reiffel JA1, Weitz JI2, Reilly P3, Kaminskas E4, Sarich T5, Sager P6, Seltzer J7; Cardiac Safety Research Consortium presenters and participants.