Case Report

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Persistent Left Atrial Appendage Thrombus Despite Apixaban Therapy

Siddharth Kumar*, Vaibhav Sharma, Thirugnanasambandam Thayumanavan, Surender Singh and Shariq Shamim

St. Louis Heart and Vascular, St. Louis, MO, USA

***Corresponding Author**
Siddharth Kumar, St. Louis Heart and Vascular, St. Louis, MO, USA.

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Abstract

73-year-old female who developed new-onset atrial fibrillation (AF) with rapid ventricular response (RVR) further complicated by an unresolving left atrial appendage (LAA) thrombus and tachycardia-induced cardiomyopathy leading to Heart Failure with reduced Ejection Fraction (HFrEF). This report discusses the management strategies employed and the patient's clinical progression over 11 months. We highlight the role, limitations, and possible alternatives of direct oral anticoagulants (DOACs) in patients with LAA thrombus and the absence of clear consensus on what constitutes treatment failure with DOACs in such patients

Keywords: Apixaban, DOAC, Left Atrial Appendage, Atrial Fibrillation.

1. Introduction

Atrial fibrillation (AF) frequently leads to thrombus formation in the left atrium, with the left atrial appendage (LAA) being the most common site, accounting for over 90% of embolic events in patients with atrial fibrillation [1]. In recent years, direct oral anticoagulants (DOACs) have become a widely adopted treatment to dissolve these thrombi, yet data on their efficacy in certain scenarios, particularly regarding what constitutes treatment failure, remains scarce [2]. Although DOACs like apixaban have shown promise in dissolving LAA thrombi, especially in patients with comorbidities such as end-stage renal disease (ESRD) [3], cases of persistent thrombi despite treatment are rare but known. When DOACs fail, clinicians often face difficult decisions regarding alternative anticoagulation strategies, as there is a lack of consensus on the best approach in such situations [2].We present the case of a 73-year-old female with AF whose LAA thrombus persisted despite apixaban therapy, ultimately resolving after switching to warfarin.

2. Case Report

A 73-year-old non-smoker female with a medical history of essential hypertension, type 2 diabetes mellitus and depression presented to the emergency department with a one-week history of dyspnea and palpitations. The patient recovered from a recent COVID-19 infection earlier in the month but denied any chest pain. On initial evaluation the patient's vitals were as follows: heart rate of 180 beats per minute and irregular, blood pressure of 122/74, afebrile and oxygen saturation of 94% on room air. Electrocardiogram demonstrated AF with RVR.

The patient was admitted for further management. Routine labs were sent, results of which are in Table 1. A transesophageal echocardiogram (TEE) revealed a large thrombus in the LAA and a significantly reduced left ventricular ejection fraction (LVEF) of 35%, decreased from 60% documented earlier in the year. Initial management focused on rate control with intravenous diltiazem; PO metoprolol succinate and digoxin were eventually added to obtain rate control. Diltiazem was discontinued after low ejection fraction diagnosis.

	HD# 1	HD 3	HD 12	HD 13	HD 23
Hb (12-16 g/dL)	11	10.8	12.3	12.1	10.9
WBC (4.5 to 11.0 × 10^9/L)	13.3	12.3	12.4	9.7	6.5
Platelet (150 to 400 × 10^9/L)	98	153	328	394	279
Na/K (133-146 mmol/L; 3.5-5.3 mmol/L)	142/2.4	141/3.4	138/4.5	138/7	138/4.8
eGFR (mL/min/1.73m^2)		46	45	29*	50
Creatinine (0.62-1.1 mg/dL)	1.03	1.23	1.27	1.81*	1.15
Pro-BNP (<300 pg/dL)	6925	8186			
Troponin (0-0.4ng/mL)	66				
PT/INR (11-13.5 seconds; 0.8-1.1)	14.9/1.4				
aPTT (30-40 seconds)	>150	39			
Albumin (3.5 - 5 g/L)				2.8	
HbA1c (4-5.6 mmol/mol)	8.1				

Table 1: Routine Investigations Through the Hospital Course. #HD=Hospital Day; *Development of AKI;

Anticoagulation was initiated with apixaban with an initial dose of 10 mg twice a day due to the LAA thrombus. A cardiac catheterization was performed to exclude ischemic cardiomyopathy as the cause of the HFrEF. No significant changes of CAD were noted on the catheterization. Her HFrEF, was felt to be tachycardia-induced cardiomyopathy, was managed with furosemide and spironolactone. Patient continued to have AF with RVR despite adequate AV nodal blocking agents, therefore Electrophysiology consult was obtained. EP added Dofetilide. During the hospital course, she had a single episode of fecal occult blood positive test and acute kidney injury, likely due to cardiorenal syndrome. Guideline-based changes to management were done based on expert recommendations. The patient was discharged after 23 days on a regimen including dofetilide,

metoprolol succinate, apixaban, dapagliflozin, insulin lispro, sacubitril-valsartan, spironolactone, buspirone, fluoxetine, and methotrexate.

The patient was managed on an outpatient basis and follow-up TEEs were performed at 6 weeks, 4 months, and 11 months after treatment initiation (Table 2, Figure 1). At 6 weeks, the LVEF had improved to 45%. By 4 months, LVEF had fully recovered to 60%. The LAA thrombus remained unchanged at these time points. The patient had spontaneously converted to NSR with dofetilide on board. The patient remained compliant with DOAC throughout her treatment which was confirmed after multiple appointments with the pharmacy. Cardiothoracic surgery was consulted to explore the possibility of surgical thrombus removal, which at this point advised continuation of anticoagulation. She was switched to enoxaparin after no improvement in thrombus at 8 weeks and later to warfarin 5 months after initial hospitalization in view of possible failure of apixaban and enoxaparin therapy. After therapeutic INR of 2-3 was achieved and maintained, a follow up TEE, 11 months after initial presentation revealed complete LAA thrombus resolution, a normal EF and left atrium size along with mild TR.

Time	Study (image)	Findings	Anticoagulation status
Before symptom onset)	Echo	• Normal LVEF (60%)	NA
day of hospitalization	TEE (A)	• LAA thrombus present • LVEF was 35-40%	Started on enoxaparin and apixaban (DOAC)
8 weeks after treatment initiation	TEE (B)	• LAA thrombus unchanged • LVEF increased to 45% • LA normal size, appearance, and function. • Mild TR and Mild PR present.	Patient continues to take Apixaban, switched to enoxaparin after the study.
17 weeks after treatment initiation	TEE (C)	• LAA thrombus unchanged • LVEF recovered completely to 60% • LA is dilated	On enoxaparin currently, switched to warfarin after the study
47 weeks after treatment initiation	TEE (D)	• LAA thrombus dissolved • LVEF normal at 60%. • LA normal in size and thrombus • Mild TR and physiological PR.	Maintaining therapeutic INR on warfarin.

Table 2: TEE and Echocardiographic Findings Correlated with Anticoagulation Treatment. (Echo= Echocardiogram, TEE=Transesophageal echocardiogram, LVEF=Left Ventricular Ejection Fraction, LAA= Left Atrial Appendage, TR=Tricuspid Regurgitation, PR= Pulmonary Regurgitation)

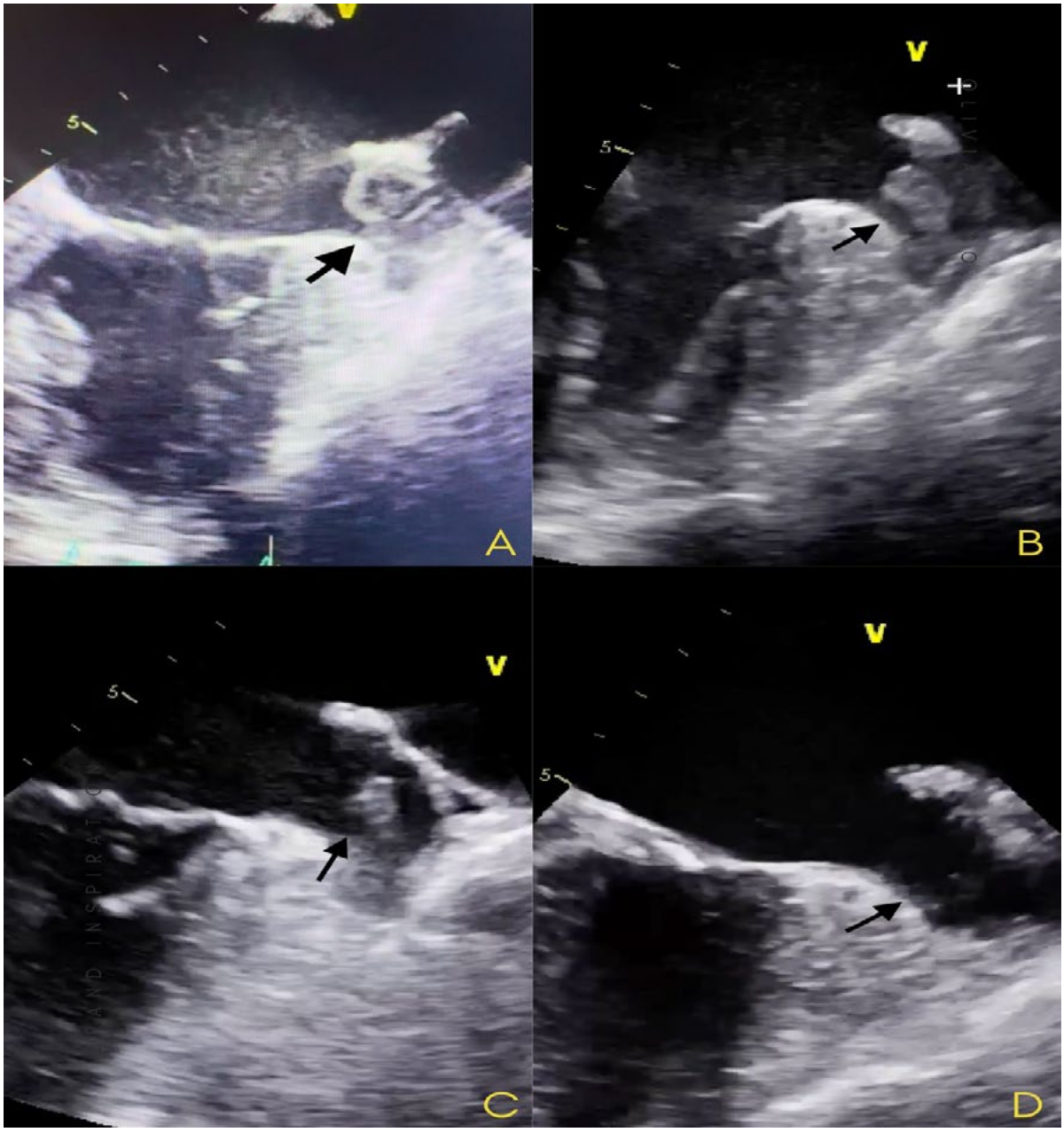

Figure 1: TEE Findings Showing the LAA (Arrow) in Chronological Order. A was on Initial Hospitalization, B, C, and D are at 8, 17, and 47 Weeks After the LAA Thrombus Diagnosis, Respectively.

3. Discussion

Atrial fibrillation with RVR can lead to complications such as tachycardia-induced cardiomyopathy, thrombogenesis, stroke, myocardial ischemia, and hemodynamic compromise. Thromboembolism, primarily from LAA thrombus, is the most serious complication of AF [4]. Rate and rhythm control are priorities, use of cardioversion depends on duration since onset, hemodynamic stability, and response to medical therapy. In AF lasting ≥ 48 hours, TEE to rule out LAA thrombus before cardioversion is advised. Anticoagulation is required if thrombus is present or cardioversion is performed [5]. DOACs are preferred in AF with LAA thrombus due to their safety and superiority over warfarin. Studies report a 79 to 94% success rate for LAA thrombus dissolution with DOACs [6]. Apixaban, a DOAC, has shown thrombus resolution as early as 16 days after treatment initiation. However, treatment failure is always a possible outcome for any drug and it is essential to recognize it before complications occur.

Failure of apixaban therapy could be multifactorial and dependent on factors such as advanced age, poor renal function, and diabetes mellitus. Genetic polymorphism in the ABCG2 drug transporter gene can lead to suboptimal drug levels, however, the impact of this interaction has not been studied in detail [7]. When considering treatment failure it is essential to check for patient compliance, as that could be another factor leading to thrombus non-resolution. When LAA thrombus persists despite chronic anticoagulation, most centers switch to another anticoagulant (e.g., from DOAC to VKA or another DOAC with a different mechanism). In some cases, low-molecular-

weight heparin (LMWH) is also considered [8]. Similarly, one study reported failure of standard dosing of rivaroxaban and suggested that increasing the dose to 15 mg twice daily could be effective. This adjustment led to LAA thrombus resolution in 46.7% of patients, it is important to consider the CHAD2S2-VASc and HAS-BLED score while making these adjustments [9]. The European Heart Rhythm Association (EHRA) survey indicates that follow-up imaging is typically performed within 3-6 weeks after anticoagulant therapy change. Currently, there's no consensus on the optimal anticoagulant, dosing, or follow-up timing [8].

Despite being compliant on optimal anticoagulation with Apixaban followed by anticoagulation with enoxaparin, our patient had no improvement in thrombus size on successive TEEs. A decision to switch to another unconventional anticoagulation regimen of warfarin was taken which led to thrombus resolution on the successive TEE after achievement of therapeutic INR range. This case highlights the need for individualized treatment approach, monitoring for treatment failure of DOACs and modification of anticoagulation strategies in complex AF cases. Warfarin still remains a reliable anticoagulant in patients with LAA thrombus who fail to respond to both the first line and an alternate agent. Future research should focus on identifying predictors of DOAC failure in LAA thrombus resolution and establishing clear guidelines for alternative anticoagulation strategies. Clinicians should remain prepared to adjust treatment plans based on patient response and imaging findings to ensure optimal outcomes.

Ethical Statement: On behalf of all the authors, I am pleased to submit our case report titled "Persistent Left Atrial Appendage Thrombus despite Apixaban Therapy" for consideration for publcation in the Journal of Future Medicine and Healthcare Innovation. This case report does not include any identifying patient details. Case reports do not require IRB approval in our institution. Verbal consent was obtained from the patient for the publication of this report. As no personal information is shared and the case is presented anonymously, further ethical approval was deemed not applicable for this publication.

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