



Rapid firing

Resolution of a warfarin and dabigatran-resistant left atrial appendage thrombus with apixaban

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ABSTRACT

The majority of embolisms associated with atrial fibrillation (AF) are from the left atrial appendage (LAA). To treat the existing thrombus, warfarin and novel anticoagulants have been used. However, there has been no clinical information regarding the difference of the effects of congealing the fibrinogenolysis system among these oral anticoagulants. Here, we report a case of persistent AF, in whom apixaban, factor Xa inhibitor resolved an LAA clot refractory to warfarin and direct thrombin inhibition. Factor Xa inhibitor, apixaban, could resolve the left appendage thrombosis refractory to warfarin and dabigatran.

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1. Introduction

The majority of clot embolisms associated with atrial fibrillation (AF) are from the left atrial appendage (LAA). Before cardioversion or catheter ablation, clot formation needs to be ruled out traditionally using transesophageal echocardiogram. To treat the existing thrombus, warfarin, and novel anticoagulants have been used [1–4]; however, there has been no clinical information regarding the differences of the effects to congealing the fibrinogenolysis system among these oral anticoagulants. We report a case of persistent AF, in whom apixaban, factor Xa inhibitor resolved LAA clot refractory to warfarin and direct thrombin inhibition.

2. Case report

A 63-year-old man with persistent AF was treated with warfarin 3.75 mg daily (prothrombin time-international normalized ratio [PT-INR] range: 1.66–2.99). His medical history included thalamic hemorrhage, hypertension, diabetes mellitus, and chronic kidney disease (CKD) (stage 3). Anticoagulation with warfarin was initiated, with a CHA₂DS₂-VASc score of two (hypertension and diabetes mellitus) and an HAS-BLED score of four (hypertension, CKD, history of thalamic hemorrhage, and labile PT-INR). As the atrial fibrillation was quite symptomatic and refractory to the medication, catheter ablation

was planned. The time course of the anticoagulation therapy is shown in Fig. 1. Initial transesophageal echocardiography (TEE) (Fig. 2A) identified mobile LAA thrombus despite approximately one year of therapeutic anticoagulation therapy with warfarin (PT-INR 1.66–2.99, percent time in therapeutic PT-INR range (TTR) of 50%, D-dimer 0.47 µg/mL). Catheter ablation was deferred and more intensive anticoagulation therapy targeting the INR range of 2.57–3.20, TTR 100% was continued for three months. Although the value of D-dimer was < 0.2 µg/mL, the second TEE showed no change in the thrombus (Fig. 2B). Therefore, warfarin was switched to the direct thrombin inhibitor, dabigatran 300 mg daily. Five months later, the third TEE (Fig. 2C) showed the mobile LAA clot (D-dimer < 0.20 µg/mL), and anticoagulation was changed to apixaban 10 mg daily. Five months later, the fourth TEE showed the resolution of the LAA thrombus (Fig. 1D). The value of D-dimer remained < 0.20 µg/mL. According to his physical examination and neurological finding, there was no evidence of cerebral and systemic embolism. Then, pulmonary vein isolation was performed without any complication; since then, the patient has been in sinus rhythm for over four months.

3. Discussion

Non-vitamin K antagonist oral anticoagulants (NOACs) are established as safe and effective first-line medications for prophylaxis of thromboembolism in patients with AF [5]. LAA thrombi are well known as high-risk findings of thromboembolism. However, little information regarding the effects of NOACs to LAA clot is available. To the best of our knowledge, this case is the first report to show the efficacy of apixaban to resolve an LAA clot, refractory to warfarin and

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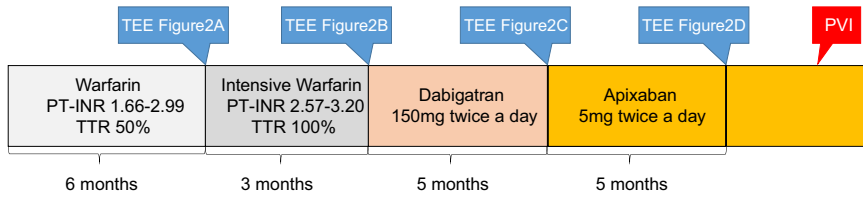


Fig. 1. Time course of anticoagulation therapy and transesophageal echocardiography (TEE).

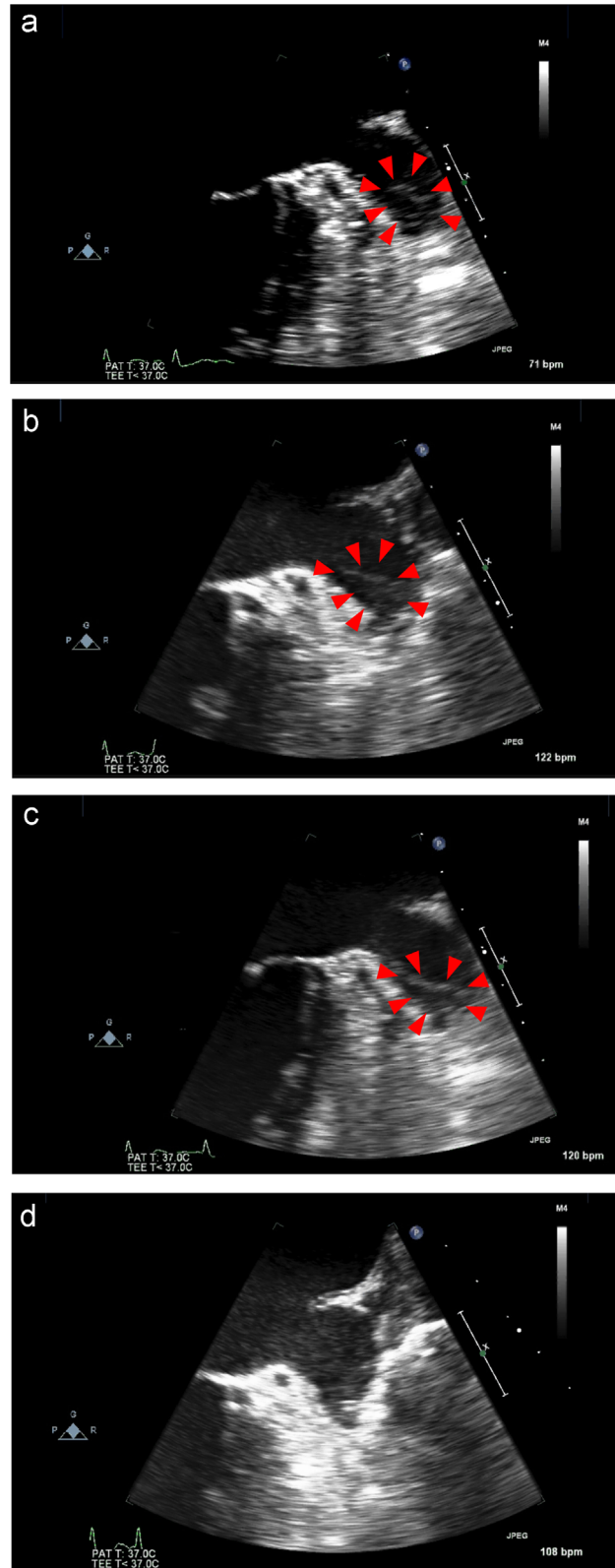


Fig. 2. Panel A: transesophageal echo shows mobile thrombus in the left atrial appendage (LAA). Panel B: no change of LAA thrombus after three months of anticoagulation with warfarin. Panel C: no change of LAA thrombus with dabigatran. Panel D: resolution of LAA thrombus after anticoagulation with apixaban.

dabigatran. Apixaban may be effective as a prophylactic anticoagulant and useful for the resolution of LAA clots. Although there has been little information on the differences of the coagulation-fibrinolysis balance among warfarin, direct thrombin inhibitor, and factor Xa inhibitor, apixaban was reported to make thrombi mobile or fragile by shifting the coagulation-fibrinolysis balance to fibrinolytic activity. Apixaban may have the optimal coagulation-fibrinolysis balance in patients with an existing thrombus. It has been suggested that the factor Xa inhibitor does not change the existing thrombin level, and will not completely suppress the thrombin production [6]. Thereby, a small amount of thrombin may be sufficient to activate high-affinity platelet thrombin receptors to maintain hemostasis. Factor Xa inhibitor inhibits the conversion of prothrombin to thrombin; however, a direct thrombin inhibitor does not inhibit the conversion [7]. In addition, factor Xa inhibitor strongly suppresses thrombin generation at a lower concentration. Perzborn et al. [8] reported a significantly low level of fibrinolytic activity at the low concentration of dabigatran compared with rivaroxaban, possibly due to the variable bioavailability of dabigatran. However, Ohyagi et al. [9] reported the case of a patient who had an embolic stroke during apixaban therapy for LAA thrombus. It is necessary to monitor patients for thromboembolic complications after the initiation of apixaban for the treatment of pre-existing LAA thrombus.

4. Conclusion

Factor Xa inhibitor, apixaban, could resolve the left appendage thrombosis refractory to warfarin and dabigatran. However, it is necessary to monitor for thromboembolic complications following the initiation of apixaban for a pre-existing LAA thrombus.

Conflict of interest

The authors declare that they have no conflict of interest.

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