

Resolution of left ventricular thrombus by edoxaban after failed treatment with warfarin overdose

A case report

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Abstract

Rationale: Although novel oral-anticoagulants are widely used in patients with atrial fibrillation (AF) for stroke prevention, there was only limited evidence for their use in left ventricular (LV) thrombus.

Patient concerns: A 41-year-old man who presented with acute onset of right-hand clumsiness and aphasia even under high international normalized ratio (INR: 7.64) from warfarin use. He was previously treated with warfarin for the LV thrombus and non-valvular AF. Brain magnetic resonance imaging (MRI) showed multiple acute infarction in the cortex of the bilateral frontal lobes, left parietal lobe, and bilateral central semiovale, which highly suggested embolic stroke.

Diagnosis: The repeated transthoracic echocardiogram still revealed LV thrombus (1.27 × 0.90 cm), which failed to respond to warfarin therapy.

Interventions: Due to acute infarctions occurred under supratherapeutic range of INR, we switched warfarin to edoxaban (dose: 60 mg/day) after INR decreased to less than 2.

Outcomes: The thrombus disappeared after receiving edoxaban for 23 days, and no more recurrent stroke was noted for more than 6 months.

Lessons: This is the first case demonstrates that while facing ineffective treatment of warfarin for LV thrombus, edoxaban could be safely and effectively used under this situation.

Abbreviations: AF = atrial fibrillation, EF = ejection fraction, INR = international normalized ratio, LV = left ventricular, MRI = magnetic resonance imaging, NOAC = novel oral anticoagulant.

Keywords: edoxaban, left ventricular thrombus, thrombolytic

1. Introduction

Left ventricular (LV) thrombus is an uncommon complication in various cardiac conditions, such as dilated cardiomyopathy, LV aneurysms or myocardial infarction. Anticoagulation with oral vitamin K antagonist is recommended to lower the risk of

embolization.^[1] However, compared with novel oral anticoagulants (NOACs), oral vitamin K antagonist required meticulous dose adjustment to achieve optimal treatment and more time to onset. NOACs are now widely used for prevention of thromboembolism in patients with non-valvular atrial fibrillation (AF); however, their efficacy in patients with LV thrombus have not been well established. There were only limited cases which reported that patients with LV thrombus received NOACs with satisfying results.^[2–4] To the best of our knowledge, there has been no previous report of edoxaban for patients with LV thrombus. Herein we report a case with LV thrombus and heart failure with reduced ejection fraction (EF), who suffered from acute ischemic stroke under overdose of the warfarin, was treated successfully with edoxaban.

2. Case presentation

A 41-year old male was in good health before. He suffered from progressive exertional dyspnea and visited an outpatient department of local hospital, but then was transferred to our hospital because of LV thrombus which was found on transthoracic echocardiogram. After admission to our ward, transthoracic echocardiogram showed global hypokinetic LV (the EF of LV was 28%), dilated LV size and a pedunculated apical thrombus measuring 1.75 × 1.68 cm (Fig. 1). Coronary angiogram was performed to rule out ischemic cardiomyopathy and it subsequently revealed no significant obstructive lesion. He

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P-HK and P-YC Both authors contributed to the work equally.

The patient has provided informed consent for publication of the case.

The authors declare that they have no competing interests.

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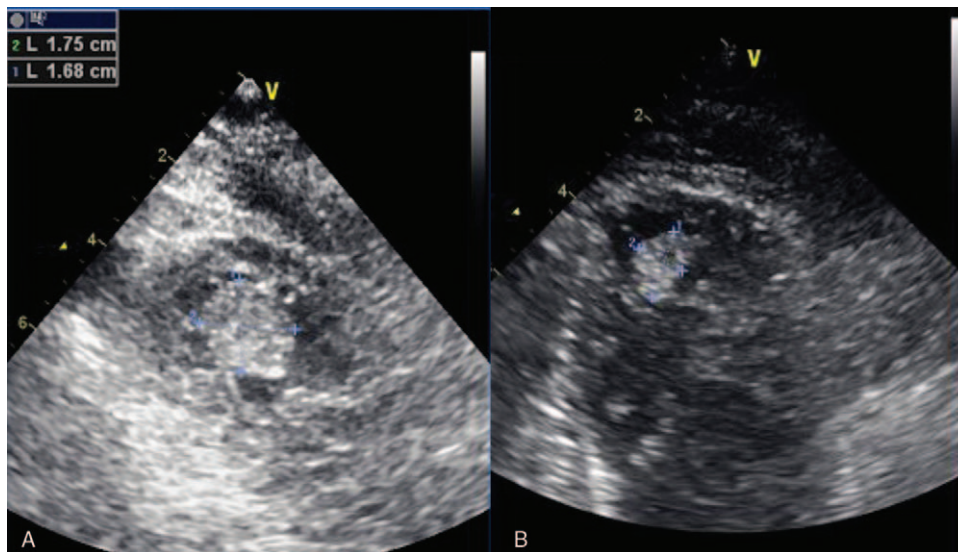


Figure 1. Transthoracic echocardiography before treatment of warfarin revealed left ventricular thrombus in size of 1.75 × 1.68 cm (A). Shrinkage of left ventricular thrombus after treatment of warfarin for 3 weeks (B).

was discharged from our hospital and had taken warfarin 3.75 mg/day for AF and LV thrombus since then.

However, he developed sudden onset of right-hand clumsiness and *expressive aphasia* after 1 month and was sent to our emergency department immediately for help. Right eye blurred vision and drooling from the right mouth angle were noted at the same time. The blood examination in the emergency department showed supratherapeutic range of prothrombin time and international normalized ratio (INR) 7.64. His symptoms totally recovered within 1 day, but the brain magnetic resonance imaging (MRI) showed multiple acute infarctions in the cortex of the bilateral frontal lobes, left parietal lobe, and bilateral central semiovale, which highly suggested embolic stroke (Fig. 2). The transthoracic echocardiogram performed on the same day of stroke still revealed LV thrombus (1.27 × 0.90 cm). Due to acute

infarction even under high INR level, we discontinued warfarin first and shifted to edoxaban (60 mg/day) use after INR decreased to less than 2.

To our surprise, follow-up echocardiography showed resolution of LV thrombus after receiving edoxaban for 23 days. The patient tolerated edoxaban well and did not get recurrent stroke in the following 6 months.

3. Discussion

Embolic events in patients with LV thrombus are common, which occurred in 10% to 40% of patients without anticoagulation.^[5] Our patient had a history of paroxysmal AF, with risk factors of hypertension and systolic heart failure, thus his annual stroke risk with AF would be 1.7% according to his score of CHA₂DS₂-

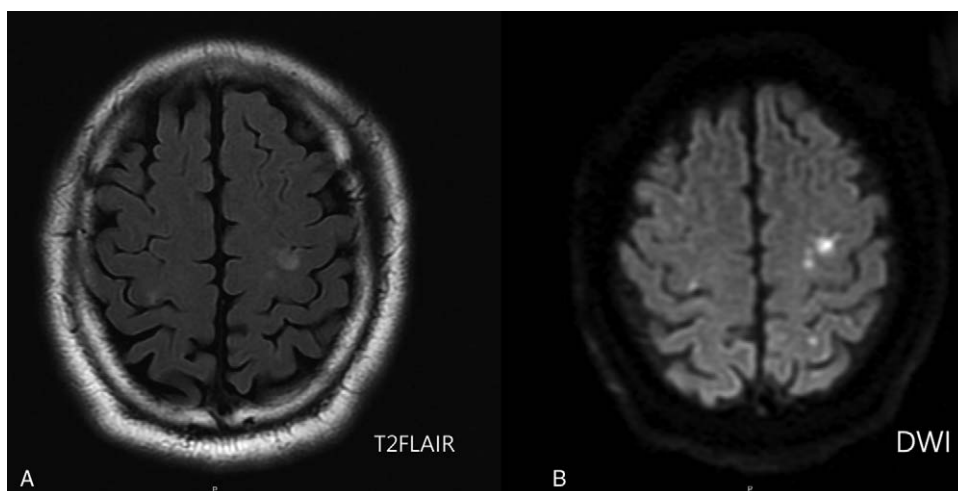


Figure 2. (A) T2 FLAIR images and (B) DWI of the brain MRI. The brain MRI showed multiple hyperintense lesions on DWI and FLAIR in the cortex of the bilateral frontal lobes and left parietal lobe, which highly suggested acute embolic infarction. DWI = Diffusion-weighted imaging, FLAIR = Fluid-attenuated inversion recovery, MRI = Magnetic Resonance Imaging.

Table 1**The experiences of using novel oral anticoagulants for thrombi in left ventricle in previous reports.**

| Age/Sex | Active disease | Basic disease | NOACs (dosage) | Other medicine | Course of thrombus | Ref |
|---------|-----------------|---------------------|--|-----------------------|--------------------|------|
| 78/M | | AF, HF | Rivaroxaban (15 mg/day) | | Resolved | [2] |
| 62/M | Anterior STEMI | | Apixaban (5 mg twice daily) | Aspirin, clopidogrel | Resolved | [3] |
| 57/M | Ischemic stroke | Anterior STEMI, AF | Dabigatran (110 mg twice daily, increased to 150 mg twice daily later) | Aspirin, clopidogrel | Resolved | [4] |
| 61/M | | HCM, HF, stroke, AF | Dabigatran (110 mg twice daily) | | Resolved | [11] |
| 52/M | Anterior STEMI | | Rivaroxaban (15 mg/day) | Aspirin, clopidogrel | Resolved | [12] |
| 75/M | Anterior STEMI | | Rivaroxaban (15 mg/day) | Aspirin, clopidogrel | Resolved | [12] |
| 69/F | Anterior STEMI | | Rivaroxaban (15 mg/day) | Aspirin, clopidogrel | Resolved | [12] |
| 77/M | | Anterior old MI, AF | Dabigatran (110 mg twice daily) | | Resolved | [13] |
| 54/M | Anterior STEMI | | Rivaroxaban (20 mg/day) | Aspirin, Clopidogrel* | Resolved | [14] |

AF=atrial fibrillation, HCM=hypertrophic cardiomyopathy, HF=heart failure, STEMI=ST-elevation myocardial infarction.

*Patient was treated with aspirin, prasugrel, and fondaparinux for STEMI until LV thrombus was found by echocardiography, which was performed 3 days after the percutaneous coronary intervention. Then prasugrel was switched to clopidogrel.

VASc=2.^[6] Therefore, the index stroke in this case was most likely resulted from LV thrombus rather than AF.

LV thrombus resolution in patients with anterior myocardial infarction, treated by warfarin and dual antiplatelet agents, was established in some previous observational studies and meta-analyses.^[7,8] We faced the difficult situation because the patient developed stroke even with warfarin overdose. There are several options for this patient, including NOACs alone, surgical thrombectomy of LV thrombus, heparin, or fibrinolytic agent. In a report of 16 patients with recent myocardial infarction and with LV thrombus, urokinase was given intravenously at a rate of 60,000U/h in a period of 2 to 8 days in combination with intravenous heparin. LV thrombi were lysed in 10 of 16 patients and there was no embolic event in any of the patients.^[9] Heik et al presented a study of 23 consecutive patients with mobile and protruding thrombi, high dose heparin was infused for 14 to 22 days then LV thrombi decreased in size in all patients with disappearance of the high-risk features, and thrombus disappeared entirely in 19 (83%) of 23 patients.^[10]

Nowadays, NOACs are widely used for stroke prevention and non-inferior to warfarin. However, efficacy and safety of NOACs in patients with LV thrombus are not yet established, although increasing evidence was showed by limited case reports in the past few years (Table 1).^[2-4,11-14] In 2016, Dr Makrides CA reported case series of resolved LV thrombus in patients with anterior myocardial infarction by rivaroxaban. As the presenting cases in the Table 1, rivaroxaban combined with dual antiplatelet were given for LV thrombus and myocardial infarction. In such situation, rivaroxaban and dabigatran may be better choice than other NOACs due to recent PIONEER AF-PCI trial and REDUAL PCI trial, although patients in both trials were treated by NOACs for AF rather than ventricular thrombus. In our case, coronary artery disease was not found by coronary angiography. Therefore, NOACs can be given solely without taking the risk of bleeding under triple therapy.

Left atrium appendage thrombus was ever successfully treated by edoxaban. But there is no literature discussing LV thrombus.^[15] In 2016, Saito et al presented 2 cases with AF and acute embolic stroke, whose left atrial appendage thrombus was treated successfully by edoxaban.^[15] The left atrial appendage thrombi in these 2 patients were detected by transesophageal echocardiogram, and the thrombi resolved on repeated transesophageal echocardiogram after administration of edoxaban for 9 to 10 days. We thought that edoxaban may also be effective in LV thrombus, thus we decided to switch

warfarin to edoxaban 60mg once daily, the same dosage for the treatment of deep vein thrombosis and pulmonary embolism, and his LV thrombus was successfully treated with full resolution. The presenting case is the first report to demonstrate the resolution of LV thrombus after administration of edoxaban in patients with acute ischemic stroke under warfarin therapy with supratherapeutic range of INR.

In conclusion, this case showed that NOACs such as edoxaban might have great potential in treating intracardiac thrombus. In addition, compared with warfarin, NOACs have fewer drug and food interactions, and also lower intracranial bleeding risk. However, large observational studies are warranted to prove its efficacy and safety.

Author contributions

Writing – original draft: Pei-Heng Kao.

Writing – review & editing: Ping-Yin Chou, Po-Chao Hsu, and Tien-Chi Huang.

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