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Case Report

Two-week administration of rivaroxaban resolved left atrial thrombus

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ABSTRACT

An 89-year-old man visited our hospital complaining of palpitation. Electrocardiography showed atrial fibrillation, and transthoracic echocardiography demonstrated a mobile thrombus of 28.6 mm × 20.8 mm in the left atrium. Administration of a direct factor Xa inhibitor rivaroxaban (10 mg/day) was started. The thrombus reduced its size and disappeared completely 2 weeks after the commencement of rivaroxaban treatment. To our knowledge, this is the first case report that rivaroxaban successfully dissolved left atrial thrombus during a short period. Rivaroxaban might have a potential, not only to prevent de novo thrombus formation, but also to dissolve established thrombi by direct inhibition of free and thrombus-associated factor Xa.

<**Learning objective:** The incidence of nonvalvular atrial fibrillation is increasing, and left atrial thrombus is the major cause of cardiogenic thrombo-embolism that we need to prevent. Recently, novel oral anticoagulants have been developed. The effects of these agents on intracardiac thrombus resolution have not been fully elucidated. Data from a large cohort study would be required to assess efficacy of novel oral anticoagulants for thrombus resolution.>

Introduction

The incidence of nonvalvular atrial fibrillation increases with age, and left atrial thrombus complicated with nonvalvular atrial fibrillation is the major direct cause of cardiogenic thrombo-embolism that we need to prevent. Intravenous heparin and oral vitamin-K antagonist warfarin have been the most popular and the most frequently used agents for the treatment of left atrial thrombus in patients with atrial fibrillation [1]. Recently, novel oral anticoagulants such as a direct thrombin inhibitor dabigatran or a direct factor Xa inhibitor rivaroxaban have been developed, and we can use these agents in the clinical settings to prevent cardiogenic thrombo-embolism in patients with nonvalvular atrial fibrillation [2]. We experienced an atrial fibrillation patient with intracardiac large thrombus, which shrunk and then disappeared during a short period after starting treatment with rivaroxaban.

Case report

An 89-year-old man visited our hospital complaining of palpitation. Blood pressure was 156/88 mmHg and electrocardiography showed atrial fibrillation with a ventricular rate of 88. Blood tests revealed hemoglobin A1c 7.9%, brain natriuretic peptide 175.6 pg/ml, D-dimer 1.7 μg/ml, prothrombin time-international normalized ratio 1.08, activated partial thromboplastin time 27.9%, and creatinine clearance 47.5 ml/min. The CHADS2 score was assessed as 3. Transthoracic echocardiography demonstrated a mobile thrombus of 28.6 mm × 20.8 mm in the left atrium (Fig. 1). We administered 4000 units of heparin intravenously and simultaneously prescribed rivaroxaban 10 mg/day. After 5 days of rivaroxaban treatment, transthoracic echocardiography showed that the thrombus shrunk to 20.3 mm × 15.6 mm (Fig. 2). After 14 days of treatment, the thrombus disappeared completely not only on transthoracic echocardiography but also on transesophageal echocardiography

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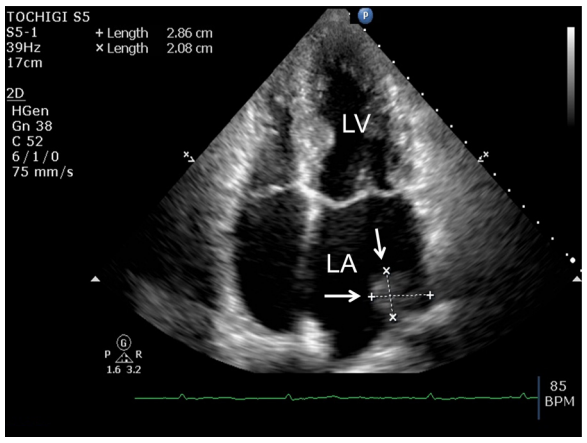

Fig. 1. Transthoracic echocardiography at visit demonstrated a mobile thrombus of 28.6 mm × 20.8 mm (arrows) in the left atrium. LA, left atrium; LV, left ventricle.

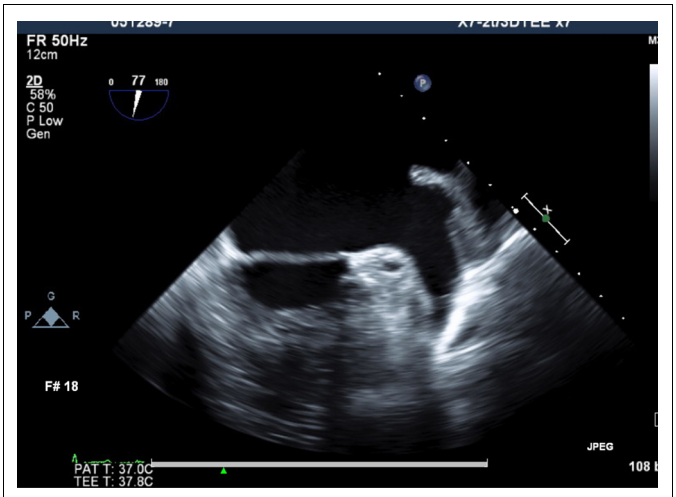

Fig. 3. After 14 days of treatment with rivaroxaban 10 mg/day, the thrombus disappeared completely on transesophageal echocardiography.

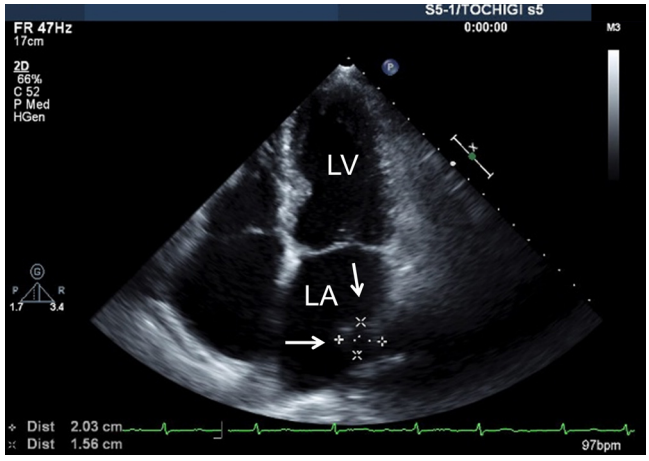

Fig. 2. After 5 days of rivaroxaban 10 mg/day treatment, transthoracic echocardiography showed that the thrombus shrunk to 20.3 mm × 15.6 mm (arrows). LA, left atrium; LV, left ventricle.

without any clinical evidence of systemic thrombo-embolism and any bleeding complication (Fig. 3).

Discussion

The effects of novel oral anticoagulants on intracardiac thrombus resolution in patients with nonvalvular atrial fibrillation have not been fully elucidated. Morita et al. [3] reported a case of thrombus of 26.0 mm × 30.0 mm in the left atrium, which disappeared after 4 months of dabigatran therapy (300 mg/day). Vidal and Vanerio [4] reported a case, in whom 6 weeks of dabigatran therapy (300 mg/day) shrunk and resolved left atrial thrombus. We also previously reported that [5] low-dose dabigatran was not sufficient to reduce the size of a left atrial thrombus. In the case, a 6-week treatment with dabigatran (220 mg/day) increased the thrombus size from 10 mm × 22 mm to 15 mm × 30 mm. After changing dabigatran to warfarin with adequate prothrombin time/international normalization ratio of 2.0–3.0, the thrombus subsequently shrunk and then disappeared 36 days after changing to warfarin. The results suggest that low-dose dabigatran is ineffective for the thrombus size reduction. On the other hand, in our present case, the left atrial thrombus of 28.6 mm × 20.8 mm had completely disappeared after only 2 weeks of treatment with rivaroxaban 10 mg/day, without any evidence of systemic thrombo-embolism and any bleeding complications, even though we did not examine by computed tomography/magnetic resonance imaging.

Dabigatran and rivaroxaban have peaks and troughs in their concentration curves. Rivaroxaban exhibits anticoagulation activity by direct inhibition of factor Xa at its peak level, but may not inhibit the coagulation cascade at the trough level. The antithrombotic effect of rivaroxaban is thought to be present even in the trough level, because of the presence of physiological coagulation inhibitors, such as tissue factor pathway inhibitor, antithrombin, protein C, protein S, and the fibrinolytic system. Therefore, once-daily intermittent anticoagulation by rivaroxaban effectively suppresses continuous thrombin activity.

The reduction of the left atrial thrombus size by anticoagulant therapy may be due to relatively predominant fibrinolytic activity rather than inhibition of thrombin activity [6]. However, the predominance of fibrinolytic activity in the trough level by the low-dose dabigatran is too weak to achieve sufficient thrombus size reduction, compared with that by rivaroxaban. In a recent study, Sadeghi et al. [7] focused on the different effects on tissue factor-mediated thrombin generation between dabigatran and rivaroxaban. According to their study, rivaroxaban inhibited the conversion of prothrombin to thrombin, whereas dabigatran did not. Unlike dabigatran, rivaroxaban exhibited strong inhibition of thrombin generation even at lower concentration. These results might explain the different effect on left atrial thrombus reduction between rivaroxaban and dabigatran in patients with nonvalvular atrial fibrillation.

From our case, we can envision that rivaroxaban might have a potential, not only to prevent de novo thrombus formation, but also to dissolve established thrombi by direct inhibition of free and thrombus-associated factor Xa. However, we need to heed that our present report is only based on a single case and data from a large cohort study would be required to assess efficacy of novel oral anticoagulants for thrombus reduction.

Multiple authorship

All authors of this paper listed have participated sufficiently in the conception and design of the work, in the analysis of the data,

and in writing the manuscript to take public responsibility for it. T. Kato designed the work. T. Adachi, T. Yabuki, and S. Toyoda analyzed the data. T. Kato, M. Yasaka, and T. Inoue wrote the manuscript. All authors revised this manuscript.

Ethics standards

The institute's ethical committee approved the access to this patient's records.

Conflict of interest

COI disclosure of M. Yasaka: lecture fees from Nippon Boehringer Ingelheim, Bayer Yakuhin, and Bristol-Myers Squibb. All other authors disclose no financial and personal relationships with other people or organizations that could inappropriately influence (bias) the work.

References

[1] Fukuda S, Watanabe H, Shimada K, Aikawa M, Kono Y, Jissho S, Taguchi H, Umemura J, Yoshiyama M, Shiota T, Sumiyoshi T, Yoshikawa J. Left atrial thrombus and prognosis after anticoagulation therapy in patients with atrial fibrillation. J Cardiol 2011;58:266–77.
[2] Yamashita T. Frontiers of anticoagulation therapy for atrial fibrillation. J Cardiol 2011;58:1–5.
[3] Morita S, Ajiro Y, Uchida Y, Iwade K. Dabigatran for left atrial thrombus. Eur Heart J 2013;34:2745.
[4] Vidal A, Vanerio G. Dabigatran and left atrial appendage thrombus. J Thromb Thrombolysis 2012;34:545–7.
[5] Tabata E, Yasaka M, Wakugawa Y, Komori M, Mori K, Tsurusaki Y, Kokuba K, Sambongi Y, Maeda K, Okada Y. Increase in the size of an intracardiac thrombus during dabigatran therapy (110 mg b.i.d.) in an acute cardioembolic stroke patient. Cerebrovasc Dis Extra 2013;3:78–80.
[6] Yasaka M, Yamaguchi T, Miyashita T, Tsuchiya T. Regression of intracardiac thrombus after embolic stroke. Stroke 1990;221:1540–4.
[7] Sadeghi N, Kahn D, Jeske W, Hoppensteadt D, Fareed J. Tissue factor-mediated activation of the prothrombin complex concentrate (PCC) is differently inhibited by dabigatran, rivaroxaban, and apixaban: potential clinical implication. Clin Appl Thromb Hemost 2013;19:589–99.