Effects of Dabigatran on the Resolution of Left Ventricular Thrombus after Acute Myocardial Infarction

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Abstract

Left ventricular thrombus (LVT) after acute myocardial infarction (AMI) is a risk factor for embolic complications. Although warfarin has traditionally been used to treat LVT, it has relevant disadvantages that limit its use. We herein describe the case of a 78-year-old man with AMI who had a history of paroxysmal atrial fibrillation. Following 10 days of urgent coronary reperfusion therapy, transthoracic echocardiography revealed a moderately sized LVT in the apex, which subsequently disappeared after 18 days of treatment with dabigatran. This case demonstrates that dabigatran may represent an alternative to warfarin as a therapeutic option in patients with LVT after AMI.

Key words: left ventricular thrombus, dabigatran, warfarin, acute myocardial infarction


Introduction

In the era of primary percutaneous coronary intervention (PCI) for acute myocardial infarction (AMI), left ventricular thrombus (LVT) continues to be reported as a relatively frequent complication (1). Although warfarin is an established anticoagulant employed to reduce the size of LVT (2, 3), the effect of dabigatran, a novel oral anticoagulant (NOAC), on LVT has not been fully elucidated. We herein describe a case in which dabigatran was effective for achieving LVT resolution after AMI.

Case Report

A 78-year-old man was transferred to our hospital due to ongoing chest pain lasting for at least six hours. Seven years earlier, he had undergone PCI for stable angina with the implantation of a sirolimus-eluting stent (SES) at the site of severe stenosis in the proximal left anterior descending (LAD) artery. His other medical history is significant for hypertension and paroxysmal atrial fibrillation. He had been taking anticoagulants, including aspirin and clopidogrel, but not warfarin, as he experienced repeated nose bleeds due to substantial fluctuation in the prothrombin time-international normalized ratio (PT-INR). The initial electrocardiogram (ECG) was notable for elevated ST segments throughout the precordial leads, and all biomarkers were markedly elevated. The creatinine clearance was calculated to be 64 ml/min, and transthoracic echocardiography (TTE) showed severe hypokinesis of the anterior wall and septum from the base to the apex of the left ventricle, although no apical thrombi were detected at that point. Emergent coronary angiography demonstrated complete occlusion of the previous SES (3.5 mm×23 mm), with a thrombus in the proximal LAD artery (Fig. 1A). After aspirating the thrombus, the coronary flow was restored, and a severe stenotic lesion became apparent in the proximal portion of the stent (Fig. 1B). We subsequently performed PCI of the lesion and implanted a zotarolimus-eluting stent (3.5 mm×38 mm) (Fig. 1C). Final angiography showed a good distal flow without residual stenosis (Fig. 1D). The level of creatinine phosphokinase (CPK) was found to be elevated up to 7,726 U/L.

TTE performed on day 10 after admission revealed an immobile thrombus (26 mm×16 mm) in the apex of the left ventricle (Fig. 2A), and treatment with dabigatran therapy (110 mg b.i.d.) was initiated. The patient did not receive thrombolytic agents, such as tissue plasminogen activator or...
Figure 1. Emergent coronary angiography demonstrated complete occlusion of the previous sirolimus-eluting stent (3.5 mm×23 mm), with a thrombus in the proximal left anterior descending artery (A, arrow). After aspirating the thrombus, the coronary flow was restored, and a severe stenotic lesion (arrow) became apparent in the proximal portion of the stent (B). We performed PCI of the lesion and implanted a zotarolimus-eluting stent (3.5 mm×38 mm) (C). Final angiography showed a good distal flow without residual stenosis (D).

Figure 2. Transthoracic echocardiography (TTE) performed on day 10 after admission revealed an immobile thrombus (26 mm×16 mm) in the apex of the left ventricle (A, arrow), and dabigatran therapy (110 mg b.i.d.) was initiated. TTE showed a significant decrease in the thrombus size after seven days of dabigatran treatment (19 mm×7 mm) (B, arrow), and complete thrombus resolution was achieved after 18 days of anticoagulant therapy with dabigatran (C). LV: left ventricle.
urokinase, due to fear of the potential for bleeding complications under dual antiplatelet therapy. In addition, intravenous heparin was not given at this time, since dabigatran, in contrast to warfarin, exhibits a rapid onset of action. Following dabigatran administration, the activated partial thromboplastin time (APTT) was slightly increased (34 sec → 44 sec), whereas the level of D-dimer was significantly decreased (10.1 μg/mL → 1.0 μg/mL). TTE showed a significant decrease in the thrombus size after seven days of dabigatran treatment (19 mm × 7 mm) (Fig. 2B), and complete thrombus resolution was achieved after 18 days of anticoagulant therapy with dabigatran (Fig. 2C). No systemic thromboembolic events occurred over the entire treatment period. While the patient has continued to receive the triple antithrombotic therapy (dabigatran plus aspirin and clopidogrel) for a six-month period after discharge, he has not developed any serious bleeding complications and has remained free of LVT recurrence.

Discussion

A recent study reported that, in the contemporary era of primary PCI, the incidence of LVT in patients with AMI is approximately 4% and the early onset of LVT is more likely in subjects with anterior AMI and a reduced ejection fraction (EF) (1). LVT is a potentially life-threatening condition, with a high risk of embolic complications. Although warfarin has traditionally been used to treat LVT (2, 3), it has many clinical limitations, including multiple food and drug interactions, a slow onset of action and narrow therapeutic range for preventing thrombosis and minimizing hemorrhagic complications. Dabigatran is an oral direct thrombin inhibitor currently indicated for the prevention of stroke and systemic embolism in patients with nonvalvular atrial fibrillation (4). Given the current patient’s past background in which he was reluctant to be prescribed warfarin to control the PT-INR, we were forced to use low-dose dabigatran instead of warfarin in this case, as we were extremely concerned about the labile PT-INR values in the setting of concomitant congestive heart failure, which may cause hepatic congestion of the blood flow and inhibit warfarin metabolism. It has also been reported that dabigatran therapy is associated with the successful treatment of LVT in patients with hypertrophic cardiomyopathy (5) and old myocardial infarction (6). To our knowledge, this is the first reported case of the resolution of LVT after AMI achieved with the administration of dabigatran.

Dabigatran is a direct thrombin inhibitor that exerts anti-coagulant effects by binding to the active site of thrombin. Thrombin modulates hemostasis by binding to its cofactor thrombomodulin, located on the surface of the endothelium, thereby attenuating fibrinolysis via the activation of thrombin-activatable fibrinolysis inhibitor (TAFI) (7). Dabigatran, at clinically relevant concentrations, is reported to enhance the susceptibility of plasma clots to fibrinolysis by reducing TAFI activation in vitro (8). These mechanisms may contribute to the antithrombotic activity of this drug.

The use of triple antithrombotic therapy is likely to increase the risk of bleeding complications. Hence, the current guidelines recommend that the duration of triple therapy be limited to the shortest time required (9). In addition, the results of the recent WOEST trial indicate that dual therapy (an oral anticoagulant and clopidogrel), rather than triple therapy, may be adequate in patients with a recent history of coronary stent placement (10). Because we implanted a new generation drug-eluting stent with a lower risk of stent thrombosis in the present case, the discontinuation of either aspirin or clopidogrel after at least six months of PCI may be viewed as a method of minimizing the risks of bleeding complications.

In conclusion, as thrombus resolution was successfully achieved in the present case, dabigatran may be a potential alternative to warfarin in patients with established LVT after AMI. Large-scale studies, however, are needed to determine whether dabigatran is effective for resolving LVT.

The authors state that they have no Conflict of Interest (COI).

References