Case report

Dabigatran for intracardiac thrombus, yet another promising role of a direct oral anticoagulant: a case report and short review of literature

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Abstract

A left ventricular (LV) thrombus is a relatively common and well-known condition associated with significant LV systolic dysfunction. However, LV thrombosis is unusual in the absence of kinetic abnormalities. The elderly gentleman presented with subacute onset of bilateral lower limb discomfort and cold extremities, but no gangrene. With normal LV function, an echocardiogram revealed a massive movable LV apical clot. He was treated with dual antiplatelets and heparin at first. He switched to dabigatran 110 mg twice a day in combination with dual antiplatelets. The thrombus had entirely vanished and leg problems had improved after a 2-week follow-up. For the next six months, he was treated with aspirin and dabigatran and was asymptomatic at follow-up. There are no specific guidelines for treating an intracardiac thrombus. Experts agree that a hypermobile and pedunculated LV thrombus with a high embolic risk should be surgically removed as soon as possible. According to ESC/ACC guidelines, all patients with LV thrombus associated with myocardial infarction should be treated with anticoagulation. Warfarin requires regular International Normalized Ratio (INR) monitoring and has a small therapeutic window; hence a direct oral anticoagulant (DOAC) could be a viable therapeutic solution. However, there are no guideline recommendations to date to guide DOAC therapy for this indication.

Keywords: d*abigatran; direct oral anticoagulants; left ventricular clot; intracardiac thrombus*

Introduction

A left ventricular thrombus is a relatively common condition, frequently linked to an acute anterior wall myocardial infarction and dilated cardiomyopathy [1]. Mobile left ventricular clot, heart failure, and atrial fibrillation are all considered to enhance the likelihood of embolic occurrences.

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As a result, it's critical to get started on proper therapy as soon as possible. The use of a vitamin K antagonist (VKA), such as warfarin, for up to 6 months is included in the current first-line treatment [2,3]. DOACs have shown similar or better efficacy with similar or better safety in patients with atrial fibrillation and venous thromboembolism. Since VKAs have several disadvantages, such as slower onset and offset of action, higher incidence of major bleeding, more interactions with food and drugs, and the need for repeated international normalized ratio (INR) monitoring, DOACs have emerged as a possible alternative. It should be noted that no DOACs have been specifically assessed in

randomized clinical trials for the treatment of LV thrombosis [4].

Case report

A 57-year-old male presented with bilateral lower limb pain and numbness of three days duration. He gave a history of intermittent claudication for 2 months with a claudication distance of around 100 meters. There was no prior history of ischemic heart disease, type II diabetes mellitus, smoking, or hypertension. General examination showed a pulse rate of 78 beats per minute which was regular with a blood pressure of 120/70 mm of Hg in the right hand in the supine position. Both lower limbs were cold from the middle one-third of the leg downwards. There were no gangrenous changes. All the distal pulses except bilateral dorsalis pedis and posterior tibial artery were present.

Arterial Doppler of both lower limbs showed an absence of color uptake in mid and distal anterior tibial and dorsalis pedis arteries suggestive of acute complete thrombosis. He was initially managed with dual antiplatelet including 150 mg of aspirin and 75 mg of clopidogrel in view of suspected left ventricular dysfunction along with low molecular weight heparin (weight adjusted). There was no ST-segment elevation or atrial fibrillation on electrocardiography and cardiac enzyme levels were normal. On admission, Transthoracic echocardiography (TTE) was done which showed a large sausage-shaped mobile mass (34×11mm) arising from the left ventricular apex with normal left ventricular systolic function (Figure 1A). Further imaging in the form of cardiac CT and MRI were done to characterize the LV mass and it was consistent with LV thrombus. MRI also showed LV thrombus attached to transmural infarcted area involving anterior septum in apical and mid cavity level (Figure 2A and 2B). After 48 hours, his leg numbness substantially improved, and dorsalis pedis and posterior tibial artery pulses were palpable. A thromboembolic etiology was considered in view of bilateral distal involvement and LV mass/ thrombus with hypermobility. To reduce further risk of thromboembolism it was considered to add direct oral anticoagulant to the existing therapy for a short duration. As the patient was already on dual antiplatelet therapy only 110 mg of dabigatran was added to reduce the bleeding risk. On follow-up two-dimensional transthoracic echocardiography conducted after two weeks of dabigatran treatment, LV thrombus disappeared completely without further thromboembolic episode (Figure 1B). We continued aspirin and increased the dose of dabigatran to 150 mg twice daily for six months after stopping clopidogrel. At 6 months of follow up the patient was doing well and remained asymptomatic.

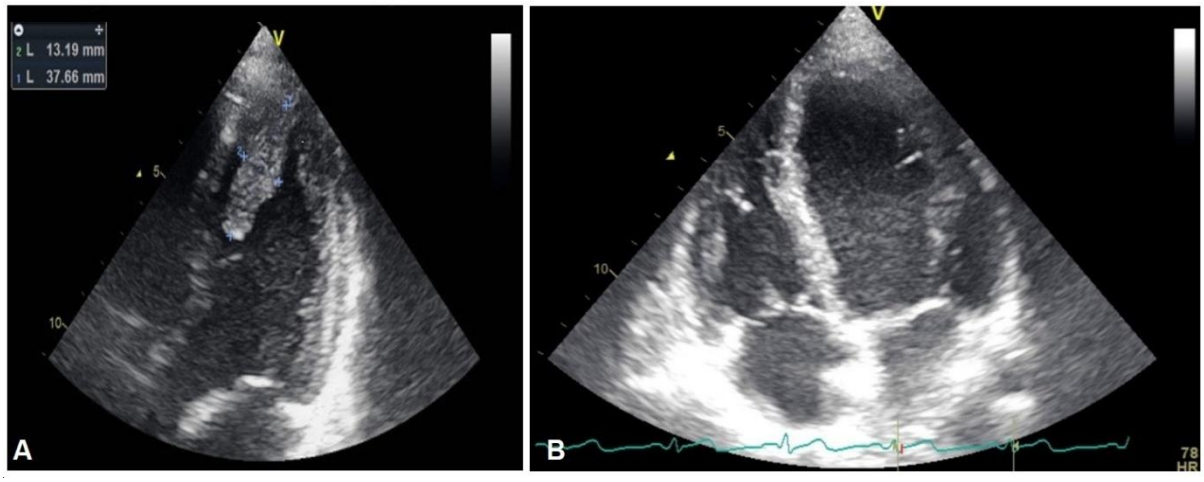

Fig. 1. Trans-thoracic echocardiography in apical four-chamber view showing (A) large sausage-shaped mobile mass (34×11mm) arising from the left ventricular apex. B: repeat echocardiography after 2 weeks of dabigatran therapy showing complete resolution of thrombus.

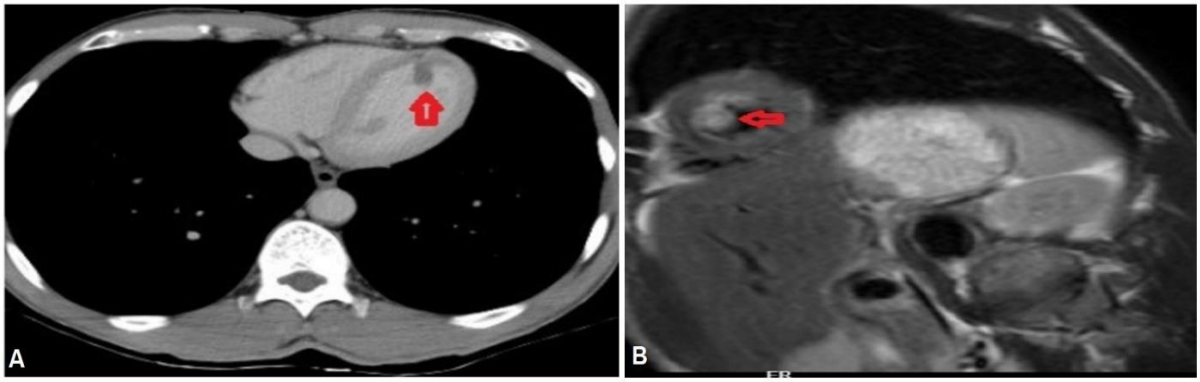

Fig. 2. A: Contrast-enhanced computed tomography scan with the arrow showing well-defined oval non-enhancing filling defect with smooth margins adjacent to the apex of the left ventricle possible thrombus. **B:** Cardiac MRI showing transmural (non-viable) infarct involving the anterior septum in apical and mid cavity level with apical thrombus.

Discussions

Patients who have had a recent or previous myocardial infarction, cardiomyopathy with significant left ventricular systolic dysfunction, myocarditis, or a left ventricular aneurysm are at increased risk of developing a left ventricular thrombus [5]. LV mural thrombus increases the risk of embolic complications. Mobility, protuberance, immaturity, filamentous character, fluctuating echo density with central liquefaction, and uneven boundaries are all high-risk thrombus characteristics for embolization. Mobile and protruding thrombi are five times more likely than immobile and non-protruding thrombi to embolize. In our case, we had a smooth and mobile sausage-shaped thrombus with regular borders [1].

There are no clear guidelines for managing intracardiac thrombus. A hypermobile and pedunculated LV thrombus with a high embolic risk, according to expert consensus, requires surgical excision as soon as possible. According to the ESC 2017 guidelines for ST-elevation myocardial infarction [5]. anticoagulation should be given for six months in patients with LV thrombus, while the ACC/AHA guidelines recommend it indefinitely in patients with a low risk of bleeding [2]. However, there is no general agreement on anticoagulation treatment and duration of anticoagulation in the absence of myocardial infarction. Because warfarin needs repeated and unending monitoring of prothrombin time/international normalized ratio, has a small therapeutic window, and has a poorly predicted therapeutic range, direct oral anticoagulants are recommended over warfarin among anticoagulation alternatives. Dabigatran, on the other hand, is a direct thrombin inhibitor approved for the prevention of stroke and systemic embolism in patients with atrial fibrillation.

Warfarin anticoagulation, according to studies, can eliminate acute ventricular thrombi but not chronic thrombi following ST-elevation myocardial infarction [6]. Dabigatran, on the other hand, has been found in recent case studies to be a successful treatment for LV thrombi [7, 8]. In our case, there are three distinguishing features. First, a large sausage-shaped thrombus formed in the left ventricular cavity, with no ventricular dysfunction on echocardiogram. Second, cardiac MRI showed transmural infarcted area in the apical septum and mid cavity level with apical thrombus, which suggest that thrombus developed in the localized ischemic area possibly due to transient endocardial dysfunction. Third, such a large thrombus has completely resolved after dabigatran therapy, with no clinically significant embolic manifestations. There is no consensus on dabigatran dose for LV thrombus because no randomized clinical studies have been conducted to date. In atrial fibrillation and venous thromboembolism studies, the dosage was 110 mg or 150 mg bid, the dose reduction being performed under pre-specified conditions. In our patient, we used a daily dose of 220 mg in combination with an antiplatelet medication. The clot had

completely disintegrated two weeks after starting dabigatran. In the previous case, dabigatran cleared LV thrombi after 4 months [7]. It is worth noting that the clot resolution speed of dabigatran is noticeably faster than that of the other DOACs [8]. The median duration for LV clot clearance with rivaroxaban, apixaban, and dabigatran was 40 days, 36 days, and 24 days, respectively, according to a systematic review encompassing 41 patients [9]. DOACs offer a significant benefit over warfarin (VKAs), which acts more slowly and the anticoagulant duration of dabigatran may be less than that of warfarin. Warfarin should be taken for at least 3–6 months in patients with LV clot, according to current guidelines [2, 3]. All patients who received DOACs reported full thrombus resolution in a large retrospective study comprising 128 individuals with LV thrombus [1].

Despite the fact that warfarin was still the most widely prescribed oral anticoagulant (87 percent vs. 3.7 percent for DOACs), only 75 percent of patients reported clot clearance after a year [1]. LV thrombus clearance was found in 87.9% of patients receiving DOACs, according to a meta-summary of case studies [10]. Similarly, during TTE follow-up, clot resolution was reported in 83 percent of patients in a single-center study of 35 patients [9]. Despite the fact that this shows that DOACs is more effective than warfarin, there has been no direct comparison of the newer drugs. The thrombus resolution success rates for rivaroxaban, apixaban, and dabigatran were found to be 81 percent, 100 percent, and 88.9 percent, respectively, in a recent systematic review [9]. All of these studies, however, only included a small number of dabigatran patients. Large-scale randomized research is required before drawing any conclusions. It's worth noting that the study's positive results with dabigatran were obtained with no major complications. There were no reports of a stroke or an embolism in the peripheral arteries.

Conclusions

Despite our extensive experience with warfarin over the years, we truly understand the drug's lack of reliability and constant monitoring in real life, as well as their known interactions. With evolving experiences with DOACs and individual cases like ours, we believe that DOACs may play a role even in patients with intra-cardiac thrombus. The true effectiveness and safety of DOACs in the treatment of these patients with intracardiac thrombus with warfarin per se must be evaluated in larger randomized controlled trials.

Competing interests

None of the authors have any conflicts of interest or financial interest to disclose.

Consent for publication

Informed consent was obtained from the patient.

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