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CASE REPORT

BEGINNER

CLINICAL CASE

Large Mobile Left Ventricular Thrombi Formation in a 32-Year-Old Despite Direct Oral Anticoagulation With Dabigatran

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ABSTRACT

Direct oral anticoagulant agents (DOACs) are widely used in the treatment of arterial and venous thrombi. We report the case of a 32-year-old patient who was receiving permanent DOAC therapy. Despite adequate use, 2 large left ventricular thrombi developed. Surgical thrombectomy was performed. The patient recovered well and received anticoagulation with phenprocoumon thereafter. (**Level of Difficulty: Beginner.**) (J Am Coll Cardiol Case Rep 2022;4:1015–1019)

HISTORY OF PRESENTATION

A 32-year-old male patient presented to our hospital with exertional dyspnea and typical angina corresponding to New York Heart Association functional class II and Canadian Cardiovascular Society stage II, respectively. His vital signs were normal (heart rate, 84 beats/min; blood pressure, 124/74 mm Hg; oxygen saturation, 98%). Apart from an obesity (body mass index, 30.07 kg/m^2; height, 173 cm; weight, 90 kg), the physical examination, including a full neurologic examination, did not reveal any significant findings.

LEARNING OBJECTIVES

- To be able to make a differential diagnosis in anticoagulated patients with chest pain and dyspnea.
- To understand the associated risk factors and imaging features of LV thrombi.

Forgotten medication (especially anticoagulation) was credibly denied.

PAST MEDICAL HISTORY

His past medical history included an unprovoked bilateral pulmonary embolism at the age of 26 years that was treated with a direct oral anticoagulant agent (DOAC) regimen (rivaroxaban, 20 mg once daily). Coagulation testing revealed a heterozygous prothrombin mutation *(G20210A)* but was otherwise unremarkable. An accumulation of risk factors (active smoker, family history of thrombosis) and the heterozygous prothrombin mutation were the reasons for a permanent anticoagulation regimen.

At the age of 30 years, the patient paused the anticoagulation therapy for a total of 1 week for lack of time to pick up a follow-up prescription. Only 1 week later, the patient experienced severe angina at night. After a delay of 2 hours, he called emergency

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ABBREVIATIONS AND ACRONYMS

CMR = cardiac magnetic resonance

DOAC = direct oral anticoagulant

LAD = left anterior descending

LV = left ventricular

STEMI = ST-segment elevation myocardial infarction

VKA = vitamin K antagonist

services and was admitted and received a diagnosis of acute ST-segment elevation myocardial infarction (STEMI). His laboratory values on admission showed no evidence of inflammation. Coronary angiography revealed total occlusion of the left anterior descending (LAD) artery by a thrombus but showed no evidence of underlying coronary artery disease. Following successful thrombus aspiration and drug-eluting stent implantation, anticoagulation therapy was resumed, now with dabigatran, at 150 mg twice daily. He received clopidogrel for 1 year, a β-blocker, and an aldosterone antagonist because of his initially moderately impaired left ventricular (LV) function (ejection fraction, 31%), and he was also prescribed statin therapy. Transesophageal echocardiography showed no evidence of an atrial septal defect. At that time, akinesia of the anterior wall was already present, but there was no evidence of an LV thrombus, and his LV function improved to mildly reduced before discharge. The patient was seen regularly by his cardiologist and general practitioner and showed excellent adherence to the prescribed medication. The ejection fraction and anterior wall akinesia remained unchanged (mildly reduced, at 52%), and his last visit was 6 months before presentation.

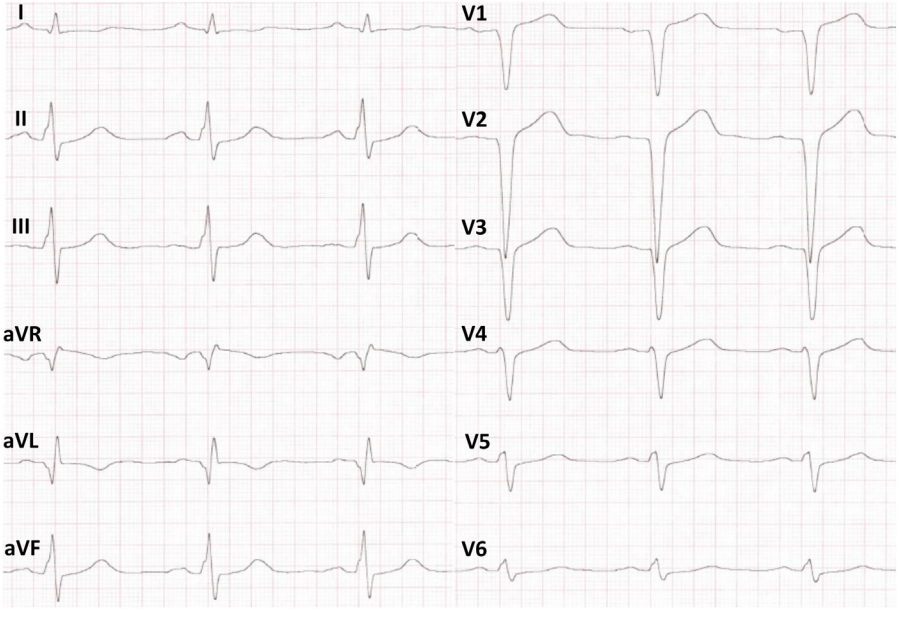
DIFFERENTIAL DIAGNOSIS

At the current admission, (partial) LAD stent occlusion, recurrent pulmonary embolism, and acute heart failure were considered as potential differential diagnoses on the basis of the patient's past medical history.

INVESTIGATIONS

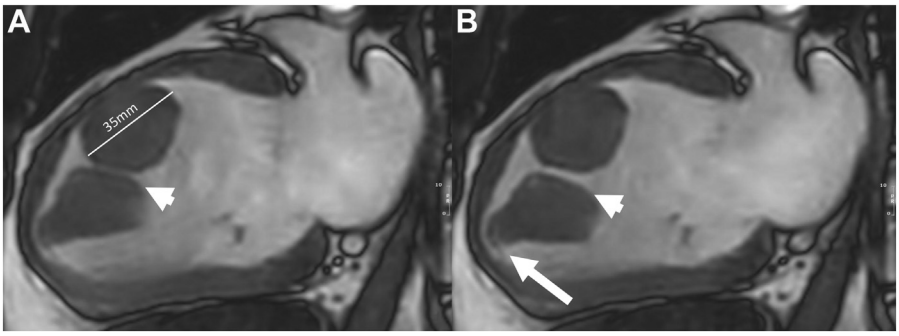
The laboratory values showed no evidence of acute myocardial injury. The electrocardiogram is shown in **Figure 1**. On transthoracic echocardiography, 2 large and partly mobile LV thrombi were detected, and these were confirmed by cardiac magnetic resonance (CMR) imaging (**Figures 2A and 2B,** Videos 1 and 2).

FIGURE 1 12-Lead Electrocardiogram



The electrocardiogram shows poor R-wave progression in the precordial leads as evidence of the previous ST-segment elevation myocardial infarction of the left anterior descending coronary artery.

FIGURE 2 2-Chamber Steady-State Free Precession Cardiac Magnetic Resonance



(A and B) The imaging shows 2 large left ventricular thrombi, 1 of which is mobile (**arrowheads;** compare **A and B**), with a very thin connection to the apex **(arrow)**.

Late gadolinium enhancement CMR (Figures 3A to 3C) revealed extensive scar tissue in the LAD artery territory.

MANAGEMENT

Given the immense size of the thrombi, the thin attachment to the wall with protrusion into the cavum, and mobility of the evolved LV thrombi with substantial risk of thromboembolism, our multidisciplinary heart team deemed a switch to a vitamin K antagonist (VKA) too risky and, alternatively, recommended surgical thrombectomy. Surgical access to the cavum following a median thoracotomy was possible through the existing anterior scar and therefore with minimal new trauma by using a left ventriculotomy. The procedure was performed successfully. The anticoagulation regimen was switched to phenprocoumon.

DISCUSSION

LV thrombus formation is a common complication following large myocardial infarctions and STEMI in particular. Reported incidences of LV thrombi after STEMI range up to 40%.[1] Current guidelines recommend anticoagulation therapy with a VKA for up to 6 months. Nevertheless, observational studies and meta-analyses of case reports suggest an equivalent therapeutic efficiency of DOACs, with reported thrombus resolution in ~90% of cases.[2-4] Although there is a lack of prospective clinical trials comparing anticoagulation regimens, DOACs are increasingly used mainly because of their superior safety profiles (eg, lower incidence of major bleeding episodes).

The present case highlights the possibility of LV thrombus formation despite sufficient DOAC therapy even in young patients. It shows that DOAC therapy is evidently not suitable for every patient and that early identification of nonresponders could aid in preventing the necessity of a surgical approach.

Regarding the underlying cause of the thrombus formation, several factors must be taken into consideration. First, the patient's heterozygous prothrombin mutation was previously associated with an increased risk for both arterial and venous thromboembolic events.[5] Second, the severe wall akinesia resulting from the preceding infarction led to both blood stasis or turbulence and endothelial dysfunction. Thus, a complete Virchow triad was present.

In recent years, growing enthusiasm for the use of DOACs can be observed.[6] In contrast, the therapeutic potency of DOACs in the treatment of LV thrombi remains unclear. Jones et al[4] outlined improved thrombus resolution by DOACs in an observational study of 2,328 patients with myocardial infarction, and this outcome was accompanied by a better safety profile. In contrast, Robinson et al[7] reported a significant association of DOAC therapy with the incidence of stroke or systemic embolism compared with VKA therapy in 514 patients with LV thrombus. However, only approximately two-thirds of patients reported by Robinson et al[7] had ischemic

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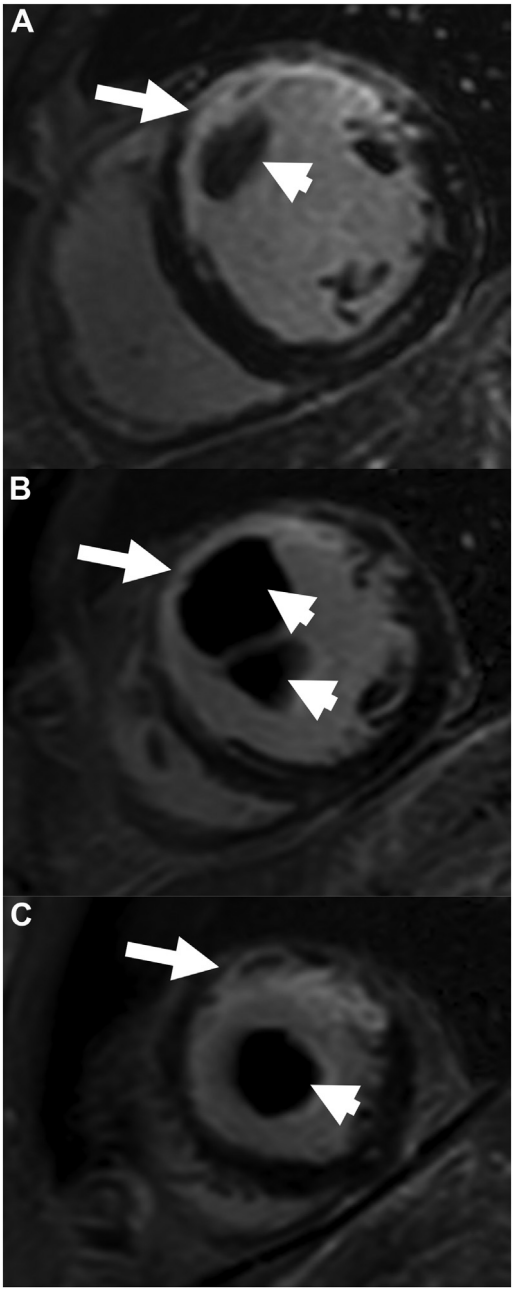
FIGURE 3 Cardiac Magnetic Resonance of Left Ventricular Thrombi



(A) Basal, **(B)** midventricular, and **(C)** apical short-axis views of late gadolinium enhancement cardiac magnetic resonance sequences (TR, 4.1 ms; TE, 1.97 ms). These images show a transmural, infarct-typical enhancement of the left anterior descending artery territory **(arrows)**. Scar burden was calculated to be 18.9% of the global myocardium. The large ventricular thrombi **(arrowheads)** show no relevant gadolinium uptake.

cardiomyopathy, and this factor could have led to the differing results. Nevertheless, failure to resolve thrombi may occur with DOACs as well as with VKAs, but no evidence exists on thrombus growth to the extent presented here during a pre-existing anticoagulation regimen.

Apart from the aforementioned anticoagulation therapy, surgical removal of LV thrombi may be the therapy of choice in selected patients. In a study of 62 patients, Lee et al[8] found no difference in post-treatment thromboembolisms between operative and other treatments, although a trend toward fewer post-treatment thromboembolisms could be observed. Especially in patients with large and mobile LV thrombi, some cases of successful surgical therapies have been described.[9,10] In our case, given the fragile connection of the thrombus to the LV wall and the subsequent substantial risk of embolism, our heart team favored surgical removal, which was conducted successfully.

FOLLOW-UP

Follow-up transthoracic echocardiography (Supplemental Figure 1) showed no residuals. At 12 months after the operation, no adverse events had occurred. The patient was asymptomatic and in good health and was resuming his normal daily activities.

CONCLUSIONS

This case demonstrates the possibility of LV thrombus formation even in anticoagulated young patients. A surgical approach remains an option in selected patients with large and mobile thrombi. Therapeutic failure is possible with both DOACs and VKAs. Regular imaging follow-up of patients with LV thrombus is advised, to react adequately if thrombus diminution cannot be observed. We confirm that this case report received proper ethical oversight.

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The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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KEY WORDS case report, CMR, DOAC, thrombus

APPENDIX For a supplemental figure and videos, please see the online version of this article.