Submassive Pulmonary Embolism and Left Atrial Thrombus

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INTRODUCTION

Left atrial appendage (LAA) and/or left atrial (LA) thrombi in the setting of nonvalvular atrial fibrillation (AF) are treated with anticoagulation. However, surgical thrombectomy and LAA ligation are frequently undertaken in patients with valvular heart disease and AF. There are no data pertaining to the management of incidentally detected large LA or LAA thrombi in the setting of acute submassive pulmonary embolism (PE). We present the case of a patient with a large thrombus seen in the left atrium with attachment in the LAA in the setting of bilateral PE and acute on chronic deep venous thrombosis and discuss the management strategies.

CASE PRESENTATION

A 72-year-old man with hypertension, AF, and history of recurrent PE presented with acute dyspnea. Three weeks before presentation, he fractured his left ankle, which was immobilized in a cast. He self-discontinued warfarin 9 months previously. His blood pressure was 181/103 mm Hg, pulse was 93 beats/min (irregularly irregular), respiratory rate was 15 breaths/min, and oxygen saturation was 91% on 4 L oxygen per nasal cannula. Computed tomographic scan with PE protocol revealed a nearly occlusive PE in the right pulmonary artery and a nonocclusive PE in the left pulmonary artery (Figure 1, *arrows*) and a mass in the left atrium (Figure 2, *arrow*).

Echocardiography showed mild to moderate right ventricular enlargement with mildly decreased systolic function and an LA mass. Left ventricular systolic function was normal. Transesophageal echocardiography (TEE) showed a large (45 × 25 mm) mass attached to the LAA wall (Videos 1 and 2, in two and three dimensions, respectively). The left atrium was moderately enlarged and LAA contractility was normal, indicated by high LAA emptying velocity (74 cm/sec; Figure 3). There was no LA or LAA spontaneous echocardiographic contrast. In addition, lower extremity ultrasound showed acute deep venous thrombosis on the left in the setting of bilateral chronic lower extremity deep venous thrombosis.

A multidisciplinary team evaluated the patient. He was not a candidate for thrombolytic therapy given the amount of thrombus in the left atrium and concern for systemic thromboembolism. Surgical thrombectomy with LA or LAA clot removal was planned in case his condition hemodynamically deteriorated on heparin. The patient's preference was to pursue anticoagulation.

The patient remained stable. The decision was made to treat with a therapeutic dose of enoxaparin twice a day and follow up in 1 month with TEE. The choice of low-molecular-weight heparin was made to ensure that the patient reached therapeutic levels and because of the possibility that this might be more helpful for the LA thrombus. Follow-up TEE showed almost complete resolution of thrombus (Videos 3 and 4, in two and three dimensions, respectively). Thrombophilia workup was negative. At this point, lifelong anticoagulation treatment with apixaban was started.

DISCUSSION

Substantial evidence guides the decision to treat acute stable submassive PE with anticoagulation,[1,2] whereas there are few data to guide treatment in the setting of coexistent large LA or LAA thrombus, as in our patient. Heparin followed by chronic anticoagulation therapy with warfarin and novel oral anticoagulant agents have been recommended for the treatment of LA or LAA thrombus in the setting of nonvalvular AF. Our patient posed a management dilemma. We contemplated the option of urgent surgical thrombectomy of unusually large LA or LAA thrombus or whether conventional anticoagulation therapy would be sufficient for its coexistence with a submassive PE. Paucity of data exist to predict the risk of systemic embolism of LA/LAA thrombus.

Systemic or catheter-based lytic therapy of PE could increase the risk of LA/LAA clot embolization. Current guidelines do not recommend systemic or catheter-directed lytic therapy of submassive PE. Systemic lytic therapy could be considered for patients with low bleeding risk and a high probability of developing hemodynamic compromise.[2] Therefore, our patient did not have clear indications for lytic therapy unless clinical deterioration occurred. In case of hemodynamic deterioration, one could also consider catheter-directed pharmacomechanical treatment of PE or using embolus aspiration only with the AngioVac, which we have done for other patients. Clinical knowledge regarding the effectiveness and safety of catheter-directed pharmacomechanical intervention for submassive PE remains rather limited.[3,4] AngioVac use, although not associated with lytic therapy, requires 22-Fr cannula use and cardiopulmonary bypass, which could trigger LA thrombus embolization.

Our patient did not have an indication for cardiac surgery. He required neither valve surgery nor surgical treatment for PE. Moreover, he had recent submassive PE, which significantly increased the periprocedural risk for further venous thromboembolic complications. In addition, the patient preferred conservative management. Thus he was treated with anticoagulation only.

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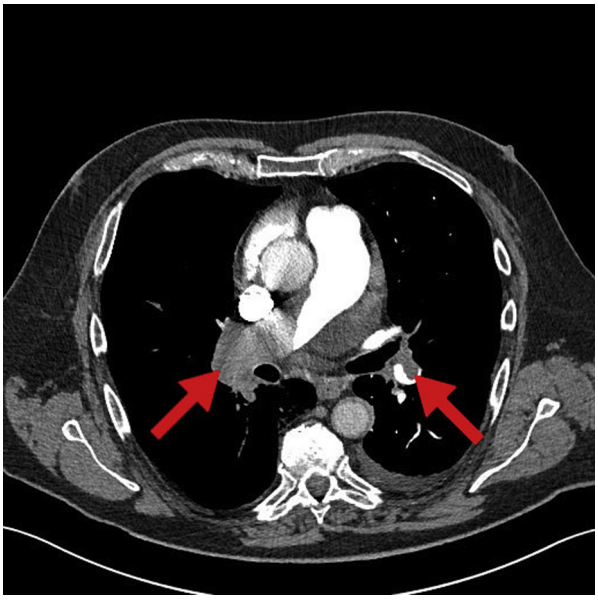

Figure 1 Chest computed tomography with PE protocol revealed a nearly occlusive PE in the right pulmonary artery and a nonocclusive PE in the left pulmonary artery (*arrows*).

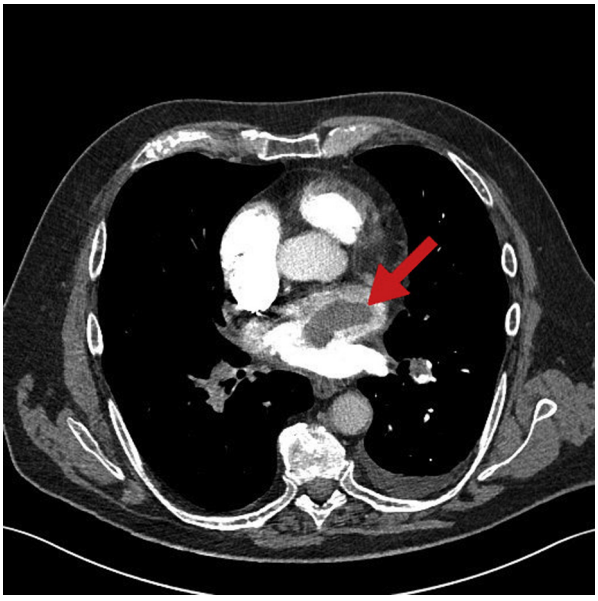

Figure 2 Chest computed tomography demonstrating a mass in the left atrium (*arrow*).

In 1995, Collins *et al.*[5] reported 14 patients with nonvalvular AF, in whom 18 thrombi were identified by TEE. Fourteen thrombi were localized in the LAA, two in the left atrium, one in the right atrial appendage, and one in the right atrium. Thrombus size varied from 5 to 20 mm, and six were considered mobile. After a median of 4 weeks of anticoagulation with warfarin, 16 of 18 thrombi (89%) had completely resolved. No patient had a clinical thromboembolic event between the transesophageal echocardiographic studies. This observation strongly suggested that anticoagulation with warfarin can achieve thrombus resolution and prevent new thrombus formation in patients with nonvalvular AF.

The observation that the majority of LA and LAA thrombi resolve with anticoagulation was further substantiated by Jaber *et al.*[6] from the Cleveland Clinic and Canavy *et al.*[7] from France. Among the 174 patients from the Cleveland Clinic with LA or LAA thrombus on TEE, 129 (80%) had thrombus resolution after a mean of 47 days. Among 35 patients with clot persistence, only 8 showed resolution on further TEE. Although thrombus size was not associated with its chance of resolution, nodular morphology was associated with nonresolution. Clinically apparent cerebrovascular events occurred in only two patients. In the French study[7] of 26 patients with LA or LAA thrombus on TEE, thrombus resolution with anticoagulation therapy occurred in 73% of patients. However, this study also raised the important issue that TEE was done for systemic embolization in 50% of these 26 patients.

The largest prospective study was performed by Bernhardt *et al.*,[8,9] who followed 43 patients with nonvalvular AF and LA or LAA thrombi with serial TEE and brain magnetic resonance imaging. All patients were anticoagulated with a target international normalized ratio of 2.5. During the follow-up period of 31 months, 72% of the thrombi disappeared. Sixteen percent had disappeared at 1 month, 42% at 3 months, 49% at 6 months, 56% at 12 months, and 72% at 31 months. Predictors of thrombus resolution were small thrombus size, lower echogenicity of thrombi, and lower LA volume. Although this study brings up the important point that complete resolution can be achieved by prolonging the duration of anticoagulation, it reveals a higher than previously appreciated incidence of cerebral embolization. Seventeen patients manifested acute cerebral diffusion abnormalities in a pattern consistent with embolic lesions. Fourteen were clinically silent, and only three were clinically apparent. Elevated peak emptying velocity of the LAA and a history of previous thromboembolism were independent predictors of cerebral embolism.

To our knowledge, only one study addressing non–vitamin K oral anticoagulant use in the setting of LA or LAA thrombus has been published.[10] This was a prospective, single-arm study of 53 patients with nonvalvular AF and LA or LAA thrombus who were treated with rivaroxaban for 6 weeks. The rate of complete thrombus resolution was 42%, while resolved or reduced thrombus was evident in 60% of patients. There were no reports of stroke or systemic embolism.

According to the data of Bernhardt *et al.*[8,9] high LAA emptying velocity suggested increased risk for cerebral thromboembolism. Although we cannot rule out a subclinical cerebrovascular event, our patient did not have a clinical stroke. Bernhardt *et al.* also reported only 16% clot resolution at 1 month, with smaller clot size and smaller LA size favoring clot resolution. In our patient, the clot almost completely resolved within 1 month of anticoagulation despite a large clot burden and moderate LA enlargement. This suggests that although the aforementioned features described by Bernhardt *et al.* may identify patients with low probability of clot resolution and high probability of possible embolic phenomena, they do not contraindicate pursuing aggressive anticoagulation. Despite the potential risk for thromboembolism, the literature supports the treatment with anticoagulation.

With multiple agents available, the choice of anticoagulation is also complex. The choice of low-molecular-weight heparin was made to ensure that the patient reached therapeutic levels and because of the possibility that this might be more helpful for the early resolution of LA or LAA thrombus. Follow-up TEE showed almost complete resolution of the thrombus, with only a small remnant in the LAA wall. At this point, lifelong anticoagulation treatment with apixaban was started. Among the group of novel oral anticoagulants, only dabigatran has shown superiority over warfarin to protect from ischemic stroke.[11] Whether this superiority would translate into better LAA and LA thrombus resolution remains to be determined.

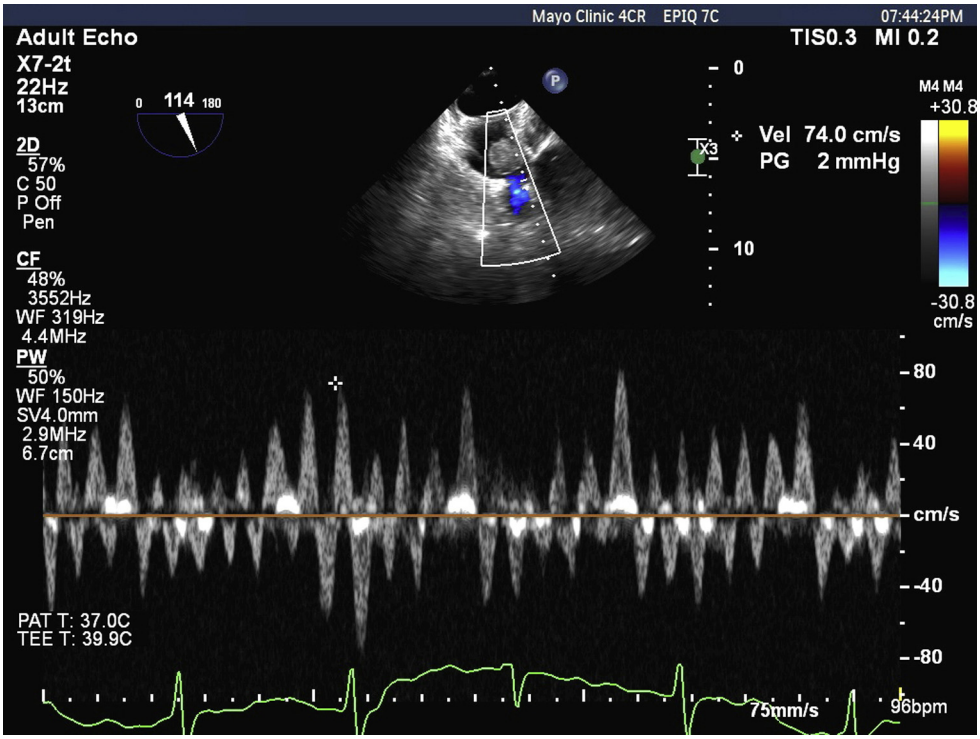

Figure 3 Pulsed-wave Doppler signal recorded from the ostium of the LAA demonstrated normal LAA emptying velocity (74 cm/sec).

CONCLUSIONS

This report suggests that aggressive anticoagulation with prolonged low-molecular-weight heparin rather than bridging to warfarin probably permitted early resolution of a large thrombus seen in the left atrium with attachment in the LAA without any clinical untoward effect. Our patient's response was more favorable than we expected given the aforementioned reports. This suggests that at present, there are no clearcut predictors, and one must pursue aggressive anticoagulation in these patients. In addition, this report points out that although thrombus size, thrombus morphology (nodularity), and preserved contractile function of the LAA can help identify those who are at high risk for thrombus persistence and embolization, prediction in individual patients is challenging. Further studies are needed, particularly for risk prediction of systemic embolization and long-term outcomes in this patient population.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.case.2017.10.007.

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