ESC European Society of Cardiology

European Heart Journal - Case Reports (2020) **4**, 1–6
doi:10.1093/ehjcr/ytaa360

CASE REPORT
Cardiac imaging

The concoction of cancer, catheter, and intracardiac clot: a case report describing a potential treatment strategy

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Received 19 March 2020; first decision 27 April 2020; accepted 10 September 2020; online publish-ahead-of-print 15 October 2020

Background Patients with cancer often pose a unique challenge to anticoagulation, as they have a higher risk of bleeding and clotting than the general population. Patients with cancer and catheter-related intracardiac thrombus are a very specific subset of people who do not have specific recommendations guiding their treatment. This article aims to address the existing knowledge gaps in this scenario and provide a possible treatment approach for these patients.

Case summary We describe the case of a 46-year-old lady with invasive breast cancer, who was on chemotherapy through a central venous catheter and was found to have a right atrial thrombus on routine echocardiography. Due to the paucity of data in this scenario and because the patient requested an oral anticoagulant which did not need frequent monitoring, we started her on apixaban for a total of 3 months. Echocardiogram was repeated at 4 and 8 weeks. In the 8-week echocardiogram, the right atrial thrombus was no longer visualized.

Discussion Malignancy and central venous catheters significantly increase the risk of thrombosis. Although low molecular weight heparin is the preferred anticoagulant to manage thrombosis in patients with cancer, direct oral anticoagulants have been proven to be non-inferior. In patients with catheter-related intracardiac thrombus, anticoagulation should be continued for at least 3 months or until the catheter is removed, whichever is longer.

Keywords Case report • Malignancy • Intracardiac thrombus • Echocardiogram • Anticoagulation • Central venous catheter • CRT (catheter-related thrombus)

Learning points

- Malignancy and the presence of vascular catheters increase the risk of developing thrombus.
- Guidelines recommend treating venous thromboembolism in cancer patients with low molecular weight heparin (LMWH) and left-sided intracardiac thrombus with warfarin.
- Low molecular weight heparin is preferred over warfarin to treat catheter-related thrombus in patients with malignancy.
- Cardiac sonographers should make an effort to carefully interrogate the catheter tip and the right atrium on each echocardiogram in patients with indwelling vascular lines to detect intracardiac thrombi.
- Direct oral anticoagulants may be an acceptable alternative to warfarin/LMWH in treating catheter-related intracardiac thrombus in patients with malignancy.

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Handling Editor: Elena Cavaretta
Peer-reviewers: Elad Asher; Pierre Deharo; Lilit Baghdasaryan
Compliance Editor: Ross Thomson
Supplementary Material Editor: Vassilios Parisis

Introduction

Malignancy is a well-known hypercoagulable state. Many patients with cancer have in-dwelling vascular lines for chemotherapy, which increases the probability of catheter-related thrombus. Low molecular weight heparins (LMWHs) are the preferred agents to manage cancer-associated thrombosis and warfarin is the preferred agent to treat intracardiac thrombus.[1–3] Although certain direct oral anticoagulants (DOACs) have been proven to be non-inferior to LMWH in preventing recurrence of venous thromboembolism (VTE) in malignancy,[4] the role of DOACs in the management of intracardiac thrombus in patients with cancer and in-dwelling venous catheters remains unclear. We present a case that illustrates a potential management option for patients who develop an intracardiac thrombus in the setting of underlying cancer and in-dwelling central venous catheters.

Timeline

April 2018	Patient diagnosed witd invasive ductal carcinoma of the right breast after having a biopsy done for an abnormal screening mammogram.
May 2018	Patient undergoes right total mastectomy with axillary node dissection.
June 2018	Central venous catheter inserted into right internal jugular vein for chemotherapy.
June 2018	Patient started on adjuvant chemotherapy with docetaxel, carboplatin, and trastuzumab.
August 2018	Routine transthoracic echocardiogram (TTE) to assess for side effects of chemotherapy reveals normal ejection fraction and cardiac structure.
November 2018	Routine TTE shows a new echodensity in the right atrium (RA).
3 days later	Transoesophageal echocardiogram describes RA density to most likely be a thrombus. Options discussed with patient and her oncologist. Patient started on Apixaban 10 mg bid × 1 week and 5 mg bid thereafter.
December 2018	Central venous catheter removed
January 2019	RA density no longer visualized on TTE. Patient continued on anticoagulation for a total 3 months.

Case presentation

A 46-year-old Caucasian lady with no significant past medical history was evaluated for an abnormal screening mammogram. She was diagnosed with invasive ductal carcinoma of the right breast and subsequently underwent right total mastectomy with axillary node dissection. A subcutaneous tunnelled vascular access port was inserted into the right internal jugular vein for the administration of chemotherapy (docetaxel, carboplatin, and trastuzumab). Apart from the chemotherapy, the patient was not on any long-term medications. Transthoracic echocardiogram (TTE) was performed every 3 months to assess the cardiac function during chemotherapy. A mobile echodensity was seen in the right atrium on routine follow-up TTE (*Figure 1*). Physical examination at this visit was unremarkable. A confirmatory transoesophageal echocardiogram was consistent with right atrial thrombus. After a discussion between the cardiologist, the oncologist, the patient, and her family, the patient was anticoagulated with apixaban 10 mg twice daily for 1 week, followed by 5 mg twice daily thereafter. The tunnelled catheter was removed after 3 weeks of anticoagulation. A computed tomography scan of the chest confirmed that there had been no pulmonary embolism secondary to the right atrial thrombus. After 8 weeks of oral anticoagulation, the right atrial thrombus was no longer present on repeat echocardiogram (*Figure 2*). Anticoagulation was planned for a minimum of 3 months, with concurrent monthly serial echocardiographic evaluation. The patient was seen in the clinic for a follow-up evaluation 5 months after the initial diagnosis of RA thrombus and an echocardiogram showed resolution of the thrombus with no recurrence.

Discussion

Current guidelines recommend treating (i) intracardiac thrombus with warfarin,[2,3] (ii) VTE in patients with cancer with LMWH or DOAC's,[1,5] and (iii) catheter-related thrombus with LMWH (*Figure 2*).[6] However, there are no guidelines outlining treatment principles for patients with the triple concurrent occurrence of cancer, catheter-related thrombus, and intracardiac thrombus on the right side of the heart. Our article aims to review the available data and to propose a potential treatment algorithm for this scenario.

The current American College of Cardiology Foundation (ACCF)/American Heart Association (AHA) guidelines recommend treating left-sided intracardiac thrombus with warfarin for at least 3 months, targeting an international normalized ratio goal of 2.0–2.5, whereas the European Society of Cardiology recommends treating for up to 6 months.[2–4] Though DOAC's have shown to be effective for managing VTE in cancer patients (*Table 1*), they have not yet been approved for treating intracardiac clots.[5,8] Compared to warfarin, DOACs have the advantage of not requiring frequent monitoring and limited interaction with food or most drugs (cytochrome p450 inhibitors). There have also been several case reports describing the effectiveness of DOACs in the treatment of left ventricular (LV) thrombus.[9,10] However, the literature describing the use of DOACs to treat right-sided thrombus is sparse and large-scale randomized control trials (RCT) are lacking in this area. Even the current recommendations to use oral vitamin K antagonists for left-sided intracardiac clots are largely based on observational studies and not RCTs, as RCTs would be rather difficult to conduct in this cohort.

Many patients with malignancy often have in-dwelling tunnelled vascular access devices.[11] These intravascular lines increase the chance of developing a thrombus due to (i) stasis of blood around the port and (ii) the thick viscosity of the drugs usually administered through the ports. Current guidelines recommend treating catheter-related thrombus (CRT) with systemic anticoagulation for at least 3 months.[7] These recommendations are similar for patients with CRT and malignancy.[7,12] Low molecular weight heparin is preferred in

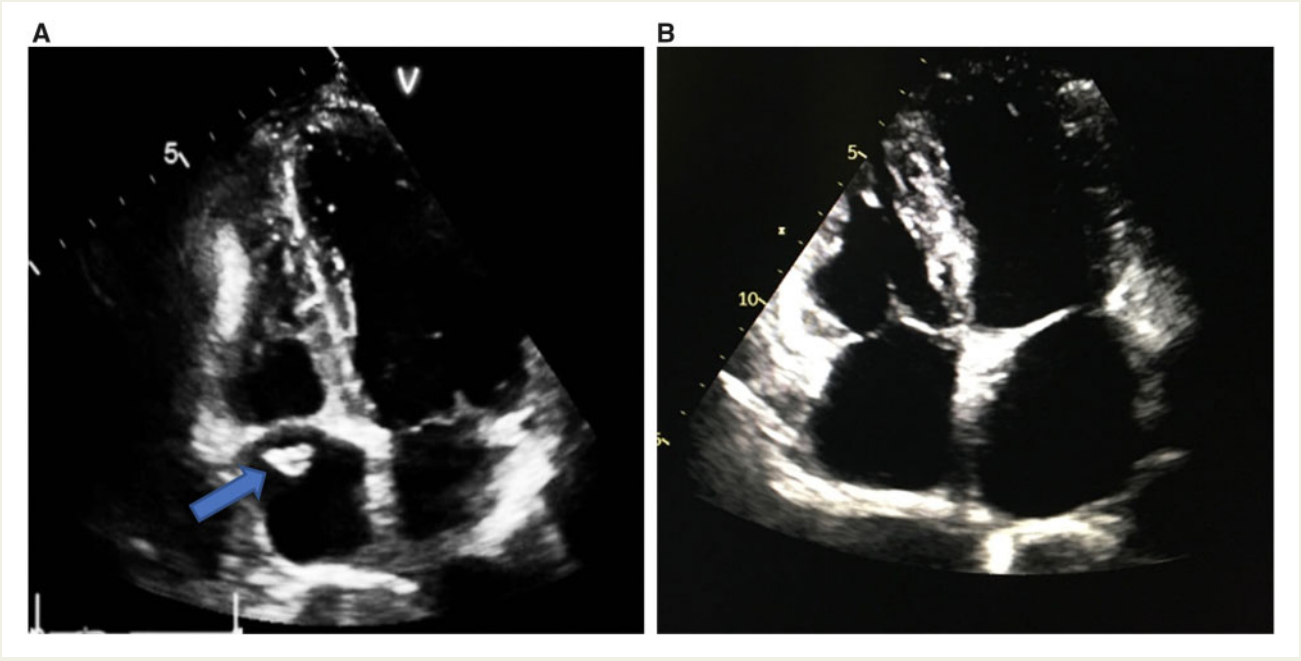

Figure 1 (*A*) Right atrial thrombus on initial ECHO. (*B*) Repeat ECHO at 8 weeks showing resolution of thrombus.

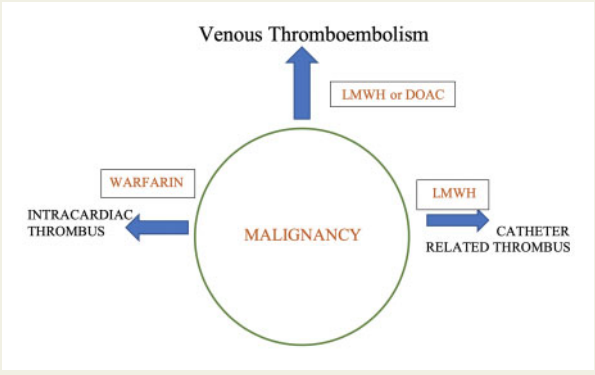

Figure 2 This figure depicts the various scenarios and their respective treatment options as per the current guidelines. DOAC, direct oral anticoagulants; LMWH, low molecular weight heparin.

patients with malignancy, as it is superior to warfarin in decreasing the recurrence of VTE.[13] The current guidelines do not necessitate the immediate removal of catheter in CRT unless it is misplaced, non-functional, or there is a concern for infection.[6,12] However, anticoagulation should be continued for as long as the catheter is in place as the risk of recurrence remains high.[6] Also, in a meta-analysis by Stavroulopoulos, it was shown that patients who underwent catheter removal had a significantly better prognosis than patients who did not.[14] Thus, it might be beneficial to consider the removal or exchange of the catheter in patients with a catheter-associated intracardiac thrombus.

There are no available guidelines to direct the duration of anticoagulation in the event of a persistent thrombus after 3 months of anticoagulation. Similar to LV thrombus, RA clots may organize and never resolve. Certain features can be used to differentiate between an acute thrombus and an organized thrombus, especially with the help of cardiac magnetic resonance imaging or deformation imaging.[15] In such cases, it may be appropriate to stop anticoagulation since the embolization potential of an organized thrombus is very low.[16] There are also no specific recommendations on the indications of surgery or thrombolysis. These are often decided on a case by case basis, and depend on the underlying comorbidities, size of the right atrial thrombus, its morphology, and the patient's prognosis.[16] Such decisions should involve a discussion between the multidisciplinary care teams involved in the patient's care.

In our patient, who was diagnosed with ductal carcinoma of the right breast and had a right internal jugular port for administration of chemotherapy, we believe the combination of the in-dwelling catheter and the malignancy lead to the right atrial clot which was detected on a routine echocardiogram. There were no clear guidelines on how to manage this unique situation and the patient preferred an oral anticoagulant that did not require frequent monitoring. Due to the efficacy and safety profile of apixaban,[17] and its success in treating intracardiac thrombus,[9,10] we decided to treat our patient with apixaban. After discussing the potential risks and benefits, the patient was started on apixaban 10 mg twice daily initially for 7 days and then 5 mg a day thereafter. Echocardiograms were repeated at 4 weeks, 8 weeks, 12 weeks, and at 5 months. The thrombus was no longer visible on these echocardiograms.

The issue of thromboembolism and anticoagulation of the cancer patient is complex because of the multiple pathophysiologies involved. In the setting of cancer, catheter, and intracardiac clot, the treatment strategy that is chosen will need to be tailored to the individual patient. We have outlined our approach to this scenario in

Table 1 Comparison of trials evaluating use of anticoagulants for VTE in cancer patients

Study name	Drugs studied	Author	Study type	Study population	Most common type of malignancy	Primary outcome	Findings	Secondary outcome	Findings
CLOT trial, published 2003.	Coumadin vs. Dalteparin	Agnes lee *et al.*	Prospective, randomized, open label, multicentre trial.	676 cancer patients with active cancer and newly diagnosed symptomatic proximal DVT, PE, or both.	Breast and colorectal	Recurrent DVT, PE, or both within 6 months.	Symptomatic recurrent DVT or PE, was lower in dalteparin group, 7.0% vs. 15% in the coumadin group. (HR 0.48, 95% CI 0.30–0.77; $P = 0.002$).	Clinically overt bleeding and death.	No difference in the rates of major bleeding (6 vs. 4%; $P = 0.27$), any bleeding (15 vs. 19%; $P = 0.09$), or death (39 vs. 41%; $P = 0.53$) between the two groups
Select-D trial, published 2018.	Rivaroxaban vs. Dalteparin	Young *et al.*	Prospective, randomized, open label, multicentre trial.	406 cancer patients with VTE.	Colorectal	Rate of recurrent VTE.	Rate of recurrent VTE was lower in the rivaroxaban group (HR 0.43, 95% CI 0.19–0.99).	Major bleeding and CRNMB	The cumulative rate at 6 months was 4% for dalteparin and 6% for rivaroxaban (HR 1.83, 95% CI 0.68–4.96)
Hokusai trial, published 2018.	Edoxaban vs. Dalteparin	Raskob *et al.*	Prospective, open label, non-inferiority study.	1050 cancer patients with VTE.	Colorectal	Composite of recurrent VTE or major bleeding during 12 months after starting treatment.	Edoxaban was non-inferior to LMWH (P 0.006 for non-inferiority).	Recurrent DVT, Recurrent PE, Major bleeding, CRNMB, death, event-free survival.	6.7% recurrent DVT in dalteparin group compared to 3.6% in edoxaban. (HR 0.56, CI -0.32 to 0.97).
Adam VTE trial, published 2020	Apixaban vs. Dalteparin	McBane *et al.*	Prospective, randomized trial.	300 patients with cancer-associated VTE.	Breast and colorectal	Major bleeding.	Major bleeding o% in apixaban group vs. 2.3% in dalteparin group (P 0.9956).	VTE recurrence	3.4% in apixaban group vs. 14.1% in LMWH (HR 0.26, 95% CI 0.09–0.80, P 0.0182)
Caravaggio trial, published 2020.	Apixaban vs. Dalteparin	Agnelli *et al.*	Prospective, multinational, randomized, open label, non-inferiority trial.	1158 cancer patients with VTE	Colorectal and lung	Recurrent VTE within 6 months, major bleeding.	Recurrent VTE occurred in 5.6% in the apixaban group vs. 7.9% in the dalteparin group. $P < 0.001$ for non-inferiority. Major bleeding occurred in 3.8% in the apixaban group vs. 4.0% in the dalteparin group (hazard ratio 0.82, 95% CI 0.40–1.69; $P = 0.60$).	Recurrent venous thromboembolism or major bleeding, CRNMB, major or CRNMB, death from any cause, and event-free survival.	Recurrent VTE or major bleeding was 8.9% in the apixaban group vs. 11.4% in the dalteparin group (HR, 0.70, 95% CI 0.45–1.07).

CRNBM, clinically relevant non-major bleeding.

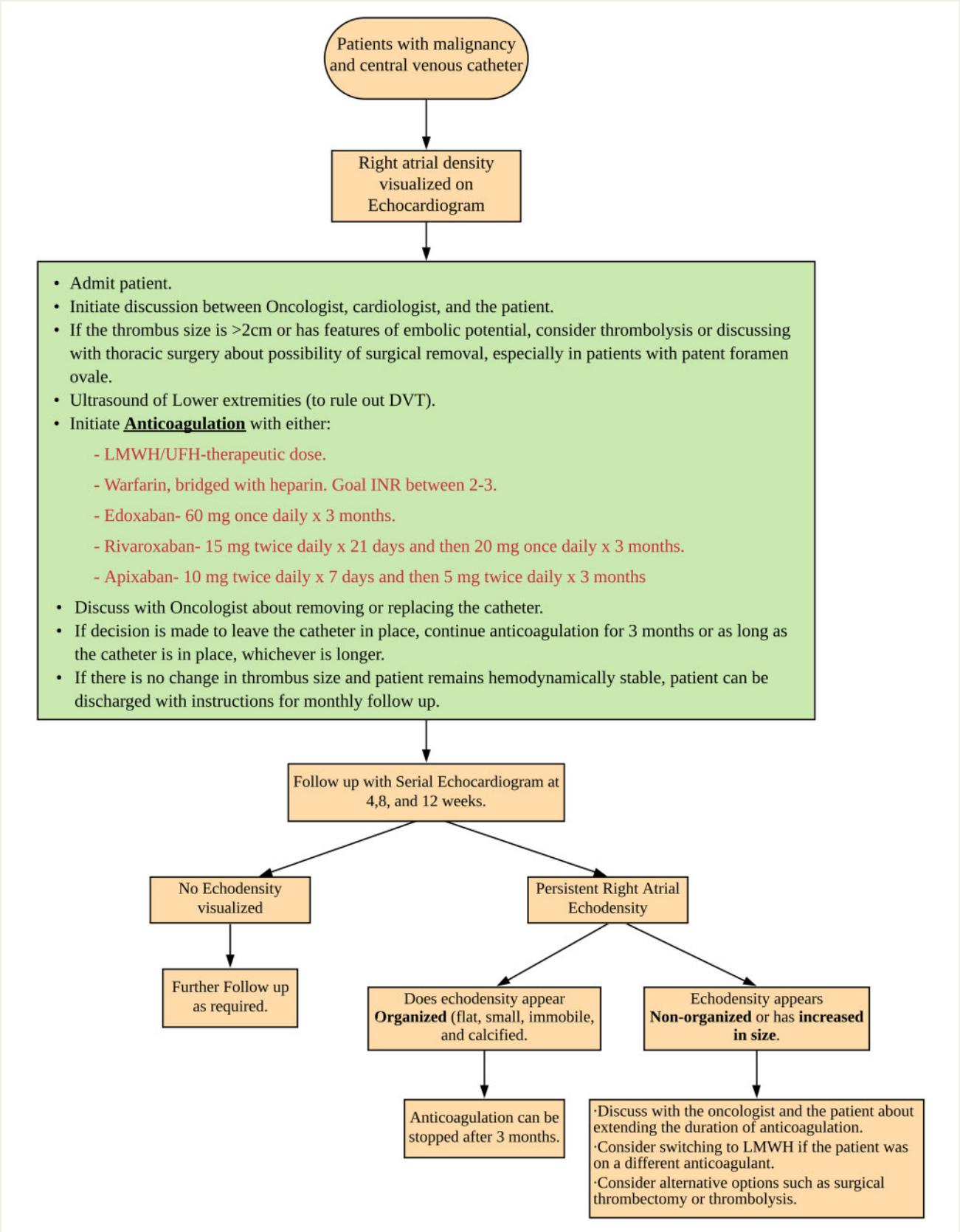

Figure 3 This flowsheet describes our approach to this unique situation based on current evidence. DVT, deep vein thrombosis; LMWH, low molecular weight heparin; UFH, unfractioned heparin.

Figure 3. Patients on chemotherapy are often assessed with serial transthoracic echocardiography to assess for LV dysfunction due to cardiotoxicity of the chemotherapeutic agents. Special attention to the right atrium and the catheter tip (if it can be visualized) is warranted. There are still questions that need to be answered: (i) Should anticoagulation be continued for longer than 3 months? (ii) How often do we need to repeat imaging in patients with catheter-related intracardiac thrombus? (iii) Can anticoagulation be stopped earlier if the thrombus is no longer visualized? (iv) When should surgery/thrombolytics be considered? It is unlikely that a randomized controlled trial can be conducted to answer these questions; we are hopeful that clinicians will continue to report their experiences in managing this scenario so that we can gain insight into the best management strategy.

Lead author biography

Dr. Nair is a third year internal medicine resident and also a Chief Resident at the Cleveland Clinic Fairview Hospital. He considers cardiology as his passion and enjoys doing clinical research as he believes it helps in advancing patient care. He has published articles in esteemed journals and also presented multiple abstracts at national and international conferences. He hopes to be cardiologist in the future and looks forward to a career with equal focus on clinical practise and scientific research.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The authors confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

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