CASE REPORT

Acute Pulmonary Embolism with mobile right ventricular thrombus successfully treated with unfractionated heparin in the Covid-19 era

Vasileios Giannakopoulos MD, Theodora Plakomyti MD, Vasileios Demou MD, Olvia Filippou MD, Joseph A Moutiris MD, PhD,

Department of Cardiology, Paphos General Hospital, Cyprus

Abstract

A male patient presented to the Emergency Department with chest pain and low grade fever and was admitted to the Medical ward with the diagnosis of bilateral pneumonia. The PCR test for Covid-19 was negative and the patient underwent a computerised tomography of the pulmonary arteries (CTPA) which detected thrombi in both pulmonary arteries and also a large thrombus in the right ventricle. The transthoracic echo (TTE) confirmed the presence of a mobile thrombus in the right ventricle. The patient received enoxaparin for 48 hours. Since there was no change on repeat TTE it was decided to discontinue enoxaparin and start infusion of aPTT-guided unfractionated heparin. Repeat TTE performed 48 hours later, showed a normally functioning right ventricle without any evidence of thrombi.

Introduction

Acute pulmonary embolism is a common disease that carries significant morbidity and mortality. The presence of right heart thrombi (RHT) in the absence of atrial fibrillation, structural heart disease, or catheters in situ is rare and almost exclusively found in the presence of clinical manifestations of pulmonary embolism (PE). In view of the reported high mortality, it constitutes a medical emergency and requires immediate treatment. Although there is a specified management strategy for acute PE, the optimal management of right ventricular thrombi is still uncertain. We present the case of a patient with a large mobile thrombus in the right ventricle that was treated conservatively with a favorable outcome.

Case report

A 22-year-old male with no prior medical history, presented at the Emergency Department complaining of low grade fever and chest pain for the last 24 hours.

The vital signs of the patient were: heart rate 110/min, blood pressure 120/80mmHg, respiratory rate 22/min, arterial oxygen saturation 93% and temperature 37.2 ^{o}C. Clinical examination revealed basal bilateral lung crackles and mild right subcostal tenderness. The electrocardiogram was in sinus rhythm and apart from sinus tachycardia, no other abnormalities were seen.

The chest X-ray revealed bilateral lung consolidations and the patient was admitted in the Medical ward for patients with high suspicion of Covid-19, which was set up in Paphos General Hospital during the first wave of Covid-19 pandemic. Based on the clinical picture and the markedly elevated D-dimers a CTPA was performed to demonstrate bilateral thrombi in the pulmonary arteries, areas of opacity in the upper segments of the lower lobes as per pulmonary infarcts as well as the presence of thrombus in the right ventricle (Fig. 1).

Transthoracic echocardiography, performed immediately after the CTPA, revealed a dilated right

ventricle with mildly reduced contractility and the presence of a large free-floating thrombus inside the right ventricle.

(Fig 2-4). In addition, ultrasound of the lower limb veins, demonstrated bilateral thrombosis in the femoral veins extending to the iliac veins. Subsequent thrombophilia tests, were negative.

Due to the hemodynamic stability and the good overall clinical condition of the patient, it was decided to follow a conservative approach with immediate administration of enoxaparin.

Cardiac echo and CTPA were repeated 48 hours later without showing any change from the baseline. It was then decided to switch to unfractionated heparin, initially 80 IU/kg as bolus followed by infusion at a rate of 18 IU/kg/h aiming to achieve an aPTT approximately 2.0-2.5 the control, in an attempt to dissolve the clots, before referring the patient to the cardiac surgeons for surgical treatment. Interestingly, 48 hours later there was no evidence of the intraventricular thrombus on transthoracic echo and no evidence of additional pulmonary embolism on a repeat CTPA. It was concluded that the clot was dissolved by the UFH.

Discussion

RHT can be identified in less than 4% of unselected patients with PE, but their prevalence may be much higher in high risk patients and are associated with excessive early mortality particularly when accompanied by right ventricular dysfunction (1).

Three patterns of RHT have been described. Type A thrombi are morphologically serpiginous, highly mobile, and associated with deep vein thrombosis and PE. It is hypothesized that these clots embolize from large veins and are captured in-transit within the right heart. Type B thrombi are nonmobile and are believed to form in situ in association with underlying cardiac abnormalities while type C thrombi elicit intermediate characteristics of both type A and type B (2). Our patient presented a serpiginous free-floating thrombus within the right ventricle compatible with a type A thrombus.

Mobile RHT is associated with RV dysfunction and higher early mortality beyond the presence of PE alone. They can easily embolize to the pulmonary arterial tree compromising pulmonary circulation, causing severe hypoxia and sudden cardiac death (3). The presence of RHT at the time of acute PE was found to predict all-cause death, PE-related death, and recurrent venous thromboembolism, particularly in patients without haemodynamic compromise (4). A meta-analysis of 6 studies including 593 patients showed a mortality rate of 16.7% (5). However, it is still unclear whether RHT are a direct cause or just an indicator of adverse outcomes. In the Right Heart Thrombi European Registry, short-term prognosis was associated with clinical and haemodynamic consequences of PE and not RHT characteristics such as size, morphology, or mobility (6).

In view of the reported high mortality, the coexistence of PE with RHT is regarded as a medical emergency and requires immediate treatment. Treatment options for PE vary, ranging between heparin alone, thrombolysis, catheter-directed therapy and surgical embolectomy. However, the optimal management of PE complicated with RHT remains unclear and can vary significantly (7).

Thrombolysis in patients with PE is currently recommended for high risk and selected intermediate-high risk patients who develop signs of haemodynamic instability while under treatment with anticoagulants (1). Thrombolysis has the potential to dissolve the clots at every location (within the heart and the venous and arterial vasculature). Good outcomes with thrombolysis were reported in some small studies (8-9). The

favorable result after thrombolysis has been related to the shorter delay between the presumed onset of symptoms and hospitalization in those patientsς (7). In one case series, half of the clots disappeared within 2 hours of thrombolysis, whereas the remainder disappeared within 12 to 24 hours. This delayed disappearance of the thrombi supports the decision to defer surgery after thrombolysis until at least 24 hours (8).

Surgical embolectomy with exploration of the right heart chambers and pulmonary arteries under cardiopulmonary bypass is another treatment option. It is recommended for patients in whom thrombolysis is contraindicated or has failed (1).

Catheter-directed therapies for PE include percutaneous catheter-directed thrombolysis or high-frequency ultrasound exposure near the surface of the clot; endovascular mechanical thrombectomy using fragmentation and a capture device; and endovascular aspiration of the clot directly from within the atrium, ventricle, or pulmonary arteries (10-12) and should be considered for patients in whom thrombolysis is contraindicated or has failed. Though there have been some successful cases reported (11, 13-15), these methods are not widely available and therefore evidence remains scarce.

Anticoagulation is recommended for virtually all PE patients and should be promptly initiated in all patients with high or intermediate probability of PE while still awaiting the results of diagnostic tests (1). In the presence of an intracardiac thrombus it can be used alone as monotherapy or as an adjunctive therapy following other interventions. The use of isolated parenteral anticoagulation is sometimes dismissed in patients with RHT because it is thought to be potentially hazardous as the thrombi may embolize to the already compromised pulmonary circulation, although thrombolysis may also pose similar risks (16). However, its use as a first line therapy in these patients is proposed in stable patients, especially when there is a high bleeding risk (17). The acute-phase anticoagulation is usually parenteral and may comprise of subcutaneous LMWH, IV unfractionated heparin or subcutaneous fondaparinux. LMWHs have many advantages over UFH (fixed doses, greater bioavailability, subcutaneous administration, longer duration of anticoagulant effect). Moreover, LMWHs or fondaparinux are preferred over unfractionated heparin in the acute phase as they carry a lower risk of major bleeding and HIT (1). UFH is recommended for patients in whom primary reperfusion is considered, as well as for those with serious renal impairment (creatinine clearance <30 mL/min), or severe obesity.

Few studies have analyzed the differential impact on mortality of the above therapies in patients with PE and RHT. Data from some case series (7, 17-18) and a meta-analysis (19) showed no differences among available treatment options. In addition, a study that compared reperfusion therapy to anticoagulation alone found no significant difference in mortality and bleeding, with a higher risk of recurrence with reperfusion therapy (20). However another meta-analysis of 177 cases presenting with RHT described an improved survival rate with thrombolytic therapy (mortality rate 11.3%) that was statistically significant when compared to either anticoagulation therapy (mortality rate 28.6%) or surgery (mortality rate 23.8%) (16). Furthermore, in 2018, a systematic review showed similar results between fibrinolysis and surgical embolectomy and recommended that the treatment of choice relies on proper individualization of the risks and benefits of both techniques (21).

Conclusion

Detection of RHT is rare and so it is highly unlikely that there will ever be a prospective randomized

study comparing different treatment arms. The choice of treatment remains mainly in the clinical judgement of the physician according both to the patient's individual characteristics and the available options. In our patient's case there was a favourable outcome with total thrombus dissemination and full recovery of the right ventricular function, after conservative treatment with heparin. Our decision to switch enoxaparin to unfractionated heparin 48 hours after the initiation of treatment was based on the suspicion of a possible resistance to enoxaparin, while still awaiting the results from the thrombophilia screening. The thrombophilia screening came back negative and therefore we have no data to claim weather the dissemination of the thrombus can be attributed to the choice of unfractionated heparin or to possibly short time of enoxaparin administration. Existing evidence suggests the superiority of thrombolysis over anticoagulation alone and most authors advocate immediate treatment with thrombolysis and/or embolectomy instead of monotherapy with anticoagulation even though there are no prospective randomized trials to support this decision. Percutaneous treatments may play an important role for the management of patients with RHT in the future, but evidence is still lacking. This case illustrates the difficulty in the management of such high risk patients in the absence of hard evidence and highlights the importance of an individualized approach. Avoiding high risk procedures should always be taken into account when the benefit is not clearly established.

References

1. S. V. Konstantinides, "2014 ESC Guidelines on the diagnosis and management of acute pulmonary embolism," European Heart Journal, vol. 35, no. 45, pp. 3145–3146, 2014.

2. G. Kronik, "The european cooperative study on the clinical significance of right heart thrombi," European Heart Journal, vol. 10, no. 12, pp. 1046–1059, 1989.

3. Chapoutot, L., Nazeyrollas, P., Metz, D., Maes, D., Maillier, B., Jennesseaux, C., Elaerts, J. (1996) Floating right heart thrombi and pulmonary embolism: Diagnosis, outcome and therapeutic management. Cardiology 87(2), 169–174

4. D. Barrios, V. Rosa-Salazar, D. Jimenez et al., "Right heart ´ thrombi in pulmonary embolism," European Respiratory Journal, vol. 48, no. 5, pp. 1377–1385, 2016.

5. Barrios, V. Rosa-Salazar, R. Morillo et al., "Prognostic significance of right heart thrombi in patients with acute symptomatic pulmonary embolism: systematic review and meta-analysis," Chest, vol. 151, no. 2, pp. 409–416, 2017

6. M. Koc, M. Kostrubiec, W. Elikowski et al., "Outcome of patients with right heart thrombi: The Right Heart Thrombi European Registry," European Respiratory Journal, vol. 47, no. 3, pp. 869–875, 2016.

7. A. Torbicki, N. Galie, A. Covezzoli, E. Rossi, M. De Rosa, and ´ S. Z. Goldhaber, "Right heart thrombi in pulmonary embolism: results from the international cooperative pulmonary embolism registry," Journal of the American College of Cardiology, vol. 41, no. 12, pp. 2245–2251, 2003.

8. E. Ferrari, M. Benhamou, F. Berthier, and M. Baudouy, "Mobile thrombi of the right heart in pulmonary embolism: delayed disappearance after thrombolytic treatment," Chest, vol. 127, no. 3, pp. 1051–1053, 2005.

9. G. Pierre-Justin and L. A. Pierard, "Management of mobile right heart thrombi: a prospective series," International Journal of Cardiology, vol. 99, no. 3, pp. 381–388, 2005.

10. T. Momose, T. Morita, and T. Misawa, "Percutaneous treatment of a free-floating thrombus

in the right atrium of a patient with pulmonary embolism and acute myocarditis," Cardiovascular Intervention and Therapeutics, vol. 28, no. 2, pp. 188–192, 2013.

11. J. Beregi, V. Aumegeat, C. Loubeyre et al., "Right atrial thrombi: ´ percutaneous mechanical thrombectomy," Cardiovascular and Interventional Radiology, vol. 20, no. 2, pp. 142–145, 1997

12. B. M. Richartz, G. S. Werner, M. Ferrari, H. Khnert, and H. R. Figulla, "Non-surgical extraction of right cardiac "thrombus in transit"," Catheterization and Cardiovascular Interventions, vol. 51, no. 3, pp. 316–319, 2000

13. R. P. Davies, J. Harding, and R. Hassam, "Percutaneous retrieval of a right atrioventricular embolus," CardioVascular and Interventional Radiology, vol. 21, no. 5, pp. 433–435, 1998.

14. B. Nickel, T. McClure, and J. Moriarty, "A novel technique for endovascular removal of large volume right atrial tumor thrombus," CardioVascular and Interventional Radiology, vol. 38, no. 4, pp. 1021–1024, 2015.

15. N. W. Shammas, R. Padaria, and G. Ahuja, "Ultrasound-assisted lysis using recombinant tissue plasminogen activator and the EKOS ekosonic endovascular system for treating right atrial thrombus and massive pulmonary embolism: a case study," Phlebology, vol. 30, no. 10, pp. 739–743, 2015.

16. P. S. Rose, N. M. Punjabi, and D. B. Pearse, "Treatment of right heart thromboemboli," Chest, vol. 121, no. 3, pp. 806–814, 2002.

17. L. Chartier, J. Bera, M. Delomez et al., "Free-floating thrombi in ´ the right heart: diagnosis, management, and prognostic indexes in 38 consecutive patients," Circulation, vol. 99, no. 21, pp. 2779– 2783, 1999.

18. R. Mollazadeh, M. A. Ostovan, and A. R. Abdi Ardekani, "Right cardiac thrombus in transit among patients with pulmonary thromboemboli," Clinical Cardiology, vol. 32, no. 6, pp. E27–E31, 2009.

19. E. L. Kinney and R. J. Wright, "Efficacy of treatment of patients with echocardiographically detected right-sided heart thrombi: a meta-analysis," American Heart Journal, vol. 118, no. 3, pp. 569–573, 1989.

20. D. Barrios, J. Chavant, D. Jimenez et al., "Treatment of right ´ heart thrombi associated with acute pulmonary embolism," The American Journal of Medicine, 2016.

21. Burgos, L. M., Costabel, J. P., Galizia Brito, V., Sigal, A., Maymo, D., Iribarren, A., Trivi, M. (2018) Floating right heart thrombi: A pooled analysis of cases reported over the past 10 years. Am. J. Emerg. Med. 36(6), 911–915.

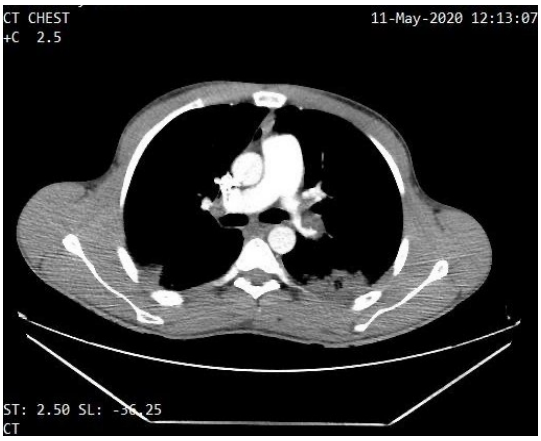

Fig 1. CT of chest

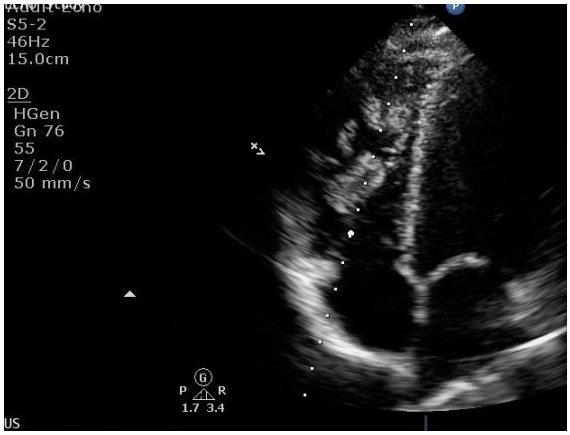

Fig 4. TTE apical 4-chamber view

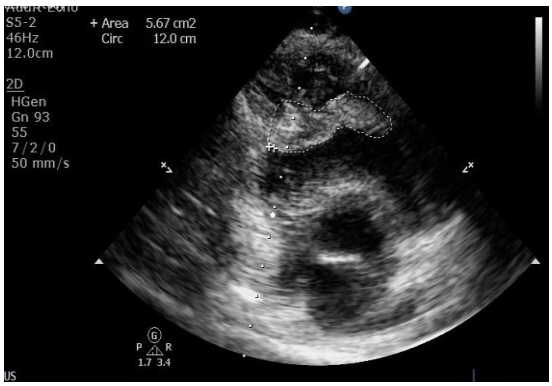

Fig 2. TTE parasternal short axis view

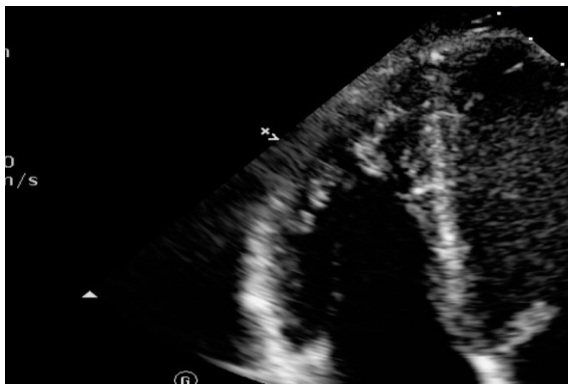

Fig 5. TTE apical 4-chamber view

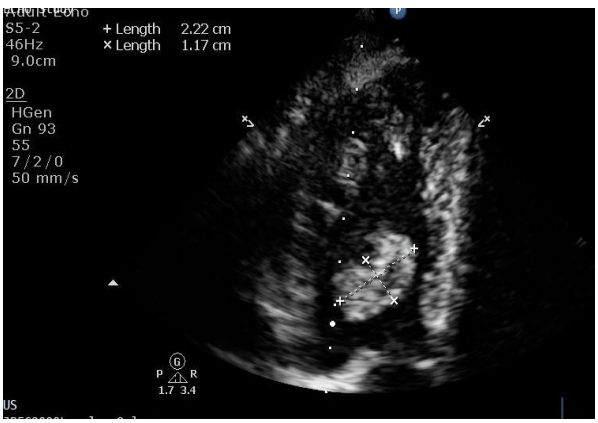

Fig 3. TTE apical 4-chamber view