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Delayed Pericardial Tamponade after Thrombolytic and Anticoagulant Treatment for Pulmonary Embolism

Sofia HC Botvid[1,4], Peter Riis Hansen[2], Jesper Kjaergaard[3] and Jens Tingleff[4]*

[1]*Department of Allergy, Venereology and Dermatology, National Research Center for Allergy, Gentofte Hospital, Denmark*

[2]*Department of Cardiology, Copenhagen University Hospital, Herlev-Gentofte, Copenhagen, Denmark*

[3]*Department of Cardiology, The Heart Center, Copenhagen University Hospital, Rigshospitalet, Denmark*

[4]*Department of Emergency Medicine, Copenhagen University Hospital Amager and Hvidovre, Hvidovre, Denmark*

Abstract

Background: Pericardial Tamponade (PT) is a life-threatening medical emergency caused by the formation of fluid in the pericardial sac. Major bleeding, including pericardial bleeding with PT, is a known adverse effect of antithrombotic therapy, e.g., heparin, thrombolytic agents, and anticoagulants. Pericardial bleeding (hemopericardium) with subsequent Pericardial Tamponade (PT) is a rare but life-threatening condition that requires emergency pericardiocentesis.

Case Report: We describe a 44-year-old woman who was admitted to our Emergency Department (ED) after syncope. Eleven days before, she was treated for Pulmonary Embolism (PE) with low molecular weight heparin, recombinant plasminogen activator, and apixaban and had an uneventful course. The patient was promptly diagnosed with PT by use of transthoracic echocardiography and treated with acute pericardiocentesis.

Conclusion: We aim to highlight this delayed and potentially fatal complication of anticoagulant and/or thrombolytic treatment. PT should be considered in patients presenting to the Emergency Department (ED) with circulatory shock, while receiving antithrombotic therapy. Rapid diagnosis of PT is of paramount importance and echocardiography should be immediately available in the ED as well as access to acute pericardiocentesis. Transthoracic Echocardiography (TTE) is the most important imaging modality for assessing the presence of pericardial effusion and its severity and in the case of severe effusion leading to PT.

Keywords: Cardiac tamponade; Pulmonary embolism; Apixaban; Reteplase

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Correspondence:
Sofia HC Botvid, Department of Emergency Medicine, Copenhagen University Hospital Amager and Hvidovre, Hvidovre, Denmark, E-mail: sofia.botvid@regionh.dk

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Introduction

Major bleeding is an adverse effect of heparin, thrombolytics, and anticoagulants. Pericardial bleeding (hemopericardium) with subsequent Pericardial Tamponade (PT) is a rare but life-threatening condition that has been described after thrombolytic treatment, primarily in patients with ST-segment elevation acute myocardial infarction or stroke [1,2]. Major bleeding during the use of vitamin K antagonists or Direct Oral Anticoagulants (DOAC) is also a well-established risk and for several therapeutic indications, e.g. non-valvular atrial fibrillation, deep venous thrombosis and Pulmonary Embolism (PE), DOACs have become preferred anticoagulation agents owing to lower risk of major bleeding, availability of fixed dosages, fewer drug interactions, faster onset of action and shorter drug half-lives [3-5]. Heparin, thrombolytic agents, and anticoagulants all have indications for treatment of PE where their use is associated with improved survival [6-9]. However, use of these agents entails risk of major bleeding including rare cases of pericardial bleeding with PT.

We here report a case of PT caused by pericardial bleeding eleven days after treatment of PE with unfractionated heparins and thrombolytic therapy, followed by a DOAC. This case underscores that in patients receiving antithrombotic therapy and presenting to the Emergency Department (ED) with circulatory shock, PT should be considered. Transthoracic Echocardiography (TTE) is the most important imaging modality for assessing the presence of pericardial effusion and its severity and in the case of severe effusion leading to PT; emergency pericardiocentesis is a life-saving procedure.

Case Presentation

A 44-year-old woman was evaluated at our ED because of a sudden and unannounced syncope. Her medical history included endometriosis treated with hormonal IUD and desogestrel, and infrequent migraine.

Eleven days before admission, the patient was diagnosed with a large saddle PE at another hospital. TTE at that time showed a dilated Right Ventricle (RV), D-shaped left ventricular cavity, with abnormal Tricuspid Annular Plane Systolic Excursion (TAPSE) of 1.1 cm. The ECG revealed new-onset incomplete right bundle branch block (Figure 1). She received tinzaparin 175 IE/kg subcutaneously. The following day the patient was tachycardia with increased shortness of breath and decreased systolic blood pressure to 90 mmHg to100 mmHg. Accordingly, thrombolytic therapy was administered with two intravenous boluses of 10 E reteplase over 5 min administered in a peripheral vein. The rest of the hospital course was uneventful and during the admission, there were only slightly abnormal liver tests

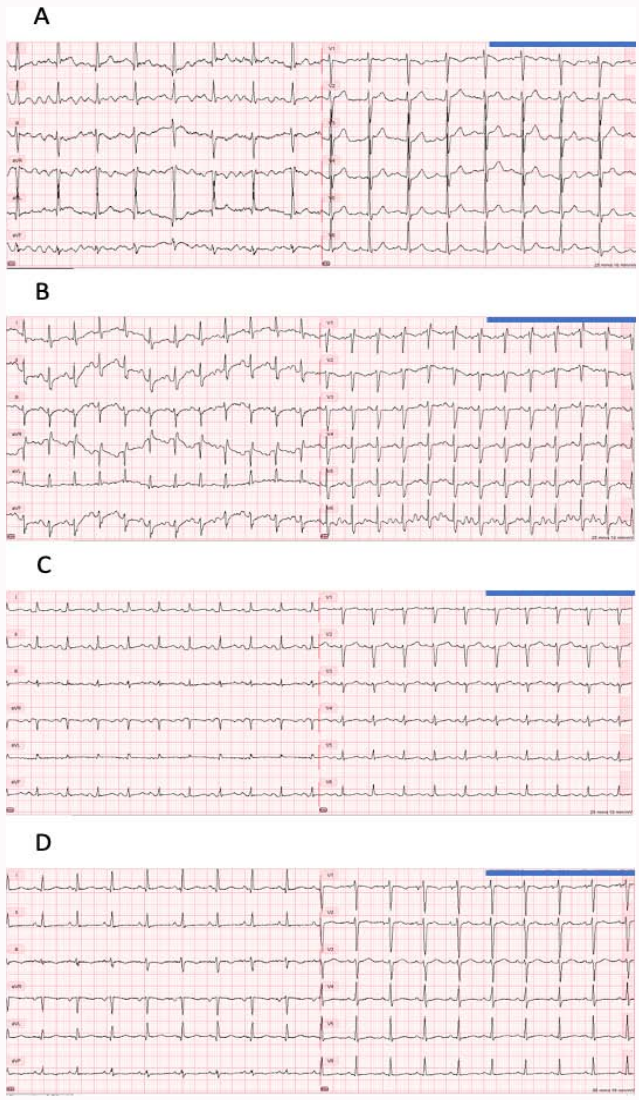

Figure 1: Case Electrocardiograms (ECGs). **(a)** Normal ECG tree years prior to acute pulmonary embolism. **(b)** ECG on day-11 showing signs of acute pulmonary embolism with new onset incomplete right bundle branch bloc. **(c)** ECG on day 0 with signs of pericardial tamponade (low voltage of the QRS complexes). **(d)** Normal ECG tree months after pericardial tamponade.

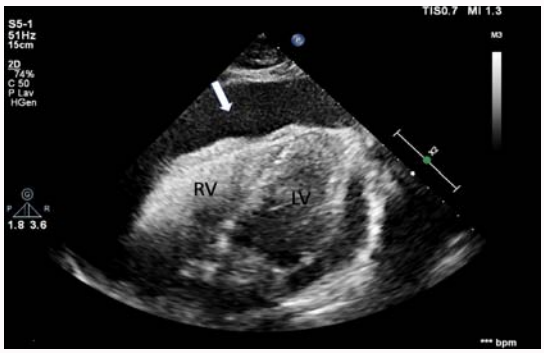

Figure 2: Transthoracic echocardiography (subcostal projection) showing pericardial tamponade Large pericardial effusion >3 cm (arrow) primarily basallyand over the Right Ventricle (RV). (LV: Left Ventricle).

(Table 2). The patient was discharged after five days with apixaban 10 mg twice per day.

On evaluation in our ED after the syncope, the patient was awake and alert in moderate distress with dyspnea and chest pain. Heart rate was 119 beats per minute, blood pressure 118/97 mmHg, respiratory rate 17 per minute, and oxygen saturation 98% while the patient was breathing ambient air. The ECG showed sinus rhythm with low voltage of the QRS-complexes (Figure 1C).

The patient was initially treated with a rapid infusion of intravenous fluids and antibiotics for suspected septic shock, possibly induced by a post-hospital-acquired infection. However, after four hours the condition quickly deteriorated with signs of hemodynamic collapse with a rapid drop in blood pressure, increased dyspnea, and acute hypoxemic respiratory failure with an oxygen saturation of 85% and arterial blood metabolic acidosis despite conventional oxygen therapy (Table 2). Therefore, high-flow nasal oxygen 50 L/min was started. Abnormal liver biochemical tests were also apparent suggestive of acute liver failure (Table 2).

Acute TTE showed PT with a massive circumferential pericardial effusion measuring up to 3 cm to 4 cm and compressing cardiac chambers and the RV in particular (Figure 2). Apixaban was discontinued and the patient was immediately transferred for emergency pericardiocentesis at the Trauma Centre in the Capital Region of Denmark. Here, 1200 ml of blood-containing fluid was drained leading to immediate improvement of the condition. During the next four hours, another 400 ml of pericardial fluid was drained. Two days later, the pericardial sac was re-drained for another 1,150 ml of blood-containing pericardial fluid. On day three, no signs of bleeding from the pericardium were apparent on repeat TTE. Therefore, tinzaparin 7000 IE twice daily was administered. A CT pulmonary angiogram revealed small remnants of arterial thrombosis in segmental arteries of both lungs and a segmental pulmonary infarction in the right lung. The patient remained hospitalized for ten days and was discharged with tinzaparin treatment. Further evaluation in the outpatient clinic showed normalization of liver tests and no signs of malignancy or thrombophilia. Forty-two days after discharge, the patient's tinzaparin was discontinued and rivaroxaban 20 mg daily was administered with subsequent uneventful complete recovery.

Discussion

Eleven days before the present admission with PT, the patient received heparin, thrombolysis, and DOAC for PE, with subsequent

Table 1: Timeline.

Timeline	Description
Day -11	Diagnosed with a large saddle pulmonary embolism. Echocardiography: Dilated right ventricle, D-shaped left ventricular cavity, TAPSE 1.1 cm (Normal TAPSE ≥ 1.7 cm). ECG: new onset incomplete right bundle branch block. Therapeutic dose of tinzaparin administered.
Day -10	Blood tests: Elevated cTnI. Blood pressure: 90-100 mmHg systolic, heart rate 120-130 bpm. Reteplase therapy: Intravenous 10 IE repeated after 30 minutes.
Day – 9	Apixaban 10 mg twice daily started.
Day – 8	Patient discharged.
Day 0 Admission	Patient presents with syncope, dyspnea, and chest pain. Apixaban stopped. Blood tests: increased liver parameters. Emergency pericardiocentesis.
Day 2	Echocardiography: recurrent pericardial effusion. New pericardiocentesis.
Day 3	Therapeutic dose of tinzaparin started.
Day 4-5	CT-chest scan: sights of minor embolism to lung segments on both sides. Infiltration in right lung. Echocardiography: minor effusion posterior to right ventricle. Right ventricle borderline dilatated. Normal TAPSE. Ejection fraction of left ventricle normal.
Day 6	Patient discharged. Tinzaparin continued.
Day 42	Echocardiography: normal. Blood tests: Normal liver parameters. Tanzanian stopped. Rivaroxaban started. Thrombophilia screen: Normal.

TAPSE: Tricuspid Annular Plane Systolic Excursion

Table 2: Case blood samples.

Variable	Reference range	Day –11 Diagnose PE	Day 0 Tamponade
Alanine aminotransferase (U/L)	15-37	50	5060
Lactate dehydrogenase (U/L)	105-205	338	6010
Creatine (mg/dL)	0.6 – 1.2	0.68	2.23
Sodium (mmol/L)	135-145	140	124
Potassium (mmol/L)	3.4-4.8	3.6	6.3
C-reactive protein (mg/dL)	<1	6.8	11.2
White cells (× 10^3/µL)	4.5-11	13	31.3
Hemoglobin (g/dL)	12-18	13.7	10.9
Platelets (× 10^3/µL)	150-400	257	310
International Normalized Ratio	<1.2	1.2	4.4
D-dimer (mg/L)	<0.5	>35	16.3
Troponin I (ng/L)	<45	299	
Troponin T (ng/L)	<14		20
Blood gases – arterial		*	**
pH	7.35-7.45	7.44	7.23
Partial pressure of carbon dioxide (mmHg)	35-42	27	11
Partial pressure of oxygen (mmHg)	80-100	97	127
Bicarbonate (mmol/L)	22-27	20.9	8.4
Base excess (mmol/L)	-6	-5.1	-22.6
Oxygen saturation (%)	92-100	98	98
Lactate (mmol/L)	0.7-2.1	3.1	10

* Nasal oxygen catheter (2 L oxygen/min); ** High-Flow Nasal Cannula oxygen therapy (50 L oxygen/min)

continued DOAC treatment. In PE, thrombolytic therapy leads to faster improvement of pulmonary artery obstruction compared with heparin alone [9]. The indication for thrombolysis in PE is determined by clinical instability and RV dysfunction [6-9]. Therefore, thrombolytic treatment for PE was well-indicated in the current case at the first admission and this condition quickly improved hereafter.

Major bleeding including intracranial hemorrhage after thrombolysis for PE is a rare albeit well-known complication [10]. Various risk score systems have focused on major bleeding risk factors after thrombolysis after PE including advanced age, recent major bleeding, ongoing antithrombotic therapy, cancer, syncope, and renal dysfunction [11,12]. The major bleeding event in the present case was PT. This complication of thrombolytic therapy has been described in patients with myocardial infarction within 1 to 2 days after treatment

[1,2]. On the other hand, in patients with PE the occurrence of PT was not reported in the last Cochrane review of the safety and efficacy of thrombolytic therapy [6]. Also, reports on risk score to predict major bleeding in PE patients receiving systemic thrombolysis did not report PT [11,12]. After the admission with PE, the patient was discharged with a DOAC (apixaban) according to current treatment guidelines. PT during treatment with DOACs is a rare complication and elderly males with renal and coagulation abnormalities appear to be at highest risk [13-15].

Our patient was diagnosed with PT eleven days after treatment of PE with pharmacological thrombolysis (reteplase) and subsequent administration of DOAC (apixaban). Major bleeding complications usually occur 24 h to 48 h after thrombolytic treatment in patients with acute myocardial infarction or stroke [1,2].

Randomized comparisons of DOACs are not available but after treatment of PT, the patient received low molecular weight heparin for weeks and then another DOAC- rivaroxaban without recurrent bleeding or other complications.

Conclusion

In patients receiving antithrombotic therapy, PT should be considered among the rare causes of circulatory shock. Immediate access to TTE and pericardiocentesis remains a clinical imperative in these cases.

Acknowledgement

Conflict of interest

Jens Tingleffis affiliated with Bayer© AG, where he receives reasonable compensation for expert consultants and sponsor speaker programs on treatment of venous thromboembolism. Approved by The Danish Medicines Agency.

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Research data

The data (vital values, ECGs, blood tests and transthoracic echocardiography) used to support the findings of this study are included within the article.

Patient consent

Written informed consent from the patient to publication of the case report has been obtained.

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