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Case Report

Recurrent Massive Pulmonary Embolism Treated by Systemic Thrombolysis

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Abstract

Massive pulmonary embolism requires rapid diagnosis and prompt treatment, systemic thrombolytic therapy, for decreasing mortality. A systematic approach, high clinical suspicion, bedside transthoracic echocardiography and D-Dimer assay, should be implemented for rapid diagnosis. Systemic thrombolytic therapy must be initiated immediately after the diagnosis of massive pulmonary embolism.

We describe a case of recurrent massive pulmonary embolism in a 26-year-old black male brought to our emergency department (ED) with dyspnea, diaphoresis and decreased consciousness.

Keywords: *Pulmonary Embolism; Massive Embolism; Thrombolysis; Echocardiography*

Introduction

Venous thromboembolic disease (VTE) occurs in 1 to 2 persons per 1000 population annually, diagnosed as deep vein thrombosis (DVT), pulmonary embolism (PE) or in combination [1,2]. VTE is responsible for over 100,000 deaths annually and is the most preventable cause of death in hospitalized patients in the United States [3]. PE, the most dreaded presentation of VTE, is the cause of over 100,000 deaths annually in hospitalized patients in United States [3]. PE is stratified, considering severity, into massive (PE causing shock), submassive (PE causing right ventricular dysfunction demonstrable by echocardiography, computed tomography or elevated cardiac biomarkers) and non-massive (PE without shock or right ventricular dysfunction). The 90-day mortality rate is 58% in patients with massive PE versus 15% in no-massive PE [4]. In patients with non-massive PE, low-risk PE, the mortality rate is less than 2% [5-7]. Systemic thrombolytic therapy (STT) reduces mortality in patients with massive PE and sub-massive PE [8,9]. Currently, with lower all-cause mortality, STT is the treatment of choice for patients with massive PE [9,10]. In the subset of sub-massive PE, use of STT reduces mortality but significantly increases the risk of major bleeding, including intracranial hemorrhage [10,11]. For this group of patients ACCP Guidelines recommend STT when cardiopulmonary deterioration is present yet shock has not occurred.

Considering the clinical importance of PE, particularly massive and sub-massive PE, I describe a case of recurrent massive PE, in a 26-year-old male, admitted in our emergency department, successfully treated by STT.

Case Report

A 26-year-old black male was brought to our emergency department (ED) with dyspnea, diaphoresis and decreased consciousness, all started one hour before the ED arrival. According to the patient's sister, he was found in the bad with dyspnea, diaphoresis, disorientation and fecal and urinary incontinence. On admission, June-02-2018, he complained of shortness of breath (SOB) and denied any comorbidity. Upon physical examination he had dyspnea, cyanosis, SaO_2 63%, respiratory rate of 28 bpm, blood pressure of 70/40 mmHg, a heart rate of 110 bpm. On auscultation normal heart and pulmonary sounds; on abdominal examination there were no signs of peritoneal irritation;

there was no edema in both legs; Glasgow coma scale (GCS) 10. Oxygen support by non-rebreathing mask, with oxygen reservoir bag and crystalloid fast infusion (3000 ml), as initial approach, were started. The oxygen saturation and blood pressure increased after oxygen delivering and crystalloid infusion (SaO_2 94% and BP 140/90 mmHg). Laboratory workup: arterial blood gas (ABG) pH 7.13 PaO_2 44 $PaCO_2$ 39 SaO_2 63% HCO_3 12 FiO_2 21%, lactate 10,9 mmol/L, hemoglobin 16 g/dl, total leukocytes 15.49 x 10^9 /L (neutrophils 12.86 x 10^9 /L), urea 1.2 mmol/L, creatinine 124 µmol/L, Na 144 mmol/L, K 6 mmol/L, CK-MB 21 U/L (Normal ≤ 25 U/L), Troponin I 1291.9 pg/ml (reference 0 - 30 pg/ml).

A chest CT scan showed bilateral diffuse pulmonary embolism characterized by filling defects in the right and left pulmonary arteries, segmental and sub segmental bilateral blanches. The main pulmonary artery dilated 3,5 cm (reference < 2,9 cm) without filling defect. Opacities in the upper and inferior left pulmonary lobes, no pleural effusion. Anticoagulation with Enoxaparin was initiated. The patient, using Oxygen support by non-rebreathing mask, became progressively dyspneic, SaO_2 80%, even though after being anticoagulated for 24 hours. Tracheal intubation was undertaken, immediately after that, the patient underwent a cardiac arrest with pulseless electrical activity (June-03-2018). Basic and advanced life supports were undertaken, such as chest compression, ventilation through the tracheal intubation and vasopressor. The return of spontaneous circulation occurred after 3 minutes of resuscitation and the patient, neurologically intact, was maintained under mechanical ventilation support and sedation. A transthoracic echocardiography (TTE), after the return of spontaneous circulation, showed-normal cardiac chamber diameters, no pericardial effusion, normal biventricular ejection fraction and no signs of acute cor pulmonale (no abnormal septal motion or flat interventricular septum).

Thrombolysis using Tenecteplase (Metalyse-Boehringer Ingelheimer Company), 50 mg intravenous bolus (weight adjusted dose) was implemented. After that the patient's oxygen saturation increases. ABG after thrombolysis: pH 7.21 PaO_2 87.5 $PaCO_2$ 41 SaO_2 94% PaO_2/FiO_2 307 HCO_3 16 Lactate 5 mmol/L. The patient was transferred to the intensive care unit (ICU), under mechanical ventilation, sedated, anticoagulated with Enoxaparin (1 mg/kg SC q12 hr) and hemodynamic stable (June-03-2018). The follow up, at the ICU, was uneventfully and after 5 days the patient, extubated, in spontaneous ventilation, anticoagulated and hemodynamic normal, was discharged to the infirmary (June-08-2018). During the infirmary stay Enoxaparin was exchanged for unfractionated Heparin (subcutaneous fixed dose - FIDO protocol). Acute and progressive dyspnea and hypoxemia (SaO_2 86%) recurred four days after ICU discharge, associated with refractory hypotension (June-12-2018). Tracheal re-intubation, mechanical ventilation and vasopressor were implemented. A bedside TTE showed signs of acute cor pulmonale (abnormal septal motion, flat interventricular septum and dilated right ventricle- (Figure 1). The diagnosis of recurrent massive pulmonary embolism was suspected. A second thrombolysis using Tenecteplase (Metalyse-Boehringer Ingelheimer Company), 50 mg intravenous bolus (weight adjusted dose) was carried out. After thrombolysis, the oxygen saturation and blood pressure gradually increased. The patient was transferred to ICU (June-13-2018). Two days later, sepsis due ventilation associated pneumonia (fever, purulent sputum, leukocytosis) and renal failure (progressive elevation of urea and creatinine) were diagnosed. Laboratory workup: hemoglobin 13.8 g/dl, total leukocytes 35.84 x 10^9 /L (neutrophils 30.10 x 10^9 /L), urea 22.3 mmol/L, creatinine 512.7 µmol/L, Na 138 mmol/L, K 5.4 mmol/L. Antibiotic, Meropenem was started June 15 and daily dialysis was initiated in June 20. A bedside TTE, three days after STT, showed normal right ventricular size and interventricular septal motion (Figure 2). ICU follow-up: gradual decrease of leukocytes, urea and creatinine, successfully weaning from mechanical ventilation and vasopressor (Table 1).

	06-15-2018	06-17-2018	06-18-2018	06-20-2018	06-23-2018	06-26-2018
Leukocytes x10^9	35.84	19.32	15.28	10.77	9.07	11.96
Bands x10^9	1.79	0.58	0	0	0	0
Neutrophils x10^9	30.10	17.00	12.68	9.37	6.44	8.01
Urea mmol/L	22.3	28.3	38.6	45.6	16.3	6.8
Creatinine µmol/L	512.7	335.9	556.9	937.0	159.1	97.2
Na mmol/L	138	141	140	137	144	141
K mmol/L	5.4	4.5	5.8	5.1	3.5	3.4
Hemoglobin	13.8	11.4	10.3	9.7	9.5	8.4

Table 1: *Laboratory follow-up at ICU.*

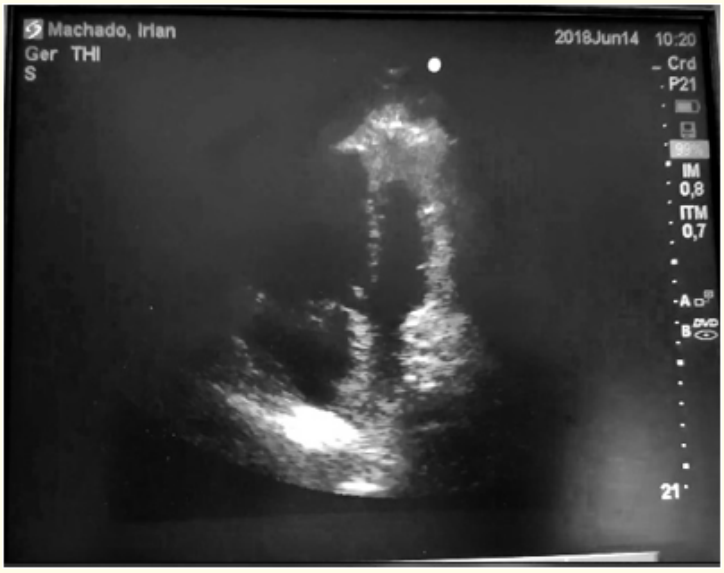

Figure 1: *Acute cor pulmonale: Dilated right ventricle and Abnormal interventricular septal motion.*

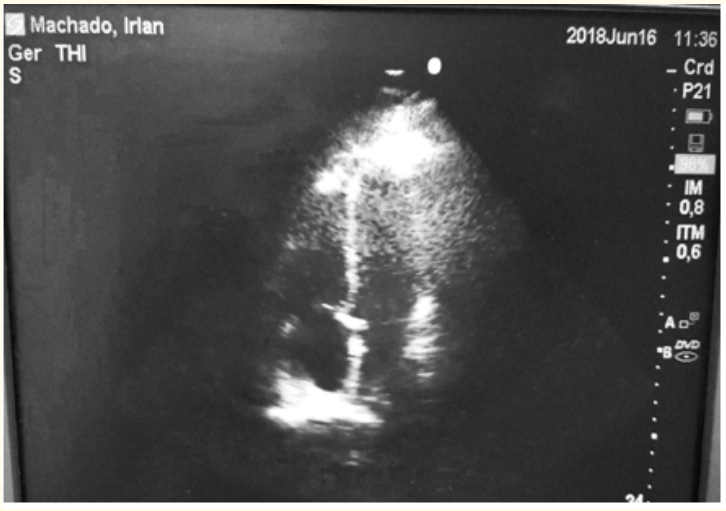

Figure 2: *Post-thrombolysis: Normal right ventricular size and Normal interventricular septal motion.*

After 13 days at ICU the patient, in spontaneous ventilation, hemodynamic normal and anticoagulated with Enoxaparin, was discharged to infirmary. In June 30, 2018 the patient was discharged to home in stable condition using Rivaroxaban for anticoagulation. He was also referred to follow-up with hematologist.

Discussion

Pulmonary embolism (PE) is the third cause of mortality by cardiovascular disease following coronary artery disease and stroke [12], it is the cause of over 100,000 deaths annually in hospitalized patients in United States [3]. However that diagnosis must be suspected in outpatients who looking for emergency assistance due acute dyspnea, associated or not with known comorbidities (clinical intuition for determining risk for PE) [12].

Our patient arrived to the ED due acute dyspnea, tachypnea and disorientation associated with hypoxemia, but without known comorbidity neither apparently etiology upon physical examination. Pulmonary embolism was suspected, according to Wells' score of 4.5 that represents an intermediate clinical probability or likely PE, an indication for D-dimer assays and chest CT scan [12]. On chest CT scan was observed bilateral diffuse pulmonary embolism compromising the right and left pulmonary arteries, segmental and sub segmental bilateral blanches. Those CT findings correspond clinically to massive pulmonary embolism, characterized by extensive embolism and shock; the patient's blood pressure was 70/40 mmHg and heart rate of 110 bpm [12]. Progressive hypoxemia and cardiovascular deterioration followed. Systemic thrombolytic therapy (STT) was implemented, in accord with current guidelines [9,10]. STT, among patients with massive PE, reduces mortality and decreases the incidence of chronic thromboembolic pulmonary hypertension (CTEPH) [8,13,14]. The patient's follow up after STT was straightforward, improvement of oxygen saturation, hemodynamic stability and weaning from mechanical ventilation. Anticoagulation with Enoxaparin was maintained during ICU stay (5 days), after that unfractioned heparin (FIDO protocol) [15], replaced Enoxaparin. At the infirmary, four days after ICU discharge, the patient suffered a recurrent massive pulmonary embolism, characterized by acute and progressive dyspnea, hypoxemia (SaO_2 86%), refractory hypotension and echocardiographic signs of acute cor pulmonale (abnormal septal motion and flat interventricular septum-Figure 1). Transthoracic echocardiography (TTE) is one of the most important tests in aiding diagnosis and risk stratification in patients with suspected PE. TTE is also useful to exclude other causes of shock, such as acute LV dysfunction, cardiac tamponade, acute valvular disease and aortic dissection [16,17]. In 80% of the patients with PE and shock TTE shows right ventricular (RV) dysfunction, characterized by: RV dilatation, RV hypokinesis and pulmonary hypertension [16,17]. TTE has low accuracy (sensitivity 51%, specificity 87%, positive predictive value 82%, negative predictive value 60%) as a test for triage in the emergency department (ED) in patients with suspected PE. In this situation other tests, such as D-Dimer and chest CT, must be used [18,19]. However, in the ICU and ED, TTE is an attractive initial test, since it is noninvasive, bedside and doesn't require the transport of an unstable patient.

In one study with the ICU patients, the most frequent TTE findings of acute PE were worsening tricuspid regurgitation (90%), pulmonary hypertension (77%), dilated RV (74%) and right heart strain (61%) [20]. Transesophageal echocardiography (TEE) can be used, as an initial screening test of PE, in patients who TTE shows a poor acoustic window. TEE provides an excellent image quality compared with TTE. For diagnosis of PE, TEE has 60 - 80% sensitivity and 95 - 100% specificity. In cases of central PE, TEE has 90 - 95% sensitivity and 100% specificity [21].

In our case the cause of the recurrent PE wasn't clear, since the patients was anticoagulated after the STT, first of all with Enoxaparin 1 mg/kg SC q12 hr and after with Heparin SC protocol FIDO, both regimens accord with current guidelines [15]. After all, the patient was discharged to home in stable condition using Rivaroxaban for anticoagulation and referred to research a probably thrombophilia with hematologist.

Conclusion

Pulmonary embolism, particularly massive or sub-massive PE, is a dreadful condition with mortality rate of 58% among massive PE subgroup [4]. However, early PE diagnosis and treatment decrease mortality and morbidity [8,13,14]. PE should be a part of the differential diagnosis in patients who present with new or worsening dyspnea, chest pain, or hypotension [22]. The three most important diseases in patients presenting with chest pain in the ED are: acute coronary syndromes, acute aortic syndromes and PE. The most common symptoms among patients with PE are: dyspnea in 80% and chest discomfort in 65% of patients [23.24]. Transthoracic echocardiography (TTE) is one of the most important tests in aiding diagnosis and risk stratification in patients with suspected PE and it is also useful to exclude other causes of shock [16,17]. In patients with suspected PE, TTE should be associated with others tests (chest CT, D-Dimer) as an initial screening of PE [18,19]. Patients with massive PE or submassive PE and cardiorespiratory deterioration should be treated with STT; its uses should be avoided only in the presence of active, uncontrollable bleeding [25].

Bibliography

1. Huang W., *et al*. "Secular trends in occurrence of acute venous thromboembolism: the Worcester VTE study (1985- 2009)". *The American Journal of Medicine* 127.9 (2014): 829-839.

2. White RH. "The epidemiology of venous thromboembolism". *Circulation* 107 (2003): 14-18.

3. "The Surgeon General's Call to Action to Prevent Deep Vein Thrombosis and Pulmonary Embolism". Rockville (MD) (2008).

4. Goldhaber SZ., *et al*. "Pooled analyses of randomized trials of streptokinase and heparin in phlebographically documented acute deep venous thrombosis". *The American Journal of Medicine* 76.3 (1984): 393-397.

5. Bova C., *et al*. "Risk stratification and outcomes in hemodynamically stable patients with acute pulmonary embolism: a prospective, multicentre, cohort study with three months of follow-up". *Journal of Thrombosis and Haemostasis* 7.6 (2009): 938-944.

6. Palmieri V., *et al*. "Troponin I and right ventricular dysfunction for risk assessment in patients with nonmassive pulmonary embolism in the emergency department in combination with clinically based risk score". *Internal and Emergency Medicine* 3.2 (2008): 131-138.

7. Post F., *et al*. "Decision for aggressive therapy in acute pulmonary embolism: implication of elevated troponin T". *Clinical Research in Cardiology* 98.6 (2009): 401-408.

8. Jerjes-Sanchez C., *et al*. "Streptokinase and heparin versus heparin alone in massive pulmonary embolism: a randomized controlled trial". *Journal of Thrombosis and Thrombolysis* 2.3 (1995): 227-229.

9. Chatterjee S., *et al*. "Thrombolysis for pulmonary embolism and risk of all-cause mortality, major bleeding, and intracranial hemorrhage: a meta-analysis". *The Journal of the American Medical Association* 311.23 (2014): 2414-2421.

10. Marti C., *et al*. "Systemic thrombolytic therapy for acute pulmonary embolism: a systematic review and meta-analysis". *European Heart Journal* 36.10 (2015): 605-614.

11. Meyer G., *et al*. "Fibrinolysis for patients with intermediate- risk pulmonary embolism". *The New England Journal of Medicine* 370 (2014): 1402-1411.

12. Bounameaux H., *et al*. "Diagnosis of venous thromboembolism: an update". *Vascular Medicine* 15.5 (2010): 399-406.

13. Kline JA., *et al*. "Prospective evaluation of right ventricular function and functional status 6 months after acute submassive pulmonary embolism: frequency of persistent or subsequent elevation in estimated pulmonary artery pressure". *Chest* 136.5 (2009): 1202-1210.

14. Sharifi M., *et al*. ""MOPETT" Investigators. Moderate pulmonary embolism treated with thrombolysis (from the "MOPETT" Trial)". *The American Journal of Cardiology* 111.2 (2013): 273-277.

15. Kearon Clive., *et al*. "Fixed-Dose, Weight-Adjusted, Unfractionated Heparin (UFH) Given Subcutaneously (sc) without Laboratory Monitoring for Acute Treatment of Venous Thromboembolism (VTE): Randomized Comparison with Low-Molecular-Weight-Heparin (LMWH)". *The Journal of the American Medical Association* 296.8 (2006): 935-942.

16. Lee JH and Park JH. "Role of echocardiography in patients with acute pulmonary embolism (Review)". *Journal of Cardiovascular Ultrasound* 16.1 (2008): 9-16.

17. Arcasoy SM and Vachani A. "Local and systemic thrombolytic therapy for acute venous thromboembolism". *Clinics in Chest Medicine* 24.1 (2003): 73-91.

18. Grifoni S., *et al*. "Utility of an integrated clinical, echocardiographic, and venous ultrasonographic approach for triage of patients with suspected pulmonary embolism". *The American Journal of Cardiology* 82.10 (1998): 1230-1235.

19. Jackson RE., *et al*. "Prospective evaluation of two-dimensional transthoracic echocardiography in emergency department patients with suspected pulmonary embolism". *Academic Emergency Medicine* 7.9 (2000): 994-998.

20. Stawicki SP., *et al*. "Transthoracic echocardiography for pulmonary embolism in the ICU: finding the "right" findings". *Journal of the American College of Surgeons* 206.1 (2008): 42-47.

21. Leibowitz D. "Role of echocardiography in the diagnosis and treatment of acute pulmonary thromboembolism". *Journal of the American Society of Echocardiography* 14.9 (2001): 921-926.

22. Righini M., *et al*. "Diagnosis of pulmonary embolism by multidetector CT alone or combined with venous ultrasonography of the leg: a randomised non-inferiority trial". *Lancet* 371.9621 (2008): 1343-1352.

23. Simonneau G., *et al*. "Surgical management of unresolved pulmonary embolism. A personal series of 72 patients". *Chest* 107 (1995): 52S-55S.

24. Stein PD., *et al*. "Clinical, laboratory, roentgenographic, and electrocardiographic findings in patients with acute pulmonary embolism and no pre-existing cardiac or pulmonary disease". Chest 100.3 (1991): 598-603.

25. Meyer G., *et al*. "Recent advances in management of pulmonary embolism: focus on the critically ill patients". *Annals of Intensive Care* 6.1 (2016): 19.

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