Successful Management of Massive Bilateral Pulmonary Embolism by Unilateral Ultrasound-Accelerated Thrombolysis after Cardiac Surgery

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Abbreviations:
ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; CDT: Catheter-Directed Thrombolysis; ceCT: Contrast Enhanced Computed Tomography; CABG: Coronary Artery Bypass Grafting; CK: Creatine Kinase; ED: End-Diastolic Dimensions; ECMO: Extracorporeal Membrane Oxygenation; FiO₂: Fraction of Inspired Oxygen; LV: Left Ventricle; UACDT: Ultrasound-Assisted Catheter-Directed Thrombolysis; BNP: Pro-Brain Natriuretic Peptide; PE: Pulmonary Embolism; RV: Right Ventricle; tPA: Tissue Plasminogen Activator

Abstract

Recently, catheter based therapies have been gaining more popularity in the management of patients with massive pulmonary embolism. We report a 57-year old Turkish woman presenting with bilateral massive pulmonary embolism causing hemodynamic instability after cardiac surgery and she was treated successfully by using unilateral ultrasound-assisted catheter-directed thrombolysis.

Introduction

Pulmonary Embolism (PE) has been regarded as to be a challenging clinical situation in terms of diagnosis and management. Although systemic anticoagulation remains as the main treatment modality in the majority of patients with pulmonary embolism, more aggressive treatment methods like systemic thrombolytic drugs, Extracorporeal Membrane Oxygenation (ECMO) or emergent surgical thrombectomy are necessary especially in patients with hemodynamic instability related to massive pulmonary embolism [1]. However, ECMO and surgical thrombectomy necessitate an appropriate infrastructure and surgical expertise. Recently, Ultrasound-Assisted Catheter-Directed Thrombolysis (UACDT) has been gathering more popularity in the treatment of hemodynamically unstable patients with PE. In this paper, we present a case of massive bilateral PE with hemodynamic instability that was treated successfully with using unilateral UACDT.

Case

A 57-year-old Turkish woman was referred to our center with the diagnosis of respiratory and hemodynamic failure related to massive pulmonary embolism (PE) from the emergency department of another nearby hospital. The patient underwent Coronary Artery Bypass Grafting (CABG) 13 days ago and early postoperative course was reported to be uneventful. She was discharged from the hospital at postoperative day 5. Her past medical history was also consistent with hypertension and diabetes mellitus. Her postoperative medications were aspirin (100 mg daily), Metoprolol (50 mg daily). On admission, she was intubated and under full sedation. She was reported to be neurologically intact before intubation. In spite of high fraction of inspired oxygen (FiO₂) (90%), she was in hypoxia (in arterial blood gas analysis PO₂: 43 mmHg (80-100 mmHg), PCO₂: 32 mmHg (35-45 mmHg), PH: 7.43 (7.35-7.45) and HCO₃⁻: 16.3 mmol/l (22-26 mmol/l) and lactate 5.6 mmol/l (0-5 mmol/l). On referral, intravenous dopamine infusion (10 mcg/kg/minute) had been already given to stabilize the worsening cardiac functions. Invasive blood pressure measurement from the right radial artery and pulse were recorded as 75/45 mmHg and 128 bpm, respectively. An emergent transthoracic echocardiography was obtained and demonstrated the signs of Right Ventricular (RV) pressure overload (a RV pressure of 60 mmHg by continuous-wave Doppler echocardiography), elevated RV end diastolic pressure, flattened interventricular septum and normal left ventricular function. Laboratory analyses revealed hemoglobin 13.1 mmol/l (12-16 mmol/l), platelets 188.000/mm³ (150-450/mm³), white blood cells 13.000/mm³ (6000-10.000/mm³), D-dimer 34.6 ug/ml (0-5 ug/ml), Creatine Kinase (CK)-MB 10.6 ng/ml (0-5 ng/ml), troponin-T 498 ng/lt (0-14 ng/lt), pro-brain natriuretic peptide (BNP) 17.011 pg/ml (0-450 pg/ml), Alanine Aminotransferase (ALT) 62 U/lt (0-50 U/lt), aspartate aminotransferase (AST) 60 U/lt (0-50 U/lt), C-reactive protein: 92 mg/lt (0-5 mg/lt), creatinine 0.5 mg/dl (0.4-1.1 mg/dl), blood urea nitrogen 20 mg/dl (5-25 mg/dl). Contrast enhanced Computed Tomography (ceCT) revealed a large thrombotic material partially occluding the proximal segment of the right Pulmonary Artery (PA) and extending into the lobar branches (Figure 1a). Additionally, lobar branches of the left PA were found to be occluded (Figure 1b). The ratio of End-Diastolic Dimensions (EDD) of Right Ventricles (RV) and Left Ventricles (LV) (RV/EDD and LV/EDD) on 4 chamber axial CT views was found to be 1.2. The patient was regarded as in the high risk group for mortality according to presence of systemic hypotension despite of moderate to high dose inotropic medication, findings for RV dysfunction (increased right ventricular pressures, EDD and pro-BNP) and positive markers for myocardial injury [1].
Although our patient did not reveal any risk factor precluding the use of systemic thrombolytic drugs, ultrasound-accelerated thrombolysis was preferred over a systemic thrombolytic drug to lessen the risk of potential fatal complications related to thrombolytic drugs. The right pulmonary bed seemed to have higher thrombus load than the left. After getting an informed consent for the procedure from the relatives, we decided to catheterize only the right side instead of doing bilateral catheterization to facilitate the procedure. In the hybrid operating theatre, the EKOS Endowave device catheter (EKOS Corporation, Bothell, Wash) was placed in a satisfactory position within the right PA via the right femoral vein (Figure 2).

Tissue Plasminogen Activator (tPA) was initiated at a dosage of 0.5 mg/h through the catheter. The infusion was continued up to 12 hours. Immediately afterwards, the patient was anticoagulated with Unfractioned Heparin (UF) infusion. The patient had started improving clinically after 24 hours of treatment with decrements in the need for the inotropes and oxygen requirement. Under FiO2 of 35%, arterial blood gas analysis revealed PO2: 134 mmHg and PCO2: 38 mmHg. After 48 hours, almost complete clearing of the thrombus was identified in the control ceCT (Figure 3a and b).

Then, all sedative drugs were tapered and extubation was planned. Although there were no lateralizing sings, the patient was unable to awake normally and seemed to be extremely agitated and disoriented. The sedatives were restarted and cranial CT and repeat pulmonary ceCT were performed. Cranial CT revealed cerebellar hemorrhage that was reported to be mild to moderate in size (Figure 4). Anticoagulation with UF was stopped to prevent the expansion of hemorrhage. After another 48 hours of support, control cranial CT demonstrated no expansion in the size of hemorrhage. Then, she was extubated uneventfully and discharged from the ICU to the ward at the day 8. She was discharged to home with oral anticoagulation at the day 20.

Figure 1: (a) Contrast enhanced CT of thorax demonstrating a huge thrombus (white arrow) extending from the right pulmonary artery into the lower lobar branches, (b) occlusion of right (dashed arrow) and left lobar branches (black arrow).

Figure 2: Correct positioning of the catheter (arrow) in the right pulmonary artery. It was extending from the orifices of segmental arteries to the pulmonary bifurcation.

Figure 3: Complete clearing of the thrombus in the right (a) and left (b) pulmonary arteries after treatment.

Figure 4: Cranial CT showing the area of hemorrhage (arrow) in cerebellum.

Discussion

Massive PE that is defined by the presence of systemic hypotension, syncope or cardiac arrest accounts for approximately 5% of all cases with PE. Recent European guidelines on the diagnosis and management of acute PE suggest a classification for PE based on the estimated risk of PE related death rate and patients with shock or hypotension are regarded as the ones with >15% risk of PE-related early mortality [1].

Systemic thrombolysis remains an accepted standard of care for patients with life-threatening massive PE. Unfortunately, it was shown that approximately half of patients presenting with massive PE might have contraindication to systemic thrombolysis [2]. Even though surgical thrombectomy and ECMO are lifesaving in very critical...
patients with massive PE, high mortality rates approaching to 20%, need for a higher level of surgical expertise and infrastructure remain as major disadvantages [2]. Besides their minimally invasiveness, catheter-based techniques for massive PE have been claimed to be associated with several benefits over systemic thrombolytics and surgical thrombectomy including that percutaneous interventions can be instituted rapidly and offer more rapid reversal of RV dysfunction related to accelerated lysis or removal of thrombus [3].

UACDT has a capacity to disintegrate thrombus or dissociate fibrin strands without causing fragmentation via low-intensity-high-energy ultrasound. It is combined with concomitant local infusion of a lytic agent that can enhance drug penetration into the thrombus and augment thrombolysis at lower doses and shorter infusion. In a study by Chamsuddin et al. [4] 10 patients with PE and RV strain were treated with the EKOS catheter and tPA infusion (mean dose, 0.86 mg/h) for a mean of 24 hours resulted in near complete thrombus resolution in 94% and partial resolution in 6% of cases. In a study by Lin et al. [5] the authors compared the efficiencies of the EKOS catheter (11 patients) with the Catheter-Directed Thrombolysis (CDT) (14 patients) in patients with massive PE. Although complete removal of pulmonary thrombus was achieved in all cases in the EKOS group, complete or partial thrombus removal was accomplished in 50% and 14% of cases in the CDT group, respectively. Furthermore, EKOS resulted in more rapid thrombolysis and less hemorrhagic complications than the CDT. Recently, Kennedy et al. [6] retrospectively analyzed the results of the 60 patients with submassive or massive PE treated by UACDT and revealed complete thrombus clearance in the 57% and near-complete clearance in the 41% of patients. The mortality was detected in 5% of the patients and all of whom had massive PE.

In the literature, the experience about the use of UACDT in hemodynamically unstable patients is limited. Stambo et al. [7] reported complete clearing of the bilateral thrombus 24 hours after bilateral UACDT with the EKOS catheter in a patient who had hemodynamically unstable massive bilateral PE. While bilateral UACDT has been advised in patients with bilateral involvement of pulmonary vasculature, [8], we preferred putting one catheter to the right PA that had higher clot burden to lessen the complexity of procedure. The treatment zone of the catheter was extending from the main PA to the lower lobar branches of the right PA. The drug infusion ports of the catheter located in the main PA might help the lysis of clots in the left PA branches.

**Conclusion**

Unilateral UACDT seems to offer a reasonable success in total clearance of thrombus from pulmonary vasculature and might help us improve patient’s outcome in acute massive PE. Moreover, although the dose of thrombolytic drugs in CDT of PE seems to be lowered in percutaneous approaches for PE, the risk of fatal bleeding should not be underestimated.

**References**