Concomitant high-risk pulmonary embolism and subdural hematoma: endo-vascular system thrombolysis as a possible solution to a difficult challenge

Vincenza Clelia Alvich, Marco Valentini, Debora Monti, Stefano Perlini, Francesco Salinaro

Emergency Medicine Unit, IRCCS Polyclinic San Matteo Foundation, Pavia; Department of Internal Medicine, University of Pavia, Italy

Abstract

Acute pulmonary embolism (PE) is a challenging and potentially fatal cardiovascular disorder. In high-risk patients, percutaneous catheter embolectomy may be considered when thrombolysis is contraindicated or has failed. We hereby discuss the case of a 60-year-old man who was found unconscious on the ground with signs of head trauma and respiratory failure. He was found to have a massive pulmonary embolism and multiple basilar skull fractures associated with slight subdural and subarachnoid hemorrhages. His acute treatment required a multidisciplinary discussion and approach. EkoSonic™ Endovascular System (EKOS) thrombolysis was successfully performed. The patient required intensive care unit (ICU) monitoring and treatment for 31 days. Upon discharge, henoxaparin 4000 UI twice per day was prescribed as anticoagulant, without any evidence of pulmonary hypertension or severe neurological sequelae.

Correspondence: Vincenza C. Alvich, Emergency Medicine Unit, IRCCS Polyclinic San Matteo Foundation, viale Camillo Golgi, 19, 27100 Pavia PV, Italy.
Tel.: +39.3299637053
E-mail: vincenzaclelia.alvich01@universitadipavia.it

Key words: pulmonary embolism; head trauma; thrombolysis; EKOS; multidisciplinary approach.

Conflict of interest: the authors declare no potential conflict of interest, and all authors confirm accuracy.

Ethics approval and consent to participate: no ethical committee approval was required for this case report by the Department because this article does not contain any studies with human participants or animals. Informed consent was obtained from the patient included in this study.

Patient consent for publication: the patient gave his written consent to use his personal data for the publication of this case report and any accompanying images.

Availability of data and materials: all data underlying the findings are fully available.

Acknowledgment: a special thanks to the intensive care unit doctor, the neurosurgeon, and the interventional radiologist who participated in managing this patient.

Funding: none.

Received: 1 July 2023.
Accepted: 22 September 2023.
Early view: 5 October 2023.

Emergency Care Journal 2023; 19:11558
doi:10.4081/ecj.2023.11558

Introduction

Pulmonary embolism (PE) represents a major global burden of cardiovascular disease.[1] Nevertheless, there is a noticeable gap in global recognition and the quality of epidemiological data between PE and diseases such as myocardial infarction and stroke.[2] Heterogeneity of clinical presentation, increasing prevalence of deep vein thrombosis risk factors, such as obesity and cancer, as well as limited literature data on high-risk patients have established PE as one of the most challenging cardiovascular disorders in emergency medicine. Although case fatality rates appear to be decreasing, PE-related mortality continues to be high,[1] reaching 7% for all patients, and 33% for those presenting with hemodynamic instability.[3]

An early diagnosis remains crucial, providing the opportunity for immediate effective treatment aimed at preventing both short and long-term sequelae. Patients with high-risk PE and a subset of patients with intermediate–high-risk PE should be considered for advanced reperfusion therapies due to higher mortality with anticoagulation alone.[4]

Advanced therapies for acute PE include systemic fibrinolysis, catheter-based intervention, surgical pulmonary embolectomy, and mechanical circulatory support. Choosing a particular advanced therapy depends on both the patient's characteristics and the hospital's expertise and/or available procedures. Catheter-based therapy (CDT) combining local fibrinolysis with mechanical thrombectomy offers the potential advantage of increased efficacy of thrombus dissolution, due to the synergic effects of higher local fibrinolytic drug concentrations and mechanical disruption with greater exposed thrombus surface area. CDT may even offer the advantage of decreased hemorrhagic complications. Although the evidence of the efficacy and safety of these techniques is becoming consistent, randomized controlled trials to evaluate clinical outcomes are still lacking.[5] The EkoSonic Endovascular System (EKOS Corporation, Bothell, Washington, USA) is the only device approved by FDA[6]

that has been found feasible, well-tolerated, and effective, despite employing only a quarter of the standard systemic rt-PA dose.[6]

Although in recent years, the scientific literature has been consolidating the role of endovascular systems in the treatment of high-risk PE patients with major bleeding risk,[7,8] poor data are available to evaluate the prognosis of patients with actual bleeding who concurrently require early pulmonary thrombus dissolution.

We herewith report a case of PE that was successfully treated with the Ekosonic endovascular system as an alternative to systemic thrombolysis, due to a concomitant subdural hematoma.

Case Report

A 60-year-old man was found in a confused state after a very likely sudden fall. He was admitted to our emergency department for a head injury, left otorrhagia, and sphincter release. During the first evaluation, he was amnesic for the event, except for a sudden feeling of dizziness just before the fall. Although conscious and reactive, he was visibly confused. No focal neurological signs were reported. Upon admission, vital parameters were as follows: blood pressure (BP) 150/88 mmHg, heart rate (HR) 115 bpm, arterial oxygen saturation (SO2) 96% on a *reservoir* mask, and respiratory rate (RR) 23 bpm (Table 1).

The electrocardiogram showed sinus tachycardia, QRS axis right deviation, and a mild anterior-lateral ST-segment depression with an incomplete right bundle branch block. Arterial blood gas analysis (ABG) on room air showed severe hypocapnic hypoxia with the following values: pH 7.37 mmHg, pCO2 24.8 mmHg, pO2 44.2 mmHg, HCO3- 14 mmol/l, SO2 78%, pO2(A-a) 75.9 mmHg, and increased lactates (8.5 mmol/L).

A point-of-care ultrasound (POCUS) revealed a minimal right pleural effusion, preserved left ventricle ejection fraction, hyperkinetic and dilated right ventricle. Compression ultrasound showed right femoral vein thrombosis.

During the evaluation, the patient had a generalized seizure, successfully treated with midazolam 3 mg.

As shown in Figure 1, a cerebral CT scan showed multiple bilateral anterior subarachnoid hemorrhages of the frontal lobes, associated with multiple subdural hemorrhages in both the frontal and the parietal right lobes. Moreover, another subdural hemorrhage along the right tentorium and the posterior part of the ipsilateral interhemispheric portion was responsible for a slight shift of the cerebral midline to the left. Further subarachnoid hemorrhages were reported in the inferior left temporal lobe, associated with a left occipital bone fracture spreading to the ipsilateral petrous bone and involving both the mastoid and the bone walls of the external auditory canal, anteriorly extending to the sphenoid wing.

A pulmonary angio-CT scan confirmed the presence of a severe bilateral pulmonary embolism, confirming the diagnostic suspicion based on ultrasound evaluations. As shown in Figure 2, thrombi were completely obstructing both pulmonary arteries, with initial pressure overload and increased transverse diameter of the right ventricle, as well as mild reversal of the physiological curvature of the interventricular septum.

The case was discussed with the intensive care unit doctor, the neurosurgeon, and the interventional radiologist. Due to progressive hemodynamic worsening (BP decreasing to 100/60 mmHg, heart rate increased to 121bpm), the poor neurological and respiratory conditions, the patient was intubated. The team decided that treatment PE was a priority while strictly monitoring the brain lesions. Catheter-directed fibrinolysis was considered the best option, and the patient was transferred to the interventional radiology lab. An ultrasound-guided left femoral approach was used with a 6 F sheath. A long 0.035" guidewire and a multipurpose catheter were advanced through the right heart chambers towards the pulmonary arteries, where multiple filling defects were confirmed. The EKOS catheter, a device characterized by a combination of an infusion catheter and an ultrasonic core, was exchanged over the guidewire and left into the right pulmonary artery with locoregional infusion of low-dose alteplase (0.8mg/h for 24h) with saline coolant at 35 mL/h. Moreover, a fixed infusion of unfractionated heparin (500 IU/h) was left in a peripheral vein.

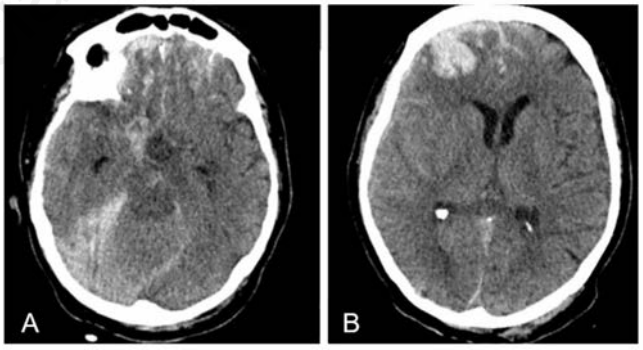

Figure 1. Basal head CT. Multiple subarachnoid hemorrhages at the anterior part of both frontal lobe and subdural hemorrhage along the right tentorium and the posterior part (**A**). A slight shift of the cerebral midline to the left (**B**).

Table 1. The clinical characteristics of the patient upon arrival in the emergency room.

Basic clinical characteristics	
Blood pressure	150/88 mmHg
Heart rate	115 bpm
Arterial oxygen saturation	96% on a reservoir mask
Respiratory rate	23 bpm
Electrocardiogram	Sinus tachycardia, QRS axis right deviation, mild anterior-lateral ST-segment depression, incomplete right bundle branch block
Arterial blood gas analysis	pH 7.37 mmHg, pCO2 24.8 mmHg, pO2 44.2 mmHg, HCO3- 14 mmol/l, SO2 78%, pO2(A-a) 75.9 mmHg, lactates 8.5 mmol/L
Point-of-care ultrasound	Minimal right pleural effusion, preserved left ventricle ejection fraction, hyperkinetic and dilated right ventricle, right femoral vein thrombosis

Anticonvulsant prophylaxis was started with levetiracetam. After 24 hours, arteriography showed almost complete dissolution of the pulmonary emboli. Therefore, the EKOS catheter was removed, and an inferior vena cava filter was placed to prevent venous clots from reaching the pulmonary circulation.

The patient was then admitted to the ICU, where he experienced initial neurological worsening. When transiently interrupting i.v. sedative treatment, the neurological assessment showed left hemiplegia. Due to the high bleeding risk, and contraindicating neurosurgery, intracranial pressure (ICP) monitoring was maintained for 12 days. After sedation and levetiracetam withdrawal, progressive improvement of the neurological deficit was observed, despite severe asthenia. The total length of stay was 32 days, during which the patient underwent mechanical ventilation through percutaneous tracheostomy. The patient was discharged home with enoxaparin 4000 UI twice a day as an anticoagulant, but even though he did not experience either pulmonary hypertension or severe neurological sequelae, he is still undergoing neurological rehabilitation.

Discussion

PE is a leading cause of cardiovascular morbidity worldwide, and rapid diagnosis and treatment are pivotal to decreasing mortality. Massive PE is generally correlated with syncope, obstructive shock, and cardiac arrest.[7] Our patient presented with confusion and otorrhagia, signs of traumatic brain injury because of syncope, concomitant with a high suspicion of high-risk PE. Indeed, ABG revealed severe hypocapnic hypoxemic respiratory failure and increased alveolar-arterial gradient, both sensitive indicators of pulmonary pathology.[9,10] Generally, ECG has a limited role in diagnosing PE but may predict a poor outcome when it shows signs of RV dysfunction (S1Q3T3 pattern, new RBBB, and T-wave inversion in anterior precordial leads).[11] Our ECG showed sinus tachycardia, RAD, and incomplete RBBB. POCUS helped us to identify acute dilation of the RV and femoral vein thrombosis. CTPA confirmed the diagnosis.

The therapeutic management for acute PE is strictly linked to a risk classification strategy, consisting of the presence of hemodynamic instability, signs of RV dysfunction, positivity of cardiac biomarkers (cTnI or T; BNP or NT-proBNP), and calculation of the PESI/sPESI score. Inter alia, our patient showed signs of progressive hemodynamic deterioration (a drop of systolic BP ^{3}40mmHg lasting longer than 15 minutes), dilation of the RV, hsTnI level of 109 ng/L, and PESI score of 152 which classified him in class V, *i.e.* a very high-risk patient.

Systemic thrombolysis would be the recommended therapy of choice for this category of patients, and its benefits in reducing mortality and hemodynamic deterioration are well established.[12] However, our patient had major contraindications to thrombolysis, due to the concomitant brain injury and simultaneous multiple intracranial hemorrhages

The presence of intrinsic bleeding risk is not so rare,[13] explaining why this treatment is underused in the real world.[14] The most frequent contraindications to fibrinolysis are recent major surgery or trauma**,** cardiopulmonary resuscitation, thrombocytopenia, and active bleeding requiring blood transfusion.[15]

As encouraged by the 2019 ESC Guidelines,[12] a multidisciplinary discussion was conducted along with the interventional radiologist, neurosurgeon, and critical care doctor. Alternative therapeutic strategies were discussed for this challenging case, including surgical pulmonary embolectomy (SPE) and catheter-directed fibrinolysis.

While CDT is emerging as a reliable therapeutic option as recommended by the European guidelines,[12] SPE is not a universally available treatment and it is associated with an in-hospital mortality rate greater than 27%.[16]

In some hospitals, PE response teams (PERTs) have been created to face such clinical challenges, due to the limited high-quality data on advanced therapies and advancing technology useful in this context.[17]

Hopefully, the widespread adoption of PERTs will reduce the heterogeneity now present within centers and across healthcare systems and will improve access to advanced therapies[18] while providing reliable data on their real-world impact.

EkoSonic Endovascular System, the only U.S. FDA-approved CDT, is characterized by a synergic action: the fibrinolytic agent provides fragmentation of the thrombus, with the concomitant ultrasound pressure waves allowing a better drug penetration by mechanically channeling the drug into the clot and contributing to its permanence within it. Such a synergy allows for to reduction of the dose of the thrombolytic drug and its possible complications, including bleeding, which is largely dose-dependent. It has been reported that a thrombus subjected to the effect of thrombolytic and ultrasound absorbs 89% more drugs in 4h than a thrombus exposed to systemic thrombolysis alone.[19]

This technique represents a new approach to improve outcomes and to modify treatment algorithms in intermediate-to-high-risk PE patients. Its increasing popularity is the effect of different promising results, which suggest rapid relief of RV pressure over-

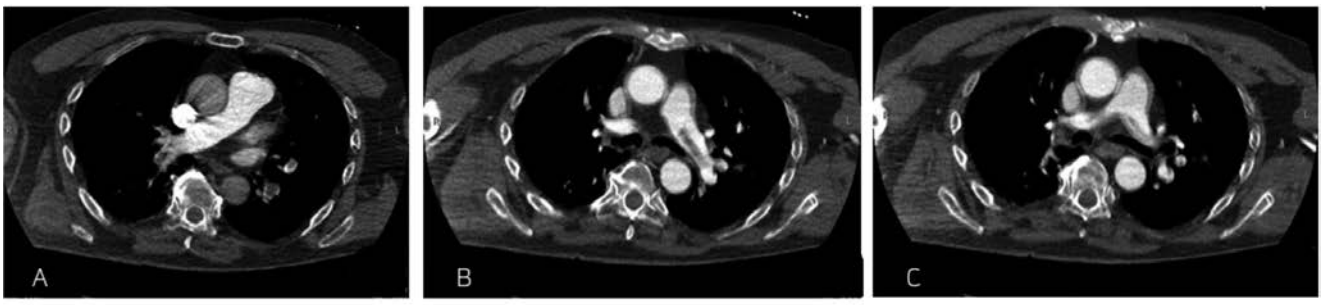

Figure 2. Acute pulmonary thromboembolism filling defects bilaterally with thrombus to the ramification of the major pulmonary arteries. Dilatation of common pulmonary artery as indirect sign of pulmonary hypertension (**A**). Greater extension of thrombus to the left side (**B**). Thrombus extended to both right and left sides (**C**).