Radiology Case Reports 13 (2018) 156–160

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Interventional Radiology

Ekosonic Endovascular System (EKOS) in a trauma patient with intracranial bleed, recent major surgery, and massive pulmonary embolus: A case report

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ARTICLE INFO

Article history:
Received 4 September 2017
Received in revised form 1 October 2017
Accepted 2 October 2017
Available online 7 November 2017

Keywords:
Pulmonary embolus
Ekosonic endovascular system
Catheter-directed thrombolysis
Interventional radiology

ABSTRACT

Pulmonary embolism is a life-threatening condition treated with anticoagulation and systemic thrombolysis when appropriate. In patients with contraindications to thrombolysis, catheter-directed thrombolysis may be considered. Here, we present a patient with massive pulmonary embolus and 3 contraindications to systemic thrombolysis who was successfully treated with pharmacomechanical thrombolysis using the Ekosonic Endovascular System.

Introduction

Pulmonary embolism (PE) is a life-threatening complication of trauma and surgical patients. Systemic anticoagulation with heparin bridged to coumadin is the initial treatment of choice. The additional use of systemic thrombolysis has been shown to reduce pulmonary hypertension and improve cardiac output in patients without contraindications. In those with contraindications, or who have failed thrombolysis, surgical thrombectomy or catheter-directed thrombolysis (CDT) may be considered. Ekosonic Endovascular System (EKOS), a form of catheter-directed pharmacomechanical thrombolysis, has been used to treat submassive and massive pulmonary emboli. It utilizes high-frequency ultrasound to enhance penetration of thrombolytic into selective targets and like CDT lowers the overall systemic dose of the thrombolytic agent, theoretically reducing the risk of bleeding complications. Recently, studies have suggested that the presence of massive pulmonary embolus and a major contraindication to thrombolytics are associated with catheter-directed intervention failure. Here, we present the successful use of EKOS on a trauma patient who presented with intracranial hemorrhage and, following major orthopedic surgery, experienced cardiovascular collapse secondary to a massive saddle embolus.

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https://doi.org/10.1016/j.radcr.2017.10.005

Case report

A 24-year-old woman, pedestrian vs motor vehicle, with a left T-type acetabular fracture and Morel-Lavallee degloving lesion of the right thigh and buttock presented to our facility from an outside hospital. Additional injuries included right occipital condyle and right temporal bone fractures with left parietal-occipital intraparenchymal and subarachnoid hemorrhage identified on outside hospital report. On presentation to our facility, the patient was hemodynamically stable with a glasgow coma scale of 14-15 and was admitted to the intensive care unit (ICU) for further observation and management.

On hospital day 1, she was taken to the operating room for orthopedic fixation of the 2-column acetabular fracture which was complicated by 3 L of blood loss requiring transfusion of 5 units of packed red blood cells, 1-unit fresh frozen plasma, and 1-unit platelets. On return to the ICU, her clinical examination showed tachycardia with heart rate in the 170s with stable blood pressures and a metabolic acidosis. An electrocardiogram showed supraventricular tachycardia and she was treated twice with adenosine with brief return to baseline heart rate only to return to the 170s. She then experienced sudden cardiovascular collapse with emergent cardiopulmonary resuscitation lasting 1-2 minutes. On return of spontaneous circulation, her heart rate continued in the 170s and she was now hypotensive and requiring vasopressor support. Due to high suspicion for pulmonary embolus, a bedside echocardiogram was performed, showing significant enlargement of the right ventricle with flattening of the interventricular septum concerning for pulmonary embolus (data not shown). Systemic anticoagulation was initiated with 5000 units of heparin.

To confirm the presence of pulmonary embolus and to plan further intervention a computed tomography pulmonary arteriogram (CTPA) was performed. A repeat head CT was also performed to verify findings of intracranial hemorrhage. The CTPA showed a massive saddle pulmonary embolus with right ventricular diameter-left ventricular diameter ratio of 2.5 confirming right heart strain (see Fig. 1A). Extension of the embolus into the distal pulmonary arteries was also demonstrated. The repeat head CT confirmed mild left parietal-occipital intraparenchymal and subarachnoid hemorrhage (see Fig. 1B).

Neurosurgery was consulted for evaluation of intracranial hemorrhage and occipital condyle fractures with recommendations to maintain patient in C-collar for possible fixation at later date. Q1 hour neuro checks were also advised, given the presence of intracranial hemorrhage. The choice of treating with anticoagulation was deferred to the primary trauma team. Cardiothoracic surgery and interventional radiology were also consulted for possible intervention. Relevant laboratories for therapeutic consideration included an international normalized ratio (INR) of 1.8, platelets of 89,000, and troponin leak of 0.75 ng/L. Central venous pressures were 22-25 cm H_2O and

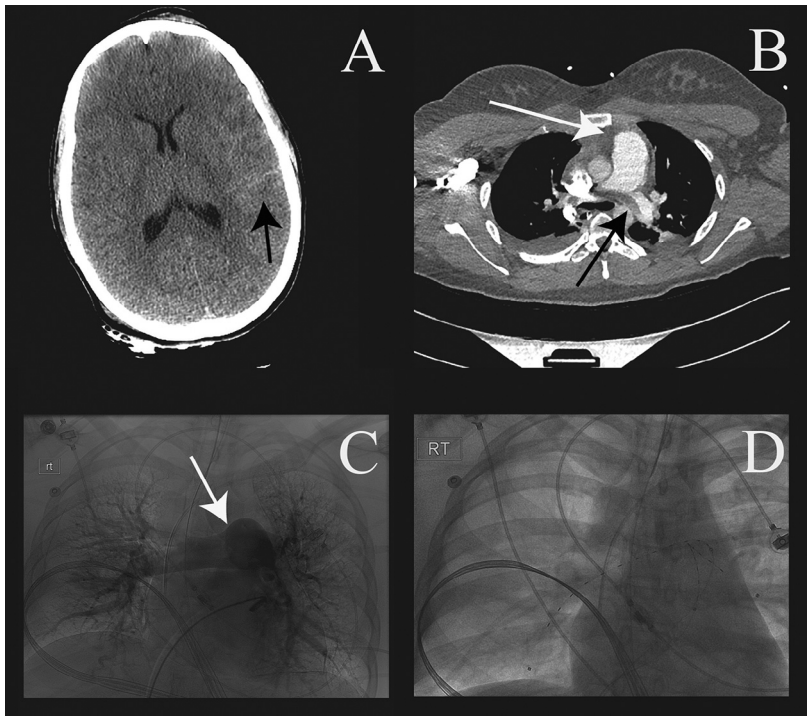

Fig. 1 – (A) Head CT showing left parietal-occipital intraparenchymal and left frontal-parietal subarachnoid hemorrhage. (B) Contrast-enhanced CTA of the chest showing large saddle embolus, RV/LV diameter ratio > 0.9, and enlargement of the main pulmonary artery. (C) Pulmonary angiogram showing large saddle embolus prior to EKOS catheter placement. (D) Fluoroscopic image showing placement of EKOS catheters in the bilateral pulmonary arteries. These were left in place for 12 hours infusing tPA at a rate of 0.5 mg/h in each catheter for a total dose of 12 mg/12 h. CT, computed tomography; CTA, computed tomography angiography; EKOS, Ekosonic Endovascular System; LV, left ventricular; RV, right ventricular; tPA, tissue plasminogen activator.

heart rate persisted in the 170s. She also required vasopressors to maintain her blood pressure. On evaluation by cardiothoracic surgery, the patient was not deemed a candidate for surgical thrombectomy, given prior trauma, recent major surgery, cardiovascular collapse, intracranial hemorrhage, and coagulopathy/thrombocytopenia. Similarly, the patient was determined to be high risk for thrombolytic therapy by any route of administration. However, considerations at this time included mechanical disruption of the clot, mechanical thrombectomy with a suction device, CDT, or continued anticoagulation with heparin.

Given that the clot had propagated distally on CTPA, mechanical disruption was felt to be less beneficial for the patient. The use of the Angio-Vac system (Angiodynamics, Latham, NY), a form of suction thrombectomy, was considered. However, this system uses a 22 Fr catheter and requires 10-20,000 units of heparin which could increase bleeding risk in this coagulopathic patient when compared with smaller access catheters commonly used in CDT. Additionally, there is an increased risk of perforating either the pulmonary arteries or right ventricle with this device. Therefore, it was not considered further. It was initially agreed by all parties involved that given the above-mentioned contraindications, a period of watchful waiting would be best with life-saving intervention (CDT) if the patient acutely decompensated. A period of 12 hours ensued with the patient continuing on systemic heparin.

When the patient's vital signs failed to normalize with medical management (systemic heparin and vasopressor support) a CDT was pursued. At this point the patient's vital signs showed sinus tachycardia with a heart rate consistently in the 170s with hypotension requiring continued vasopressor support. Central venous pressures were unchanged in the range of 22-25 cm H_2O. The troponin leak had increased to 0.8. INR was now 3.0 and she had been transfused 2 units of platelets, now at 135,000. Ekosonic Endovascular System (EKOS, BTG Interventional Medicine, Bothell, WA) was selected for use, given its smaller catheter size and ability to deliver a targeted dose of thrombolytic to the pulmonary arteries typically at 24 mg/12 h. Given coagulopathy and contraindications to thrombolysis, we opted for half that dose, 12 mg/12 h, and without heparin infusion. After 12 hours had elapsed the plan was to reassess the patient and determine if continued thrombolysis was needed, based on the clinical picture, or if it could be discontinued.

The risks and benefits of pharmacomechanical thrombolysis were explained to the patient's family who ultimately elected for emergent procedure despite the risk of a potentially fatal bleeding complication, given her history of intracranial hemorrhage and recent surgery. She was transported to the interventional radiology suite. Sedation was carried out by an anesthesia team. The left groin was selected as an access site for both EKOS catheters which were placed in tandem due to large surgical incision on the right hemipelvis (from the degloving injury) and patient in C-collar due to right occipital condyle fracture. Two 7 Fr sheaths were placed in tandem in the left common femoral vein using ultrasound guidance. Prior to placement of EKOS infusion catheters, a thoracic angiogram was performed which redemonstrated a massive saddle embolus (see Fig. 1C). EKOS catheters were placed in the pulmonary arteries per manufacturer's recommendations and thrombolytic therapy was performed for a total of 12 hours with a tissue plasminogen activator (tPA) flow rate of 0.5 mg/h per catheter (see Fig. 1D). The catheters were removed at bedside once the patient had shown signs of clinical improvement. The total dose of tPA administered was 12 mg (6 mg per each pulmonary artery over 12 hours), half the amount normally given for CDT. Saline was run through the other 2 ports on the catheters at rates of 35 and 25 mL/h as coolant and to prevent thrombosis of the catheters. Heparin was not given due to the aforementioned contraindications. She returned to the ICU for the remainder of her recovery.

At the time the catheters were removed, her heart rate was in the 110s and she was no longer requiring vasopressor support. Bedside echocardiogram prior to removal (not shown) demonstrated normal right ventricular volume without interventricular septal bowing or flattening. Over the next 2-3 days her heart rate trended toward normal limits in the 80s. Likewise, her troponin level improved to 0.17 ng/L by that time. Central venous pressures also normalized to 4-5 cm H_2O and the central lines were subsequently removed. There were no changes in her baseline neurologic status during this time nor were there any long-term sequelae. There were no immediate bleeding complications from her prior surgical incisions or EKOS catheter access sites. She is now 1-year post trauma and without significant morbidity related to pulmonary embolus or EKOS treatment.

Discussion

Acute PE accounts for an estimated 50,000-200,000 fatalities per annum [1]. It ranks third in the cardiovascular causes of death behind coronary artery disease and stroke [1]. Pelvic or lower extremity trauma and prior surgery increase the risk of PE. In patients with massive pulmonary embolus and who experience cardiovascular collapse, the in-hospital mortality rate may be as high as 50% [2]. This accentuates the need for rapid diagnosis and effective intervention in such cases.

As in the case presented above, a bedside echocardiogram can be expediently performed and is a good modality for rapidly evaluating right heart dysfunction but is poor at evaluating the presence and extent of thrombus. A bedside echocardiogram was suspicious for PE in this case. A confirmatory CTPA was then performed. Right heart strain can be accurately evaluated with CTPA. The findings of right heart strain are right ventricular-left ventricular ratio of greater than 0.9 (ratio of 2.5, as above), dilatation of the main pulmonary artery suggesting acute high-grade obstruction or pulmonary hypertension (our patient measured 33 mm), and bowing of the interventricular septum [3]. An elevated troponin in the setting of right heart strain is concerning for possible irreversible myonecrosis and long-term functional disability (right heart failure). Likewise, the elevation of pro brain natriuretic peptide (pBNP or N-terminal BNP), a marker of myocardial stretch, may be seen in patients with right ventricular dilatation and has been shown to indicate an increased risk of early death and a complicated hospital course [4]. A BNP, unfortunately, was not drawn as a part of the laboratory evaluation in the present case.

Initial treatment of PE or suspected PE is with intravenous unfractionated heparin for 5 days bridged to coumadin with

a target INR of 2.0-3.0. This is the preferred method of anticoagulation in patients with renal failure, high bleeding risk (as in the case above), severe hypotension (as in case above), extremes of body weight, and in the elderly [5]. Once PE is confirmed, systemic thrombolysis may provide further benefit and has been shown to promptly reduce pulmonary artery pressure and resistance with concomitant increase in cardiac output [6]. Altepase is a commonly used thrombolytic for this purpose and is typically given at 100 mg over 2 hours. Absolute contraindications to systemic thrombolysis include stroke or hemorrhagic stroke, history of ischemic stroke within the past 6 months, central nervous system neoplasm, major trauma, surgery, or head injury within the past 3 weeks [5]. In the case presented above, the patient had 3 absolute contraindications to thrombolysis: major trauma, recent surgery, and head injury.

For patients who have contraindications to systemic thrombolytics or who have failed thrombolysis, surgical thrombectomy, mechanical disruption of the clot, suction thrombectomy, or CDT are additional options to consider. Risk stratification of patients after a review of surgical outcomes in patient's status, post-surgical thrombectomy has determined that those experiencing preoperative cardiac arrest or who are in extremis are far less likely to survive surgical intervention, making this option extremely risky [7]. Even with the technical advances with extracorporeal assist systems that have been made, the case fatality rate remains high, in excess of 23% [8]. For these reasons, in agreement with the cardiothoracic surgery team, thrombectomy was not considered in this case.

Because the saddle embolus had propagated too far distally, mechanical disruption was not considered to be beneficial in this case. Suction thrombectomy with the Angio-Vac system was also considered. However, this system utilizes a 22 Fr catheter and requires high doses of systemic heparin on the order of 10-20,000 units, which potentially increases the risk of bleeding complication from both catheter size and additional heparin requirements. Additionally, there is high risk of perforating the pulmonary arteries or right ventricle during placement. In a small case series of 5 patients with massive pulmonary embolus, 4 patients died within a mean of 7 days post procedure, 1 secondary to right ventricular perforation after the use of Angio-Vac [9].

A catheter-directed approach allows for specific targeting of thrombus at lower doses of tPA (24 mg over 12 hours) than does systemic thrombolysis (100 mg over 2 hours). When our patient's vital signs failed to normalize with systemic heparin and vasopressor support, we opted to treat her saddle embolus with pharmacomechanical thrombolysis using EKOS. EKOS uses high-frequency (2 MHz) sound waves to augment the penetration of thrombolytic while causing the reversible disaggregation of uncrosslinked fibrinogen [10–12]. In a randomized controlled trial of ultrasound-assisted catheter-directed thrombolysis vs systemic anticoagulation with heparin alone, there was a statistically significant resolution of right heart strain within 24 hours of treatment in the ultrasound-assisted group. There was no significant difference in bleeding risk between the 2 groups [13]. In the Seattle II trial which evaluated the safety and efficacy of catheter-directed low-dose thrombolysis using the EKOS system, there was a reduction in right ventricular strain and pulmonary artery hypertension within 48 hours post treatment. Moderate bleeding events were reported in up to 10% of cases with 1 severe groin bleed reported. There were no complications of intracranial hemorrhage [14]. In a head-to-head comparison of EKOS vs traditional CDT, EKOS was shown to be superior to CDT with 100% of patients achieving complete thrombus removal vs 50% for CDT. The mean time to thrombolysis was also shorter by approximately 8 hours with EKOS. Importantly, treatment-related hemorrhagic complications were 0% and 21% for EKOS and CDT, respectively, suggesting the superiority of EKOS over conventional CDT in both safety and efficacy [15]. We therefore opted to treat with EKOS. However, given the above-mentioned contraindications in this patient, we treated the patient with a lower dose, 12 mg tPA given over 12 hours with saline coolant running through the additional ports instead of heparin.

Within 12 hours of treatment, our patient experienced improvement in cardiac function based on repeat bedside echocardiogram and decreasing troponin. However, without post-treatment CTPA to confirm a reduction in clot burden we cannot definitively say that this response was solely due to our therapy. Optimization of medical management as well as intrinsic vasogenic factors may also have contributed to her recovered cardiac function. However, given the lack of improvement after 12 hours of heparin therapy coupled with the rapid improvement post treatment is highly suggestive of successful thrombolysis. The effectiveness of EKOS at reducing clot burden was determined by follow-up CTPA and was shown to be as high as 57% complete clearance vs 41% partial clearance in 1 recent study [16].

CDT has also been used in patients with contraindications to systemic thrombolysis. In a study of 15 patients with submassive or massive PE, treated with CDT and at least 1 contraindication to systemic thrombolysis, 14 experienced a rapid hemodynamic recovery with 1 major non–life-threatening bleeding complication [17]. The authors concluded that CDT should be considered first line in patients with acute PE, right ventricular dilation, and contraindication to systemic thrombolysis. There was 1 periprocedural fatality reported in the study, however.

It is assumed that catheter-directed interventions (CDIs) provide similar benefits to that of systemic thrombolysis while lowering the overall dose of thrombolytic and the associated complications. A recent study has shown that they are not without significant risk. In a review of 102 patients receiving standard CDI or ultrasound assisted intervention, there were 15 failures of therapy, 8 were secondary to clinical decompensation and 7 were due to a major bleeding event. The factors associated with CDI failure and major bleeding included massive PE, age ≥ 70 years, and a major contraindication to thrombolytics [18]. The authors further suggest that the lytic dose within the low-volume range administered in CDI and the type of CDI (standard or ultrasound assisted) seem to have no impact on adverse events. Therefore, the potential risks should be seriously considered prior to any CDI regardless of the anticipated dosage of thrombolytic or type of intervention used (CDT or ultrasound-assisted catheter-directed thrombolysis). In contrast, a multicenter meta-analysis of 860 patients with massive and submassive pulmonary emboli treated with CDI demonstrated a low rate of complication, with 0.35% having intracranial hemorrhage and 4.65% having major bleeding

requiring transfusion, the majority of which involved the access site [19]. Indeed, there are many conflicting reports regarding the safety of CDI in this patient population.

In summary, we report the successful use of EKOS in the treatment of a massive saddle embolus in a critically ill patient with 3 absolute contraindications to systemic thrombolysis and who experienced complete cardiovascular collapse requiring emergent resuscitation. Although both standard CDT and EKOS have been shown to rapidly improve right heart strain and pulmonary hypertension, the long-term morbidity when compared with anticoagulation alone appears to be similar between the 2 treatment modalities [20]. To date, our patient has been without cardiopulmonary morbidity for up to 1-year post treatment. The use of EKOS as well as other CDI techniques is not without significant risk to the patient, the most common being bleeding at the access site, but can be as serious as death. In patients with contraindications to systemic thrombolysis and who have failed to improve with medical management, EKOS may be considered as a possible treatment modality. However, the use of EKOS in such patients should be weighed against the potential risks and should occur in consultation with cardiopulmonary specialists and tailored to the individual patient. More research will be needed in the assessment of safety and efficacy in patients with massive PE and absolute contraindications to thrombolysis.

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