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Case Report

Successful pharmacomechanical intervention with ultrasonic-accelerated thrombolytic catheter for massive pulmonary embolism

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ABSTRACT

An 86-year-old male with history of metastatic prostate carcinoma and hypertension was admitted due to acute onset dyspnea and lower extremity pain and swelling. Transthoracic echocardiography revealed a large right atrial thrombus extending in to the right ventricle. Within 12 h, the patient developed severe hypoxemia, tachypnea with sustained hypotension and cardiogenic shock due to presumed massive pulmonary embolism. The patient underwent emergency pulmonary angiography which showed large emboli in the right main pulmonary artery extending in to the middle and lower lobe branches. An ultrasonic-accelerated thrombolytic catheter was placed in the right main pulmonary artery for continuous infusion of alteplase for 20 h. Repeat pulmonary angiogram showed resolution of the large pulmonary emboli, with normal flow in to the distal pulmonary arteries. Significant improvement of hemodynamics, symptoms and hypoxemia occurred as well.

1. Introduction

Acute pulmonary embolism (PE) is the third most common cause of death among hospitalized patients.[1]

Therapeutic escalation beyond anticoagulation with heparin is necessary and of extreme importance in acute massive pulmonary embolism (MPE), defined by persistent systemic hypotension and cardiogenic shock and hemodynamic instability, as well as in a highly selected group of patients with submassive PE, in which there is objective evidence of right ventricular (RV) dysfunction by transthoracic echocardiography (TTE) or computed tomographic angiography (CTA) of the chest and elevated biomarkers of myocardial injury.[2] In recent years, the best current evidence suggests that pharmacomechanical interventions represent a novel therapeutic modality for a variety of thromboembolic conditions, including

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peripheral occlusive arterial disease, ischemic stroke, and venous thromboembolism (VTE) spectrum of disorders.[3]

Endovascular techniques for MPE may be indicated in compromised patients who are unsuitable to receive systemic thrombolysis due to high-risk of bleeding complications. Ultrasonic-accelerated catheter-directed thrombolysis (UCDT) works by displaying a high-frequency low intensity ultrasound waves in order to accelerate clot dissolution by dissociating the fibrin strands, thereby reducing treatment time and the incidence of systemic thrombolysis-related complications, especially hemorrhagic complications.[4] In some experienced centers, UCDT strategies are being advocated as a replacement for systemic thrombolysis.

We present the case of a patient who was successfully treated with UCDT strategy within few hours post-admission to the hospital for further work-up of significant acute PE.

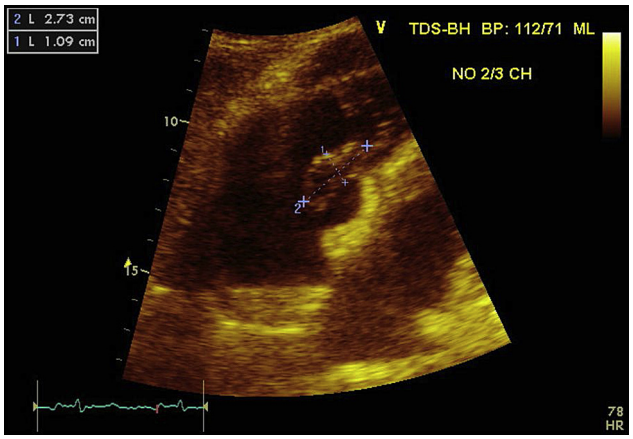

Fig. 1 – Transthoracic echocardiogram (TTE) showing large right atrial thrombus.

2. Case presentation

An 86-year-old male with history of metastatic prostate carcinoma and hypertension was admitted due to 4-day history of left lower extremity swelling, severe pain and redness that had been progressively worse.

Associated symptoms included a 3-day history of dyspnea, progressively worse to the point to be worsened upon minimal activities. He denied orthopnea, paroxysmal nocturnal dyspnea, recent surgeries, prolonged immobilization, fever, chills, cough, hemoptysis or chest discomfort.

Physical examination revealed the following vital signs: heart rate 87 beats/min, blood pressure of 111/79 mmHg, 24 respirations/min, and oxygen saturation (O_2Sat) at 95% on 2 L by nasal cannula. Cardiovascular examination significant for 2/6 systolic murmur in left mid sternal border, no gallops, splits or rubs. He had 2+ pitting edema up to the upper third of the left calf, no cyanosis; and calves nontender to palpation.

Remarkable laboratory findings included abnormal blood urea nitrogen (BUN) of 47 mg/dl and creatinine of 1.8 mg/dl, as well as elevated brain natriuretic peptide (BNP) of 999 pg/ml, troponins, prothrombin time (PT), partial thromboplastin time (PTT), and INR were within normal limits. Electrocardiogram showed normal sinus rhythm without acute abnormalities (e.g. sinus tachycardia, right axis deviation, T wave inversion in precordial leads or indirect signs of RV dilatation/hypertrophy). Chest radiograph was unremarkable.

TTE was immediately obtained, revealing a large right atrial thrombus measuring 2.7 × 1.4 cm, extending in to the RV (Fig. 1). The patient was empirically placed in enoxaparin 1 mg/kg subcutaneously (SQ) adjusted for his creatinine clearance every 12 h, however, within 12 h after admission to our institution and while awaiting ventilation/perfusion (V/Q) lung scan results, the patient developed severe hypoxemia (O_2 needs significantly increased to 15 L while in face mask with reservoir in order to keep O_2Sats >92%), with sustained hypotension (75/45 mmHg) with cardiogenic shock due to presumed MPE. The patient underwent emergent pulmonary angiography after briefly discussing that benefits will outweigh the risks of such invasive procedure, being a life-saving intervention. It showed large emboli in the main pulmonary artery extending in to the right middle and lower lobe branches of the right main pulmonary artery (Fig. 2a). An ultrasonic endovascular system (EKOS Corporation, Bothell, Washington) catheter was placed in the right main pulmonary artery for continuous infusion of recombinant tissue

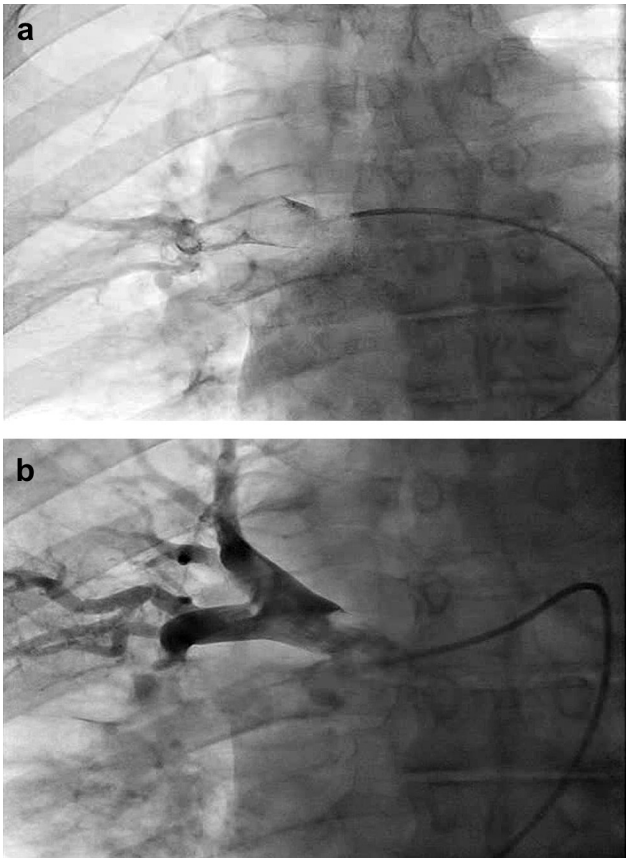

Fig. 2 – a: Pulmonary angiogram demonstrating the right main pulmonary artery with large extensive thromboemboli, involving the right middle and lower lobar arterial branches. b: Pulmonary angiogram showing patient right main pulmonary artery with adequate distal filling of the entire pulmonary vasculature after successful use of ultrasonic-accelerated catheter-directed thrombolysis (UCDT).

plasminogen activator (r-TPA) for 1 mg/h for 20 h. Repeat pulmonary angiogram showed resolution of MPE, with normal flow in to the distal pulmonary arteries (Fig. 2b).

Significant clinical improvement, as well as pulmonary hemodynamics, symptomatology and hypoxemia occurred as well during the patient's hospitalization, being discharge home to hospice care given his advanced malignancy as well as on life-long parenteral anticoagulation with enoxaparin SQ every 12 h.

3. Discussion

MPE, characterized by circulatory collapse and hemodynamic instability, has been associated with a 3-fold increased inpatient and up to 50% 3-month mortality.[1] In recent years, interest has risen regarding the use of a variety of endovascular strategies in selected patients with MPE involving catheter-based techniques.[5–7] UCDT, which uses low intensity high ultrasonic energy, represents a novel treatment strategy. The acoustic streaming energy dissociates the fibrin strands and increases the fibrin porosity without causing distal fragmentation or embolization, allowing the utilization of intrapulmonary thrombolytic agents at lower doses and infusion rates, achieving a more complete thrombolysis.[2,8]

Two recent clinical studies (one case series and one comparative study) analyzed the therapeutic outcomes of a catheter-directed thrombolysis versus UCDT-based strategy for MPE, demonstrating acceptable effectiveness, thrombus burden resolution, and improvement in hemodynamic parameters.[6,7] Lin et al noted an overall reduction in hemorrhagic complications in the group using the UCDT strategy.[7]

Engelhardt et al[9] studied retrospectively 24 patients, with 19 with submassive and 5 with massive PE, by using UCDT, they found a significant reversal in RV dysfunction by performing pre and post intervention by CTA imaging right to left ventricular dimension ratio (RV/LV ratio) ($p \leq 0.001$), and without reporting any significant or serious hemorrhagic complications upon discharge from the hospital.

Kuo et al[10] performed a meta-analysis of 594 patients with MPE treated with modern catheter-directed therapeutic interventions, clinical success was achieved in 86.5%, with success being defined as stabilization of hemodynamics, resolution of hypoxemia, and survival upon hospital discharge. Also, when injected locally, the required dose of thrombolytics is likely to be lower when compared with systemic thrombolysis, demonstrated a lower risk for significant hemorrhagic complications.[10] Indeed, the rate of major complications (e.g. pulmonary hemorrhage from pulmonary artery rupture or dissection) from modern catheter-directed interventions has proven to be only 2.4%.[10,11] Interestingly, this meta-analysis clearly demonstrated that the pool frequency of clinical success was higher when patients received UCDT strategies compared with percutaneous mechanical thrombectomy (PMT) without local thrombolysis (91.2% vs 86.3%; $p = 0.01$).[10,11]

Recently, the ULTIMA trial (Ultrasound-accelerated Thrombolysis of Pulmonary Embolism) was just completed and the results were presented. In this prospective double-blind study, 59 patients were prospectively randomized to receive anticoagulation or UCDT via the Ekosonic endovascular system (EKOS®). Within 24 h of therapy, patients treated with UCDT strategy demonstrated statistically significance reduction in RV enlargement (improvement of the RV/LV ratio, 23% $p < 0.001$) with no adverse events from the invasive procedure.[12] The ongoing single-arm, multicenter SEATTLE-II trial is currently looking in to the efficacy and safety of UCDT using the EKOS® catheter, with a primary end-point of decreasing RV/LV ratio measured by CTA post-48 h after UCDT catheter-based strategy in 150 patients with MPE and submassive PE.[13]

4. Conclusions

The best current emerging evidence suggests that UCDT represents an attractive and promising endovascular technique for the treatment of MPE as an early and first-line of therapy in order to achieve rapid clot debulking. The use of these particular endovascular techniques appear to be a promising option in order to reduce the incidence of chronic thromboembolic pulmonary hypertension, while avoiding the hemorrhagic risks of full-dose systemic thrombolysis.

Further research on UCDT focusing on MPE and submassive PE is needed in order to refine existing protocols and to evaluate long-term outcomes. Rapid and efficient risk stratification in the setting of acute.

Despite cumulative evidence regarding the use of UCDT, there are many limitations regarding this therapeutic modality, including the absence of standardized protocols and the lack of experienced operators. Ongoing prospective randomized controlled trials will help standardize therapeutic protocols and guidelines for its use in the setting of massive and submassive PE.

Conflicts of interest

All authors have none to declare.

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Obituary

Prof. H.S. Rissam

Dr. H.S. Rissam, Director, Clinical Cardiac Sciences & Senior Interventional Cardiologist at Max Heart & Vascular Institute, New Delhi expired recently. He did his cardiology at PGIMER, Chandigarh. He had a particular interest in preventive cardiology.

Dr. H.S. Rissam was widely known and was active in many fields of cardiology including the activities of Cardiological Society of India. The Government of India awarded him Padmashree in the year 2006. He had a special interest in writing and has authored "Scalpel" a book on medical mystery. A very affable person, we will all miss him badly in cardiology circles.

The CSI Executives joins me in expressing deepest condolences to the bereaved family.

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Dr. K. Sarat Chandra
Hony. Editor
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