Successful low-dose thrombolysis of submassive pulmonary embolus in a pregnant patient

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Lesson
Low-dose thrombolysis was effective and safe in a pregnant woman with acute pulmonary embolism causing severe right ventricular dysfunction.

This is the first reported case of successful thrombolysis for pulmonary embolus in pregnancy in the absence of shock.

The case
A 37 year-old primigravida at 34 weeks’ gestation was admitted with progressive dyspnea over four days such that she was symptomatic at rest. She had no significant medical history and was on no regular medication.

She was subjectively dyspnoeic with preserved oxygen saturations. She was tachycardic (125/min) with a respiratory rate of 32–36 breaths/min. Her blood pressure was 122/87 mmHg. She had signs of a right leg deep vein thrombosis. Arterial blood gas analysis with no supplemental oxygen showed a compensated metabolic acidosis (pH 7.47, PO₂ 11.42 kPa, PCO₂ 2.94 kPa, HCO₃ 15.9 mmol, lactate 2 mmol/L). Her electrocardiogram demonstrated sinus tachycardia. Routine blood tests and chest radiography were unremarkable. Perfusion imaging confirmed multiple bilateral pulmonary emboli and she was started on heparin.

Transthoracic echocardiography revealed that her right ventricle was severely dilated with moderate to severe impairment in systolic function. The right ventricular free wall was hypokinetic. Her septum was deviated towards the left ventricle. She had moderate tricuspid regurgitation and her right ventricular systolic pressure was 37 mmHg. Her inferior vena cava was dilated >2 cm and did not collapse in respiration. The left ventricle was normal in size and function (Figure 1(a)).

She was monitored on a high dependency unit. Foetal cardiotocography was within normal limits.

Despite 72 h of optimal anticoagulation, the patient remained subjectively and objectively unwell. She had ongoing chest discomfort and remained dyspnoeic. She was persistently tachypnoeic (respiratory rate 26 to 30 breaths/min) and tachycardic (heart rate above 120/min) but remained normotensive. She now required supplemental oxygen (2 L/min) to keep her oxygen saturations above 96%. Her base deficit and elevated lactate levels persisted. Serial bedside echocardiograms failed to demonstrate any improvement in right ventricular size or function. At this point, we decided to offer the patient thrombolytic therapy.

After informing the patient and obtaining consent, we administered a lower dose of recombinant tissue-type plasminogen activator (Alteplase 10 mg loading dose and 40 mg over 2 h) with continuous maternal and foetal monitoring. Heparin therapy was re-commenced on completion of lytic therapy.

Within 2 h of treatment completion, the patient was asymptomatic. Observations from 2 h post-thrombolysis demonstrated reduction in heart rate and respiratory rate, reduction in supplemental oxygen requirements and an increase in urine output. Blood gas analysis revealed improvement in gas exchange and reduction in base deficit (Table 1). No minor or major bleeding was observed. Foetal monitoring remained reassuring.

Repeat echocardiography the following day revealed clear improvement in haemodynamics of the right ventricle with normalisation in size, function and septal position (Figure 1(b)).

The patient was switched over to low-molecular weight heparin and was subsequently discharged a week later. She laboured spontaneously at 38 weeks’ gestation; her anticoagulation was interrupted to allow labour and she had a normal vaginal delivery with normal blood loss.
Discussion

Thrombolysis is recognised as first-line treatment for massive pulmonary embolus and may improve clinical outcomes in normotensive patients with other adverse features.\(^1\) The use of thrombolysis in treatment of pulmonary embolus in the absence of shock remains debated. The American Heart Association recommends that thrombolysis may be considered for submassive pulmonary embolus with clinical evidence of adverse prognosis including severe right ventricular dysfunction.\(^2\) The most feared complication of thrombolysis is major bleeding, in particular intracerebral haemorrhage, estimated at 3%.\(^3\) This has caused reluctance in the use of thrombolysis for symptomatic pulmonary embolus without shock.

Pulmonary embolus is a leading cause of maternal death in pregnancy.\(^4\) Due to the presumed risk of placental abruption and foetal compromise, pregnancy is
a relative contraindication for thrombolysis. Several reports have demonstrated successful outcomes from thrombolysis for pulmonary embolus with shock in pregnancy.\(^3\)\(^,\)\(^6\) Reported risks of thrombolysis are 1% for maternal death, 6% for foetal death and 8% of haemorrhage, mainly from the genital tract.\(^7\) Recombinant tissue-type plasminogen activator (Alteplase) does not cross the placental barrier.\(^4\)

Right ventricular dysfunction is associated with increased mortality in acute normotensive pulmonary embolus.\(^3\) Our case patient had normal systemic arterial blood pressure but had echocardiographic evidence of severe right ventricular dysfunction. The plasma lactate level in this patient persisted ≥2 mmol/L despite fluid and heparin treatment. Patients with pulmonary embolism and elevated plasma lactate level are at high risk of death and adverse outcomes independent of hypotension or shock.\(^8\)

We decided to thrombolise the patient as she was deteriorating subjectively and objectively despite optimal anticoagulation, and had biochemical and echocardiographic features which conferred adverse prognosis. We opted for half the standard dose of thrombolysis due to risk of maternal and foetal haemorrhage and the absence of shock. A 50 mg/2 h dose of recombinant tissue-type plasminogen activator (Alteplase) has been shown to have similar efficacy to the Food and Drug Administration approved dose of 100 mg/2 h regimen in acute pulmonary embolus with a reduction in bleeding tendency.\(^9\) The lungs are the only organs that receive the entire cardiac output. This uniqueness suggests that a lower dose of thrombolytic therapy may be used to achieve re-perfusion in acute pulmonary embolism. A recent prospective trial\(^10\) of low-dose thrombolysis in patients with submassive pulmonary embolus demonstrated reduction in pulmonary hypertension and hospital stay compared to heparin alone with no difference in bleeding complications.

As far as we are aware, this is the first case report of successful thrombolysis in a pregnant patient with acute pulmonary embolus in the absence of shock. We further demonstrated that a lower dose of thrombolysis may produce good outcomes in pulmonary embolus. With constant monitoring, the benefits of thrombolysis treatment outweighed the risks given worsening symptoms, clinical and biochemical parameters, and severe right ventricular dysfunction despite optimal conventional anticoagulation. The clinical and haemodynamic response to treatment was excellent, with no maternal or foetal complications.

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