Bilateral massive pulmonary thromboembolism in a young patient treated with supportive measures and an inferior vena cava filter with excellent outcome

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Acute pulmonary embolism (PE) is a common and often fatal disease with a mortality rate of more than 30% in untreated patients. There is a twofold increase in mortality in patients with massive PEs who do not receive treatment. Recurrent embolism is the most common cause of death. A 48-year-old woman presented to Tan Tock Seng Hospital, Singapore, on December 16, 2009, with a massive pulmonary thromboembolism. She was admitted to the intensive care unit and treated with supportive measures, ventilatory support, antibiotics and ionotropes. The patient was diagnosed with urosepsis with septicemic shock, disseminated intravascular coagulation, acute renal

failure, high anion gap metabolic acidosis, iron-deficiency anemia secondary to menorrhagia, and a uterine mass with high cancer antigen 125, although malignancy was ruled out. Anticoagulation or thrombolysis could not be provided in view of coagulopathy. The patient subsequently underwent inferior vena cava filter insertion on December 31, 2009. The patient showed clinical improvement over the next two weeks with antibiotics and supportive measures. If there is a contraindication to anticoagulation or thrombolysis, massive pulmonary thromboembolism should be treated aggressively with supportive measures. Inferior vena cava filter insertion should be instituted early to prevent recurrent PE, which can be fatal. It may take weeks before the patient displays clinical improvement.

Key Words: High CA 125; Inferior vena cava filter; Massive pulmonary embolism; No anticoagulation; No thrombolysis

Acute pulmonary embolism (PE) is a common and often fatal disease with a mortality rate of more than 30% in untreated patients (1). There is a twofold increase in mortality in patients with massive PEs who do not receive treatment (2).

CASE PRESENTATION

A 48-year-old woman presented to Tan Tock Seng Hospital, Singapore, on December 16, 2009, with symptoms of shortness of breath of one day in duration, and abdominal distension. The patient's history included an expanding mass in the pelvis for the past three years and menorrhagia. The patient had not sought medical attention and resorted to traditional Chinese medicines.

On examination, she was tachypneic, pale and febrile. Her blood pressure (BP) was 90/60 mmHg, heart rate was 94 beats/min and O₂ saturation was 100% on 100% inspired O₂. A systemic examination revealed a pelvic mass measuring 6 cm × 6 cm extending from the hypogastric region to the umbilicus, with free fluid in the abdomen. She was admitted to the medical intensive care unit due to worsening respiratory distress and shock. Blood investigations on December 17, 2009, revealed a hemoglobin level of 4.6 g/dL, white blood cell count of 45.1×10⁹/L (neutrophils 90.4%, lymphocytes 4.9%, monocytes 4.7% and eosinophils 0%), platelet count of 774×10⁹/L, iron level of 2 µmol/L, transferrin level of 2.8 g/L, iron saturation of 3%, ferritin level of 45 µg/L, normal folate and vitamin B₁₂ levels, sodium level of 144 mmol/L, potassium level of 6.4 mmol/L, creatinine level of 229 µmol/L, urea level of 14.5 mmol/L, activated partial thromboplastin time (APTT)

of 36.9 s, prothrombin time (PT) of 21.1 s, international normalized ratio (INR) of 1.88, D-dimer level of greater than 10 µg/mL, fibrinogen level of 2.8 g/L, C-reactive protein (CRP) level of 153.1 mg/L, creatine kinase (CK) level of 695 U/L, CK-MB level of 13.4 µg/L, troponin I level of 0.77 µg/L, albumin level of 29 g/L, bilirubin level of 31 µmol/L, alanine aminotransferase (ALT) level of 2637 U/L, aspartate aminotransferase (AST) level of 4090 U/L and an alkaline phosphatase (ALP) level of 199 U/L. The patient's arterial blood gas test revealed a pH of 7.18, partial pressure of CO₂ of 26 mmHg, partial pressure of O₂ of 125 mmHg, bicarbonate level of 9 mmol/L and O₂ saturation of 97%. After a full examination and microscopic examination of the urine, pyuric and cellular cultures revealed *Streptococcus agalactiae* (group B). Follow-up investigations on December 19, 2009, revealed a hemoglobin level of 8.8 g/dL, white blood cell count of 29.5×10⁹/L (neutrophils 96%, lymphocytes 0%, monocytes 4% and eosinophils 0%), platelet count of 330×10⁹/L, sodium level of 146 mmol/L, potassium level of 3.9 mmol/L, creatinine level of 201 µmol/L, urea level of 21 mmol/L, APTT of 36.7 s, PT of 25.1 s, INR of 2.38, CRP level of 171.1 mg/L, procalcitonin level of 17.77 µg/L, albumin level of 28 g/L, bilirubin level of 46 µmol/L, ALT level of 2123 U/L and an ALP level of 246 U/L. On December 22, 2009, follow-up tests revealed an albumin level of 23 g/L, bilirubin level of 47 µmol/L, ALT level of 709 U/L, AST level of 171 U/L and an ALP level of 136 U/L. On December 23, 2009, her cancer antigen (CA) 19-9 level was 261 U/mL and CA 125 level was 543 U/mL; her alpha-fetoprotein and carcinoembryonic antigen levels were normal.

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The patient was diagnosed with urosepsis with septicemic shock, disseminated intravascular coagulation, acute renal failure, transaminitis secondary to ischemic hepatitis, high anion gap metabolic acidosis, iron-deficiency anemia secondary to menorrhagia and a uterine mass with a high CA 125 level, although malignancy was ruled out.

She was initially given intravenous ceftriaxone, which was subsequently escalated to piperacillin and tazobactam. She was also started on inotropes (dopamine and adrenaline) due to hypotension attributed to septicemic shock. She was given four packed-cell transfusions – one whole blood and three fresh frozen plasma. She had episodes of supraventricular tachycardia on December 18, 2009, which were attributed to infection and inotropes in the intensive care unit and were remedied with adenosine and verapamil. On December 19, 2009, she underwent two-dimensional echocardiography, which revealed a left ventricular ejection fraction of 55%. Her right atrium and ventricle were moderately dilated, with increased pressure and moderate pulmonary hypertension.

Computed tomography (CT) of the abdomen and pelvis on December 21, 2009, showed a midline grossly heterogeneous pelvic mass inseparable from the uterus with a hypodense core and hyperenhancing peripheries, measuring 20 cm × 14 cm × 22 cm, and compression of the sigmoid colon, although no evidence of large bowel dilation. Gross ascites with thickening of the small bowel wall with normal enhancement were noted. There was no peritoneal thickening or nodularity. There was a left adnexal rim-enhancing cystic mass measuring 5.3 cm × 5.3 cm closely related to the uterine fundus, and another cystic mass more inferiorly. She was referred to a gynecologist, who recommended draining the ascites and performing cytology to confirm her CA level in view of her previous high CA 125 level and CT scan results. Abdominal paracentesis was deferred.

In view of persistent tachycardia and unresponsiveness to antibiotics, a CT pulmonary angiogram was performed on December 21, 2009, which revealed extensive bilateral pulmonary thrombosis, primarily involving the distal aspect of both main pulmonary arteries and their bifurcations (Figure 1). In view of her anemia, continued vaginal bleeding and coagulopathy, the patient was considered to be unsuitable for anticoagulation. A Doppler scan of the legs indicated deep vein thrombosis (DVT) of the left external iliac, common femoral, superficial femoral and popliteal veins.

On December 28, 2009, her follow-up investigation revealed a sodium level of 144 mmol/L, potassium level of 4 mmol/L, creatinine level of 43 µmol/L, urea level of 1.5 mmol/L, APTT of 33.2 s, PT of 14.2 s, INR of 1.10, D-dimer level of greater than 10 µg/mL, fibrinogen level of 2.8 g/L, CRP level of 49.7 mg/L, CK level of 695 U/L, CK-MB level of 13.4 µg/L, troponin I level of 0.77 µg/L, albumin level of 21 g/L, bilirubin level of 25 µmol/L, ALT level of 113 U/L, AST level of 30 U/L and an ALP level of 99 U/L. Additional follow-up indicated a hemoglobin level of 8.9 g/dL, white blood cell count of $10.1 \times 10^9/L$ (neutrophils 85%, lymphocytes 6.6%, monocytes 7.5% and eosinophils 0.6%) and a platelet count of $234 \times 10^9/L$. On December 31, 2009, a temporary inferior vena cava (IVC) filter was inserted. Following IVC filter insertion, she showed clinical improvement over the next two weeks with antibiotics and supportive measures. An abdominal paracentesis performed

Figure 1) Computed tomography pulmonary angiogram showing extensive bilateral pulmonary thrombosis, primarily involving the distal aspect of both main pulmonary arteries and their bifurcations

one week later demonstrated no evidence of malignancy. On January 12, 2010, the two-dimensional echocardiography was repeated, which revealed an ejection fraction of 70%, and no evidence of increased right heart pressure or pulmonary hypertension. The patient was discharged on January 18, 2010.

She underwent a modified radical hysterectomy on February 9, 2010, at KK Women's Hospital, Singapore. The histopathology report showed adenomyosis with extensive necrosis and infarction, but no malignancy. A repeat CT pulmonary angiogram was performed on February 2, 2010, indicating a complete resolution of PE and no evidence of lung parenchymal damage.

The patient returned for follow-up in the vascular medicine clinic on March 22, 2010. The examination revealed no ascites or pelvic mass, and a systemic examination was normal. She underwent successful IVC filter removal on April 1, 2010.

In view of persistent DVT of the left limb, an ultrasound Doppler scan was repeated and the patient was started on anticoagulation. Anticoagulation was planned for a course of six months, and the patient was asked to repeat a follow-up Doppler scan of the left limb in six months to determine the status of DVT.

DISCUSSION

Acute PE is a common and often fatal disease, with a mortality rate of greater than 30% in untreated patients (1,3-5). There is a twofold increase in mortality in patients with massive PEs who do not receive treatment (2). Massive PE occurs in patients with PE who present with hypotension, defined as a systolic BP of less than 90 mmHg or a drop in systolic BP of 40 mmHg or greater from baseline for a period of longer than 15 min. Recurrent embolism is the most common cause of death. Right ventricular (RV) dysfunction due to PE predicts increased PE-related mortality if normotensive and hypotensive patients are considered together. This was illustrated by a meta-analysis (2) of seven studies (3395 normotensive or hypotensive patients with PE), which found that RV dysfunction was associated with a twofold increase in PE-related mortality. Bilateral massive pulmonary thromboembolism is a life-threatening condition wherein patients present with circulatory and respiratory collapse. These patients require either thrombolysis or an intervention such as thrombectomy

performed by a specialized cardiovascular thoracic surgeon to obtain a good outcome. The indications for thrombolysis in PE are presence of hypotension related to PE, presence of severe hypoxemia, substantial perfusion defect, RV dysfunction associated with PE, and extensive DVT (6). For patients with confirmed PE who are persistently hypotensive due to PE (systolic BP of lower than 90 mmHg or a drop in systolic BP of 40 mmHg or greater from baseline) and who do not have an increased risk of bleeding, the recommended treatment is thrombolytic therapy followed by anticoagulation, rather than anticoagulation alone.

Surgical embolectomy is typically limited to large medical centres because an experienced surgeon and cardiopulmonary bypass are required. Whether surgical or catheter embolectomy is performed depends on the expertise and resources of the institution. Although systemic hypotension due to PE in a patient in whom thrombolysis is contraindicated is the usual indication for surgical embolectomy, echocardiographic evidence of an embolus trapped within a patent foramen ovale, the right atrium or the right ventricle has also prompted surgery (7).

Our patient had a massive PE and was not able to receive thrombolysis or anticoagulation. The patient was very ill, and our centre did not have the facilities or expertise to offer surgical embolectomy. Due to her fragile condition, this patient was not initially in a position to be transferred to a centre offering surgical embolectomy.

She underwent IVC filter insertion to prevent further recurrence of PE. She was treated with antibiotics, ventilatory support, inotropes and intravenous fluids. She recovered completely, with no evidence of pulmonary hypertension.

CONCLUSION

In the case of absolute contraindication to anticoagulation or thrombolysis, massive pulmonary thromboembolism should be treated aggressively with supportive measures. IVC filter insertion should be instituted early to prevent recurrent PE, which can be fatal. It may take weeks before the patient shows clinical improvement.

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