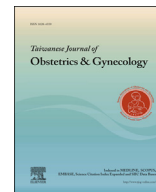




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Research Letter

Pulmonary embolism after cesarean section and successful treatment with early application of extracorporeal membrane oxygenation system and anticoagulant agents



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Pulmonary embolism (PE) is defined as the obstruction of the main arteries of the lung by a substance (such as thrombus, fat, or amniotic fluid) that has traveled through the bloodstream. PE remains a leading cause of maternal mortality in the United States [1]. It is a rare, unpredictable, and unpreventable life-threatening complication of pregnancy, with incidence rates ranging from 0.11 to 0.73 per 1000 deliveries [2].

Because the maternal hypercoagulable state is part of a normal physiological preparation for delivery, hypercoagulability during pregnancy is associated with a 5-fold increased risk in venous thromboembolism [3]. Early detection of thromboembolism during pregnancy or during the postpartum period enables identification of patients who require anticoagulant treatment.

According to the International Cooperative Pulmonary Embolism Registry, the death rate from massive PE among hemodynamically unstable patients is 52% [4]. In this report, we describe a case in which massive PE developed 2 days after the cesarean section; the patient was successfully treated with early application of the extracorporeal membrane oxygenation (ECMO) system, catheter-directed thrombectomy, and anticoagulants. We further describe the use of the ECMO system as a bridge therapy to support patients through the diagnostic workup for suspected PE and further treatment.

A 37-year-old woman (G2P1) at a gestational age of 37 weeks and 2 days with P1 through natural spontaneous delivery presented with symptoms of labor. Upon arriving at our ward, the patient showed a cervix dilatation of 5 cm. A cardiotocogram revealed regular uterine contraction at intervals between 4 minutes and 10 minutes. No signs of infection were evident and laboratory tests were within normal limits.

During labor, a nonreassuring fetal heart rate was noted and an emergent cesarean delivery was performed. After the surgery, the patient had bed rest for 2 days because of bilateral lower-limb weakness. Consciousness disturbance with weakness in all four limbs suddenly developed after mobilization on postoperative Day 3, followed by unstable hemodynamic status, hypotension (46/20 mmHg), tachycardia (121 beats/minute), low oxygen saturation (85%), tachypnea (32 breaths/minute), hypoxemia, and respiratory alkalosis. Endotracheal tube insertion was performed for impending respiratory failure. An immediate electrocardiogram showed sinus tachycardia with an SIQ III TIII pattern (Fig. 1), suggestive of PE. The echocardiogram showed a left ventricle ejection fraction of 32.7%, pulmonary arterial hypertension, and right heart dilatation. Cardiopulmonary resuscitation was performed for 10 minutes because of pulseless electrical activity. Because of acute right heart failure, venoarterial ECMO system was initiated. Multidetector chest computed tomography (CT) was arranged after stabilizing the patient's hemodynamic status, which revealed a filling defect in the pulmonary trunk before the right and left pulmonary arteries (Fig. 2). Massive PE was diagnosed and emergent catheter-directed thrombectomy was performed, followed by continuous low molecular weight heparin (LMWH) infusion.

After 5 days of heparin treatment, the patient presented with abdominal distension and pain. The bedside ultrasonography revealed massive ascites. Abdominal CT revealed internal bleeding with hemoperitoneum in the left pelvic region. Heparin infusion was stopped temporarily, and an emergent transcatheter arterial embolization of the left uterine artery was performed. We removed

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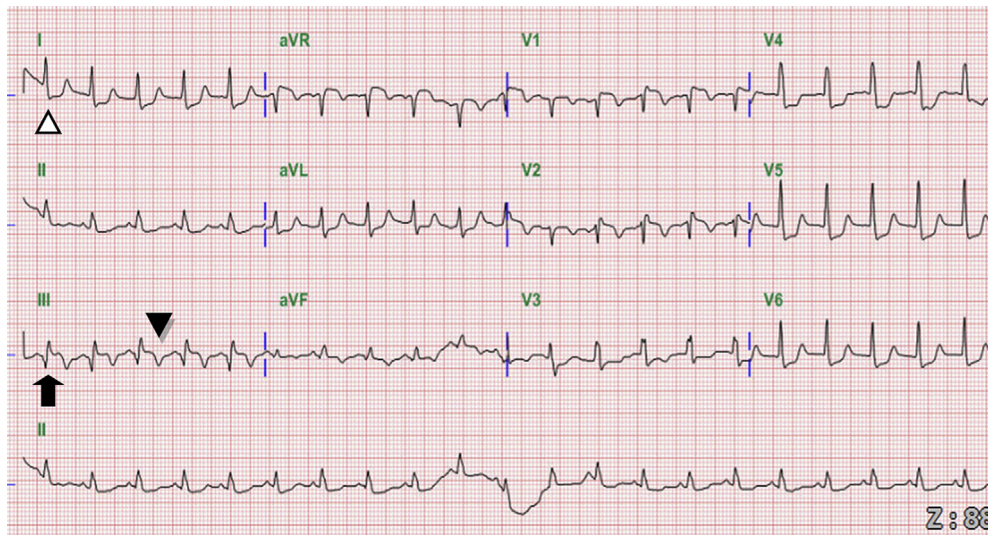


Fig. 1. The electrocardiogram of the patient demonstrates an SI QIII TIII pattern, in which an S wave is seen in lead I (hollow arrowhead), a Q wave in lead III (arrow), and inverted T waves in lead III (arrowhead).

the ECMO system smoothly on the 6th day of ECMO use and substituted the heparin infusion for enoxaparin and warfarin. Extubation was performed on the 8th day. Screening for inherited thrombophilia during admission revealed 107% antithrombin III, 40% protein C, and 21.2% protein S.

The patient recovered quickly after extubation. Once in a stable condition and the wound was healing sufficiently, she was transferred to a general ward for observation. The patient made a full recovery without developing any neurological sequelae.

PE is difficult to diagnose. Clinical signs and symptoms include sustained hypotension, dyspnea, chest pain, tachycardia, and tachypnea. Severe cases of PE can lead to cardiogenic shock, cardiopulmonary arrest, and sudden death. Determination of PE symptoms such as chest pain and shortness of breath from normal physiological changes brought about by pregnancy should be made with caution to avoid fatal misdiagnosis.

Amniotic fluid embolism (AFE) is defined as the passage of amniotic fluid into the maternal bloodstream to trigger an allergic

reaction. The United Kingdom Amniotic Fluid Embolism Register recommends the following entry criteria for suspected AFE: acute hypotension, acute hypoxia, and coagulopathy or severe hemorrhage, all of which occur during labor, cesarean delivery, or within 30 minutes postpartum, and in the absence of other explanations [5]. The management of AFE is resuscitative. In critically ill patients with acute respiratory distress syndrome or cardiopulmonary failure, use of aggressive management such as the ECMO system for cardiovascular and respiratory support has been reported [6].

Pulmonary thromboembolism and AFE are responsible for approximately 20% of perinatal maternal mortality in the United States [1,7]. The differential diagnosis of these conditions is critical to a successful outcome because they should be managed differently. The management of AFE is supportive and focuses on early recognition, rapid cardiopulmonary stabilization, and adequate oxygenation. In patients with suspected thromboembolism, treatment with LMWH, unfractionated heparin (UFH), and thrombolytic therapy should be started immediately to reduce mortality [8].

The diagnosis of acute pulmonary thromboembolism remains a challenge to clinical physicians because the signs and symptoms vary widely, from asymptomatic conditions to sustained hypotension and cardiopulmonary arrest. The diagnostic workup consists of a clinical probability assessment, the D-dimer test, echocardiography, venous ultrasonography, multidetector CT, and a ventilation–perfusion scan [3]. These surveys should be modified according to the severity of the clinical presentation based on the patients' hemodynamic status. In the initial assessment, patients with suspected PE are categorized into low, intermediate, or high clinical probability based on their Wells score [9].

Agnelli and Becattini [10] suggested that, for hemodynamically stable patients with a low or intermediate clinical probability of PE, a normal D-dimer result indicates a low probability of PE, and clinical exclusion from further investigation is recommended. In patients with a high clinical probability of PE or with an elevated D-dimer level, multidetector CT should be considered. Agnelli and Becattini [10] also suggested a ventilation–perfusion scan as an alternative if CT is unavailable or if CT is contraindicated for the patient. However, the European Association of Nuclear Medicine currently recommends a ventilation–perfusion scan as the gold standard for the diagnosis of PE [11]. In hemodynamically unstable

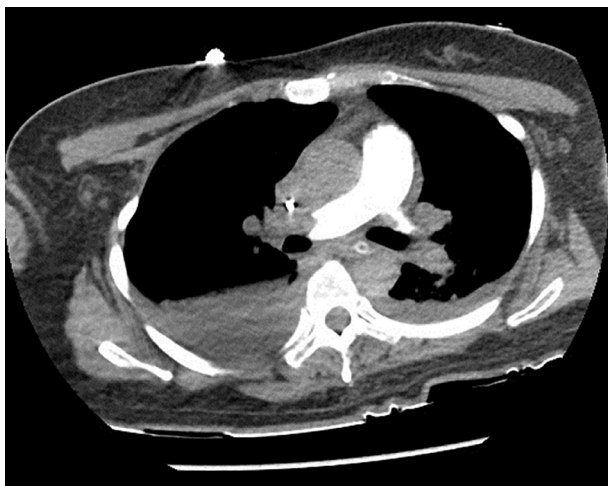


Fig. 2. Computed tomographic (CT) scan of the patient showing a filling defect within the pulmonary trunk, right and left pulmonary arteries, left superior and inferior pulmonary arteries, and right inferior pulmonary artery.

patients, Agnelli and Becattini [10] suggested that CT should be performed immediately because of its sensitivity in detecting emboli in the main pulmonary arteries. If CT is not available or the patient is critically ill, bedside echocardiography should be performed to evaluate right ventricular function.

Because the patient in this case was hemodynamically unstable, transport was unfeasible. According to Well's prediction rule, the coexistence of tachycardia and recent surgery, and the fact that an alternative diagnosis was less likely than PE, strongly supported PE as the most probable diagnosis, and, thus, diagnostic imaging was required for confirmation [3,9]. Therefore, bedside echocardiography was used to confirm the presence of right ventricular dysfunction and to eliminate other possible causes of shock, such as myocardial infarction, cardiac tamponade, and aortic dissection. The ECMO system was applied to the patient as a supportive treatment for the unstable hemodynamic status caused by acute right heart failure because the patient had responded poorly to medication and cardiopulmonary resuscitation. The diagnosis of PE was confirmed by detecting thromboemboli in the main pulmonary arteries using multidetector CT after stabilizing the patient's hemodynamic status.

PE can be divided into massive, submassive, and low-risk PE. A massive PE is characterized by acute PE with sustained hypotension (systolic blood pressure <90 mmHg), pulselessness, or persistent profound bradycardia (heart rate <40 bpm). A submassive PE is characterized by either right ventricular dysfunction or myocardial necrosis without systemic hypotension. A low-risk PE is neither massive nor submassive [12]. In patients with suspected pulmonary thromboembolism, immediate therapeutic anticoagulation should be initiated, followed by long-term treatment with vitamin K antagonist aiming for a target prothrombin time/international normalized ratio of 2–3 for 6–12 weeks [13]. The first-line treatment of acute pulmonary thromboembolism includes LMWHs, fondaparinux, and UFH. These anticoagulants should be continued throughout pregnancy and for 6 weeks–6 months postpartum [12,14]. LMWHs (enoxaparin: 1 mg/kg every 12 hours or 1.5 mg/kg daily) and fondaparinux (5–7.5 mg daily) are easier to use compared to UFH (intravenous bolus of 333 IU/kg followed by an infusion of 250 IU/kg every 12 hours, adjusted according to the target-activated partial thromboplastin time—i.e., 1.5–2.5 times the normal value) [13]. UFH is preferred for the treatment of patients with renal failure because LMWHs and fondaparinux are excreted by the kidneys [8].

Patients with a single prior episode of PE have a risk of recurrence. The recurrence risk was found to be twice as high in patients with thrombophilia. Inherited thrombophilias such as protein C and protein S deficiencies may play an important role in causing PE and its recurrence [15]. Screening for thrombophilia should be performed 4–6 weeks after completion of anticoagulation. In our case, we will screen our patient for inherited thrombophilia (anti-thrombin III, protein C, protein S) and acquired thrombophilia (antiphospholipid syndrome, lupus anticoagulant) 4–6 weeks after completing the treatment with oral anticoagulants.

Thrombolytic therapy is recommended in patients with massive and submassive PE who have a low risk of bleeding [12]. Available thrombolytic drugs include streptokinase (250,000 IU IV bolus followed by 100,000 IU/hour infusion for 12–24 hours), urokinase (4400 IU/kg bolus followed by 4400 IU/kg/hour for 12–24 hours), and alteplase (100 mg IV infusion over 2 hours) [12]. There is no difference in efficacy between the various thrombolytic agents. However, streptokinase should be avoided in patients who have received it previously because of the likely presence of neutralization antibodies [16]. A recent surgery or trauma is a contraindication to thrombolysis because of the increased risk of bleeding complications. According to the American Heart Association, catheter-directed embolectomy and fragmentation is suggested in patients with massive PE who have contraindication to

thrombolysis or who remain hemodynamically unstable after receiving thrombolysis [10,12]. A recent meta-analysis of a case series demonstrated that catheter-directed therapy had a clinical success rate of 86% in the treatment of massive PE [17]. The patient in our case received an emergent catheter-directed thrombectomy after being diagnosed with massive PE. However, the procedure was not satisfactorily effective. Anticoagulant was maintained at a dosage designed to keep the activated partial thromboplastin time at 1.5–2 times the control value. Internal bleeding developed 5 days after heparin use, which was immediately controlled through transcatheter arterial embolization.

The diagnosis and management of PE have been discussed extensively. As previously mentioned, early recognition of PE and early identification of patients who are to be treated with anticoagulants are the keys to a successful outcome. We conclude that, for patients with suspected PE, treatment with anticoagulants should start immediately and continue until the diagnosis of thromboembolism is eliminated [8]. For our patient, the ECMO system decompressed the acutely overloaded right heart and maintained hemodynamic stability. This demonstrates that such patients can be rapidly treated and successfully supported by the ECMO system while awaiting a definitive diagnosis.

Conflicts of interest

The authors declare no conflict of interest.

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