Case Report

Can we predict and take a proper treatment for postpartum pulmonary embolism? A single institution review of five cases

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Postpartum pulmonary embolism (PPE) is a rare disorder in the puerperium that can present a wide range of symptoms after childbirth. This condition can lead to death and is the most common cause of maternal mortality, accounting for about 10% of all maternal deaths in the United States. A previous study conducted over 3 years (2014-2016) followed five patients diagnosed with postpartum pulmonary embolism, two of whom died. As PPE is characterized by a variety of symptoms, patients suspected of this condition require prompt diagnosis and treatment. Based on the previous investigation of five patients, the present study aimed to elucidate considerations for early treatment and diagnosis. Maternal mortality can be minimized by proper treatment and early detection using contrast-enhanced chest computerized tomography and echocardiography in women during or after delivery, particularly those with suspected embolism.

Keywords
Postpartum; Pulmonary embolism; Deep vein thrombosis

1. Introduction
Postpartum pulmonary embolism (PPE) is a rare disorder, occurring in 1 in 80,000 pregnancies [1]. PPE encompasses amniotic fluid embolism (AFE), venous thromboembolism (VTE), and others; it is characterized by a variety of symptoms ranging from relatively minor, such as sudden chest pain or difficulty breathing after delivery, to serious symptoms such as coagulopathy, renal failure, and cardiac arrest. However, it is associated with fatal complications in pregnancy and childbirth. PPE manifests in a variety of ways immediately after delivery, making diagnosis more difficult and challenging, unless it is suspected clinically. Moreover, clinical outcomes vary, ranging from recovery and discharge to death, depending on circumstances and prompt treatment. Advance preparation is critical, as there is no time to prepare when it occurs.

2. Cases series
2.1 Case 1
A 33-year old woman, gravida 2, visited our hospital with chief complaints of vaginal bleeding after normal spontaneous vaginal delivery (NSVD) on the day of the visit, a sensation of pressure in her chest, and unstable vital signs (blood pressure, 80/40). Her findings on prenatal exam were non-specific. At the time of this visit, the patient’s blood pressure (BP) was 50/30, pulse rate (PR) was 157, oxygen saturation (SaO₂) was 94%, and hemoglobin/hematocrit (Hb/Hct) was 5.4/16.4. Contrast-enhanced chest computerized tomography (CT), cardiac marker testing, and echocardiography were performed. She recovered after a massive transfusion, uterine artery embolization, and administration of dopamine and diuretics, followed by conservative treatment. She was discharged after about 2 weeks.

2.2 Case 2
A 28-year old woman, gravida 2, intra-uterine pregnancy (IUP) at 35 weeks, visited our hospital with a chief complaint of left flank pain and labor pain. Her prenatal exam revealed a history of gestational hypertension, and she received conservative treatment. The labor pain persisted, resulting in NSVD. She suddenly complained of chest pain at 6 hours after delivery. Her vital signs were unstable, with BP of 60/40 and PR of 180. Chest X-ray and Contrast-enhanced chest CT were performed. Despite conservative treatment, including extracorporeal membrane oxygenation (ECMO) and inotropics, the patient died after 6 hours.

2.3 Case 3
A 27-year old woman, gravida 3, IUP 38 + 3 weeks, underwent repeated cesarean section. On prenatal exam, the findings were non-specific. She had dyspnea on the day after delivery, low BP (74/44), PR of 164, and SaO₂ of 85%. Under a diagnosis of ‘rule out pulmonary embolism’, she was admitted via the emergency room (ER). Fig. 1 shows pulmonary thromboembolism at both main pulmonary arteries, both descending pulmonary arteries, truncus anterior, segmental branch of left upper, descending pulmonary artery. The patient was transferred to the intensive care unit (ICU) and underwent ECMO, dopamine infusion, hyperbaric oxygen therapy (HBOT), anticoagulation (heparin), and transfusion after a week of conservative treatment, she was discharged.
Fig. 1. Contrast-enhanced chest CT shows pulmonary thromboembolism at both main pulmonary arteries, both descending pulmonary arteries, truncus anterior, segmental branch of left upper, descending pulmonary artery.

Fig. 2. Contrast-enhanced chest CT shows pulmonary thromboembolism in both main pulmonary artery and segmental branches of BLL († thrombi). (B) Chest X ray shows pulmonary edema on both lungs, bilateral moderate amount of pleural effusion and R/O pulmonary embolism.
2.4 Case 4

A 23-year old woman, gravida 3, IUP at 38 + 3 weeks, tertiary cesarean section, was diagnosed with pre-eclampsia of pregnancy on prenatal exam. She was found collapsed on the day after delivery and admitted to our hospital’s ER as a paramedic administered chest compressions. Her vital signs were BP 67/46, PR 174, respiratory rate (RR) 16, and SaO\textsubscript{2} 93%. Fig. 2 shows Contrast-enhanced chest CT shows pulmonary thromboembolism in both main pulmonary artery and segmental branches of BLL (\textsuperscript{1}thrombi). The patient was transferred to ICU and received hypothermia treatment, BP control (epinephrine), thrombolytic agent (tissue plasminogen activator (tPA), clexane), transfusion, and HBOT. Disseminated intravascular coagulation (DIC)-induced abdominal hemorrhage was detected 3 days after treatment. The patient’s guardian refused additional management. On day 2 of conservative treatment, she died.

2.5 Case 5

A 34-year old woman, gravida 2, IUP 35 + 5 weeks, underwent repeated cesarean section. On prenatal exam, she was diagnosed with pre-eclampsia. She received a transfusion due to severe blood loss during surgery. On the third postpartum day, she was admitted to our hospital via the ER with chief complaints of palpitation and shortness of breath. At the time of admission, her vital signs were BP 100/70, PR 147, and SaO\textsubscript{2} 96%. Fig. 3 shows chest x-ray shows pulmonary edema on both lungs, bilateral moderate amount of pleural effusion and rule put (R/O) pulmonary embolism.; lab tests were also performed. The patient was transferred to the ICU, where she received input/output monitoring (Lasix), BP control (beta blocker), transfusion, and HBOT. The patient improved after conservative treatment and was discharged.

3. Discussion

Postpartum pulmonary embolism (PPE) is a rare disorder in the puerperium, and it is the most common cause of maternal mortality, accounting for about 10% of all maternal deaths in the United States \cite{2}. In this series, two of five PPE patients died.

The early signs of PPE may progress to potentially fatal conditions including low blood pressure, cardiac arrest, co-
agulopathy, and multi-organ failure, sometimes leading to death. At even a slight suspicion, aggressive diagnosis and treatment should be performed concomitantly. Given that management and prognosis vary by condition, as seen in the discussion below, differential diagnosis in an emergency department is very important. However, accurate diagnosis is difficult based on medical examinations and inquiries in an emergent situation. Clinical experience and medical facilities for differential diagnosis, an expert medical team, and senior doctors to offer appropriate recommendations are thought necessary. When patients with suspected symptoms of PPE visit the hospital, adequate supplies of oxygen can be attempted preferentially. Then, more accurate diagnosis and treatment can be achieved by screening cardiac output, systemic vascular resistance (SVR), pulmonary vascular resistance (PVR), and other predictors via hemodynamic monitoring after the insertion of a pulmonary catheter. However, this procedure may be challenging in emergent circumstances. And treatment should be initiated after contrast-enhanced chest CT and echocardiography for differential diagnosis, to identify the exact cause of the condition (Table 1).

PPE is known to be influenced by coagulopathy of cardiovascular origin, such as hypertension, toxemia of pregnancy, preeclampsia, or hemolysis, elevated liver enzymes, and low platelets (HELLP syndrome) in pregnancy [3]. In the current study, three of five patients had medical histories of cardiovascular disorders associated with toxemia of pregnancy. Previous studies have examined the postnatal effects of respiratory diseases during pregnancy [4], but none of the patients in our study had a history of lung disorder. Because hypoxia, hypotension, and shock immediately after delivery are predominantly of pulmonary or cardiovascular origin, differential diagnosis between PPE and other diseases is crucial.

Contrast-enhanced chest CT is the first-line imaging approach for diagnosing PPE; by contrast, simple chest PA is not useful in making a diagnosis of PPE. In cases of pulmonary embolism (PE), several considerations are crucial. First, the increased risk of PE is recognized to result from the hypercoagulable state associated with pregnancy and puerperium [2], and pregnancy-induced venous stasis and damage in vein endothelial cells are known to increase the risk of complications such as deep vein thrombosis (DVT) [5]. For these reasons, PE should be primarily considered in pregnant women with symptoms such as hypoxia, tachycardia, hemoptysis, and so forth. Second, PE should be differentiated from pneumonia because they present with similar symptoms. Third, immune system changes during pregnancy and intrapartum aspiration may also increase the risk for infection, and acute respiratory distress syndrome (ARDS) is one of the known complications during pregnancy [6].

Amniotic fluid embolism (AFE) is a rare but fatal obstetric condition characterized by cardiorespiratory collapse. The causes of AFE are considered to include pregnancy in women aged ≥ 35 years, Cesarean section, forceps delivery, placenta previa, abruptio placenta, and pre-eclampsia-eclampsia, among others [7]. Many studies have reported that AFE is associated with cardiovascular and hemodynamic changes [8–11]. Women who are pregnant and have severe pre-eclampsia-eclampsia require especially close attention. In this study, three of five patients had histories of conservative treatment after being diagnosed with gestational hypertension and toxemia of pregnancy on prenatal examination; furthermore, these conditions occurred in those three women after cesarean delivery. The process of labor and delivery itself causes significant hematological changes, and mothers can be exposed to multiple problems during postpartum recovery. Pregnant women with gestational hypertension appear to be particularly prone to PE due to severe hematological changes related to blood pressure regulation after delivery or postpartum hemorrhage. This seems to be attributable to the fact that, unless uterine atony occurs, C-section delivery is more likely to result in greater blood loss and transfusion and less stable hematological parameters than NSVD.

Because PPE may be associated with disseminated intravascular coagulation (DIC) and systemic inflammatory responses and early manifestations include septic shock, an immediate supply of oxygen and fluid is needed in cases where PPE is suspected. However, excessive fluid supply should be avoided because PPE is often associated with right ven-

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**Table 1. Early response protocols for suspected Postpartum pulmonary embolism (PPE).**

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<td>1</td>
<td>Basic physical examinations including vital signs, oxygen saturation (SaO₂), neurologic exam, hemorrhage and ECG, hemoglobin test, arterial oxygen tension, assessment of cardiac markers, screening tests of DIC and others should be performed, and, if necessary, central vein catheterization can be conducted.</td>
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<td>2</td>
<td>When patient conditions suddenly aggravate, the possibility of AFE and hemorrhage should be taken into consideration and CT should be attempted primarily for differential diagnosis. When intrapartoneal hemorrhage is not present, AFE can be suspected and fluid therapy and vasopressors (norepinephrine, epinephrine, dopamine, dobutamine, etc.) should be administered.</td>
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<td>3</td>
<td>When dyspnea, tachycardia and low SaO₂ are manifested but, severity of symptoms do not worsen (cardiac arrest, etc.), PTE and postpartum cardiomyopathy can be suspected. For differential diagnosis, ECG and CT should be performed. PPE can be discriminated from other conditions, because the signs of DVT such as leg swelling are associated in most cases. When PTE is confirmed, anticoagulation therapy using low-molecular-weight heparin (LMWH) or heparin should be started. In case of postpartum cardiomyopathy, treatment is the same as for heart failure and diuretics are initially administered to prevent deterioration of pulmonary edema.</td>
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<td>4</td>
<td>Pneumonia should be considered when fever is associated.</td>
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<td>5</td>
<td>When ECG and cardiac biomarkers indicate suspected myocardial infarction, coronary angiography should be performed.</td>
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tricular failure. Treatment for both PPE and DIC should be started simultaneously. When starting treatment, DIC should be simultaneously managed to improve patient outcomes. ECMO can be considered but, generally, the use of ECMO is not recommended. Coagulation therapy is initially started for the management of pulmonary thromboembolism (PTE), thereby reducing the risk of heart failure associated with PTE. Aggressive treatment can be initiated, including ECMO and other approaches, in severe cases.

PPE must also be discriminated from postpartum cardiomyopathy (PPCM), as it can mimic PPCM. PPE may be suspected in patients with congestive heart failure and left ventricular dysfunction without other heart diseases. In such cases, the cardiac ejection fraction (EF) is reduced below 45%, and clinical signs mostly manifest within the first week postpartum. Echocardiography seems to be essential to discriminate embolism from other heart problems.

Given that management and prognosis vary by condition, as seen in the discussion above, differential diagnosis in an emergency department is very important. However, accurate diagnosis is difficult based on medical examinations and inquiries in an emergent situation.

4. Conclusions
When PPE is suspected, after various causes are considered, early and adequate management and accurate diagnosis via contrast-enhanced chest CT and echocardiography can prevent conditions that could cause death in pregnant women with high blood pressure during the antepartum or intrapartum period, those at risk for intrapartum or postpartum hemorrhage, and those with symptoms of heart problems such as dyspnea and hypotension during or after delivery.

Ethics approval and consent to participate
The article does not contain any studies with human participant or animal performed by any of the authors.

Author contributions
All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

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Conflict of interest
The authors declare no competing interests.

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