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Treatment of Pulmonary Embolism during Cesarean Section with Recombinant Tissue Plasminogen Activator

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ALTHOUGH pulmonary embolism is a rare complication of pregnancy, it is one of the leading causes of maternal mortality.[1,2] It was estimated that two thirds of deaths caused by pulmonary embolism occur during the first hour after the event, and the remainder occurred within 4 to 6 h.[3] Therefore, we believe that early detection and subsequent treatment of pulmonary embolism are important clinical challenges. In this report, we describe a patient with abruptio placenta and preeclampsia who underwent general anesthesia for cesarean section, in which life-threatening pulmonary embolism developed intraoperatively and was treated with recombinant tissue plasminogen activator (rt-PA).

Case Report

A 35-yr-old woman, at 29 weeks' and 4 days' gestation, was admitted from an outside institution for the treatment of abruptio placenta and preeclampsia, which was diagnosed by hypertension, proteinuria, and edema of her limbs. There was no external vaginal bleeding. The patient had undergone previous cesarean section for preeclampsia and prematurity and had no history of pulmonary disease or deep venous thrombosis. Ultrasonography revealed an estimated fetal weight of 1,212 g, and the fetal heart rate was > 100 beats/min. Results of blood tests performed at admission showed the following: hemoglobin level: 7.6 g/dl (11.8 < normal < 13.0); erythrocyte count: $3.30 \times 10^6/\mu l$ (3.74×10^6 < normal < 4.29×10^6); and hematocrit level: 23% (35 < normal < 45). Coagulation tests disclosed the following: platelet counts: $92 \times 10^3/\mu l$ (131×10^3 < normal < 362×10^3); prothrombin activity: 56.5%; and fibrin degradation products: more than 70 μg/ml (normal < 10). Because of an acute decrease in fetal heart rate, the patient was scheduled for emergency cesarean section.

General endotracheal anesthesia was induced using a rapid-sequence technique with cricoid pressure. Bilateral breath sounds were normal. Oxygen saturation by pulse oximetry (Sp_{O_2}) was 99% and end-tidal carbon dioxide (ET_{CO_2}) was 26–28 mmHg.

Just after cesarean delivery of a neonate, methylergometrine maleate was administered intravenously. A few minutes later, ET_{CO_2} decreased suddenly to 9 mmHg. Simultaneously, it became difficult to ventilate the lungs, and 3 min later, Sp_{O_2} decreased from 99% to 19%. (fractional inspired oxygen tension, FI_{O_2} = 1.0) Systolic blood pressure progressively decreased from 140 to 80 mmHg, and the heart rate increased to 142 beats/min. Eight milligrams ephedrine was administered intravenously, and systolic blood pressure recovered to 120 mmHg. Fifteen minutes after the decrease in blood pressure, an intraarterial catheter was inserted, and arterial blood gas analysis revealed *p*H = 6.93; P_{O_2} = 20.7 mmHg; arterial carbon dioxide tension, Pa_{CO_2} = 67.3 mmHg; base excess = −19.1. Dopamine infusion was started at a rate of 10 $\mu g \cdot kg^{-1} \cdot min^{-1}$ and increased to 17 $\mu g \cdot kg^{-1} \cdot min^{-1}$. Nevertheless, systolic arterial blood pressure decreased to 62 mmHg, and the heart rate decreased to 38 beats/min. Epinephrine was started at a rate of 0.133 $\mu g \cdot kg^{-1} \cdot min^{-1}$, with an increase in blood pressure to 100/60 mmHg. Sp_{O_2} and ET_{CO2} monitoring showed 0% and 16 mmHg, respectively.

Despite a ventilation with 100% oxygen, Sp_{O_2} remained in the range of 0 to 34% for approximately 40 min. Based on a provisional diagnosis of pulmonary embolus, 5,000 units heparin followed by 5,000 units/h was administered. Sp_{O_2} increased to 50–60%. However, the patient continued to be hypoxic for 1 h, and her condition gradually deteriorated. A bolus of 1,800,000 units followed by 12,000,000 units/h rt-PA was then administered. Ten minutes later, Sp_{O_2} dramatically increased to 100%. Arterial blood gas showed the following: *p*H: 7.328, P_{O_2}: 451.1 mmHg; P_{CO_2}: 49.2 mmHg; base excess: −0.5 (FI_{O_2} = 1.0).

Chest radiography performed in the operating room was unremarkable. The patient was transferred to the intensive care unit. Three hours later, she recovered consciousness without neurologic compromise. However, her abdomen gradually became distended. There was external evidence of severe ongoing coagulopathy with bleeding from the vagina and the abdominal incision. Multiple transfusions of blood components were transfused for the next 35 h. Exploratory laparotomy for hemostasis of bleeding was performed through a midline incision the next day. Although postoperative transfusions were necessary, coagulation test results returned to normal levels and bleeding decreased gradually. Fourteen days after delivery of a neonate, the

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patient was transferred to the obstetric ward. Pulmonary ventilation/perfusion scan 2 weeks after the operation was compatible with a large embolism to the left upper lobe; the patient eventually made a complete recovery.

Discussion

In the current case, because heparin and rt-PA were effective, pulmonary thromboembolism was the most likely cause of the intraoperative pulmonary event. The patient had preeclampsia and abruption, both of which may increase the risk of thromboembolism. In addition, the characteristics of disseminated intravascular coagulation (DIC) were noted preoperatively in the current patient. Amniotic fluid embolism is another possible cause of the pulmonary embolism in the current patient. Because amniotic fluid has a potent thromboplastic action, disseminated deposition of fibrin clots may be induced in pulmonary vasculature.[4] Esposito *et al.*[5] reported a case of amniotic fluid embolism, in which emergency pulmonary thromboembolectomy was performed successfully.

Treatment of pulmonary thromboembolism may include anticoagulation, thrombolysis, and pulmonary embolectomy.[4] Administration of anticoagulants, such as heparin, reduces morbidity and mortality by treating thromboembolism and by preventing recurrence. If administration of heparin is not effective or if a patient is unstable, thrombolytic therapy or pulmonary embolectomy is recommended. Streptokinase and urokinase have been used as fibrinolytic agents.[6] Sharma *et al.*[7] demonstrated that acute thrombolysis of pulmonary embolism with urokinase and streptokinase followed by heparin improved pulmonary capillary blood volume. Recombinant tissue plasminogen activator, more specifically a thrombolytic agent, which preferentially activates plasminogen in the presence of fibrin, reduces bleeding complications compared with urokinase and streptokinase.[8]

However, perioperative thrombolysis for the treatment of pulmonary embolism may be limited because bleeding complications are more likely to occur with thrombolysis than with heparin.[9] Obstetric delivery and major surgery within 7–10 days were classified as major relative contraindications by the National Institutes of Health (NIH) Consensus Conference because thrombolytic therapy also lyses other tissue clots.[6] In the current patient, despite continuous resuscitation, hypoxia continued for approximately 1 h, and circulatory condition gradually became worse. We thought that rt-PA therapy was worth trying, regardless of the possible complications. As a result, the patient's cardiopulmonary status improved, but massive hemorrhage developed. She was fortunate to survive.

In summary, life-threatening pulmonary embolism can occur during cesarean section, and subsequent treatment may be necessary. In addition to supportive therapy, heparin may be administered to a patient in which thromboembolism is suspected. In a patient with thrombotic pulmonary embolism for which heparin is effective but not sufficient for cardiopulmonary state to recover from the critical level, rt-PA may be worth considering, although we need to consider the possibility of severe complications.

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