

# Maternal anaphylactic shock in pregnancy

## A case report

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### Abstract

**Rationale:** Anaphylaxis is a very rare event in pregnancy, triggering maternal hypotension leading to intrapartum hypoxic-ischemic encephalopathy in infant. Furthermore, cesarean sections are performed at a high rate in anaphylactic pregnant women.

**Patient concerns:** A 34-year-old pregnant woman presented with maternal anaphylaxis following prophylactic antibiotic injection for cesarean section. Within a few minutes after initiation of intradermal skin test with cefotetan, the pregnant woman developed generalized itchy rash, chest tightness, and dyspnea.

**Diagnoses:** Several minutes after the injection of antibiotics, a diffuse urticarial rash was detected over her face and trunk followed by complaints of chest tightness and dyspnea. She was diagnosed with hypotension and hypoxia. Further, fetal heart tones showed bradycardia. A presumptive diagnosis of anaphylactic reaction induced by cefotetan was made for surgical prophylaxis.

**Interventions:** The patient was managed for anaphylaxis, via administration of epinephrine, glucocorticoid, and antihistamine. Emergency cesarean section performed under general anesthesia resulted in a favorable perinatal outcome for the fetus.

**Outcomes:** Maternal and fetal outcomes were good after prompt treatment for anaphylaxis and emergency cesarean section.

**Lessons:** This is the first reported case of anaphylaxis following cefotetan administration in pregnancy. Cefotetan, a second-generation cephalosporin, is a commonly prescribed antibiotic used to treat a wide range of bacterial infections. The case demonstrated life-threatening anaphylactic reaction during pregnancy. Even a skin test using antibiotics alone triggered anaphylaxis.

**Abbreviation:** BP = blood pressure.

**Keywords:** anaphylaxis, cefotetan, fetal distress, pregnancy, surgical prophylaxis

### 1. Introduction

Anaphylaxis is a rare event occurring during pregnancy. It is characterized by generalized hypersensitivity reaction, which is life-threatening and typically results in maternal hypotension and/or fetal morbidity as a consequence of intrapartum asphyxia. Anaphylaxis is typically triggered by exposure to foods, insect venom, natural rubber latex, or medications through an IgE-mediated mechanism.<sup>[1]</sup> Cefotetan, a second-generation cephalosporin, is commonly used for surgical prophylaxis in cesarean section. The management of anaphylaxis during pregnancy is difficult, with severe consequences for both mother and fetus. We report a patient undergoing skin prick test with cefotetan leading to intrapartum cefotetan-induced anaphylaxis during pregnancy, and prevention of devastating complications of hypoxic brain damage in a term neonate.

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### 2. Case report

A 34-year-old multigravida was hospitalized for a cesarean section at 37 weeks of gestation. Her obstetrical history included no term births/abortions, but 1 preterm birth, and 1 living child. Her surgical history included McDonald operation and Cesarean section. During her prenatal visits, the patient was treated with vaginal cerclage attributed to previous preterm birth history. The patient had no histories of medical or drug allergy. Cefotetan was administered several times previously with no adverse reaction.

Upon admission, the patient's vital signs were: blood pressure (BP) 110/80 mm Hg, heart rate 76 beats per minute, respiratory rate 19 per minute, and temperature 36.4°C. The general physical examination revealed no remarkable findings. A singleton pregnancy at 37 weeks of gestation and in cephalic presentation was documented. Electronic fetal monitoring indicated reactive fetal heart tracing, with a baseline heart rate of 140 beats per minute and nonuterine contractions.

Following admission, antibiotic skin testing of cefotetan was performed for prophylaxis in cesarean section. Intradermal skin test on forearm with a 0.04-mL injection of the 1:100 diluted solution, interpretation of the test after 20 minutes of injection, with a positive result defined as raising a 3-mm wheal. At the beginning of the antibiotic skin test, the patient complained of diffuse itching and burning, and within seconds she experienced shortness of breath, cough, and chest tightness. Several minutes later she experienced dyspnea, and a diffuse urticarial rash was observed over her face and trunk, followed by emesis. Her BP was 90/60 mm Hg, heart rate was 133 beats per minute, oxygen saturation was 93% with high-flow humidified supplemental 100% oxygen (5 L/min by mask). Further, the fetal heart revealed bradycardia (80–90 beats per minute). The presumptive diagnosis of anaphylactic reaction caused by cefotetan was made. The

patient was immediately placed in a lateral recumbent position and oxygen was administered via a face mask (10L/min). A second intravenous access was obtained, and normal saline infusion was administered. The patient received an intravenous of 50mg H1-antihistamine and 200mg hydrocortisone treatment, except epinephrine, which was effective, although abdominal pain persisted. To prevent fetal adverse outcome such as fetal hypoxia, the patient was rushed to the operating room for emergency cesarean section under general anesthesia. The maternal vital signs remained relatively stable throughout the operation. A male infant weighing 2950g was delivered with Apgar scores of 5 and 8 at 1 and 5 minutes, respectively. The infant responded to ventilation with 100% oxygen by bag and eventually breathed spontaneously.

The mother was transferred to the intensive care unit for further care at the end of surgery. After the surgery, the urine output decreased, followed by pleural effusion and pulmonary edema. Pulmonary edema was adequately controlled by Lasix and the rest of her hospital course remained uneventful. The patient was discharged home.

The study was approved by the Institutional Review Board of Soonchunhyang University Cheonan Hospital. Written informed consent was obtained from the patient for publication of this case report and accompanying images.

### 3. Discussion

Anaphylaxis is a serious life threatening, and systemic allergic or hypersensitivity reaction with immediate onset.<sup>[2]</sup> The prevalence of anaphylaxis has been reported to be 0.05% to 2%.<sup>[3]</sup> Anaphylaxis is a relatively infrequent event during pregnancy but can result in adverse outcome for the mother and fetus.<sup>[2,4]</sup> Anaphylaxis has been reported during pregnancy following exposure to insect venom, natural rubber latex, food, or medications such as antibiotics through an IgE-mediated mechanism.<sup>[1]</sup> The most common cause of drug-induced anaphylaxis is antibiotics, especially penicillin. Cefotetan-induced anaphylaxis has rarely been observed.<sup>[5,6]</sup> The incidence of cefotetan-induced anaphylactic reaction was 1.4% for surgical prophylaxis in cesarean sections.<sup>[5]</sup> Our patient was exposed previously to cefotetan antibiotics several times without any allergic reactions, suggesting that the immunologic changes in pregnancy may have triggered a new onset of sensitization. An altered immunologic status due to increased progesterone level during pregnancy may predispose pregnant women to anaphylaxis.<sup>[7,8]</sup>

Symptoms involve respiratory and gastrointestinal (eg, dyspnea, vomiting, abdominal pain), skin and mucosal (eg, urticaria, itchy rash), and cardiovascular and central nervous systems (eg, hypotension, feeling faint, seizures).<sup>[9]</sup> Pregnancy-related symptoms include lower back pain, vaginal and vulvar itching, fetal distress, and preterm labor.<sup>[10]</sup> Maternal hypotension and hypoxia present with potentially life-threatening complications for mother and fetus. Maternal hypotension and vasoconstriction decrease uterine blood flow, and maternal hypoxia triggers intrapartum asphyxia resulting in ischemic encephalopathy, severe central nervous system damage, developmental disorder, or death.<sup>[4,10,11]</sup>

Anaphylaxis was diagnosed clinically without confirmation by laboratory testing. Most immediate reactions to cephalosporins are characterized by positive results to skin prick tests and detection of serum-specific IgE antibodies.<sup>[12]</sup> Specific serum IgE levels cannot be detected during labor. Skin prick test has been

the most generalized approach for diagnosing immediate hypersensitivity, despite its variable sensitivity.<sup>[12]</sup>

Management of anaphylaxis in pregnancy is similar to that in nonpregnant women. The recommendations for management of acute anaphylactic episodes include immediate cessation of the triggering factors, airway and BP support, prevention of hypoxia with 100% oxygen, aggressive fluid resuscitation with normal saline and various medications, such as epinephrine, antihistamines, and corticosteroids.<sup>[2]</sup>

However, several aspects involving the management of life-threatening onset during pregnancy are still disputed. Epinephrine is usually recommended in nonpregnant patients as a vasopressor. The dosage of epinephrine has been standardized (0.01mg/kg of 1:1000, 1mg/mL solution) and administered intramuscularly in the mid-outer thigh.<sup>[9]</sup> Although epinephrine improves maternal hypotension, it may induce uterine vasoconstriction, resulting in hypoxic damage to the fetus as well as ventricular arrhythmias, hypertensive crises, and pulmonary edema. Therefore, epinephrine was not administered to the mother to avoid hypoxic injury to the fetus.<sup>[9,13]</sup>

Instead, the patient was immediately treated with oxygen supplementation, normal saline infusion.

To the best of our knowledge, this case is the first reported anaphylaxis characterized by maternal shock and fetal bradycardia induced by cefotetan exposure in pregnancy for surgical prophylaxis in cesarean sections. With prompt treatment, including the administration of glucocorticoids, and emergency cesarean section, the mother and the fetus showed a favorable outcome. Several reports of antibiotic anaphylactic shock during pregnancy were published previously.<sup>[14]</sup> However, it usually occurs after intravenous injection, and this is the only case triggered with the intradermal skin test. It was the first incidence of anaphylaxis following multiple previous treatments, which failed to trigger any hypersensitive reaction. Therefore, even if the drug has been used safely, skin tests should be conducted carefully every time. Nevertheless, the sensitivities of the cephalosporin drugs used for the prevention of anaphylactic reactions have been reported to be as low as 30.7% to 69.7% in a few studies,<sup>[15]</sup> suggesting the safety of cephalosporin antibiotics. The clinical value of the reaction test is limited and cannot be absolute.

This case of anaphylactic shock was observed only with intradermal skin test. Since antibiotic dilution methods for skin reaction tests are not known for accuracy, further skin tests are needed. Further, the antibiotic skin test needs to be confirmed for safety each time it is performed.

Prompt intervention and first aid are the most important factors to treat anaphylactic shock during pregnancy under uncertain conditions.

Controversies still exist regarding the optimal timing and mode of delivery of the neonate following anaphylaxis during pregnancy.<sup>[16,17]</sup> The neonatal risks of maternal anaphylaxis are associated with neonatal morbidity and mortality with maternal hypoxemia, hypotension, or both. Anaphylaxis has devastating effect on fetal oxygenation and circulation. Fetal oxygenation is directly compromised by maternal hypoxemia and indirectly compromised by maternal hypotension leading to reduced uterine blood flow. The fetus compensated for hypoxemia and hypotension by means of redistribution of blood to vital organs, especially the brain. When this mechanism fail, the fetus have hypoxic-ischemic encephalopathy and permanent central nervous system damage.<sup>[18]</sup> In the face of inadequate maternal resuscitation, immediate cesarean delivery might yield a

better outcome for the baby. On the contrary, continuing and aggressive hemodynamic resuscitation of the mother until fetal bradycardia is resolved can potentially avert an emergency.

A limitation is predicting acute hypersensitivity reactions of cefotetan has not been standardized, although the intradermal skin test has been widely used for hypersensitivity.<sup>[19]</sup>

A second limitation of this case is the lack of information on long-term neonatal outcome about neurology.

It is therefore critically important that concerted effort is needed to design a treatment protocol that protects both mother and neonate from the disastrous consequences of anaphylaxis and standardized guidelines for antibiotic skin testing are needed for the safe.

## Author contributions

**Conceptualization:** Hye Ji Jeon, Aeli Ryu.

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