

## Case Report

# Suspected Systemic Anaphylaxis to Fresh Frozen Plasma during a Cesarean Section in a Young Primigravida with HELLP Syndrome

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Anaphylaxis is a severe allergic reaction, associated with high morbidity and mortality if not detected and treated rapidly. In the United States, 1-17% of the population is at risk for anaphylaxis, of which 0.02% is at risk for fatal reactions. The incidence of intra-operative anaphylaxis is between 1:3500 and 1:20,000 [1]. Currently, patients are up to 1000-times more likely to experience non-infectious serious hazards of transfusion (NISHOT) than an infectious transfusion reaction. We report a case of anaphylactic reaction to fresh frozen plasma in a young primigravida with HELLP syndrome during an emergency cesarean delivery under general anesthesia.

**Introduction**

The case of a 20 year old primigravida with preeclampsia and HELLP syndrome in early labor, who developed an anaphylactic reaction to Fresh Frozen Plasma (FFP) during emergency cesarean section, is described. Following the cesarean, the patient was noted to have a diffuse total body rash and edema. Her endotracheal leak test was consistent with laryngeal edema. Serum tryptase levels sent within 30 minutes of noticing the rash was negative. She responded to intravenous medications and was extubated uneventfully the following day with no sequelae.

**Consent for publication**

The patient has given written permission for the authors to publish the case report.

**Case Description**

A 20 year old primigravida presented in early labor, complicated by pre-eclampsia and HELLP syndrome, as diagnosed by the obstetrician per the patient's clinical symptoms and the decreased platelet number and increased liver enzymes. Her past medical history was significant for childhood psychosis and migraine headaches, treated with antidepressants and antipsychotics in the past. She had no known drug allergies or previous incidents of anaphylaxis. The patient received magnesium for seizure prophylaxis and penicillin for Group B streptococcal (GBS) bacteriuria. Her platelet count was deemed adequate for neuraxial anesthesia and she had an uneventful epidural catheter placement. Patient-controlled epidural analgesia was inadequate despite additional boluses of lidocaine and bupivacaine. The epidural catheter was replaced 8 hours later in the setting of anxiety and poor pain control.

The decision to perform a cesarean delivery was made for failure to progress in labor and the worsening clinical status of the parturient. Her repeat laboratory values showed a decreasing platelet count

from 120,000 to 66,000. The epidural catheter was bolused with 2% lidocaine with epinephrine and sodium bicarbonate, her sensory level was confirmed as T3 and the surgeon was asked to proceed. Since she denied any history of medication allergies, she received IV Cefazolin per the obstetric pre-operative antibiotic protocol at our institution.

Despite a negative clamp test, the patient experienced sharp pain on incision. Rapid-sequence, general anesthesia was induced with a 6.5 of endotracheal tube. The patient received Propofol, Succinylcholine, Fentanyl, ephedrine, phenylephrine and oxytocin during the procedure.

Her baseline systolic blood pressure was in the range of 150-175mmHg and diastolic 90-100mmHg with a heart rate of 100-120bpm. After induction, her blood pressure dropped to approximately 105/50 for about 20 minutes and was eventually responsive to small incremental doses of ephedrine and phenylephrine.

In the setting of a low platelet count and fibrinogen level, a 6-pack of platelets was infused followed by 1 unit of fresh frozen plasma soon after induction. The cesarean delivery was performed and the baby was delivered with APGAR scores of 1 and 7 at one and five minutes respectively.

After the procedure, the patient was noted to have a diffuse rash on her abdomen, legs, and arms, described as red and hives-like. She also had facial and total body edema. She was afebrile. Her rash improved with diphenhydramine 50mg IV and dexamethasone 10mg IV. An endotracheal tube cuff-leak test was performed and it was consistent with the presence of laryngeal edema. The patient was transferred intubated to the surgical intensive care unit for further monitoring and interventions as she continued to have facial, laryngeal, and total body edema at the time of transfer. There was no difficulty in ventilating the patient post-operatively; neither poor gas exchange/compliance nor residual hypotension was observed after the procedure. She was monitored in the ICU overnight and

extubated the following morning with no sequelae.

## Discussion

With the declining risk of transfusion-transmitted infectious disease, noninfectious serious hazards of transfusion (NISHOTs) have emerged as the leading complication of transfusion. Currently, a patient is up to 1000-fold more likely to experience a NISHOT than an infectious complication of transfusion. Furthermore, the FDA has reported that death rates due to hemolytic reactions alone are more than twice those due to all infectious hazards of transfusion.

Transfusion reactions associated with hives (in the absence of other symptoms) are termed “urticarial”. These are estimated to occur in 1% -3% of transfusions. In addition to urticaria, “allergic” reactions may include edema, pruritus and angioedema.

Major “anaphylactic” reactions can also occur with hypotension, bronchospasm, stridor, and gastrointestinal symptoms. These are relatively rare, occurring 1 in 20,000 to 1 in 50,000 transfusions. Immunoglobulin Ig E or anti-IgA antibodies are often implicated in severe reactions, although the cause and effect are not always evident [1-4].

The cause of less severe allergic reactions is often unclear, but several different mechanisms have been implicated, including the presence of pre-existing antibodies to serum proteins (eg, albumin, complement components, IgG, and IgA), human leukocyte antigen antibodies, transfusion of allergens, and passive transfer of IgE antibodies.

Elevated levels of serum tryptase occur in both anaphylactic and anaphylactoid reactions, but a negative test does not exclude anaphylaxis. Tryptase is a mast cell enzyme and is released into the serum during mast cell activation and degranulation. Serum tryptase levels peak in 1 to 2 hours and may return to normal within 3 to 4 hours, but it can remain elevated for up to 48 hours. Serum tryptase has never been studied as a potential diagnostic marker for anaphylactic or anaphylactoid transfusion reactions or to differentiate anaphylaxis secondary to transfusion from TRALI. Serum tryptase deserves further study as a potential marker for severe allergic transfusion reactions, with or without anaphylaxis.

Rapid onset of increased secretions from mucous membranes, increased bronchial smooth muscle tone, decreased vascular smooth muscle tone, and increased capillary permeability occur after exposure to an inciting substance. Cardiovascular effects result from decreased vascular tone and capillary leakage. These effects are produced by the release of mediators, which include histamine, leukotriene C4,

prostaglandin D2, and tryptase.

In the classic form, mediator release occurs when the antigen (allergen) binds to antigen-specific immunoglobulin E (IgE) attached to previously sensitized basophils and mast cells. Mediators are released almost immediately when the antigen binds. In an “anaphylactoid” reaction, exposure to an inciting substance causes direct release of mediators, a process that is not mediated by IgE.

The most common inciting agents in anaphylaxis are parenteral antibiotics (especially penicillins), IV contrast materials, *Hymenoptera* stings, and certain foods (most notably, peanuts). Oral medications and many other types of exposures also have been implicated. Anaphylaxis also may be idiopathic.

With regard to the patient presented here, evaluation for IgE-mediated hypersensitivity was negative for succinylcholine, Lidocaine, Fentanyl, and Propofol. Her serum tryptase level obtained around the time of the reaction was reassuringly normal, reducing the likelihood of a robust anaphylactic reaction to these medications. Patient had no history of allergy to cephalosporin which was administered in earlier days. Two grams of cephalosporin were given 3 hours prior to the procedure without noted reaction. Her latex-specific IgE was also negative. The most likely inciting agents, based on the temporal relationship to the rash and edema, were blood products. She had received a 6-pack of platelets and 1 unit of fresh frozen plasma during the procedure; however, discussion and tests with the blood bank (antibody screen and DAT) revealed no evidence of a hemolytic transfusion reaction or serologic incompatibility. The blood bank consultants did feel, however, that acute allergic reaction to transfusion was a possibility, given the timing of the reaction. Of note, the testing did not evaluate for non-IgE-mediated hypersensitivity reactions and non-hypersensitivity reactions (such as the non-allergic side effects of medications). As a result, if these medications are to be used in the future, we recommend evaluation for non-IgE-mediated reactions.

## References

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