Surviving Anaphylactoid Syndrome of Pregnancy: A Case Study

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ABSTRACT

Anaphylactoid Syndrome of Pregnancy (ASP) is a rare complication of delivery in mother and/or infant during the process of birth. Known as either Anaphylactoid Syndrome of Pregnancy or Amniotic Fluid Embolism, the maternal mortality rate worldwide for this complication is between 10 and 16% while the fetal mortality rate is upwards of 30%. The majority of maternal survivors are expected to have long - term neurologic deficit. While the majority of infants will survive, the majority will also incur some form of neurologic defect. This report is of a case in which both the mother and infant survived with discharge occurring at eleven days for the mother and eighteen days for the infant.

ABBREVIATIONS: ASP - Anaphylactoid Syndrome of Pregnancy, AFE - Amniotic Fluid Embolism, DIC - Disseminated Intravascular Coagulation, FFP - Fresh Frozen Plasma

INDEX TERMS: Anaphylaxis/ therapy, Disseminated Intravascular Coagulation/ physiopathology, Embolism, Amniotic Fluid/ physiopathology, Multiple Organ Failure/ complications, Postpartum Hemorrhage, Pregnancy Complications/ physiopathology

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Patient History

A 35-year-old Caucasian woman, 33 weeks pregnant and considered to be of high risk due to her age and four prior pregnancies, presented to the Emergency Department with complete placenta previa (abnormal positioning of placenta close to or over cervix) and bleeding. At 18 weeks gestation, both placenta previa and placental lakes (enlarged spaces in the placenta filled with maternal blood) were demonstrated by MRI. At 22 weeks another MRI was performed in order to determine if placenta accreta (abnormally deep attachment of the placenta into the myometrium) was a concern for the patient. Although there were limited views of the posterior placenta, anterior accreta was not seen. At 26 weeks a third MRI was performed and the fetus looked to be growing at a normal rate, but there was an increased number of placental lakes seen and the posterior previa is still noted, with an anterior involvement at this time. At 27 weeks the patient was admitted with vaginal bleeding and was given two doses of betamethasone (a glucocorticoid steroid) to decrease inflammation. After five days, the patient was discharged and placed on bed rest. At 30 weeks enlarged placental lakes were seen with the largest at 17 centimeters in diameter. During this visit, plans were put in place to administer "rescue steroids" at 33 weeks 5 days, and a Repeat Low Transverse Caesarian section (RLTCS) similar to a previous delivery was to be performed at 34 weeks. One day after the administration of the steroids, the woman was seen in the emergency department (ED).

Given her clinical presentation in the ED, an emergency C-section was performed. After the neonate was delivered, it was noticed that the uterus became flaccid or atonic. The patient was already on intravenous oxytocin so 0.2 mg of methylergonovine maleate was given intramuscularly to the patient. These agents firmed up the uterus slightly but blood continued to pool in the lower uterus. The patient then experienced a tonic spasm, became bradycardic and hypotensive

signaling a complete circulatory collapse. Chest compressions were started, and an emergency hysterectomy was initiated to stop blood loss. To correct the blood loss, the patient had a central venous line placed and multiple units of compatible packed red blood cells, fresh frozen plasma, platelets and cryoprecipitate were transfused.

Historical Overview

First widely recognized in 1941 article by Steiner and Luschbaugh, the histopathology findings in the lungs of women dying of sudden shock during labor and delivery include amorphous eosinophilic material, mucin, and squamous cells.[1] The first well-documented case of maternal survival was published by Resnik, et al in 1976.[2] The syndrome can be detected during the second trimester up to 48 hours post partum. Risk factors are not consistently seen and currently this condition is not considered to be preventable.[3] Table 1 lists some of the more commonly seen signs of ASP onset.

Table 1. Risk Factor Assessment of possible ASP. Some common signs of potential ASP. All of these risk factors are not consistently found in all patients.

Advanced maternal age
Cervical laceration
Chorioamnionitis
Intrauterine fetal death
Male fetal sex
Multiparity
Oxytocin use
Previous caesarian section
Placenta accreta
Uterine rupture

At present, a biphasic model of pathophysiology has been proposed.[4] During the initiating phase, amniotic fluid and fetal cells enter the maternal circulation stimulating biochemical mediators causing vasospasm and constriction in the pulmonary artery. The resulting pulmonary hypertension causes elevated right ventricular pressure leading to hypoxia. The cascade of myocardial and pulmonary damage causes left heart failure and acute respiratory distress syndrome. The second phase is characterized by uterine atony, hemorrhage, and disseminated intravascular coagulation. If treated properly and immediately, this syndrome is manageable, however, one of the most serious potential sequellae of this syndrome is mental deficiency in some form, in either the mother or fetus.[5]

Pathogenesis

The acute hypotension (cardiac arrest), acute hypoxia (respiratory arrest), and Disseminated Intravascular Coagulation (DIC) can occur during the birthing process or postpartum. In this case the patient experienced a complete cardiovascular collapse consistent with the first two criteria of the diagnosis. Soon after, the patient experienced DIC, as the entire hemostatic system was triggered as a response to systemic trauma. In the classic description of DIC, it is noted that massive hemorrhage is the first sign of this complication since the thrombi created to stop the massive bleeding are not working properly. [6]

Anaphylactoid syndrome of pregnancy is often referred to as the common cause for the majority of maternal deaths during pregnancy and labor.[7] This is a rare syndrome with an occurrence of between 1:8,000 to 1:83,000 births but accounts for up to eighteen percent of maternal deaths.[8] This patient had a high overall risk of maternal fatality as she was within the older age group, had four previous pregnancies, a history of previous C-Sections with one planned for this pregnancy, placenta previa, large placental lakes, DIC, and massive blood volume loss.

The two largest factors in successful treatment are access to available blood and/or blood products, and the speed with which they can be available and transfused. Presently, there is no laboratory tests that can be performed ahead of time in order to warn of such a reaction, and no fast acting definite treatment. There is some thought that serum tryptase can be measured to give an idea of increased risk, although most clinical laboratories do not perform this in-house. As such, while a valuable piece of evidence, it is not available in a time frame necessary for use. Tryptase is a degranulation product of basophil and mast cell stimulus that is released at the same time as histamine and other vasoactive amines that contribute to vascular collapse. Tryptase is measured using a fluoroimmunoenzymatic assay which measures total tryptase and there are multiple companies that utilize this assay. Total tryptase has a reference range of 1-15 mg/dL in normal serum. It has been seen that an increase in serum tryptase coincides with symptoms of ASP or other anaphylaxis related syndromes.[9] The

problem with using this test as a marker for the syndrome, is that the serum levels do not peak until one to two hours after the first onset of the syndrome. This along with the lengthy turn around time, makes this test more of a confirmatory test as opposed to a test to screening test.

Maternal mortality rates have been reported to range from 26 to 86%.[10] This vast range is due to the relatively low knowledge about this syndrome and the variety of symptoms that can be associated with this syndrome. Not every case of ASP will have all three of the major signs; hypotension, hypoxia and coagulopathy as DIC is not present in all cases. In those cases where it is present, such as this case, mortality is on the higher end of the range.[2] This patient was in the group with the overall highest chances of maternal fatality due to previous C-section; 30-39 age group; DIC; more than four pregnancies; placenta previa; placental lakes; and massive blood volume loss.[6] With all of these factors her chances of survival were slim.

Relevant Laboratory Data

Prior to admission, the patient's blood specimen was tested and found to be Group A positive with a negative antibody screen. Four units of packed red blood cells were originally cross-matched and ready for the surgery. During the critical moments of this syndrome, most of the laboratory results are non-informative as the patient is experiencing vascular collapse at a critical rate and specimens take time to collect, transport, test, and report result. Given this, the laboratory's value is to confirm that the treatment is working and not harming the patient. However, in this case, the availability of the first four units allowed time to prepare and release the additional components.

Since one of the main problems in this case is DIC, the coagulation levels are very important. The two most critical specimens showing the severity of the patient's DIC were taken thirty minutes apart (Table 2). The first specimen (drawn after onset of symptoms) had a Prothrombin Time (PT) of 25.7 seconds; an Activated Partial Thromboplastin Time (aPTT) of 27.6 seconds; the fibrinogen was 84 mg/dL; and the D-Dimer was above analytical range (the analyzer used has an upper analytical range of 20 mg/dL). The D-Dimer was measured on the STA-R Evolution using a photometric method. In this method when monochromatic light is allowed to pass through the suspension of patient plasma and latex particles, the light that is detected by the sensor is used to determine the concentration in the sample.

Table 2. Laboratory Results over time during ASP

	Pre-ASP Sample drawn at 0705	First Sample Drawn at 0845	Second Sample Drawn at 0915
PT (seconds)	13.1	25.7	22.1
aPTT (seconds)	23.4	27.6	68.3
Platelet Count (10^9/L)	213	58	136
Fibrinogen (mg/dL)	326	84	110
D-Dimer	Not Performed	>Analytical Range	>Analytical Range
Hemoglobin (g/L)	110	87	89
Hematocrit (L/L)	0.317	0.250	0.257

The second specimen had a PT of 22.1 seconds; an aPTT of 68.3 seconds; the D-Dimer was again above analytical range; and the fibrinogen was 110 mg/dL. Platelet counts were 58 x 10^9/L from the first specimen, and 136 x 10^9/L in the second specimen. All five key results support a diagnosis of DIC.

The extensive blood loss caused hemoglobin and hematocrit values of 87 g/L and 0.25 L/L in the first sample and 89 g/L and 0.257 L/L in the second. These levels were significantly lower when compared to the patient's previous hemoglobin and hematocrit results of 116g/L and 0.34 L/L, which were from the most recent prenatal checkup. The massive hemorrhage also caused a metabolic acidosis characterized by a decrease in blood pH and bicarbonate concentration. The patient's pH dropped from 7.520 in the first sample to 7.120 within 30 minutes. The pH stayed acidic until the patient finally began to stabilize. The bicarbonate also follows this trend showing that this acidosis is caused by the excessive loss of blood.[4] All of these laboratory results are typical of ASP.

Treatment and Prognosis

Treatment for this syndrome includes controlling the hemorrhaging, restarting the cardiovascular system, replacement of blood loss and correction of the DIC.[11] Each problem needs to be dealt with separately and in order of severity.

The largest issue for this patient was the massive hemorrhage. The surgeons cauterized, sutured and tied

off any large sections of hemorrhages seen in order to slow the bleeding. The next issue to solve was the blood loss, as this may correct multiple problems at once. A central venous line was placed so that blood could be transfused. The patient received multiple units of blood and blood products in order to compensate for the massive loss. All told, 27 units of packed red blood cells, 16 units of fresh frozen plasma, three units of platelets and one unit of cryoprecipitate were used to stabilize the patient. The platelets, fresh frozen plasma and cryoprecipitate were pivotal in replacing the hemostatic components consumed by the DIC, and the packed red blood cells replaced the amount lost due to the hemorrhage and corrected the hypoxia.

Patient Follow Up:

Since a common secondary sequella is mental deficiency (to either mother, child, or both), a psychiatric evaluation was performed on the patient after she had recovered from this traumatic episode. She suffered from a panic attack after a minor bleeding incident when sutures were removed. For the panic attack the patient was given 0.5 mg of lorazepam. At the time of discharge, there were no noticeable mental impairments but the patient was advised to follow up with a therapist for post traumatic stress disorder (PTSD).

Case Conclusion

The outcome of this situation was made possible by the early notification of the laboratory to the potential of a high-risk delivery. That this notification included the evaluation of the placenta previa and increasing size of the placental lakes supported the preoperative testing of compatible blood products. The ability of the blood bank to release these units immediately upon request certainly played a role in the reestablishment of the circulatory system and in supporting minimal oxygen saturation early on in the crisis. The timely reporting of hemostasis testing supported the medical decision to begin infusing the fresh frozen plasma, platelets and cryoprecipitate. Due to the rapid response, both mother and child survived. They were both released from the hospital within a relatively short time and at the time of discharge neither mother nor child had any adverse sequellae. The fear of delayed symptoms was eased when the patient returned for her postpartum check up and no mental disabilities were noted in mother or child. Both seemed to be in excellent physical health.

REFERENCES

1. Steiner PE, Lushbaugh CC. Maternal pulmonary embolism by amniotic fluid as a cause of obstetric shock and unexpected deaths in obstetrics. JAMA 1941;117:1245-54.
2. Resnik R, Swartz WH, Plumer MH, Benirschke K, et al. Amniotic Fluid Embolism with Survival. Obstet Gynecol 1976;47:295-8.
3. Peterson, EP, Taylor, HB. Amniotic fluid embolism. An analysis of 40 cases. Obstet Gynecol 1970;35:787.
4. Clark, SL, Montz, FJ, Phelan, JP. Hemodynamic alterations associated with amniotic fluid embolism: A reappraisal. Am J Obstet Gynecol 1985;151:617.
5. Clark, SL, Hankins, GD, Dudley, DA, et al. Amniotic fluid embolism: Analysis of the national registry. Am J Obstet Gynecol 1995;172:1158.
6. Mant MJ, King EG. Severe acute DIC. Am J Med 1979;67:557-63.
7. Gilmore DA, Wakim J, Secrest J, Rawson R. Anaphylactioid syndrome of pregnancy: A review of the literature with latest management and outcome data. AANA J 2003;71(2):120-6.
8. Stein P, Matta F, Yaekoub A. Incidence of amniotic fluid embolism: reaction to caesarian section and to age. JWH 2009;18(3):327-9.
9. Schwartz, LB. Diagnostic Value of tryptase in anaphylaxis and mastocytosis. Imunol Allergy Clin N Am; 2006;26:451-63.
10. DeJong MJ & Fausett MS. Anaphylactoid Syndrome of pregnancy: A devastating complication requiring intensive care. AJCC 2003;23(6):42-8.
11. Moore J and Baldisseri MR. Amniotic fluid embolism. Crit Care Med 2005;33:10 (Suppl.)

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