

Suspected Amniotic Fluid Embolism Following Amniotomy: A Case Report

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Amniotic fluid embolism (AFE), also referred to as anaphylactoid syndrome of pregnancy, is a rare obstetric emergency that may manifest itself at any time during pregnancy. AFE is believed to occur when the constituents of amniotic fluid enter the maternal circulation, leading to varying degrees of multiorgan compromise. AFE was first described in 1926, gaining widespread recognition in 1941.

This article describes the pathogenesis of AFE, including theories of its immunological mediation available in the literature. The most current diagnostic and treatment

modalities are discussed, including several novel therapies. A case report of a 40-year-old parturient who suffered probable AFE following amniotomy, with the development of cardiopulmonary compromise, neurologic involvement, fetal distress, and coagulopathy, is outlined. The patient survived emergency cesarean delivery and hysterectomy with no residual physiologic deficits.

Key words: Amniotic fluid embolism, anaphylactoid syndrome of pregnancy, disseminated intravascular coagulation, obstetric emergency.

Obstetric emergencies present unique challenges to anesthesia providers, because interventions must be directed at achieving the best possible outcomes for both the parturient and the fetus. Amniotic fluid embolism (AFE) is a rare obstetric condition that may present as a true emergency, requiring immediate intervention by skilled clinicians. In 1926, Meyer¹ described the presence of vernix caseosa in the pulmonary vasculature of a parturient who died peripartum. A major emphasis was not placed on AFE until 1941, when Steiner and Lushbaugh² published an article outlining postmortem examination findings of amniotic fluid constituents, including fetal squamæ, mucin, lanugo hairs, and occasional meconium in the pulmonary vasculature of 8 parturients who died during the peripartum period. Thompson and Budd³ later refuted the presence of amniotic fluid constituents in the pulmonary vasculature as diagnostic of AFE. They argued that small amounts of fetal squamæ enter the maternal circulation, even in the absence of suspected AFE. There is a strong correlation between embolization of amniotic fluid and peripartum morbidity and mortality. Since 1926, more than 300 reports of AFE have appeared in the medical literature.⁴

There is no singular clinical presentation for AFE. Most likely, many subfulminant cases occur yearly. Half of all patients present with dyspnea, tachypnea, and cyanosis, while 25% present with shock that seems inconsistent with estimated blood loss.⁵ Pulmonary edema develops in 25% of cases, and 25% of patients die within the first hour after embolization.⁵ A small subset of patients, 10%, present with seizure activity, as is described in the case report presented in this article.⁵

The hallmark signs of AFE are respiratory failure, neu-

rologic symptoms, hypotension, and disseminated intravascular coagulation (DIC).⁶ Whatever the precise presentation in a particular patient, the diagnosis of AFE can be made with great confidence, after taking into consideration the suddenness, severity, and timing of symptom onset, while being able to eliminate other causative factors.⁴ Care is supportive and directed at treating the suspected underlying cause and ensuing symptoms. The mainstays of treatment include hydration, cardiopulmonary resuscitation, administration of blood products, and the use of vasopressors.⁷ Surgical and pharmacologic measures are instituted as needed.

Masson⁸ links AFE to several predisposing conditions, including advanced maternal age, tumultuous labor, intrauterine fetal demise, high parity, fetal macrosomia, placenta accreta, uterine rupture, and cesarean delivery. Prerequisites for the embolization of amniotic fluid have been described in the literature. These include ruptured amniotic membranes, ruptured cervical or uterine blood vessels, and the presence of a pressure gradient between the uterus and its vasculature, such as that created by rupture of amniotic membranes, intrauterine saline infusion, and the use of uterine stimulants.⁹⁻¹¹

Several theories exist for the pathophysiological progression of the response to AFE. Bradykinin, trypsin, complement activation, leukotrienes, and antigen-antibody responses have been implicated in its pathogenesis.¹²⁻¹⁵ Perhaps with a better understanding of the precise mechanism of the physiologic response to this condition clinicians will be able to tailor interventions to improve outcomes for patients.

Case Summary

A 40-year-old woman was admitted to the labor floor at a

major tertiary referral center, at 41 weeks' gestation, for postterm induction of labor. The patient had previously delivered vaginally at term, with no reported complications, and denied any history of abortions.

Medical history included gestational diabetes, during the current pregnancy, that was questionably controlled by diet alone. No other medical or surgical history or allergies were reported. The patient said that she was not currently taking any medications.

Induction of labor was carried out with intravenous (IV) oxytocin for initiation and augmentation of uterine contractions and cervical misoprostol to induce cervical ripening. Fetal heart rate monitoring revealed an appropriate rate and pattern throughout induction.

At 4-cm dilation, 80% cervical effacement, and -2 station, the patient reported severe discomfort associated with onset of contractions. The anesthesia service team was consulted for management of labor pain.

The patient's history was reviewed and the anesthesia team performed a physical examination. Continuous epidural and combined spinal-continuous epidural neuraxial analgesia options were discussed. The patient consented to a combined spinal-continuous epidural.

Laboratory analyses on admission revealed hematocrit (HCT) level, 33.1%; hemoglobin (HGB) level, 10.8 g/dL; platelet count, 198,000/L; potassium level, 3.9 mEq/L; blood urea nitrogen level, 8 mg/dL; creatinine level, 0.5 mg/dL; and blood glucose level (BG), 123 mg/dL. Pulse rate was 103/min; blood pressure (BP), 113/54 mm Hg; oxygen saturation on room air, 99%; and respirations, 23/min. An 18-gauge IV catheter was in place with lactated Ringer's solution infusing at 125 mL/hour.

An atraumatic combined spinal-continuous epidural insertion was performed at approximately the L4 to L5 spinal interspace using a 17-gauge Touhy epidural needle with loss of resistance to saline at 6.5 cm. A 27-gauge Whitacre spinal needle was advanced through the epidural needle with a palpable dural puncture and flow of clear cerebrospinal fluid without blood. Fentanyl, 15 µg, and 0.25% bupivacaine in 8.25% dextrose, 0.5 mL, were given intrathecally, as per protocol at this facility. The spinal needle was withdrawn, 2 mL of preservative-free normal saline was injected through the epidural needle, and a 19-gauge epidural catheter was advanced easily and secured at 11.5 cm at the skin. Aspiration for blood through the catheter was negative. The patient denied paresthesias or discomfort throughout the procedure. Strict sterile technique was used. A continuous epidural infusion of 0.083% bupivacaine with fentanyl, 3.3 µg/mL, in a preservative-free normal saline base was begun at 12 mL/hr. Continuous epidural infusion pump settings were verified twice.

At the end of the procedure, the patient reported relief of labor pain with a thoracic 9 dermatome sensory level to cold. Vital signs before and after the procedure re-

mained stable. A urethral catheter was inserted to provide bladder emptying and assess urine output, as per obstetric service protocol at this facility. Approximately 90 minutes after initiation of epidural infusion, the patient reported continued comfort during contractions, with no motor blockade.

Approximately 3 hours after initiation of labor analgesia, the anesthesia service team was called emergently to the patient's room. When the anesthesia team on call arrived, the patient was unresponsive to verbal or tactile stimuli, with eyes open and fixed in the midline. Oxygen saturation by pulse oximetry was 96% on room air, with evidence of airway obstruction. Oxygen was applied at 15 L/min via Ambu bag, and chin tilt was performed. The patient's jaw was clenched tightly, so an oral airway could not be inserted. Oxygen saturation increased to 100%, so insertion of a nasal airway was not attempted. Other vital signs were BP, 82/38 mm Hg; pulse rate, 110/min; and respirations, 28/min. Fetal heart rate ranged from 60 to 70/min by external monitor, with little discernable variability. Intravenous phenylephrine, 50 µg, was given, which resulted in an increase in BP to 104/49 mm Hg. The continuous epidural infusion was turned off and the epidural catheter was capped.

The obstetrician said that approximately 5 to 10 minutes following amniotomy for augmentation of labor the patient became rigid and unresponsive, and her left hand twitched rapidly. Before amniotomy, the patient was calm, pleasant, communicative, and reported excellent labor analgesia. Given the low fetal heart rate, obvious need for immediate cesarean delivery, inability to maintain an effective airway, and the patient's change in mentation, the decision was made to secure the airway before transport to the operating suite. Cricoid pressure was applied and orotracheal intubation was facilitated with propofol, 50 mg IV; phenylephrine, 50 µg IV; and succinylcholine, 100 mg IV. The trachea was intubated under direct visualization with a 7.0-mm endotracheal tube. Positive bilateral breath sounds, chest rise, and condensation in the endotracheal tube were observed, and cricoid pressure was released. Mean arterial pressure (MAP) increased by 5 mm Hg after intubation, maintaining 100% oxygen saturation. Fetal heart rate continued to range from 60 to 70/min, with continued loss of variability. Chest auscultation revealed bilateral coarse crackles. Furosemide, 80 mg IV, was ordered by the obstetrician for suspected pulmonary edema. An additional 18-gauge IV catheter was inserted and a lactated Ringer's infusion begun. The patient's bedside BG level was 110 mg/dL. The anesthesia and obstetric teams agreed that the suddenness and severity of symptoms, and their correlation with artificial rupture of membranes, were consistent with the textbook presentation of AFE. The patient was transported to the operating suite for emergency cesarean delivery, with Ambu bag-endotracheal tube ventilation.

When the patient arrived at the operating suite, her breath sounds were positive bilaterally, and positive end-tidal carbon dioxide was detected. Vital signs were: oxygen saturation level, 100%; BP, 78/33 mm Hg; and pulse rate, 125/min. Inhaled anesthesia was induced with nitrous oxide, 1.5 L/min, and oxygen, 1.5 L/min. Mechanical ventilation was initiated at a rate of 10 breaths/min, tidal volume at 650 mL, positive end-expiratory pressure of +5 cm H₂O, and inspiration:expiration ratio of 1:2. Peak airway pressure was 23 cm H₂O. End-tidal carbon dioxide measurement was 39 mm Hg 5 minutes after initiation of mechanical ventilation. Intravenous phenylephrine, 50 µg per bolus, was titrated 3 times before delivery to maintain systolic BP above 100 mm Hg. Intravenous lactated Ringer's solution was initiated at moderate free flow through both IV catheters. Bispectral index (BIS) analysis was instituted after induction, with a reading of 48 to 56 throughout surgery. Core body temperature was measured by oesophageal temperature probe, ranging from 35.2°C to 36.3°C throughout surgery. An upper body forced-air warming blanket was applied.

Skin incision was made 4 minutes after arrival in the operating suite, and the fetus was delivered 3 minutes after skin incision. A large amount of meconium was noted in the amniotic fluid. The neonate was transferred to the care of the neonatal resuscitation team. APGAR (The American Pediatric Gross Assessment Record) score at 1 minute was 1, and the score at 5 minutes was 5. Immediately after delivery, midazolam, 5 mg IV, and fentanyl, 200 µg IV, were given. Muscle relaxation was achieved with rocuronium bromide, 30 mg IV. Additional doses of rocuronium bromide were given throughout the procedure, in increments of 10 mg, to maintain a 1-twitch response to a train-of-four stimulus.

Immediately after delivery, 40 units of oxytocin were placed in a liter of lactated Ringer's solution and maximal free-flow IV administration was begun. Approximately 4 minutes after delivery, the uterus remained atonic, with heavy bleeding from incision margins and placental implantation site. Oxytocin infusion was continued. Additional midazolam, 5 mg, and fentanyl, 100 µg IV, were given, as administration of an inhaled volatile anesthetic agent was contraindicated. Methylergonovine maleate, 0.2 mg, was given intramuscularly (IM), without increase in uterine tone. Carboprost tromethamine, 0.25 mg, was given IM 3 minutes after methylergonovine maleate, with continued uterine atony. Both methylergonovine maleate, 0.2 mg IM, and carboprost tromethamine, 0.25 mg IM, were each repeated once within 10 minutes after delivery, with continued heavy bleeding. Additional carboprost tromethamine, 0.5 mg, was given directly in the myometrium by the obstetrician, approximately 15 minutes after delivery, without resolution of bleeding.

Twenty-five minutes after delivery, and despite aggressive pharmacologic and surgical intervention, estimated operative blood loss totaled more than 3,000 mL, with no indication of resolution. DIC was suspected. The decision was made to initiate hysterectomy. Ten units of type-specific packed red blood cells, 24 units of pooled platelets, 8 units of cryoprecipitate, and 8 units of fresh frozen plasma were ordered. A 20-gauge right radial arterial catheter was inserted with good waveform and correlation with noninvasive BP measurement. Blood samples were sent for complete blood count, coagulation studies, and arterial blood gas (ABG) analysis. A peripheral venous blood sample was also sent for pathological examination for fetal squamous cells, despite the recommendation that only blood aspirated from the pulmonary artery be sent for this screening test. Transfusion of 2 units of previously typed and cross-matched packed red blood cells was begun.

Initial laboratory results revealed HCT level, less than 15%; HGB, 5.2 g/dL; platelet count, 58,000/L; BG, 116 mg/dL; prothrombin time, 18.4 seconds; and activated partial thromboplastin time, 51 seconds. Initial ABG readings were: pH level, 7.48 mm Hg; partial pressure of carbon dioxide level, 43 mm Hg; partial pressure of oxygen level, 221 mm Hg; bicarbonate level, 29.2 mEq/L; and base excess level, 0.3. Transfusion of ordered type-specific blood products was continued through a fluid warmer, in order to maintain a HCT above 25%. The patient's urine was hematuric, totaling 150 mL 70 minutes after administration of furosemide. Urine output was responsive to crystalloids and continued blood product administration. MAP ranged from 52 to 78 mm Hg during surgery, quickly responsive to boluses of phenylephrine, 50 µg IV, as needed to maintain MAP above 60 mm Hg.

After ligation of the uterine vasculature was achieved, oxytocin administration was stopped. Additional fentanyl citrate, 250 µg, and midazolam, 5 mg IV, were given. Moderate to severe oozing was still noted in all incision margins after hysterectomy. Recombinant coagulation factor VIIa was given at a dose of 200 µg/kg over 30 minutes. After administration of factor VIIa, oozing subsided and vital signs remained stable. Additional minor oozing was treated as needed with electrocautery. After satisfactory hemostasis was achieved, the abdomen was closed, and the patient was transported to the surgical intensive care unit (SICU) with Ambu bag and monitors.

Total operative time was approximately 210 minutes. Final fluid counts were: blood loss, 8,500 mL; packed cells, 12 units; cryoprecipitate, 8 units; platelets, 18 units; fresh frozen plasma, 8 units; crystalloids, 3,300 mL; and urine output, 380 mL. Laboratory studies in the SICU revealed HCT, 27%; HGB, 9.4 g/dL; platelets, 108,000/L; BG level, 143 mg/dL; prothrombin time, 18.1 seconds; and activation partial thromboplastin time, 47

seconds. ABG readings were: pH, 7.43 mm Hg; partial pressure of carbon dioxide level, 38 mm Hg; partial pressure of oxygen level, 211 mm Hg; bicarbonate level, 25.8 mEq/L; and base excess level, -0.1. Vital signs were BP, 98/58; oxygen saturation, 99%; pulse rate, 102/min; and core temperature, 36.3°C. The patient did not require vasoactive agent infusion. Mechanical ventilation was initiated in assist-control mode with a respiratory rate of 12, tidal volume of 700 mL, inspired oxygen concentration of 50%, inspiration:expiration ratio of 1:2, and positive end-respiratory pressure level of +8 cm H₂O. Peak airway pressure was 24 cm H₂O. Continuous IV administration of propofol was started at 50 µg/kg per minute for sedation. Epidural preservative-free morphine sulfate, 4 mg, was given by the anesthesia team in the SICU, and the catheter was left in place with epidural infusion of preservative-free normal saline at 3 mL/h for normalization of coagulation studies before removal.

Laboratory studies returned to within 10% of baseline on postoperative day 1, and the epidural catheter was removed. The patient met extubation criteria on postoperative day 2 and her trachea was extubated. On postoperative day 3, oxygen saturation was 98% on oxygen at 2 L/min by nasal cannula, with no obvious neurologic deficits. She was awake, alert, oriented, and obviously shaken by the events of the preceding days. Vital signs were stable, with the exception of arterial hypertension with a MAP of 104 to 115 mm Hg, requiring titration of continuous IV nicardipine infusion. The patient reported no history of hypertension. She was transferred to a surgical step-down unit on postoperative day 5 and was discharged home on postoperative day 7. Neonatal outcome was not available.

Few fetal squamous cells were found in the peripheral venous blood sample sent for pathologic evaluation. Other diagnoses, such as acute congestive heart failure, fluid volume overload with resultant pulmonary edema, high inadvertent spinal anesthetic level, anaphylactic reaction to a medication or substance, electrolyte imbalance, acute seizure, and undiagnosed eclampsia, were suggested and quickly ruled out. These other diagnoses failed to account for the suddenness and severity of the symptoms described in this patient. Especially telling was the correlation of symptom onset with artificial rupture of membranes. All findings were consistent with AFE. The obstetric team agreed with the anesthesia team's conclusions, and indicated their agreement in the medical record.

Discussion

The estimated maternal mortality rate in the United States from 1991 to 1999 was 11.8 deaths per 100,000 pregnancies. The goal for maternal mortality outlined by the Healthy People 2010 report is only 3.3 deaths per 100,000 pregnancies.¹⁶ The most common causes of ma-

ternal death in the United States are primary postpartum uterine hemorrhage, infection, eclampsia, preeclampsia, pulmonary thromboembolism, and AFE.¹⁷ Fatality rates for AFE are globally and widely divergent, ranging from more than 50% in England to a US rate of about 26%.¹⁵

A review of pregnancy-related mortality in the United States from 1987 to 1990 placed AFE as the second leading cause of maternal death, with 100 to 150 deaths per year.¹⁸ This is similar to the fatality rate reported in England from 1997 to 2004, which cited AFE as contributing to 1 death in every 120,000 pregnancies.¹⁹ Appropriate diagnosis and treatment of AFE would significantly decrease maternal morbidity and mortality in the United States and England.

Some parturients seem to be predisposed to AFE. A synthetic formulation of oxytocin for elective induction and augmentation of labor was first made available and went into widespread use in the 1960s and 1970s. Although the precise mechanism is unclear, there appears to be a correlation between the use of uterine stimulants and AFE.¹¹ There is evidence to support a correlation between the use of misoprostol and AFE, with a number of cases reported to the US Food and Drug Administration. The decision to use misoprostol should be entered into with caution, especially in patients who have other risk factors for AFE, such as advanced maternal age, tumultuous labor, intrauterine fetal demise, high parity, fetal macrosomia, placenta accreta, uterine rupture, and cesarean delivery.^{8,11} AFE has also been linked to the use of continuous saline amnioinfusion. Dorairajan and Soundararaghavan¹⁰ described 2 patients who had fatal AFE during saline amnioinfusion. Similar cases may go unreported because of the lack of a clear causal relationship between AFE and amnioinfusion.

A case report also exists describing the occurrence of AFE in a patient who underwent second trimester dilatation and curettage for intrauterine fetal death, with development of shock, respiratory arrest, pulseless electrical activity, hemorrhage, and DIC. The authors of this case report reported that the pathophysiological features of AFE are similar to a type-1 hypersensitivity reaction, ranging from mild allergy to anaphylaxis and shock.⁷

The precise immunologic mechanism that mediates the response to embolization of amniotic fluid is unclear. Two hypotheses describe a maternal immune response to fetal antigens. The first hypothesis states that clinical symptoms result from mast cell degranulation and release of histamine.¹⁵ This mechanism underlies anaphylaxis.¹⁵ This hypothesis has caused some individuals to rename AFE "anaphylactoid syndrome of pregnancy." The second hypothesis states that illness results from massive activation of the complement pathway. Complement activation occurs in seriously ill patients who develop adult respiratory distress syndrome.¹⁵ The literature suggests a potential role for bradykinin release in the pathophysiology of

AFE. Serial measurement of serum bradykinin level in a parturient who had AFE showed low levels shortly after the initial insult, with increasing levels as symptoms progressed.²⁰ The data do not support bradykinin's implication in initiating the more sudden and immediate symptoms following AFE. A role for tryptase activation in AFE, with the use of serum tryptase level as a diagnostic test, has been suggested, based on a rat model. This model suggests that the degranulation of cells to release tryptase may be the important cause of the body's exaggerated response to AFE, with particular evidence pointing to mast cell activation.¹³

Postmortem findings in a parturient who had AFE during the 40th week of pregnancy revealed eosinophilic inflammatory infiltrates in the lungs, hepatic portal system, and, especially, the heart. These findings suggested a specific hypersensitivity reaction to fetal antigens. Macrophage infiltration of the lungs supports a nonspecific immune response to amniotic fluid.¹⁴ Leukotrienes and placental arachidonic acid metabolites may play a role in the mediation of the response to AFE.¹²

The bleeding diatheses caused by AFE are not well understood. As many as 50% of patients who survive the first hour after AFE onset go on to develop exaggerated bleeding, secondary to DIC.⁴ DIC is characterized by exaggerated activation of coagulation factors, which occurs when hemostatic autoregulation is overridden by procoagulant disorders, such as AFE.²¹ Activation of the coagulation mechanism in AFE is usually explosive, resulting in the rapid consumption of coagulation factors, with hemorrhagic consequences.⁶

An *in vitro* thromboelastography study using amniotic fluid to assess coagulation and platelet function on whole blood exposed to amniotic fluid has been reported. Findings of this study did not support the hypothesis that primary fibrinolysis occurs following AFE, as was suggested by one case report that described findings suggestive of primary fibrinolysis rather than DIC in a single patient.^{22,23} Most of the available literature, however, supports the hypothesis that the hemorrhagic consequences of AFE are consistent with DIC. The common obstetric causes of DIC include placental abruption, AFE, acute fatty liver of pregnancy, and eclampsia.²⁴ These other causes may account for the occurrence of DIC during the peripartum period and should be ruled out when a diagnosis of AFE is made based solely on the presence of coagulopathy.

Cardiopulmonary compromise commonly results from AFE. Symptoms include respiratory arrest, cardiac arrest, pulseless electrical activity, and dysrhythmias. Animal studies based on injection of amniotic fluid into the pulmonary circulation of pregnant ewes demonstrated an increase in pulmonary vascular resistance, pulmonary hypertension, right ventricular failure, and a decrease in systemic vascular resistance.^{25,26} Initial chest radiographs

of 5 women who survived suspected AFE indicated findings consistent with aspiration pneumonitis or adult respiratory distress syndrome. Resolution of radiograph findings was rapid in all of the subjects.¹⁹ Porat and colleagues⁶ described transesophageal echocardiography findings during the acute phase of AFE. The researchers were able to detect large asymptomatic intracardiac thrombi that disappeared within days of the initial insult, with likely disintegration of the intracardiac masses and asymptomatic embolization of their fragments into the pulmonary vasculature in the days following embolization. Leibowitz and colleagues also described 2 case reports of transesophageal echocardiography following AFE. Both cases revealed right ventricular failure and leftward deviation of the interventricular septum with severe tricuspid regurgitation. The findings in these case reports were more consistent with the animal model findings discussed previously.

The catastrophic nature of the symptoms associated with AFE has led to the application of numerous novel therapies. Nuclear factor-kappa B activity, a possible contributor to the pathogenesis of pulmonary injury from AFE, has been reported to increase greatly with entrance of amniotic fluid into blood. Studies conducted on rats demonstrated that IV dexamethasone may inhibit Nuclear factor-kappa B activity, possibly ameliorating the pulmonary injury caused by AFE.²⁷

The use of inhaled nitric oxide in the therapeutic regimen of acute pulmonary embolism also has been described. The increased pulmonary vascular resistance following acute pulmonary embolism results from mechanical obstruction of the pulmonary vasculature and pulmonary arteriolar vasoconstriction caused by a neurogenic reflex and release of vasoconstrictors. Therefore, the vasodilatory effects of inhaled nitric oxide may oppose the pulmonary hypertension that occurs in AFE.²⁸

Van Heerden and colleagues²⁹ described the use of inhaled aerosolized prostacyclin as a powerful pulmonary vasodilator in the treatment of severe refractory hypoxemia. Hence, there may be some applicability of this inhaled agent to the treatment of the severe hypoxemia that commonly accompanies AFE.

The use of intraoperative cell salvage for autotransfusion in obstetric surgery has been hindered by the theoretical concept that the use of this type of transfusion may lead to iatrogenic AFE. Catling and Joels³⁰ of Singleton Hospital in the United Kingdom routinely use autotransfusion in their obstetric surgery practice. They have described its safe use in cases of placental abruption, laparotomy for severe postpartum hemorrhage, undiagnosed extrauterine placenta, and in cases of anticipated large volume blood loss during cesarean section, such as with the presence of massive fibroids and placenta previa. The use of standard cell salvage filters effec-

tively removes amniotic fluid from aspirated blood, eliminating the possibility of AFE caused by autotransfusion during obstetric surgery.²³ This is further reinforced by findings by Rebarber and colleagues,³¹ who found no increased risk of suffering any adverse condition from autologous blood collection and autotransfusion during cesarean section in a multicenter study.

Several approaches have been used to treat the coagulopathy of AFE, with its ensuing blood loss. Transfusion of multiple blood products is the standard treatment, along with surgical intervention as warranted. The use of recombinant clotting factor VIIa (NovoSeven, Nordisk, Princeton, New Jersey) was cited in a case report as efficacious in the treatment of severe postpartum hemorrhage secondary to AFE.³² Haas et al³³ made a strong argument for the use of NovoSeven in their report of 5 patients who exhibited severe continuous bleeding, not amenable to surgical intervention, who responded favorably to a single mean dose of 90 µg/kg of NovoSeven (range 90-120 µg/kg). In all patients, bleeding from wound surfaces stopped within minutes of the administration of NovoSeven.

Hysterectomy for refractory postpartum hemorrhage may be physically and psychologically detrimental to the patient, because it precludes future pregnancy and carries surgical risks. Goldszmidt and Davies³⁴ reported the clinical course and management of 2 women who had AFE, with 1 woman having cardiopulmonary arrest and 1 having respiratory failure and alteration in neurological status. Both developed severe postpartum hemorrhage, effectively managed by percutaneous uterine artery embolization. Neither patient required hysterectomy.

Cardiovascular collapse resulting from AFE may range from mild, as seen in the case summarized in this report, to complete cardiac arrest. Fluid administration, transfusion of blood products, use of vasopressors, and initiation of cardiopulmonary resuscitation are the mainstays of therapy. A scant number of cases of AFE with refractory cardiovascular collapse treated with heroic measures have been reported. There is 1 case report of the use of transesophageal echocardiography to diagnose catastrophic pulmonary vasoconstriction following AFE, with initiation of cardiopulmonary bypass during stabilization with heparin, epinephrine, and high-dose steroids. These heroic measures led to a successful outcome.³⁵ There also is 1 case report of the successful application of extracorporeal membrane oxygenation and the use of intra-aortic balloon counterpulsation in a patient suffering from AFE.³⁶

Conclusion

Patients who develop symptomatic amniotic fluid embolism present unique challenges to their providers. These patients require prompt, aggressive therapy to achieve the best possible outcomes. As the body of

knowledge about the pathophysiology of AFE increases, interventions will become more tailored and morbidity and mortality will decrease. Any anesthesia provider who cares for patients at risk for developing AFE should have a basic understanding of the pathogenesis, diagnosis, and treatment of this rare condition.

REFERENCES

1. Meyer JR. Embolia pulmonar amnio-caseosa. *Bras Med.* 1926;2:301-303.
2. Steiner PE, Lushbaugh CC. Maternal pulmonary embolism by amniotic fluid, as a cause of obstetric shock and unexpected death in obstetrics. *JAMA.* 1941;117:1245-1254,1341-1345.
3. Thompson WB, Budd JW. Erroneous diagnosis of amniotic fluid embolism. *Am J Obstet Gynecol.* 1965;91:606-620.
4. Hussain SA, Damanpaul SS, Munir A, Rosner F. Amniotic fluid embolism with late respiratory failure. *Hospital Physician.* 2001;37(10):40-43.
5. McDougall RJ, Duke GJ. Amniotic fluid embolism: a review of the literature. *Can J Anaesth.* 2001;48:88-98.
6. Porat S, Leibowitz D, Milwidsky A, Valsky DV, Yagel S, Anteby EY. Transient intracardiac thrombi in amniotic fluid embolism. *BJOG.* 2004;111(5):506-510.
7. Ray BK, Vallejo MC, Creinin, MD, et al. Amniotic fluid embolism with second trimester pregnancy termination: a case report. *Can J Anaesth.* 2004;51(2):139-144.
8. Masson RG. Amniotic fluid embolism. *Clin Chest Med.* 1992;13(4):657-665.
9. McLaren P. Women's Health Australia. Amniotic fluid embolism. <http://www.medicineau.net.au/clinical/womenshealth/amnioemb.html>. Accessed March 29, 2006.
10. Dorairajan G, Soundararaghavan S. Case report: Maternal death after intrapartum saline amnioinfusion—report of two cases. *BJOG.* 2005;112:1331-1333.
11. Wagner M. From caution to certainty: hazards in the formation of evidence-based practice—a case study on evidence for an association between the use of uterine stimulant drugs and amniotic fluid embolism. *Paediatr Perinat Epidemiol.* 2005;19(2):173-176.
12. Steiner PE, Lushbaugh CC. Landmark article, Oct. 1941: maternal pulmonary embolism by amniotic fluid, as a cause of obstetric shock and unexpected death in obstetrics. *JAMA.* 1986;255(16):2187-2203.
13. Zhou XW, Shang T, Tang Y, Tian S, Du SM, Feng LY. Activity and role of tryptase after entrance of amniotic fluid into blood in rats [in Chinese]. *Zhonghua Fu Chan Ke Za Zhi.* 2005;40(12):815-817.
14. Balazic J, Rott T, Jancigaj T, Popovic M, Zajfert-Slabe M, Svirgelj V. Amniotic fluid embolism with involvement of the brain, lungs, adrenal glands, and heart. *Int J Legal Med.* 2003;117(3):165-169.
15. Benson MD, Kobayashi H, Silver RK, Oi H, Greenberger PA, Terao T. Immunologic studies in presumed amniotic fluid embolism. *Obstet Gynecol.* 2001;97(4):510-514.
16. Chang J, Elam-Evans LD, Berg CJ, et al. Pregnancy-related mortality surveillance—United States, 1991–1999. *MMWR Surveill Summ.* 2003;52(2):1-8.
17. Christiansen LR, Collins KA. Pregnancy-associated deaths: a 15-year retrospective study and overall review of maternal pathophysiology. *Am J Forensic Med Pathol.* 2006;27(1):11-19.
18. Berg CJ, Atrash HK, Koonin LM, Tucker M. Pregnancy-related mortality in the United States, 1987-1990. *Obstet Gynecol.* 1996;88(2):161-167.
19. Tuffnell DJ. United Kingdom amniotic fluid embolism register. *BJOG.* 2005;112(12):1625-1629.
20. Robillard J, Gauvin F, Molinaro G, Leduc L, Adam A, Rivard GE. The syndrome of amniotic fluid embolism: a potential contribution of bradykinin. *Am J Obstet Gynecol.* 2005;193(4):1508-1512.

21. Taylor FB Jr, Kinasewitz GT. The diagnosis and management of disseminated intravascular coagulation. *Curr Hematol Rep.* 2002;1(1):34-40.
22. Harnett MJ, Hepner DL, Datta S, Kodali BS. Effect of amniotic fluid on coagulation and platelet function in pregnancy: an evaluation using thromboelastography. *Anaesthesia.* 2005;60(11):1068-1072.
23. Biron-Adr ani C, Morau E, Schved JF, H don B, Dechaud H. Amniotic fluid embolism with haemostasis complications: primary fibrinogenolysis or disseminated intravascular coagulation. *Pathophysiol Haemost Thromb.* 2003;33(3):170-171.
24. Furlong, MA. eMedicine. Disseminated intravascular coagulation. <http://www.emedicine.com/emerg/topic150.htm>. Accessed March 28, 2006.
25. Reis RL, Pierce WS, Behrendt DM. Hemodynamic effects of amniotic fluid embolism. *Surg Gynecol Obstet.* 1969;129(1):45-48.
26. Rodgers BM, Staroscik RN, Reis RL. Effects of amniotic fluid on cardiac contractility and vascular resistance. *Am J Physiol.* 1971;220:1979-1982.
27. Tian S, Shang T, Zhou XW. Activity of nuclear factor kappa B in rat pulmonary tissue after entrance of amniotic fluid into blood and inhibition by dexamethasone [in Chinese]. *Zhonghua Fu Chan Ke Za Zhi.* 2005;40(2):95-98.
28. Tanus-Santos JE, Theodorakis MJ. Is there a place for inhaled nitric oxide in the therapy of acute pulmonary embolism? *Am J Respir Med.* 2002;1(3):167-176.
29. Van Heerden PV, Webb SA, Hee G, Corkeron M, Thompson WR. Inhaled aerosolized prostacyclin as a selective pulmonary vasodilator for the treatment of severe hypoxemia. *Anaesth Intensive Care.* 1996;24(1):87-90.
30. Catling S, Joels L. Cell salvage in obstetrics: the time has come. *BJOG.* 2005;112(2):131-132.
31. Rebarber A, Lonser R, Jackson S, Copel JA, Sipes S. The safety of intraoperative autologous blood collection and autotransfusion during cesarean section. *Am J Obstet Gynecol.* 1998;179(3):715-720.
32. Lim Y, Loo CC, Chia V, Fun W. Recombinant factor VIIa after amniotic fluid embolism and disseminated intravascular coagulopathy. *Int J Gynaecol Obstet.* 2004;87(2):178-179.
33. Haas T, Innerhofer P, Huhbacher G, Fries D. Successful reversal of deleterious coagulopathy by recombinant factor VIIa. *Anesth Analg.* 2005;100(1):54-58.
34. Goldszmidt E, Davies S. Two cases of hemorrhage secondary to amniotic fluid embolus managed with uterine artery embolization. *Can J Anaesth.* 2003;50(9):917-921.
35. Stanten RD, Iverson LI, Daugherty TM, Lovett SM, Terry C, Blumenstock E. Amniotic fluid embolism causing catastrophic pulmonary vasoconstriction: diagnosis by transesophageal echocardiogram and treatment by cardiopulmonary bypass. *Obstet Gynecol.* 2003;102(3):496-498.
36. Hsieh YY, Chang CC, Li PC, Tsai HD, Tsai CH. Successful application of extracorporeal membrane oxygenation and intra-aortic balloon counterpulsation as lifesaving therapy for a patient with amniotic fluid embolism. *Am J Obstet Gynecol.* 2000;183(2):496-497.

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