Lipid Emulsion Rescue of Amniotic Fluid Embolism-Induced Cardiac Arrest: A Case Report

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Amniotic fluid embolism (AFE) is a rare and often fatal complication that occurs in the peripartum period. We present a patient with an AFE who developed disseminated intravascular coagulation and cardiovascular collapse who may have benefitted from intravascular lipid emulsion rescue. This is the first published case in which lipid emulsion was a part of the successful treatment of AFE. (A&A Case Reports. 2017;8:64–66.)

Amniotic fluid embolism (AFE) is a rare and often fatal complication of the peripartum period.[1] The severity of its consequences, rapid onset, and limited treatment options make recognition of this syndrome of vital importance for those caring for patients in the peripartum period. The term AFE may be somewhat of a misnomer in that this condition may be the final common expression of a unique maternal immunologic response to various foreign antigenic stimuli originating in the fetal compartment.[2] However, the term AFE is sufficiently embedded in the literature and describes the syndrome that presents with the classic triad of hypotension, hypoxia, and coagulopathy. A patient presented with AFE in cardiovascular collapse who had return of spontaneous circulation temporally related to the administration of IV lipid emulsion therapy after prolonged cardiac arrest and cardiopulmonary resuscitation. Potential mechanisms for the beneficial results in this scenario based on previous research findings are presented.

CONSENT FOR PUBLICATION

The patient has reviewed the case and gave written permission for the authors to publish this report.

CASE REPORT

A 28-year-old otherwise healthy, nonsmoking, 76-kg primigravid woman presented at 41 weeks of gestation for vaginal misoprostol induction of labor. Initial examination and review of systems were unremarkable. After 6 hours, a labor epidural catheter was placed without complication, and a ropivacaine 0.2% epidural analgesic infusion was initiated at 10 mL/h. An oxytocin infusion was administered for labor augmentation, and an intrauterine pressure catheter was placed. Occasional fetal heart decelerations occurred soon afterward, and the oxytocin infusion was stopped with the resolution of decelerations. Bleeding was then noted from the epidural catheter site. The patient had no history of coagulopathy, and there was no bleeding from any other site. The epidural catheter site was inspected, and a pressure dressing was applied. An hour later, the slow hemorrhage from the epidural catheter site had continued and coagulation studies including prothrombin time (PT) with international normalized ratio (INR), fibrinogen, and D-dimer were performed. Late decelerations returned and vaginal examination showed complete dilation and complete effacement. The neonate was then vaginally delivered with vacuum assistance resulting in a third-degree perineal laceration. The patient developed postpartum hemorrhage that did not improve despite oxytocin, misoprostol, carboprost, and methylergonovine administration. The etiology of the hemorrhage was suspected to be coagulopathy. Coagulation studies showed an increased PT of 22.6 seconds and INR of 2.0 (normal range PT 11–14 seconds and INR 0.8–1.1). Disseminated intravascular coagulation was suspected. Additional IV catheters were placed, 2 units of crossmatched red blood cells (RBCs) were ordered for transfusion, and intrauterine tamponade with a Bakri balloon was performed to attempt to slow the vaginal hemorrhage. A perineal laceration was repaired despite the fact that it was not considered to be the major source of hemorrhage. Forty-seven minutes after completion of transfusion of crossmatched blood but before intensive care unit transfer, the patient suddenly reported dyspnea and angina and rapidly developed an altered mental status. The patient then became hypotensive and tachycardic. Tracheal intubation was performed emergently, facilitated by intravenous administration of 10 mg etomidate and 100 mg succinylcholine when maintaining cricoid pressure. The tracheal tube was placed easily with a grade I laryngoscopic view. Shortly thereafter, pulses were absent on femoral and carotid artery examination. The presumed diagnosis was AFE presenting with disseminated intravascular coagulation and cardiovascular collapse. Advanced cardiac life support (ACLS) and cardiopulmonary resuscitation (CPR) were immediately initiated during which a femoral central venous catheter and radial arterial catheter were placed and 6 units of crossmatched RBCs with 4 units of fresh frozen plasma were administered to treat ongoing vaginal hemorrhage. The arterial catheter waveform suggested adequate peripheral perfusion from chest compressions. Bedside rescue transesophageal echocardiography (TEE) revealed right heart strain with moderate tricuspid regurgitation, no obvious saddle embolus on midesophageal short-axis view of the ascending aorta, and severely depressed left ventricular systolic function with adequate left ventricular end-diastolic volume as seen on the

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transgastric short-axis view of the left ventricle. A finding suspicious for a thrombus was seen in the inferior vena cava near the liver. This was a small, slightly echogenic irregularity within the inferior vena cava less than 1 cm in diameter.

Despite several administrations of ACLS medications including vasopressin, sodium bicarbonate, calcium chloride, atropine, and a total of 6 mg epinephrine, the patient's heart rhythm fluctuated between profound bradycardia and asystole for a prolonged period of 40 minutes. Other diagnoses were considered such as local anesthetic systemic toxicity (LAST) despite the fact that her epidural analgesia infusion was well within the normal dosing range for ropivacaine and worked well providing effective analgesia throughout her labor. An inspection of the infusion revealed the expected amount of ropivacaine left in the bottle and no evidence of pump malfunction. The patient received an initial 8-mL bolus of ropivacaine 0.2% totaling 16 mg followed by an infusion of 10 mL/h for 6 hours, totaling 120 mg over 6-hour period, well below the maximum recommended dose limit for ropivacaine (3 mg/kg). As a last resort, IV lipid 20% emulsion (1.5 mL/kg) was administered as a bolus. Within 30 to 90 seconds, the patient had return of spontaneous circulation, normal sinus rhythm, and dramatic improvement in left and right ventricular function, shown clearly by TEE. After several minutes, the patient's condition slowly deteriorated once again to asystole, at which time CPR was once again started and a second lipid emulsion bolus (1.5 mL/kg) was administered and followed with an infusion at 0.25 mL/kg/min. Within 30 to 60 seconds, the patient again had a return of spontaneous circulation with normal sinus rhythm. In addition, she also exhibited spontaneous movements of her extremities.

She was transferred to the intensive care unit where she regained consciousness and was able to follow commands. Lipid emulsion infusion was discontinued shortly after arrival. Initial coagulation studies revealed fibrinogen levels <60 mg/dL and D-dimer levels >20 μg/mL (normal range fibrinogen 150–400 mg/mL and D-dimer <0.5 μg/mL). Because of ongoing vaginal hemorrhage, she required an additional 6 units of RBCs, 5 units of fresh frozen plasma, 1 unit of platelets, and 2 units of cryoprecipitate. Initially, she required vasopressor support with epinephrine and norepinephrine until hemostasis and hemodynamic stability were achieved later that evening. She was sedated and ventilated overnight and monitored closely.

The patient developed profound reperfusion injuries in both hands with severe ischemic changes. In addition, she experienced acute renal failure that required 4 sessions of dialysis. The next day, sedation was discontinued, and the patient was extubated after meeting all extubation criteria. The patient was fully oriented without any obvious neurologic sequelae. The epidural catheter had been left in place because of her coagulopathy but was removed on hospital day 3 after normalization of coagulation studies. Follow-up at 6 months revealed no neurologic sequelae other than modest sensory-related deficits in bilateral hands related to reperfusion tissue injury. After discharge, the patient was able to fully participate in her activities of daily living and care for her newborn. Further hematologic investigation revealed no evidence of any underlying coagulopathic or hypercoagulopathic condition that may have provided alternative etiologies of the cardiovascular collapse.

DISCUSSION

AFE is a leading cause of maternal morbidity and mortality.[1] AFE is likely not because of an actual embolus of definable material, but more likely, it is the final common expression of a unique maternal immunologic response to various foreign antigenic stimuli originating in the fetal compartment.[2] The diagnosis of AFE is based on the clinical presentation, and it is a diagnosis of exclusion.[1,3] Diagnosis of AFE is suspected in a patient in the peripartum period who is experiencing sudden hypoxia, hypotension or cardiac arrest, altered mental status, and coagulopathy.[2,3] Although there have been many proposed identifying laboratory markers, to date, none have been found to be of significant diagnostic or clinical use to discretely identify AFE.[2]

The differential diagnosis in this patient included AFE, LAST, myocardial infarction, and pulmonary thromboembolus. LAST was unlikely because of the fact that her clinical presentation did not follow the normal pattern of seizures followed by cardiac arrest. In addition, the patient's dose of ropivacaine was far below generally accepted toxic doses, and the event occurred well after the initial bolus of ropivacaine through her epidural catheter and an effective analgesic level had been established. Furthermore, the patient specifically denied tinnitus or other mental status changes typically associated with LAST in conversation with her after the event and, in contrast, had dyspnea and angina as her presenting symptoms. In addition, her profound coagulopathy cannot be reconciled by LAST. A serum ropivacaine concentration was ordered during the arrest period, but the sample was lost when sent to the outside laboratory for testing. An acute hemolytic reaction or anaphylaxis from the transfused RBCs was unlikely because of the fact that the blood was crossmatched without evidence of clerical error and the patient's acute decompensation did not occur until 47 minutes after completion of the transfusion. In addition, the patient did not develop a rash, fever, flank pain, or airway edema nor did she develop problems with subsequent transfusions or have a positive direct antiglobulin (Coombs) test. An acute, idiopathic myocardial event in an otherwise healthy individual was also felt to be unlikely without any preceding signs or symptoms and would also not explain her coagulopathy. Pulmonary embolism was also thought to be unlikely given no particular risk factors for deep venous thrombosis besides pregnancy and no direct evidence of thrombus on TEE, and it is not consistent with coagulopathy and hemorrhage. The sudden development of a coagulopathy is a key factor that is not better explained than by AFE. Her clinical scenario did fit perfectly with the expected clinical sequelae associated with AFE, that is, the triad of hypoxia, hypotension, and coagulopathy.

There is no specific treatment for AFE, and the management is primarily supportive.[2,3] Maintenance of oxygenation, cardiac output and perfusion as well as blood product transfusions for the treatment of severe coagulopathy and massive hemorrhage is vital.[2,3] Unfortunately, despite these treatments, AFE is frequently fatal.

IV lipid emulsion is composed of an emulsion of soybean oil, egg-yolk phospholipids, and glycerol and has historically been used in the formulation of total parenteral nutrition. In addition, lipid emulsion has quickly become

the standard treatment for LAST.[4] New reports suggest its benefit in the treatment of overdoses in a wide spectrum of lipid soluble medications.[4] The most commonly available lipid formulation in the United States is Intralipid® (Baxter Pharmaceuticals, Baxter Healthcare Corporation, Deerfield, IL). An early proposed mechanism of action was described as a partitioning phenomenon in which the lipid solubility of local anesthetics in lipid emulsion and the high binding capacity of these emulsions were thought to account for the reversal of toxicity.[4] However, more recent evidence suggests that the mechanism is much more complex and is associated with fatty acid oxidation and inhibition of mitochondrial permeability transition pore opening.[5] Recently, Fettiplace et al[6] showed that lipid emulsion exerts a rapid, positive inotropic and lusitropic effect on the anesthetized rat heart and theorized that this may also play a role in the reversal of cardiotoxicity because of the overdose of lipophilic drug.

Umar et al[7] demonstrated that lipid emulsion plays a role in preventing and rescuing fatal pulmonary hypertension and right heart failure in a rat model. In addition, γ-linolenic acid, 1 of the key essential fatty acids in the Intralipid® formulation, has been shown to be protective against doxorubicin-induced cardiotoxicity.[8] Furthermore, genistein, a soy-derived phytoestrogen found in Intralipid®, has been shown to reduce pulmonary hypertension.[9] γ-linolenic acid is a precursor of prostacyclin, a substance well known to induce pulmonary vasodilation that has been used in the treatment of pulmonary hypertension. Prostacyclin binds to the I2 (prostacyclin) receptor (IP) that causes adenylate cyclase and subsequent cyclic adenosine monophosphate activation resulting in vascular relaxation and platelet aggregation. Therefore, lipid emulsion may provide a prostacyclin-like effect leading to pulmonary vasodilation.[10] Prostacyclin has a similar effect on pulmonary vasculature as nitric oxide, which has been previously used in the successful treatment of critical hemodynamic compromise in a parturient with AFE.[11] Prostacyclin induces relaxation of vascular smooth muscle in the pulmonary vasculature by stimulating the production of cyclic adenosine monophosphate. Nitric oxide directly relaxes vascular smooth muscle through the stimulation of soluble guanylate cyclase and increased production of intracellular cyclic guanosine monophosphate.[12] The known effects of prostacyclin on lowering pulmonary vasculature resistance give further credence to the use of lipid emulsion in the treatment of AFE, which is known to cause early pulmonary hypertension and right heart failure.[3] Because our patient had clear echocardiographic evidence of acute right heart strain, she might have benefited from a potentially pulmonary arterial vasodilatory effect of lipid emulsion therapy.

Although Eldor and Kotlovker[13] were the first to suggest a possible benefit of lipid emulsion therapy in the treatment of AFE, this is the first published instance in which a patient received intravenous lipid emulsion temporally related to the recovery from cardiovascular collapse associated with amniotic fluid embolism. The main limitation is the fact that AFE is a diagnosis of exclusion; however, other differential diagnoses are less likely. There is TEE evidence that shows overall improvement of cardiac function temporally related to administration of lipid emulsion. The patient had return of spontaneous circulation occurring shortly after the administration of lipid emulsion on 2 different occasions after exhausting all other ACLS options, suggesting that lipid emulsion may have been responsible for the successful resuscitation. In addition, after the initial improvement, a relapse occurred, which was treated with a second bolus of lipid emulsion after which the same improvement in clinical and cardiac function occurred. Full neurologic recovery was noted after significantly prolonged cardiovascular collapse with chest compressions (40 minutes) and exhaustion of other standard ACLS medications. The excellent neurologic recovery emphasizes the importance of high quality and sustained CPR. Furthermore, a possible physiologic mechanism for the cardiopulmonary recovery is presented and is based on scientific models from previous research on the effects of lipid emulsion and its components. This report suggests a possible benefit of lipid emulsion therapy in the treatment of cardiovascular collapse caused by AFE, and further research will be required to elucidate the role of lipid emulsion therapy in the setting of AFE.

DISCLOSURES

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