

CASE REPORT

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Atypical amniotic fluid embolism successfully treated with a novel protocol: A case report

Abigail Berry, Andrea Salcedo, Christopher Riba

ABSTRACT

Introduction: Amniotic fluid embolism (AFE) is a rare complication of pregnancy with a high morbidity and mortality rate for the gravida. Due to a lack of consensus on diagnostic criteria and treatment, there is great need for further research.

Case Report: We present a 26-year-old female patient who experienced cardiorespiratory distress following labor and, through exclusion, was determined to have atypical AFE. She was successfully treated with both standard supportive care and a novel protocol of atropine, ondansetron, and ketorolac (A-OK) first suggested by Copper et al.

Conclusion: Not only does this case add to the variety of ways in which atypical AFE can present, but the patient's full recovery gives support to the further study and utilization of the A-OK protocol as a treatment for AFE.

Keywords: A-OK protocol, Atypical amniotic fluid embolism, AFE

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INTRODUCTION

Amniotic fluid embolism (AFE) is a rare but potentially devastating complication of pregnancy. The estimated incidence is between 1.9 and 11 per 100,000 deliveries [1–3]. Despite the low incidence, 13.7% of all maternal deaths in the United States are due to AFE [2]. Maternal mortality rate is between 20% and 40%, while the perinatal mortality rate is 20–25% with 50% of neonates suffering from neurologic impairment [3]. Amniotic fluid embolism is a clinical diagnosis of exclusion, hypothesized to occur when disruption of the maternal-fetal membranes allows amniotic fluid to enter the maternal circulatory system resulting in the occlusion of pulmonary vasculature and the activation of humoral and immunological processes due to the presence of the foreign fetal tissues. The current diagnostic criteria for AFE is the presence of the following tetrad: sudden cardiorespiratory arrest (or both hypotension and respiratory compromise), disseminated intravascular coagulation (DIC), onset during labor or within 30 minutes of placental delivery, and absence of fever as defined as a temperature greater than or equal to 38.0°C [4]. Notably, not all AFE cases meet the four diagnostic criteria. Atypical amniotic fluid embolisms are rare occurrences in which one or more of these criteria are not met, yet the patient is suspected to have an AFE through exclusion or histologic examination. At the time of writing, case reports describing atypical AFE without DIC are few and there is no definitive consensus involving successful treatment methods. The current standard treatment is supportive and includes oxygenation and ventilation, along with fluid and blood administration to maintain blood pressure and to correct coagulopathy [4]. Importantly, in 2013, Copper et al. reported success with a proposed treatment regimen that is intended to improve cardiovascular function and block the cause of coagulopathy rather than simply providing cardiovascular

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support and replenishing clotting factors [1, 5]. This protocol involves the use of atropine, ondansetron, and ketorolac (A-OK) to treat vasomotor overstimulation and to increase vagal tone, to inhibit the release of inflammatory mediators, and to prevent coagulopathy, respectively [6]. This study aims to give further support to the use of the A-OK protocol to treat AFE. We present the case of a 26-year-old female patient with suspected atypical AFE without DIC who reached full recovery after management with hemodynamic and respiratory support measures plus the addition of the A-OK treatment protocol.

CASE REPORT

This is the case of a 26-year-old G4P2012 female patient who developed an atypical amniotic fluid embolism without DIC approximately 45 minutes post-partum and was successfully managed utilizing the A-OK protocol. The patient was admitted for premature rupture of membranes at 40 weeks and 2 days while experiencing painful contraction at 5-minute intervals. Her past medical and obstetric history was notable for postpartum hemorrhage and remote tetrahydrocannabinol use. The current pregnancy was negative for group B streptococcus and other complications. Cervical exam found her to be 3 cm dilated and 70% effaced with a -3 cm fetal station. Electronic fetal heart monitoring revealed a category 1 fetal heart tracing. The patient received epidural anesthesia for labor pain relief. Labor progressed normally, and she delivered a viable neonate via spontaneous vaginal delivery 8 hours after admission with normal blood loss. Due to the patient's history of postpartum hemorrhage, misoprostol 1000 mcg rectally was administered prophylactically immediately after delivery. Approximately 45 minutes postpartum the patient had a fever of 100.8°F, chills, and developed tachycardia of 140 bpm. Maternal respiratory rate became tachypneic with a respiratory rate of 32 and stridor. She developed hypertension at 150/120 mmHg and her oxygen saturation decreased to 50–60%. She was arousable, but in acute respiratory distress. A code blue was initiated, and she was intubated after her oxygen saturation decreased to 48% on 8 L of oxygen via face mask. Based upon the acute time frame and the patient's cardiovascular signs and symptoms, a diagnosis of amniotic fluid embolism was strongly suspected among other differential diagnoses, such as pulmonary embolism (PE), myocardial infarction, and sepsis. The A-OK protocol was initiated during the resuscitation, and the patient received atropine 1 mg intravenous (IV), ondansetron 8 mg IV, ketorolac 30 mg IV, and following intubation her SpO₂ rapidly normalized to 100%. Her vital signs stabilized. Blood and urine cultures taken at the time were negative for growth, urinalysis was within normal limits, and a coagulation panel revealed levels normal for pregnant physiology. As a precaution, she received 24 hours of IV ampicillin and gentamicin after delivery. Computed tomography (CT) angiogram of the chest and chest X-ray (CXR) showed no evidence

of PE or other abnormalities. Bedside echocardiography revealed appropriate left and right heart function. She was successfully extubated postpartum day 1, had a routine postpartum course with no further respiratory distress, and remained hemodynamically stable. She was discharged home on postpartum day 3 and had a normal recovery.

DISCUSSION

Amniotic fluid embolism is a diagnosis of exclusion made with a tetrad criterion which aids in ruling out other potential diagnoses [4]. The presence of DIC distinguishes AFE from hypovolemic shock secondary to postpartum hemorrhage, myocardial infarction, anesthetic accidents, or pulmonary thromboembolism. The acute time frame indicates the disease process is a result of an acute inflammatory mediator release. The sudden onset of the cardiorespiratory arrest without a temperature ($\geq 38^{\circ}\text{C}$) allows for sepsis and septic shock to be ruled out with a significant degree of confidence. Although helpful to distinguish AFE from similarly presenting conditions, a lack of consensus on the diagnostic criteria persists and presents an obstacle for diagnosis [5]. This is due in part to atypical AFE, a known rare occurrence in which one or more of these criteria are not met, yet the patient is diagnosed with AFE through clinical exclusion or histologic examination of amniotic cells in the vasculature. Stafford et al. reported that approximately 12% of AFE presented atypically [7]. The most common presenting signs and symptoms included hypotension, respiratory distress, and cyanosis, which were detected in up to 100% of women, DIC in approximately 50%, seizures in 20%, and cardiac arrest in between 30–87% [3]. Of note, atypical presentations in which coagulopathy or severe fetal bradycardia are the initial or even the singular presenting feature have been reported in the literature [3].

In this case report, the patient did not meet three of the four diagnostic criteria as she had a fever, did not exhibit DIC, and was beyond the 30-minute postpartum time frame. There are multiple factors that must be considered to explain this patient presentation. Firstly, the fever of 100.8°F could be secondary to epidural anesthesia or an adverse reaction to misoprostol given to prevent postpartum hemorrhage. Secondly, the patient's lack of DIC was likely influenced by the administration of ketorolac. Thirdly, the patient was noted to be symptomatic approximately 45 minutes after the delivery, however the symptoms easily could have started within the 30-minute time frame but were not yet drastic enough to raise clinical suspicion. Ultimately, her presentation allowed us to rule out other diseases on the differential. She presented with sudden and acute onset of the cardiorespiratory distress after labor, exhibited lack of growth on blood and urine cultures which effectively rule out sepsis, and showed a clear CT and CXR which effectively ruled out pulmonary thromboembolism. Therefore, we were led to suspect atypical AFE. Although

AFE without DIC has been reported, it is relatively rare [8]. The presence of AFE without DIC in this case report is therefore significant as it reveals how the presentation of a patient with AFE is altered when coagulation factors are still present at physiologic levels. Further, we argue that AFE should still be considered when all other diagnoses have been excluded, even if the patient lacks coagulopathy.

Beyond the challenge of diagnosis lies the need for systematic treatment. In addition to traditional supportive measures such as fresh frozen plasma and packed red blood cells to treat DIC, some studies have reported positive outcomes and full recovery by utilizing the A-OK treatment protocol (Table 1). This protocol is intended to improve patient outcome by inhibiting the three major processes that cause the sudden cardiorespiratory arrest

seen in AFE. Atropine improves the patient’s vasomotor tone by antagonizing the muscarinic receptors which are overactivated by the body’s vagal reflex causing systemic hypotension. The NSAID (non-steroidal anti-inflammatory drugs) ketorolac mitigates consumptive coagulopathy by inhibiting the release of inflammatory mediators like thromboxane and other coagulation activators. Additionally, the serotonin 5-HT₃ receptor antagonist ondansetron prevents serotonin from aggravating pulmonary vasoconstriction and inhibits the activation of platelets which would contribute to consumptive coagulopathy. While there is no standardized treatment for AFE, the success of the A-OK protocol as shown in this case report strongly supports its use in the management of AFE.

Table 1: Use of the A-OK protocol in previous case reports of patients with likely atypical amniotic fluid embolisms

Authors	Gestational age	Presenting symptoms	AFE diagnostic criteria	Treatment (in order of events)	Outcome
Rezai et al. [5]	38 1/7 weeks	<ul style="list-style-type: none"> - Fever (102.2°F) - Blood pressure 119/73 mmHg - Maternal tachycardia (144 bpm) - Tachypnea (24 bpm) - Oxygen saturation of 97% - Fetal tachycardia (211 bpm) 	<p><i>Met:</i></p> <ul style="list-style-type: none"> - Sudden onset cardiorespiratory arrest - Clinical onset during labor <p><i>Unmet:</i></p> <ul style="list-style-type: none"> - No fever - Overt signs of DIC 	<ul style="list-style-type: none"> - Intravenous hydration - Broad spectrum antibiotics - Cesarean delivery - 1800 mcg/mL IV phenylephrine - 0.2 mg Atropine - 8 mg Ondansetron - 15 mg Ketorolac - 50 units of Oxytocin - 2 doses of Carboprost - 3 units of pRBC - 1 unit FFP - 3500 mL IV fluid 	Full recovery
Parfitt et al. [6]	40 weeks	<ul style="list-style-type: none"> - Shortness of breath - Full cardiac arrest 	<p><i>Met:</i></p> <ul style="list-style-type: none"> - Sudden onset cardiorespiratory arrest - Clinical onset during labor - No fever <p><i>Unmet:</i></p> <ul style="list-style-type: none"> - Overt signs of DIC 	<ul style="list-style-type: none"> - Advanced cardiac life support measures administered - Cesarean section performed - 8 mg of ondansetron - 1 mg of atropine 	Full recovery

Abbreviation: DIC: disseminated intravascular coagulation, FFP: fresh frozen plasma, pRBC: packed red blood cells

CONCLUSION

An amniotic fluid embolism can present without the classic diagnostic tetrad and therefore should still be considered in the differential diagnoses of patients

presenting with acute postpartum cardiorespiratory distress. Furthermore, patients with an amniotic fluid embolism can be managed successfully utilizing the A-OK protocol.

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Author Contributions

Abigail Berry – Acquisition of data, Analysis of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Andrea Salcedo – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation

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Christopher Riba – Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.

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