

CASE REPORT

Embolism by the water of life

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Abstract

A 33-year-old multiparous woman in the process of labour was admitted to our hospital after developing a cardiorespiratory arrest immediately after manual rupture of the membranes in a home setting. On arrival, she was quickly stabilised and approached from the very beginning in a multidisciplinary fashion, working through the differential diagnosis of a peripartum collapse resulting in the highly suggestive diagnosis of amniotic fluid embolism (AFE) complicated with disseminated intravascular coagulation (DIC). In this brief report we describe a case of peripartum cardiorespiratory collapse due to AFE, review the diagnostic and therapeutic considerations involved in this scenario with a special emphasis on the phenomenon of DIC.

Introduction

We report a case of a 33-year-old multiparous woman admitted to our intensive care unit (ICU), who developed a severe cardiopulmonary collapse during labour. Although spontaneous circulation returned, the clinical course was complicated by overt disseminated intravascular coagulopathy (DIC) and neonatal death. We discuss this case and review the differential diagnosis of peripartum cardiorespiratory collapse, its approach, and the pathophysiology involved.

Case report

The patient was a 33-year-old multiparous pregnant woman without significant previous medical history. The pregnancy had developed uneventfully until the 41st week of gestation. Shortly after manual rupture of the membranes by her midwife, in the setting of a home delivery, at four centimetres of cervical dilatation and with regular uterine contractions, the patient became acutely cyanotic and a few seconds later unconscious with an abnormal breathing pattern. The midwife could not feel a pulse and cardiopulmonary resuscitation was initiated.

An ambulance arrived ten minutes later and documented the return of spontaneous circulation. However, the patient was still unresponsive (Glasgow Coma Score 3), and endotracheal intubation was performed. Subsequently the patient was transported to our emergency department.

On arrival, the patient was mechanically ventilated, she had a body core temperature of 37 °C, was tachycardic at 120 beats per minute, and normotensive with similar blood pressure levels on both arms. There were no cardiac rhythm abnormalities and her ECG was normal. Transthoracic cardiac ultrasound did not show wall motion abnormalities or right ventricular dilatation. An obstetrician onsite performed a pelvic/foetal ultrasound, manifesting a regular foetal heartbeat of 150 beats/min and no signs of abruption placentae or uterine rupture. Vaginal examination revealed complete cervical dilation. On site blood analysis showed a normal haematocrit, leucocytosis of $34 \times 10^9/l$ (normal range: $4-10 \times 10^9/l$) and a normal platelet count. Electrolytes were within normal ranges and C-reactive protein was elevated at 48 mg/l (normal range: 0-5 mg/l). Renal function and liver function analysis were within normal ranges. Coagulation studies were abnormal with a prolonged prothrombin time (PT) of 62 seconds (normal range: 12-15 seconds), INR of 4.2, activated partial thromboplastin time (APTT) of 120 seconds (normal range: 25-32 sec), D-dimer of more than 5000 ng/ml (normal range: < 500 ng/ml) and a fibrinogen of 0.4 gram/l (normal range: 2-4 gram/l). In this particular case the patient was further tested for insulin-growth factor-1 (IGF-1) and compliment factors with the following results: IGF-1: 237 mg/l (normal range: 37-85 mg/l), compliment factors: C1q 72 mg/l (normal range: 102-171 mg/l); C3 0.7 g/l (normal range : 0.9-2.0 g/l); C4 127 mg/l (normal range: 95-415 mg/l).

The cardiotocogram (CTG) performed at the emergency department did not suggest that the foetus was in acute distress. Since complete cervical dilatation was present in a

multiparous woman a vaginal delivery was deemed a faster and safer option as compared with caesarean section. Owing to the high risk of potential haemorrhage during and after delivery the patient was transported to the ICU for delivery under controlled and safe circumstances. She was given ten units of fresh frozen plasma, two units of packed cells, and a right central venous jugular line was placed. Concomitantly, the patient was administered intravenous oxytocin for maximal uterine contractility and within minutes a successful delivery was performed. The foetus was born with severe respiratory insufficiency, a pH of 6.9 and a deep lactic acidosis, needing intubation and further care in the neonatal ICU. In retrospect, the CTG performed in the emergency department, which suggested that the foetus was not in distress, may have been deceiving since at that time the circulation of mother and child had been restored after a previous episode of circulatory arrest. Postpartum the patient remained haemodynamically stable, and no active blood loss was seen. In a time lapse of about an hour all sedation was stopped including vasopressive support. Once awake the patient was extubated. Abnormal behaviour was observed and direct contact with her was not possible. The neurologist was asked to evaluate the patient. No lateralisation was observed, but taking into account a prolonged hypoxic event at the time before her intubation, an MRI of her brain was preformed to exclude cerebral injury secondary to anoxia. This last procedure revealed the absence of cerebral damage. Thirty hours postpartum she was in the obstetric ward, fully conscious with a normal neurological examination. Unfortunately her child did not recover and died a few days later in the neonatal ICU.

Peripartum cardiorespiratory collapse

The differential diagnosis of an obstetric patient with cardiovascular collapse is diverse. It includes eclampsia, uterine rupture, placenta abruption, peripartum cardiomyopathy, amniotic fluid embolism (AFE), pulmonary thromboembolism, air embolus, anaesthetic complications, drug-induced allergic anaphylaxis, myocardial infarction, cardiac arrhythmia, aortic dissection, pulmonary aspiration, and sepsis.¹ The initial common approach to all these critical clinical situations is the stabilisation of the mother. Stabilisation in the context of a cardiorespiratory collapse entails securing the airway by endotracheal intubation followed by aggressive haemodynamic and circulatory control. From 20 weeks gestation onwards a left uterine displacement (left lateral tilt) is of great importance to facilitate venous return. An urgent caesarean section should be considered as a resuscitative procedure to be performed primarily in the interest of maternal survival. If deemed necessary it should be done as quickly as possible, certainly if resuscitation continues beyond four minutes of the collapse.² Once maternal stabilisation is achieved, the intensive care specialist has the challenge of reaching a diagnosis with

the available diagnostic procedures in the shortest time possible, keeping in mind the safety of the mother at all times. As in the present case, a multidisciplinary approach is recommended, formed by an intensive care, obstetric, haematological, cardiological and neonatal team. Ultrasound is the imaging modality of choice for diagnosing maternal-related abnormalities. In expert hands, pelvic ultrasound can help us exclude or diagnose a significant number of clinical complications including uterine abruption, placental abruption and postpartum haemorrhage.³ Transthoracic cardiac ultrasonography is utilised to investigate signs of myocardial infarction, massive pulmonary embolism, and aortic dissection and can guide us into further decision-making strategies.⁴ More conventional diagnostic tools include ECG, blood count and coagulation studies.

In the present case, the fact that the patient was afebrile and was not reported to have had earlier signs of infection made the clinical diagnosis of sepsis unlikely. She was normotensive with similar blood pressure readings in both arms, making aortic dissection less plausible and because she was normotensive, the diagnosis of eclampsia was doubtful. The absence of signs of right heart ventricular distress or wall motion abnormalities in cardiac ultrasound made possible diagnoses of pulmonary thromboembolism, peripartum cardiomyopathy and myocardial infarction less likely. The pelvic ultrasound showed no signs suggestive of uterine rupture or placental abruption. The relative exclusion of these pathologies, together with the haematological presentation compatible with DIC, was highly suggestive for AFE. Further diagnostic workup, in particular a CT scan, was considered but disregarded because the major possible diagnoses had already been largely excluded including an unlikely diagnosis of a massive pulmonary embolism (large enough to cause a cardiac collapse but without alteration of the cardiac right ventricle).

Amniotic fluid embolism

AFE remains a leading cause of mortality in the pregnant population. Its precise incidence is unclear but varies between 1:15,000 and 1:50,000 deliveries in North America and Europe respectively.⁵ Its case fatality rate and perinatal mortality are 13-30% and 9-44%, respectively.¹ AFE is usually a complication that occurs during or within 24 hours after labour. There are no specific diagnostic criteria for this disease but it can present with acute severe hypoxic respiratory failure, DIC, confusion and seizures.⁶ Among survivors, persisting neurological impairment is reported in up to 61% of women and 50% of infants.⁷ Older maternal age and induction of labour are associated with AFE.⁸ AFE typically occurs during labour and delivery, or in the immediate postpartum period, with most cases (70%) starting before delivery.¹ Although the underlying mechanisms of AFE are poorly understood, it is accepted that the aetiology is related to the transfer of amniotic fluid into

the maternal circulation. How this event then translates to the varied clinical expression of this disease is still based on theoretical models.

There are three phases in the development of AFE. The first phase is characterised by an abrupt onset of dyspnoea, seizures, hypotension, cyanosis, cough, cardiac arrest, and coma, with 50% of deaths occurring within the first hour of onset of symptoms. Those who survive the initial insult enter the second phase characterised by DIC-associated haemorrhages and shock, and ultimately, the third phase consists of multiorgan failure which may lead to death.⁹ Many theories have been proposed to explain the pathophysiology of AFE. It is multifactorial and poorly understood. Anaphylactic reaction to foetal debris and/or compliment activation are suggested to play an important role in this process.^{10,11} The fact that amniotic fluid contains vasoactive and procoagulant products may help explain the prevalence of DIC in AFE. However, an alternative explanation for this association is an immune-mediated response producing compliment activation, which is consistent with the decreased C3 and C4 concentrations found in some of these patients.^{12,13} Alternatively exposure of the pulmonary microvasculature to amniotic fluid components may induce capillary leak, negative inotropic effects and bronchospasm, resulting in respiratory distress and left ventricular failure leading to pulmonary oedema and shock. These events ultimately culminate in a neurological response to the cardiorespiratory injury, with seizures, confusion, or coma as a result.

Diagnosis of AFE

No specific laboratory tests are available for making a diagnosis of AFE, yet several tests have been proposed to increase the index of suspicion for this diagnosis. The identification of foetal debris (squamous cells) in the maternal pulmonary arterial circulation is not pathognomonic for the diagnosis of AFE.^{7,14,15} Diagnostic markers on peripheral blood analysis have been suggested; these include zinc coproporphyrin (a characteristic component of meconium), sialyl Tn antigen (a foetal antigen present in amniotic fluid and meconium), tryptase and complement factors.¹⁶⁻¹⁸ Legrand suggests the use of insulin-like growth factor binding protein-1 as a marker for DIC in AFE patients.¹⁹ IGF-1 is an important regulator of foetal growth and can be measured in amniotic fluid. Indeed, in our patient blood testing showed a significantly increased IGF-1 (237 mg/l) in the maternal serum, which was interpreted as further proof that our diagnosis of AFE was correct. Also decreased complement factors are reported. In this particular case the patient was further tested for compliment factors C1q, C4, C3. Concentration levels of compliment factors C1q and C3 were low in the serum but whether these decreased complement levels are associated with the diagnosis of AFE or reflect active DIC remains to be elucidated.

Disseminated intravascular coagulation during amniotic fluid embolism

Dissimilar obstetric calamities may trigger DIC.²⁰ One of these calamities is AFE. AFE leads to activation of coagulation,²¹ but the exact pathophysiological mechanism by which AFE induces coagulation is incompletely understood.²² However, studies have shown that amniotic fluid contains high levels of tissue factor, phospholipid-like phosphatidylserine, thrombin, and lower concentrations of plasmin and plasminogen activators. Due to the strong procoagulant activity of tissue factor, haemostasis will be activated, leading to an enormous production of intravascular thrombin. Then, thrombin will convert fibrinogen to fibrin deposition, especially within the small vasculature. Subsequently, fibrinolysis will be activated resulting in DIC. Normally thrombin formation will be controlled by antithrombotic mechanisms. Due to the relatively large amount of tissue factor, the thrombin formation overwhelms the capacity of the regulatory antithrombotic pathways. The large amount of thrombus formation in a very large area of arterioles, capillaries and venules results in consumption of both coagulation factors and platelets. Together with the large amount of fibrin degradation products as a result of fibrinolysis, bleeding complications may occur due to consumptive coagulopathy. Laboratory tests usually show a prolonged PT and APTT, low platelet count, a low level of fibrinogen and a high D-dimer.

This patient presented with a cardiopulmonary arrest and had to be resuscitated due to AFE. Besides obstruction of the circulation, anaphylactic reactions to the amniotic fluid contents may play a role. This hypothesis is supported by laboratory tests at the time of presentation. As seen earlier, at admission the patient had a prolonged PT and APTT in combination with an immeasurably high D-dimer. In addition the fibrinogen concentration was below the lower detection limit. Additional testing showed a low complement C3 and C1q and low normal value of C4. High fibrinogen consumption, depletion of clotting factors, formation of fibrin degradation products and use of complement are all in agreement with a diagnosis of DIC. However the platelet count of $248 \times 10^9/l$ (normal value: $150-400 \times 10^9/l$) was not as low as expected. Studies have shown that mild thrombocytopenia is a common finding in patients with DIC, however, this is not specific. During follow-up, the fibrinogen, PT and APTT normalised. The D-dimer also fell initially, but not to normal levels with a value of 3400 ng/ml. After a longer follow-up, all the values normalised, which underscores that this disorder may resolve spontaneously once the stimulus, in this case the amniotic fluid, disappears.

Conclusion

AFE is a rare but catastrophic obstetric emergency with a high maternal and perinatal fatality rate. Its diagnosis is primarily

based on clinical observation and most of the diagnostic workup is directed to excluding other possible aetiologies. The rarity of this complication together with its diagnostic difficulties makes its underlying pathophysiology difficult to study, and to date the exact pathophysiology remains to be elucidated. AFE is strongly associated with DIC. Although the exact pathophysiology is unknown, DIC is an important contributor to the morbidity and mortality. In rare pathologies, case reports remain an important source of knowledge, and with the lack of evidence-based protocols, sharing experiences with positive outcomes (maternal survival in this case) help construct a path to the management of these patients.

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