Amniotic fluid embolism in an HIV-positive parturient

Penfold PR, FCA(SA), MMed(Anaes)(Wits)
Corbett C, FCA(SA)
Bortolan L, FCA(SA)
Department of Anaesthesia, Chris Hani Baragwanath Hospital, Johannesburg, South Africa
Correspondence to: Dr P Penfold, e-mail prpenfold@mweb.co.za
Keywords: amniotic fluid embolism; anaphylaxis; human immunodeficiency virus

Abstract

We present a case of a parturient infected with human immunodeficiency virus, who developed amniotic fluid embolism during the delivery of her twins by elective Caesarean section. Our management and the available literature are briefly discussed, and consideration is given to a possible association between the two pathologies.

Ⓟ Peer reviewed. (Submitted: 2010-02-01, Accepted: 2010-06-04) ***S Afr J Anaesthesiol Analg 2010;16(4):43-47***

Introduction

Amniotic fluid embolism is a rare and potentially catastrophic syndrome in pregnancy. It ranks among the most important causes of maternal mortality, with an incidence varying between 1:8 000 and 1:83 000 live births.[1] Reported mortality rates vary widely, most probably due to difficulties in accurately diagnosing the syndrome and in distinguishing it from that of anaphylactic shock. Most series report a consistently high mortality and morbidity.[2]

Risk factors for amniotic fluid embolism are well documented, although numerous incidences have occurred in women without any risk factors.[2,3] Human immunodeficiency virus (HIV) infection in pregnancy has not been investigated as a potential risk factor. The maternal death rate in South Africa is higher than in developed countries, and this is frequently attributed to the high prevalence of HIV infection.[4,5]

We report a case of an HIV-positive parturient who survived an amniotic fluid embolism following the delivery of her twins by Caesarean section.

Case report

A 33-year-old gravida 4 para 3 presented for an elective Caesarean section for a term twin pregnancy with an abnormal lie of the second twin. She was HIV positive with a clinical diagnosis of Stage 1 disease (asymptomatic, with no clinical features of AIDS or other associated conditions). She had been diagnosed with HIV infection during her pregnancy and had elected to delay further investigation until after the delivery of her babies. The patient was not on antiretroviral therapy and had no history of other medical problems or surgery. Her current pregnancy had been uncomplicated, with no features of gestational hypertension or pre-eclampsia. Her previous pregnancies had also been uncomplicated, and she had delivered by spontaneous vaginal delivery in all three. She had no history of any allergies or atopic symptoms. Preoperative full blood count and urea and electrolyte testing were normal. She was graded as ASA II, and she consented to a spinal anaesthetic.

An 18-gauge intravenous cannula was inserted, and an infusion of Ringers lactate was commenced at 80 ml per hour. Sodium citrate 30 ml orally and metoclopramide 10 mg intravenously (IV) were given immediately prior to the induction of anaesthesia. Amoxycillin-clavulanic acid 1.2 g was given IV as prophylaxis against wound sepsis. She was placed in a sitting position, and she was monitored with a three-lead electrocardiogram (ECG), non-invasive blood pressure measurement and pulse oximetry. Using an aseptic technique, the subarachnoid space was located on the first attempt, using a 26-gauge pencil-point spinal needle. Two point five millilitre of 0.5%

hyperbaric bupivacaine was administered slowly. The procedure was uneventful.

The patient was then placed supine with a 15-degree left lateral tilt. A 30-minute delay in the start of surgery followed due to a logistical issue. The patient remained haemodynamically stable throughout.

A Caesarean section was performed by an experienced consultant obstetrician via a Pfannenstiel incision. The first twin was female and was delivered 90 seconds after incision. Her Apgar scores were 9/10 and 10/10. The second twin was male and extensive manipulation of the uterus was required for delivery due to his abnormal lie. He was delivered after five minutes, with Apgar scores of 8/10 and 10/10. Oxytocin 2 IU was administered as a slow intravenous bolus.

Within two minutes after the delivery of the second twin, the patient had a generalised tonic clonic seizure. One hundred per cent oxygen was administered via face mask, propofol 50 mg and succinylcholine 50 mg were injected IV and her trachea was intubated. The seizure aborted with induction of anaesthesia. No gastric contents were seen in the oropharynx. Placement of the endotracheal tube was confirmed. Intermittent positive pressure ventilation with 100% oxygen was commenced. An intravenous bolus of 500 ml of Ringers lactate was infused. Blood pressure and heart rate were immediately noted to be 100/62 mm Hg and 93 beats/min, and oxygen saturation was 92%. Within a minute, the patient developed widened QRS complexes on the dynamic ECG trace. This rapidly progressed into cardiac arrest with pulseless electrical activity. Cardiopulmonary resuscitation was commenced, including intermittent boluses of adrenaline (total dose 2 mg). After two minutes, a return to spontaneous circulation occurred. Sinus tachycardia with a rate of 120 beats/min and hypertension with a blood pressure of 170/105 mm Hg were documented. Oxygen saturation was 80–85% on 100% oxygen, and compliance of the lungs was poor.

Two minutes later, a second cardiac arrest with pulseless electrical activity occurred, once again preceded by a wide complex bradycardia. Resuscitation continued and again spontaneous circulation returned after two minutes. A radial arterial line, a right internal jugular double-lumen central venous catheter and a large-bore 14-gauge peripheral intravenous line were placed. The patient's blood pressure was very labile and an adrenaline infusion was started at 0.5 ug/kg/min. A 500 ml colloid bolus was commenced. Magnesium sulphate 30 ug/kg IV as well as lignocaine 1 mg/kg IV was given. Arterial blood gas analysis showed slightly low levels of calcium and potassium, which were corrected, and a haemoglobin concentration of 9.2 g/dl. Other indices were within the normal range. Hydrocortisone 200 mg IV was given. After another 10 minutes, the patient had a third cardiac arrest. Once again, spontaneous circulation returned after two minutes of resuscitation.

Surgery had continued during the cardiac arrests and haemostasis had been easily obtained, the uterus sutured closed and the procedure completed. The uterus had been clearly noted as being well contracted. Following the third return of spontaneous circulation, the patient appeared to stabilise haemodynamically and mean blood pressure was maintained above 50 mm Hg on an adrenaline infusion of 0.1-0.5 ug/kg/min. The patient became restless and opened her eyes. She was subsequently given midazolam 2 mg IV and isoflurane 0.8% was commenced. Intermittent positive pressure ventilation was continued with 100% oxygen. Her nasopharyngeal temperature was 37.5 degrees Celsius.

After 15 minutes, significant blood loss was observed per vagina and abdominal distension was noted, with bleeding from the incision site. Fresh bleeding was also observed from the central venous pressure (CVP), arterial and peripheral line insertion sites. A disseminated intravascular coagulopathy was presumed. The uterus was re-examined by the obstetrician and deemed atonic. A decision was made to perform a subtotal hysterectomy in an effort to control any possible surgical bleeding. Arterial blood gas measurement at this stage revealed a haemoglobin level of 6 g/dl. An 8F intravascular sheath was placed in the left internal jugular vein to further facilitate rapid transfusion of blood and blood products.

The second surgical procedure took 45 minutes, despite the hysterectomy having been performed in 10 minutes. Internal iliac arteries were clamped in an attempt to regain haemostasis. Abdominal packs were also placed. During the operation, increasing dosages of the adrenaline infusion were required to maintain haemodynamic stability. Five units of packed red blood cells, four units of fresh frozen plasma, a megaunit of platelets and tranexamic acid (1g) were administered to correct the patient's clinical coagulopathy (the results of laboratory investigations were not available yet). After 40 minutes, haemostasis was achieved, the packs were removed and the abdomen was closed.

The Intensive Care Unit (ICU) of the hospital is 1.2 km from the obstetric theatre complex, and patients require an ambulance transfer by road. In view of this, we elected to continue stabilisation and observation of

the patient, prior to attempting transfer. Full intensive care management was continued. After two hours, no further haemorrhage was noted. No further cardiac arrests occurred and the ECG remained normal. By the time of transfer, the adrenaline infusion had been stopped. Urine output had remained more than 1 ml/kg/hr throughout. Gross neurological examination revealed appropriate responsiveness on weaning of volatile anaesthetic, in other words movement of all limbs and equal, reactive pupils bilaterally.

The patient was transferred to the ICU intubated and ventilated and given a further dose of midazolam 2 mg IV. She remained haemodynamically stable throughout the transfer. Her arterial blood gas on arrival in the ICU was normal, aside from a haemoglobin level of 8.0 g/dl. No further bleeding occurred and no further transfusions were necessary. She was normothermic on arrival.

Blood results of specimens taken just after the patient's third cardiac arrest revealed a low Hb of 7 g/dl and a raised INR of 1.6. C3 and C4 complement levels were both low, but unfortunately specimens for neither serum tryptase nor zinc coproporphyrin levels could be measured by our laboratory. Her urea and electrolytes, as well as her liver functions were all normal.

The patient's ICU stay was uneventful. A transthoracic echocardiogram on admission showed acute left ventricular dysfunction with an ejection fraction of 35% and mildly dilated ventricles. The pulmonary artery pressures were not measured. A dobutamine infusion of 7.5 µg/kg/min was started, and her ejection fraction improved to 60%. A chest X-ray revealed pulmonary oedema but no significant cardiomegaly. Furosemide diuresis was commenced and dobutamine was weaned and discontinued. The patient was extubated the following morning, and a subsequent echocardiogram showed normal cardiac function. Her neurological examination was completely normal. She gave a full recollection of the birth of both her twins. The patient was discharged from the ICU to a general postnatal ward two days after delivery. She consented to the use of her details in this report. On the fourth day post delivery, both she and her twins were discharged home.

Discussion

Confirming the diagnosis of amniotic fluid embolism has been the subject of many authors.[6,7] The clinical scenario we describe in our report fits well with the presumptive diagnosis, namely peripartum acute collapse with cardiac arrest, hypoxia, neurological signs and coagulopathy,[8] and as such we made the diagnosis on clinical grounds. Laboratory investigations that served to confirm the diagnosis included the deranged INR and the low complement levels. The typical late findings of acute left ventricular dysfunction were found on the echocardiogram.[9,2,4] Our patient also had a number of risk factors for amniotic fluid embolism – she was multiparous, she had a twin pregnancy with an abnormal foetal lie and she delivered by Caesarean section,[9]

The management of this event is largely symptomatic, with interventions aimed at maintaining delivery of oxygen and reversing the coagulopathy,[9,10] A high index of suspicion and rapid institution of resuscitative measures are required. Organ support is frequently required, and survivors are usually managed in an ICU setting,[11]

We were fortunate to have enough clinicians available to institute management almost immediately, and the surgeon on duty was particularly proficient. Because of the inherent delay associated with transfer to ICU in our hospital, we elected to manage the patient for slightly longer in the operating theatre so that the transfer would be as uneventful as possible.

Evidence exists to suggest that the syndrome of amniotic fluid embolism has numerous similarities with that of anaphylaxis, and recent investigations have considered management along the same lines.[12] With this in mind, we administered a dose of steroid. Unfortunately, the serum tryptase level of our patient was not determined.

Anaphylaxis under anaesthesia, despite its varied reported incidence from 1:4 000 to 1:25 000 cases, is still far more common than amniotic fluid embolism. Beta-lactamase antibiotics are responsible for almost 60% of these cases.[13] Although mortality from anaphylaxis under anaesthesia is rare, the reported cases of death are almost exclusively due to the IV administration of beta-lactamase antibiotics.[14] There does not appear to be any variation in incidence among races; however, women do display a slightly increased incidence.[14.15] Antibiotic anaphylaxis usually occurs via a hapten-mediated IgE hypersensitivity reaction, and hence patients with an atopic history are not predisposed to the syndrome.

The presentation of anaphylaxis is also inconsistent and can be broadly classified as either immediate (occurring within the first hour) or non-immediate (occurring any time after the first hour) and possibly even exhibiting a biphasic pattern of remission and then recurrence for up to 32 hours post exposure[16,17]

This classification refers to the onset of clinical signs and symptoms following initial exposure to the trigger. Immediate reactions are usually IgE mediated and non-immediate reactions are more commonly T-cell mediated.

Clinical diagnosis of anaphylaxis is likely if one of the following three criteria is satisfied within minutes to hours post exposure[18]:

- Acute signs of mucosal involvement or cutaneous manifestations accompanied by one of either respiratory compromise, hypotension, or end organ dysfunction.
- At least two of the following having developed rapidly post exposure – hypotension, respiratory compromise, gastrointestinal tract (GIT) symptoms or mucocutaneous signs.
- Hypotension > 30% less than the patient's baseline, following exposure to a known allergen for that specific patient.

Respiratory compromise, and hence hypoxia, may occur in up to 69% of cases. Both the lower airways, in the form of bronchospasm and increased pulmonary vascular pressures, and the upper airways, in the form of angioedema and stridor, may be involved.[14]

Hypotension occurs in 41% of cases and may be followed by complete circulatory collapse.[14] Myocardial ischaemia, conduction abnormalities, ventricular arrhythmias, nonspecific T-wave abnormalities in addition to cardiogenic and distributive shock may all occur. Whether these are due to direct mediator effects on the myocardium, exacerbation of pre-existing myocardial insufficiency due to hypotension or catecholamine effects on the myocardium as a result of the endogenous release or exogenous administration of adrenaline is unknown.[14] Mast cells also accumulate on atherosclerotic coronary plaques and may result in plaque rupture, resulting in further myocardial ischaemia. Direct H1 receptor stimulation by histamine can cause coronary artery vasospasm, ischaemia and negative inotropy.[14] Echocardiographic findings are variable as a result of the inconsistent pathophysiology; however, significantly reduced pre-load and afterload with a markedly reduced ejection fraction and left ventricular end diastolic volume are almost always noted, with a picture predominantly that of acute left ventricular failure.[14]

The presentation of amniotic fluid embolism is also variable.[7] The respiratory failure has a multifactorial aetiology. Initially it was thought to be due to pulmonary oedema with increased pulmonary capillary wedge pressures, which develops as a result of acute left ventricular failure. New data favour evidence that a sudden massive increase in pulmonary vascular resistance occurs on the basis of inflammatory mediator release as a result of the presence of foetal squames and amniotic fluid particles in the pulmonary vasculature.[19] A further mechanism may be that amniotic fluid is procoagulant and may result in the development of significant microthrombi within the pulmonary vasculature.[20] This sudden increase in pulmonary arterial pressures is believed to cause an initial acute right ventricular distension, acute right ventricular failure and a reverse Bernheim effect. It is also believed that the left ventricular failure occurs only later as a result of these changes.[19]

The only reported case of echocardiography in the hyperacute setting of amniotic fluid embolism displayed acute right ventricular failure, with supra-systemic right-sided pressures, bulging of the interventricular septum into the left ventricle and an almost totally collapsed left ventricle as a result.[19]

Clearly, further investigation into the cardiovascular manifestations of amniotic fluid embolism is warranted. Early transoesophageal echocardiographic studies may provide useful information regarding ventricular function. Obvious limitations to this mode of investigation would be the availability of the transoesophageal echocardiogram (TOE) probe in an obstetric theatre, the low incidence of amniotic fluid embolism, the need for the immediate institution of resuscitatory measures, as well as the risks associated with the placement and manipulation of the TOE probe in a severely coagulopathic patient.

Our patient did not develop bronchospasm, upper respiratory signs or any mucocutaneous signs typical of anaphylaxis. The patient had a seizure that was apparently unrelated to hypoxia. Furthermore, the sudden development of an atonic uterus and the acute onset of a disseminated intravascular coagulopathy are more in keeping with a diagnosis of amniotic fluid embolism than one of uncomplicated anaphylaxis.

It is unknown whether HIV infection presents an added risk factor for the development of amniotic fluid embolism. Numerous immunological changes occur in the setting of HIV and these changes to the immune system may well create a scenario of increased risk; however, this is purely speculative.

Amniotic fluid embolism continues to present both diagnostic and management-related difficulties. New research into the management of amniotic fluid embolism is examining the efficacy of selective pulmonary vasodilators for use in the proposed hyperacute setting of severe pulmonary hypertension

and right ventricular failure, as well as the possible efficacy of recombinant activated Factor VIIa for the treatment of the disseminated intravascular coagulation (DIC).[21] Hopefully, these measures will provide useful insight into this syndrome.

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