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Amniotic Fluid Embolism

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ANAESTHESIA
TUTORIAL OF THE WEEK
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Before reading this module begin with this scenario. This scenario is based on an actual case report of an amniotic fluid embolism.

You are covering the delivery suite you are called to attend urgently because a patient has just collapsed. On arrival you find the response team performing CPR on a 35 year old parturient (G₂P₀) of 41 weeks and 6 days gestation who presented in spontaneous labour earlier in the day. She is not making any respiratory effort and no pulse is detectable. The defibrillation pads are just being applied.

Approximately 2 minutes later a palpable pulse is restored corresponding with a sinus tachycardia on the defibrillation monitor. This is soon followed by return of spontaneous respiratory effort and some purposeful movement in the upper limbs. On talking to the midwife you discover that the patient initially complained of difficulty breathing and then appeared to lose consciousness and have a seizure.

Post arrest the fetus is compromised with a heart rate of 60 bpm. The mother remains unconscious. Clinically her cardiac output has normalised, so a decision is made to deliver her baby emergently in theatre. A caesarean is performed under general anaesthesia. A live male infant is delivered. After delivery the mother's haemodynamic and respiratory status deteriorates. Her oxygen requirements increase and high doses of noradrenaline are required to support her circulation.

It becomes apparent that a coagulopathy has rapidly developed and approximately one hour after the arrest her coagulation studies reveal an INR of 1.7, APTT 78s, fibrinogen 0.9 g/L, platelets 169 x 10⁹ /L and a Hb of 12.2 g/dL. This is treated with blood and blood product administration and transfer is arranged to the Intensive Care Unit (ICU).

The mother deteriorated further in the ICU, requiring large doses of vasopressor and inotropic therapy in addition to further blood products to correct her coagulopathy. Echocardiography revealed severe right ventricular failure with elevated pulmonary artery pressures. After treatment measures were instituted for the pulmonary hypertension she made a rapid recovery. She was extubated on the second ICU day and discharged from ICU on the fourth day. The neonate suffered from meconium aspiration syndrome but both the mother and baby survived with no long term medical issues.

Introduction

Amniotic Fluid Embolism (AFE) is a rare but potentially fatal syndrome that is unique to pregnancy. It most commonly presents in the intra-partum or immediate post-partum period. AFE classically presents as a sudden cardiovascular collapse associated with respiratory compromise, fetal distress and the development of a coagulopathy. However non-classical presentations may also occur and the clinician must always consider the possibility of AFE when dealing with an unwell obstetric patient.

Although AFE was first identified as a clinical entity in 1941 it remains an unpredictable condition and treatment is still largely supportive. AFE has emerged as one of the leading causes of direct maternal death within developed countries such as Australia, the UK and the USA. It is also associated with significant morbidity of surviving mothers and their babies.

The aetiology of AFE remains unclear. Initially AFE was thought to be secondary to the mechanical obstruction of the maternal circulation by amniotic fluid. More recent theories suggest that AFE is an immune mediated response to the presence of amniotic fluid in the maternal circulation. This has led some authors to suggest that the name AFE is a misnomer.

Despite deficiencies in our understanding of this condition, it is highly likely that improvements in medical care, in conjunction with the inclusion of less severe cases, has contributed to a decline in the mortality rate associated with AFE. Traditionally AFE was associated with an 80% mortality rate. More recent reports would suggest the mortality is between 20-40%, with some reports being as low as 13%. Neonatal outcomes, if AFE develops whilst the fetus is still in utero, are usually poor. Neonatal mortality rates range from 21-32%; however up to 50% of survivors have long term neurological impairment.

Incidence

The actual incidence of AFE remains unknown with commonly reported incidences ranging from 1:8000 to 1:80 000 deliveries. A recent review analysed and compared data from the USA and Europe and found that the pooled incidence in North America was 1:15 200 deliveries and in Europe 1:53 800 deliveries. It is difficult to attribute the reported differences in incidence to clinical differences between the various populations. It is more likely that AFE is under-reported in many medical communities as it remains a diagnosis of exclusion with no specific diagnostic test. In particular non-fatal cases may be undiagnosed given the common misconception that AFE is frequently fatal.

Risk factors

Risk factors that have been found to be associated with AFE include:

1. Maternal age > 35 years
2. Placental abnormalities: placenta previa, placental abruption
3. Caesarean delivery or forceps/vacuum assisted
4. Eclampsia
5. Fetal distress
6. Induction/augmentation of labour A young maternal age (<20 years) has been found to be protective against the development of AFE.

Amongst maternal AFE survivors there are a number of case reports of subsequent successful pregnancy without AFE. Whilst numbers are small the current evidence suggests that a history of AFE is not in itself a risk factor.

Pathogenesis

The pathogenesis of AFE is yet to be conclusively determined. Traditionally AFE was thought to be due to obstruction of the maternal pulmonary vasculature by amniotic fluid, thus the term amniotic fluid embolism. This however failed to explain all of the physiological changes that were seen in AFE, in particular the coagulopathy that develops in most women.

A humoral mechanism was subsequently proposed. Amniotic fluid has been found to contain a number of substances that could potentially contribute to the clinical picture of AFE, either directly or indirectly via the activation of secondary mediators. Proposed mediators have included platelet activating factor, bradykinin, leukotrienes, prostaglandins and tissue factor. Manifestations of AFE explained by this theory include coagulopathy, increased vascular permeability, vasoconstriction and bronchoconstriction.

Both of these theories have been largely discarded following the discovery that amniotic and fetal cells are a common finding in the vasculature of pregnant women (most of whom have no clinical evidence of AFE). Furthermore in animal studies AFE has not been reliably reproduced by direct injection of autologous, or human, amniotic fluid, with or without meconium, into the venous circulation.

More recently an immunologic mechanism has been proposed – AFE occurring in susceptible women upon exposure to fetal material. Many authors have identified the clinical similarities between AFE and septic or anaphylactic shock. Whilst subsequent research has failed to find evidence of mast cell degranulation, thus disputing the role of anaphylaxis, several studies have revealed reduced complement levels suggesting complement activation by antibody-antigen complexes could play a role.

The term AFE now appears to be a misnomer. Proposed new names include “sudden obstetric collapse syndrome” and “anaphylactoid syndrome of pregnancy”.

Clinical presentation

AFE typically occurs during labour and delivery or in the immediate postpartum period (usually within 5 minutes). However it can occur up to 48 hours post partum and at other points during pregnancy e.g after blunt abdominal trauma, cervical suture removal and during transabdominal amniocentesis. Classically the onset is sudden and catastrophic with cardiovascular collapse, respiratory distress, coagulopathy and fetal compromise. Atypical presentations can occur, for example, with gradual onset or isolated coagulopathy.

The most common signs and symptoms associated with AFE include: hypotension, fetal distress, pulmonary oedema/ARDS, cardiopulmonary arrest, cyanosis, coagulopathy, dyspnoea and seizures.

The most recent triennial report of maternal deaths within the UK (CEMACH: Confidential Enquiry into Maternal and Child Health) found that the majority of women that died from AFE had premonitory symptoms before collapse. These included: "breathlessness, chest pain, light headedness, restlessness, distress, panic, a feeling of pins and needles in the fingers, and nausea and vomiting". These early warning signs could act as indicators of at risk patients triggering the initiation of increased monitoring.

Cardiovascular Changes

Based on echocardiography studies in the acute setting, the haemodynamic response to AFE is thought to be biphasic. Initially there is thought to be severe pulmonary hypertension secondary to pulmonary vasoconstriction, which can precipitate right heart failure. This vasoconstriction may extend to the systemic circulation which can account for the transient hypertension that is occasionally seen. If the patient survives this acute insult then it can be followed by left heart failure. This left heart failure is probably secondary to a combination of a shift of the interventricular septum secondary to right heart failure, myocardial depression by activated mediators and myocardial ischaemia secondary to the initial hypoxia. Hypotension is attributed to the left heart failure but may also be contributed to by a distributive vasodilatory process, arrhythmia or haemorrhage.

Haematological Changes

Activation of a consumptive coagulopathy causes a rise in APTT and PT with a fall in fibrinogen levels. This typically appears within 4 hours of the initial presentation.

Respiratory Changes

Hypoxia is an early feature and likely attributable to three processes. Early on the main causes are pulmonary vasoconstriction and cardiogenic pulmonary oedema secondary to left heart failure. Later as these two primary processes resolve hypoxia is maintained by the development of an inflammatory capillary leak within the pulmonary vasculature leading to non-cardiogenic pulmonary oedema.

Neurological Changes

Hypoxia associated encephalopathy is a common cause of morbidity in AFE survivors. Seizure activity, which occurs in approximately half of all patients with AFE, possibly exacerbates this neurological injury.

Diagnosis

Currently the diagnosis of AFE is one of exclusion and determined on clinical grounds. Consensus varies as to the exact criteria that must be met for a diagnosis. Many diagnostic criteria do not include atypical presentations of AFE. Below is a set of diagnostic criteria commonly used in the USA and UK. Given that many of these signs and symptoms are non-specific, alternative diagnoses should always be considered. In particular conditions with specific treatments should be excluded.

Diagnostic Criteria for Amniotic Fluid Embolism

(Adapted from Stafford et al²)

- Acute hypotension and/or cardiac arrest
- Acute hypoxia diagnosed by dyspnoea, cyanosis and/or respiratory arrest
- Coagulopathy or severe clinical haemorrhage in the absence of other explanations

All of these occurring during labour, caesarean delivery or dilation and evacuation, or within 30 min postpartum with no other explanation for the findings

Table 1: Differential Diagnosis of AFE

| Pregnancy Specific Diagnosis | Anaesthetic Specific Diagnosis | Other Diagnosis |
|------------------------------|--------------------------------|----------------------|
| Acute Haemorrhage | High Regional Block | Pulmonary Embolism |
| Uterine Rupture | Local Anaesthetic Toxicity | Air Embolism |
| Eclampsia | | Anaphylaxis |
| Peripartum Cardiomyopathy | | Sepsis |
| | | Cardiac Ischaemia |
| | | Arrhythmia |
| | | Transfusion Reaction |

There is currently no test to confirm AFE. Traditionally the presence of amniotic fluid contents in the pulmonary circulation was considered pathognomonic but as explained previously this is no longer the case.

Treatment

The treatment of a suspected AFE episode is essentially supportive. A number of specific interventions such as cardiopulmonary bypass, nitric oxide and plasmapheresis have been described in exceptional circumstances.

Early and aggressive resuscitation is vital to maternal and neonatal survival in AFE

Alarmingly in the most recent CEMACH report, substandard care was considered to have contributed to 41% (7/17) of maternal deaths attributable to AFE. In the majority of these cases the main failing was a delay in active resuscitation – either through failed recognition of the severity of the woman’s condition or the lack of preparation for such an event.

In the event of cardiorespiratory arrest CPR should be administered immediately. There are 3 additional considerations when performing CPR on a pregnant woman:

1. Resuscitation should occur with left lateral tilt to reduce the impact of aortocaval compression on venous return.
2. Due to the high maternal oxygen consumption and reduced FRC maternal desaturation occurs rapidly and impacts adversely upon the mother and the fetus. This necessitates early intubation to secure the airway. The most experienced clinician present should perform this procedure due to the increased risk of difficult intubation in pregnancy.
3. If there is no response to CPR after 4 minutes of traditional resuscitation measures and the fetus is over 20 weeks gestation a perimortem caesarean should be performed with the aim of achieving delivery within 5 minutes. This will improve resuscitation efforts by removing aortocaval compression and will also potentially improve the efficacy of chest compressions.

Resuscitation in the non-arrest situation should follow an A, B, C style approach with the aim of maintaining oxygenation and organ perfusion. Coagulopathy should be anticipated and corrected with appropriate blood products. If unborn, the baby should be delivered as quickly as possible followed by transfer of the mother to a high dependency area for ongoing monitoring and treatment.

Frequently these women will require endotracheal intubation and a high inspired concentration of oxygen. The development of non-cardiogenic pulmonary oedema/ARDS may require complex ventilation strategies. If alveolar capillary disruption is severe, consideration of non-pulmonary gas exchange strategies (e.g. Extra Corporeal Membrane Oxygenation (ECMO)) may be required.

Haemodynamic changes can be complex and will frequently necessitate the monitoring of central venous pressure and potentially the insertion of a pulmonary artery catheter (to determine cardiac output, PCWP, pulmonary arterial pressure and systemic vascular resistance). Information from these devices along with information from echocardiography, if available, can help guide fluid, inotrope and vasopressor therapy.

Haemorrhage should be anticipated necessitating the insertion of large bore intravenous cannulae and early ordering of blood products. If post-partum haemorrhage occurs, other causes of ongoing bleeding should also be considered (e.g. tone, tissue, trauma). The successful use of recombinant activated factor VII has been reported in patients with AFE and bleeding unresponsive to conventional blood product therapy.

Other therapeutic modalities that have been utilised successfully in case reports of AFE include: cardiopulmonary bypass, ECMO, continuous haemofiltration (aiming to eliminate amniotic fluid), intra-aortic balloon counter-pulsation for left ventricular failure and pulmonary vasodilators including inhaled prostacyclin and nitric oxide.

Summary

- Amniotic Fluid Embolism is a condition unique to pregnancy and a leading cause of maternal death.
- With modern resuscitation techniques and intensive care treatment survival is much improved such that AFE is no longer a post mortem diagnosis.
- Aggressive and early resuscitation of parturients with AFE is frequently associated with good long term maternal and neonatal outcomes.
- Atypical presentations occur so the diagnosis of AFE should always be considered in acutely unwell parturients.

References

1. Conde-Agudelo A, Romero R. Amniotic fluid embolism: an evidence based review. *Am J Obstet Gynecol* 2009; 201; 445.e1-13
2. Stafford I, Sheffield J. Amniotic Fluid Embolism. *Obstet Gynecol Clin N Am* 2007; 34: 545- 53

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