Case Report

Early coagulopathy in amniotic fluid embolism

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Abstract

Background: Amniotic Fluid embolism (AFE) is a life-threatening complication in the peripartum period, especially during delivery due to the entrance of amniotic fluid into the maternal circulation. A typical patient may present with the triad of hypoxia, hypotension followed by coagulopathy. Neurological deficits may follow due to hypoxia. This immunological, anaphylactoid type reaction is due to the chemical nature of the amniotic fluid.

Case report: This atypical AFE was presented with an initial prodromal period (chills and a rash) followed by an early bleeding and atony of uterus. She delivered stillbirths. Even with investigation guided blood and blood product transfusions, she rapidly progressed to become hypoxic and hypotensive. She died of disseminated intravascular coagulation (DIC). The clinical picture and the presence of fetal parts in the maternal pulmonary circulation at the post mortem were positive findings for the diagnosis.

Conclusion: Bleeding in peripartum period or uterine atony may be an "atypical case" of AFE. Although these cases are being managed symptomatically, the presence of DIC will be a challenge to the team. Early detection, suspicion of the causes and correct use of early investigations may help. Unfortunately, even with careful timely interventions, the outcome may not be pleasant.

Key words

Amniotic fluid embolism, Incidence, Typical clinical features, Complications, Immunology, Diagnosis, Post mortem findings of AFE.

Introduction

Amniotic fluid can cause drastic reactions in the maternal life, in case it enters the maternal circulation (amniotic fluid embolism) as it contains ions, bioactive substances, fetal excretions and salts. It produces a chemical reaction in maternal life, hence the name "anaphylactoid reaction of pregnancy" [1]. This may go unnoticed or may produce reactions at various degrees.

The majority of cases occur at the time of induction of labor and during delivery. Polyhydramnios, uterine rupture, abruption, instrumentation, and caesarean deliveries are some high-risk associations. Even though a typical presentation would be a maternal collapse following hypoxia and hypotension, atypical cases can happen, misleading the diagnosis.

Case report

A twenty nine year old, medically uncomplicated twin-pregnant mother, at her 37 weeks of gestation was referred for delivery as one of the twins had been diagnosed of having a diaphragmatic hernia.

She suddenly developed a transient bout of chills and a rash. Soon afterwards, she went into labor with dribbling. She was prepared for an emergency caesarean section.

A subarachnoid block (SAB) using heavy bupivacaine and fentanyl at L3-L4 level achieved an adequate sensory block up to T4. Systolic blood pressure had been around 90- 110 mmHg. Blood-stained urine was noted once she was catheterized following the SAB. Both twins were dead by the time they were delivered.

Despite the usual oxytocin, ergometrine, uterine massage and B-Lynch wiring she had continuous bleeding with uterine atony. Following a blood loss of 2L, she underwent a hysterectomy and bilateral internal iliac artery ligation, under general anesthesia. Blood pressure (BP) dropped significantly with continuous bleeding. During the delivery period and afterwards two liters of saline, 1200ml of packed red cells, 900ml of fresh frozen plasma (FFP) and five bags of platelets were transfused to maintain blood pressure, to correct hemoglobin (Hb) and bleeding as investigations showed Hb 6g/dL, platelet count of 80 000/µL and INR of 5. There were no features suggestive of placental abruption.

Adrenaline 0.4 µg/kg/min and noradrenalin 0.4 µg/kg/min were added to maintain blood pressure. Initial chest X-ray, after 4 hours, was slightly hazy, bilaterally. The saturation was 95 to 99% with 70 to 80% oxygen. Hb remained low around 6g/dl, platelets dropped and remained low at around 30,000/µL. INR and APTT were high, even with several transfusions of blood and blood products. Vasopressin and dobutamine were added to maintain blood pressure. Saturation was below 90% with 100% Oxygen. The 2nd chest X-ray after 10 hours showed features of pulmonary edema. The abdomen was re-opened and packed with surgical towels. Thrombo-elastography showed features of disseminated intravascular coagulation (DIC).

After repeated attempts at resuscitations, she passed away, about eighteen hours after delivery. The post mortem revealed some fetal squamous cells, mucins and lanugo hair in mother's pulmonary circulation.

Discussion

Incidence

Incidence may vary from center to center, country to country, and on the method of analysis and the definition. It ranged from 1.9/ 100 000 maternities (UK) to 6.1/ 100 000 maternities (Australia) [2].

The latest Confidential inquiry into maternal deaths in the UK and Ireland (MBRRACE 2017) reports 8 out of 202 deaths due to AFE during 2012- 15 period. This figure has been changing from 7 to 16 in the last decade [3].

Analysis of US national registry finds 70% of AFE happens during labor. 11% and 19% AFE may occur after vaginal delivery and during caesarean sections respectively.

Presentation

She complained of a transient bout of chills and a nonspecific skin rash before the development of labor pains. Prodromal features may include sudden onset dyspnea, cough, sweating, anxiety, agitation, chills and rigors [4]. This prodromal period may go unnoticed due to non-specificity and it is transient.

Typical AFE may present with a triad of sudden onset hypoxia, hypotension followed by coagulopathy during labor and delivery. Hypotension is considered the most common finding. This may be due to anaphylactoid type reaction. Respiratory signs and symptoms may include severe shortness of breath and cyanosis leading to sudden desaturation. Uterine atony is common. Encephalopathic features may range from agitation, altered mental state to tonic-clonic seizures, thought to be secondary to hypoxia. Fetal bradycardia and death may occur due to hypoxia.

This mother developed prodromal features and labor almost together and progressed to coagulopathy very rapidly, within less than an hour. She delivered stillbirths and went into severe persistent uterine atony.

Pathophysiology

The entry of amniotic fluid into the maternal circulation was initially reported by J.R. Meyer in 1926 [5]. In 1941, after examining 32 autopsies, Steiner and Lushbaugh concluded that the presence of fetal squamous cells in maternal pulmonary circulation causing a possible obstruction may play a role in pathology. They described it as a "syndrome of sudden peripartum shock" [6].

Amniotic fluid contains several vasoactive as well as procoagulant chemicals. Bradykinin, thromboxane, leukotrienes, arachidonic acid, platelet-activating factor, tissue factor and tissue factor pathway inhibitor may explain coagulation disturbances, which lead to disseminated intravascular coagulation (DIC). The rise in endothelin concentration in maternal circulation following the entry of amniotic fluid may be contributing to the broncho-pulmonary and coronary vasoconstriction which leads to cardio-respiratory collapse [7]. These findings have made to believe that the chemical or immunogenic theory is more favored than obstruction by the fetal particles in producing AFE as it may explain respiratory, cardiovascular and coagulopathic features. This is further suggested by the reaction, following AFE which is very much similar to anaphylaxis, hence the name "anaphylactoid reaction of pregnancy".

The immunologic theory is further suggested by the activation of complement cascade by the observation that these patients have marked reduction in C3 and C4 levels plus the rise in histamine and tryptase levels [8]. These findings may suggest the difficulty in differentiating AFE from anaphylaxis as these are common to both.

Host response to an antigen varies from person to person. Atopic individual's response may be higher. This idiosyncrasy may play a vital role in producing different responses and outcomes.

In a typical AFE, the initial hypoxia develops due to vasospasm and pulmonary hypertension following the entry of vasoactive substances into the pulmonary circulation. This may end up in right heart failure. In the second phase, the hypoxia continued due to pulmonary edema following left ventricular failure (LVF) and leaky capillaries in the pulmonary circulation following endothelial damage. LVF and systemic vasodilatation (due to SIRS like reaction with proinflammatory cytokines) proceed to cardiovascular collapse.

Procoagulant factors in amniotic fluid, with the tissue factor release following endothelial damage, leads to activation of the coagulation pathway and DIC.

Diagnosis

The clinical picture is considered the best to make the diagnosis.

Typical scenario includes sudden onset hypoxia and cardiovascular collapse followed by coagulopathy with the possibility of neurological features. The clinical diagnosis will be difficult in atypical cases. Differential diagnoses such as myocardial infarction, peripartum cardiomyopathy, deep vein thrombosis (DVT), placental abruption, anaphylaxis, sepsis and transfusion reactions should be excluded.

Fetal squamous cell and mucins, which were found in the lungs at the post-mortem of the patient can be positive findings. Epithelial squamous cells shed from the fetal skin, lanugo hairs, vernix caseosa, mucin and bile pigments derived from the meconium have been found in the pulmonary circulation following death due to AFE [9]. Mere presence of these in post mortem findings should be carefully analyzed, as these may be present in other circumstances as well.

Zinc coproporphyrin, sialyl-Tn antigen, insulin-like growth factor binding protein have been identified and tested in research. It is noted, that the levels of C3, C4 and C1 esterase inhibitor (C1INH) were also low in cases of AFE [10]. C1INH acts on complement pathways preventing auto-activation of the classical pathway and acts as an inhibitor of plasmin, helping in the stabilization of clots. C1INH has drawbacks, as a biomarker, as it's level in pregnancy is usually low. Tryptase, which is raised in anaphylactoid or anaphylactic reactions, may be high in some cases of AFE, suggesting the anaphylactic type of pathology as well. All these biomarkers are not considered specific.

Management

The management is essentially on a symptomatic basis, which includes,

1. Stabilization of airway, possibly with an endotracheal tube and ventilation to prevent hypoxia
2. Fluids and inotropes to maintain the blood pressure.
3. Transfusion of blood and blood products (FFP, cryoprecipitate and platelets) appropriately to replace the losses and to correct disturbed coagulation. The amount of replacement depends on the speed and the amount of blood loss. Even though a rapid replacement may be needed initially, laboratory testing should be done as early as possible. Point of care testing like thrombo-elastography will be very useful as these are relatively fast and give an idea of the ongoing function of platelets, clotting and thrombolysis.

Consent

Sincere thank goes to the husband of the patient for giving consent, for the publication without divulging the identity of the patient.

Conclusion

Bleeding in peripartum period or uterine atony may be an "atypical case" of AFE. Although these cases are being managed symptomatically, the presence of DIC will be a challenge to the team. Early detection, suspicion of the causes and correct use of early investigations may help. Unfortunately, even with careful timely interventions, the outcome may not be pleasant.

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