www.jmscr.igmpublication.org
Impact Factor 5.244
Index Copernicus Value: 83.27
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v4i10.37

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Amniotic Fluid Embolism: A Nightmare

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Abstract
The disastrous entry of amniotic fluid into the maternal circulation leads to dramatic sequelae of clinical events, characteristically referred to as Amniotic fluid embolism (AFE). AFE can occur during labour, caesarean section, dilatation and evacuation or in the immediate postpartum period where the role of anaesthetist is prudent. The pathophysiology is believed to be immune mediated which affects the respiratory, cardiovascular, neurological and haematological systems. Undetected and untreated, it turns into fulminant pulmonary oedema, intractable convulsions, disseminated intravascular coagulation (DIC), malignant arrhythmias and cardiac arrest. Usually the diagnosis is made clinically however definite diagnosis can be confirmed by identification of lanugo, foetal hair and foetal squamous cells in blood aspirated from the maternal right ventricle. The cornerstone of management is early recognition and aggressive resuscitation with multidisciplinary approach that increases the probability of maternal and neonatal survival.
Keywords: *Amniotic fluid embolism, pulmonary oedema, hypoxia, coagulopathy, cardiac arrest.*

Introduction

Amniotic fluid embolism (AFE) is a rare, potentially fatal syndrome unique to pregnancy. The entry of amniotic fluid into the maternal circulation stimulates the sudden onset of severe dyspnoea, tachypnoea, and cyanosis during labour, delivery or early post-partum. The exact mechanism of this catastrophic condition is not yet clearly understood. However the disease course may vary from minor subclinical to rapidly fatal organ dysfunction resulting into coagulo-pathy, cardiovascular collapse and death wherein crucial role in management is played by anaesthetist. The incidence of AFE has been reported to range from 1 in 8000 to 1 in 80,000 deliveries[1]. The estimated mortality (death) rate is 70-90%. Despite advances in the care of critically ill patients, no management or interventions have been found to prevent the occurance or improve the survival or long-term outcome of woman with AFE.

Amniotic fluid embolism was first reported by Ricardo Meyer in 1926[2]. It was in 1941, when Steiner and Lushbaugh reported the clinical and pathological findings of 42 women who died suddenly during or just after labor[3]. Clarke et al have proposed renaming of the syndrome as "Anaphylactoid syndrome of pregnancy" because of the various humoral and immunologic factors implicated.[4,5] He studied the histopathology of the pulmonary vasculature of these women which included mucin, amorphous eosinophilic material, and squamous cells indicating that the syndrome results from bronchial mediators that are released after embolization .

In recent years the improvement in morbidity and mortality is likely to be secondary to a number of factors, like greater awareness of the condition among clinicians, developments in resuscitation and intensive care, as well as multidisciplinary training for the management of the collapsed obstetric patient.

Following four criteria are considered in a broader way to diagnose AFE clinically.

1. Acute hypotension or cardiac arrest
2. Acute hypoxia
3. Coagulopathy or severe clinical haemorrhage in the absence of other explanations
4. All above findings occurring during labour, caesarean delivery, or dilation and evacuation or within 30 minutes postpartum with no other explanation for the clinical findings.

Pathophysiology

The exact mechanism is not yet clearly understood, hence many theories have been put forward. The proposed mechanism of Amniotic fluid embolism suggests that foetal antigen in amniotic fluid stimulates the maternal endogenous immune mediators, producing a reaction similar to anaphylaxis; while the biochemical mediators trigger the anaphylactoid reaction with multisystem involvement. Clarke et al suggested that the syndrome of acute peripartum hypoxia, hemodynamic collapse, and coagulopathy should be described as anaphylactoid syndrome of pregnancy[4].

The mechanism of clinical signs can be explained phase wise.

Phase 1*:* Amniotic fluid and fetal cells enter the maternal circulation resulting in the release of biochemical mediators which cause pulmonary artery vasospasm followed by pulmonary hypertension. This results in elevated right ventricular pressures and right ventricular dysfunction, which will lead to hypoxaemia and hypotension with associated myocardial and capillary damage. Phase 1 may last up to 30 min.

Phase 2*:* This occurs in patients who survive the initial insult. Left ventricular failure and pulmonary oedema sets in. The biochemical mediators trigger DIC leading to massive haemorrhage and uterine atony.

Phase 3: Tissue hypoxia and end organ failure comprise the last phase.

In the first manifestation the amniotic microemboli trigger the release of arachidonic acid metabolites causing transient pulmonary vasospasm[6] resulting into pulmonary hypertension, intrapulmonary shunting, bronchoconstriction and severe hypoxia[7]. The increase in maternal plasma endothelin concentration causes pulmonary and coronary vasoconstriction which may contribute to respiratory and cardiovascular collapse[8]. Meconium may play a role in this mechanism. The second manifestation includes negative inotropism and left ventricular failure resulting in increasing pulmonary edema and hypotension quickly leading to shock. The third manifestation is a neurological response to the respiratory and hemodynamic injury, which may include seizures, confusion, or coma[9]. Given proper treatment almost 50% patients who survive this phase generally land into disseminated intravascular coagulation, the phase of uncontrolled uterine and puncture site bleeding. This coagulopathy is precipitated by procoagulant components of amniotic fluid, thromboplastin, which initiates the extrinsic pathway of the clotting cascade and results in excessive fibrino-

lytic activity. This is supported with Complement activation and markedly decreased C3 and C4 concentrations. The release of histamine and tryptase is due to reaction of immunoglobuline E with foetal antigen.

The incidence of recovery from this injury is very low. The consequences like severe lung or brain injury, multi-organ failure, infection are the major causes of mortality[6].

Clinical presentation

Amniotic fluid embolism occurs during labour or delivery, the immediate postpartum period,after caesarean section, amniocentesis, removal of placenta, or with therapeutic abortion. Other cases have been associated with abdominal trauma, cervical suture removal, ruptured uterus or intrapartum amnioinfusion.[10,11,12]

The sudden occurance of severe chills, shivering, sweating and coughing followed by respiratory distress, evidenced by cyanosis,tachypnea and bronchospasm, raises the suspicion of AFE. These symptoms turn into pulmonary edema and cardiovascular collapse and convulsions[10].

Hypoxemia explains the cyanosis, restlessness, convulsions, and coma whereas reflex tachypnea results from the decreased arterial oxygen saturation and cardiovascular collapse heralded by hypotension, tachycardia, and arrhythmia which may end in cardiac arrest.

In some patients convulsions may be the early manifestation and death may occur due to cerebral ischemia. There is a subset of patients in whom severe hemorrhage with DIC may be the first presenting sign.

Diagnosis

To diagnose Amniotic fluid embolism, the clinical presentation is supported with the ECG showing ST-T wave changes, tachycardia and right ventricular strain pattern.Pulse oximetry shows drop in saturation followed by hypotension and cardiovascular collapse. Central venous pressure (CVP) shows an initial rise due to pulmonary hypertension and eventually a profound drop due to severe haemorrhage as patient enters into the phase of DIC. The evidence of disseminated intravascular coagulation ensues decreased platelet count, decreased fibrinogen and afibrinogenemia, prolonged PT, aPTT, and presence of fibrin degradation products. Echocardiography may demonstrate acute left heart failure, acute right heart failure or severe pulmonary hypertension. The diagnosis is further confirmed by Chest X-Ray showing an enlarged right atrium and ventricle and prominent proximal pulmonary artery and pulmonary edema.The lung scan can demonstrate some areas of reduced radioactivity in the lung field. However, a definitive diagnosis is usually made by demonstration of amniotic fluid material in the maternal circulation, in the small arteries, arterioles, and capillaries of the pulmonary vessels; identification of lanugo or foetal hair and foetal squames in an aspirate of blood from the maternal right heart[13].Fetal squames have been recovered in the maternal sputum in some cases[14]. The other method used is immunostaining of the antimucin monoclonal TKH-2 antibodies in the maternal serum and lung tissue. TKH-2 reacts with meconium and mucin and stains the lung tissue in patients with AFE[15]. One more rapid diagnostic marker is the measurement of Zinc coproporphyrin, a component of amniotic fluid found in maternal serum, which is elevated in patients with AFE[16].

Differencial Diagnosis

The conditions which mimic AFE are

1) Thrombotic pulmonary embolism: it presents with chest pain and occurs in late postpartum period with evidence of venous thrombosis in the lower limbs[17]. 2) Air embolism: Water wheel murmur is heard over pericardium[18]. 3) *Aspiration of gastric contents* into the lungs causes cyanosis, tachycardia, hypotension, and pulmonary edema (similar to AFE). However, acid aspiration is usually seen in an unconscious patient with loss of the cough reflex or during induction or emergence from general anesthesia[17].

Management

Early recognition, prompt resuscitation for cardiopulmonary stabilization and adequate oxygenation to the vital organs with delivery of foetus are the key factors in the management of AFE. Elective LSCS is indicated though decision is individualized. After delivery of baby uterine tone can be achieved by using Oxytocin, ergometrine, and prostaglandins such as carboprost and misoprostol.

Monitoring of such patients should include Continuous cardiac telemetry monitoring with pulse oximetry, EtCo2, CVP monitoring, Arterial blood gas analysis, electrolyte monitoring, Pulmonary artery catheterisation and transesophageal echocardiography. Essencial laboratory data such as complete blood count, platelets, electrolytes and ABG, coagulation profile with fibrin degradation products and D-Dimer study help in the diagnosis and prognosis of the patient. Emergency resuscitative management is done by anaesthetist in post anaesthesia care unit or in intensive care unit.

Oxygen supplementation by Ventilatory support with PEEP is mandatory to prevent hypoxia, end-organ hypoperfusion leading to organ system failure and subsequent severe neurologic impairent. Fluid resuscitation is imperative to counteract hypotension and hemodynamic instability. Transthoracic or transesophageal echocardiography may guide fluid therapy with evaluation of left ventricular filling[19]. An arterial line and pulmonary catheter is also helpful for monitoring of cardiac output as well as the gas analysis. Epinephrine may be the first-line agent of choice in refractory hypotension, as it is used in other anaphylactoid reactions. Dopamine or noradrenaline may be ideal agent because of the additional β-adrenergic effects, which improves cardiac function in addition to the α-adrenergic vasoconstriction[20]. Inotropic support is given with dobutamine. High doses of steroids are suggested.

Patients with coagulopathy must be treated with blood component therapy such as Fresh frozen plasma, platelets and cryoprecipitate. The maintenance of tissue oxygenation should be preferably achieved by packed red blood cells transfusion. Fresh frozen plasma and platelets are given to replace antithrombin III and platelets that are consumed in clotting process. Cryoprecipitate has a significant role where fibrinogen is low and volume overload is a concern, so also in severe ARDS secondary to amniotic fluid embolism. Cryoprecipitate is rich in opsonic alpha 2 surface-binding glycoprotein, also known as fibronectin, which aids the reticuloendothelial system in the filtration of antigenic and toxic particulate matter. Recombinant factor VII is used in massive haemorrhage. At times hysterectomy with internal iliac ligation is required if bleeding is profuse and pharmacological support is unsuccessful.

The newer strategies are put forward in the management of AFE viz: Cardiopulmonary bypass for catastrophic pulmonary vasoconstriction, Plasma exchange transfusion, Extracorporeal membrane oxygenator, Serum protease inhibitors and Aprotinin to manage DIC, Inhaled prostacyclines used as pulmonary vasodilator to combat severe hypoxemia etc.Use of inhaled nitric oxide has also been reported for acute right ventricular failure and pulmonary hypertension being a selective pulmonary vasodilator[21].

Conclusion

Amniotic fluid embolism syndrome is an unexpected catastrophic complication of pregnancy and its unpredictability increases the risk. Diagnosis is based on a spectrum of clinical signs and symptoms .The mortality is regardless of quality of care rendered. Improved understanding of the pathophysiology of AFE may lead to the development of preventive measures and more effective and specific treatment. Although ongoing research may change the scenario, a high index of suspicion, a multidisciplinary approach with the input of consultant anaesthetists, obstetricians, haematologists, intensivists and rapid resuscitation efforts are essential to have a desirable clinical outcome.

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