Amniotic Fluid Embolism

Amniotic fluid embolism is a catastrophic and potentially fatal disease whose mechanism of injury is poorly understood, with few means to predict who and when the condition will affect an otherwise healthy parturient; right heart failure that progresses to left heart dysfunction, rapidly developing pulmonary edema, neurologic symptoms, and hematologic abnormalities are the main clinical features of this syndrome; a high index of suspicion is needed to make the diagnosis & prompt and aggressive supportive treatment is required to lessen an otherwise dismal outcome, which may include death or permanent disability

ANESTHETIC CONSIDERATIONS:

- Emergency situation
  - Emergent delivery of fetus if not yet delivered
- General considerations of the pregnant patient
  - Physiologic changes etc.
  - Two patients
- Respiratory failure:
  - hypoxemia
  - non cardiogenic pulmonary edema
- Hemodynamic instability:
  - Cardiovascular collapse with biventricular failure
  - Hypovolemia: DIC / uterine hemorrhage
- Postoperative disposition: ICU
  - Potential for postoperative MI, renal failure & neurological deficits

ANESTHETIC GOALS:

- Maintenance of oxygenation
- Maintenance of circulation
- Correction of coagulopathy

HISTORY

- Can occur during TA, labor, vaginal delivery or C/S
- Risk factors
  - Tumultuous labor, strong contractions, uterine stimulants, uterine rupture, sudden fetal expulsion
  - cervical laceration, chorioamnionitis
  - Increased fetal size, Multiple gestations
  - Advanced age
  - Meconium
  - Fetal death
- AMPLE history

PHYSICAL

- **GENERAL**
  - Earliest sign is sudden tachypnea and decrease in saturation
  - Cardinal signs – respiratory distress, cyanosis, CV collapse, coma
  - Review monitors: loss / drop $EtCO_2$, low BP, low saturation with low output waveform, tachycardia / arrhythmia
- **RESP**
  - Distress (tachypnea, accessory muscles, cyanosis); pulmonary edema (frothy pink sputum); dyspnea; pleuritic chest pain; cyanosis; ↑ RR; ↓ SaO_2
- **CVS -** CV collapse; ↑ HR; ↓ BP; pulmonary HTN with RV failure
- **CNS -** Anxiety; shivering / sweating; seizures; coma; hyperreflexia
- **HEME -** Hemorrhage, thrombolysis, DIC
- **OB -** Fetal distress; uterine atony

INVESTIGATIONS

- **Labs**
  - CBC (anemia, thrombocytopenia), lytes, BUN, Cr & serum tryptase
  - INR & PTT (prolongation)
  - Fibrinogen (decreased) & FDP (increased)
  - ABG
    - Hypoxemia with mixed metabolic acidosis & respiratory alkalosis
  - Consider blood sample from pulmonary circulation
    - Blood should be drawn from the distal lumen of a wedged PAC
    - The first 10 mL of blood is discarded & a second is drawn, heparinized and analyzed utilizing Papanicolaou's method looking for squamous cells & mucous
- **Imaging**
  - EKG
    - Non-specific ST & T-wave changes
    - RBBB, right atrial strain & RAD
  - CXR
    - Infiltrate, pleural effusion, atelectasis & elevated hemidiaphragm
  - ECHO
    - Pulmonary HTN & biventricular failure

Table 1. Cardinal signs/symptoms of amniotic fluid embolism syndrome

Hypoxemia
Shock (typically obstructive, cardiogenic, or distributive)
Coagulopathy/disseminated intravascular coagulation
Altered mental status/hypoxic encephalopathy

Table 2. Other common presenting signs/symptoms of amniotic fluid embolism

Seizure activity
Confusion
Agitation
Constitutional (fever, chills, headache, nausea, vomiting)
Evidence of fetal distress (late decelerations, bradycardia)

Table 3. Differential diagnosis of amniotic fluid embolism

Pulmonary thromboembolism
Air embolism
Hemorrhage
Aspiration of gastric contents
Anesthetic complications
Anaphylaxis
Sepsis/systemic inflammatory response syndrome
Myocardial infarction
Cardiomyopathy
Eclampsia
Transfusion reactions

MANAGEMENT OF ANESTHESIA

- Management via an ABC approach, with goals towards maintenance of oxygenation, circulatory support and correction of coagulopathy
- **Airway**
  - Place patient on 100% O_2 to maintain SaO_2
  - A majority of patients require securing the airway and placement on 100% O_2 via mechanical ventilation through an ETT
    - **Early oxygenation** is the most consistent factor in preventing poor neurological outcome!
- **Breathing**
  - Listen over both lungs to rule in / out other etiologies
  - Assess degree of pulmonary edema
    - Consider PEEP if evidence of pulmonary edema
- **Circulation / C-section**
  - Cycle all vitals and scan monitors
  - Initiate CPR if indicated
  - Maintain left uterine displacement to minimize aortocaval compression
  - Secure two good IVs and hang fluid
  - Consider the Rapid Infuser if indicated
  - Support BP
    - Early utilization of phenylephrine (direct acting vasopressor) to maintain afterload
    - Change to dopamine / dobutamine for inotropy / chronotropy
      - Dopamine 2-20 mcg/kg/min
      - Dobutamine 10-30 mcg/kg/min
      - Norepinephrine 0.1-0.5 mcg/kg/min
      - Epinephrine 0.1-0.3 mcg/kg/min
    - Some cases may require afterload reduction (milrinone, NTG) or diuresis
  - Place IJ / subclavian line to float PA catheter
    - Will help guide therapy as some patients may need afterload reduction to improve cardiac performance
    - Others may need diuresis to reverse pulmonary edema
    - Consider TEE
  - Monitor fetus & facilitate delivery
    - If the baby is not yet delivered then a stat c-section is needed
      - Only 50% of babies delivered post-AFE end up neurologically intact
      - C-section may still be performed within 5 minutes of maternal arrest and death (perimortem c-section)
  - Treat uterine atony – oxytocin, hemabate
  - Anticipate and treat acute ARDS
- **Disability**
  - GCS, gross assessment of focal neurological findings and evaluation for seizure-like movements may help narrow the differential diagnosis (rule in / out seizure activity)
  - If the patient who received neuraxial blockade ends up surviving an AFE, use frequent neurological assessments to rule out epidural hematomas in the setting of a coagulopathy
- **Anemia / Coagulation**
  - As per standard DIC protocol, utilizing cells, FFP, platelets and cryoprecipitate
  - If volume overload is an initial concern have a lower threshold to move straight to cryoprecipitate as this is a concentrated source of factors (VIII, XIII, fibrinogen, vWF)

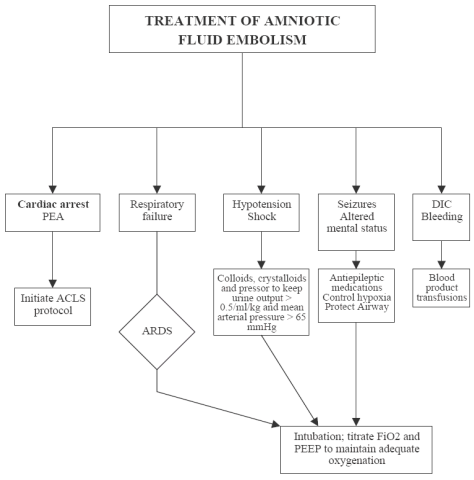

Fig. 2. Treatment of amniotic fluid embolism. ACLS, advanced cardiac life support; ARDS, acute respiratory distress syndrome; PEA, pulseless electrical activity; PEEP, positive end expiratory pressure.

Table 4. General supportive measures in the treatment of amniotic fluid embolism

1. Treat hypoxia with 100% oxygen.
2. Treat hypotension by fluid resuscitation with isotonic solutions and vasopressors.
3. Treat left ventricular diminished contractility with fluids and inotropic therapy.
4. Treat DIC and coagulopathy with FFP, cryoprecipitate, fibrinogen, and factor replacement.
5. Treat hemorrhage with RBC transfusions and thrombocytopenia with platelets.

DIC, disseminated intravascular coagulation; FFP, fresh frozen plasma; RBC, red blood cells.

Table 5. Newer strategies in the treatment of amniotic fluid embolism

1. Intra-aortic balloon counterpulsation (41)
2. Extracorporeal membrane oxygenation (41)
3. Cardiopulmonary bypass (17)
4. Plasma exchange transfusions (42, 43)
5. Uterine artery embolization (40, 44)
6. Continuous hemofiltration (43)
7. Cell-salvage combined with blood filtration (45)
8. Serum protease inhibitors (46)
9. Inhaled nitric oxide (46)
10. Inhaled prostacyclin (46)
11. High-dose corticosteroids (46)

- **Other Treatments:**
  - There are case reports of successful use of cardiac bypass and thrombolectomy
  - Corticosteroids
    - Due to the similarity of AFE to anaphylaxis
    - Clark and co-workers recommend giving 500 mg of hydrocortisone IV q6h until improvement of the patient or death occurs
    - Epinephrine may also be given
  - Cryoprecipitate as a source of fibronectin
    - There are case reports in AFE, multiple trauma, and sepsis of cryoprecipitate dramatically improving cardiac function
    - It contains fibronectin, which aids the reticuloendothelial system in filtering toxic / antigenic matter from the body
  - Consider ECMO

DISPOSITION & MONITORING

- ICU / monitored setting
- Outcome – 50% mortality in first hour, total mortality > 80%

PATHOPHYSIOLOGY

- **Incidence**
  - Approximately 1:8000 to 1:80,000 – accounting for 9-12% of all maternal deaths
  - Mortality rate of 60-86%
    - ⅔ of deaths occur in the first 5 hours
    - In one study only 25% of survivors were neurologically intact, others as low as 16%
- **Etiology**
  - An anaphylactoid syndrome of pregnancy?
    - The pathophysiology of this syndrome is believed to be humoral
    - The clinical picture is believed to share common pathways with sepsis and anaphylaxis, hence the suggested term anaphylactoid syndrome of pregnancy
    - It is postulated that exposure to fetal products incites an immunologic response in the mother that unleashes a cascade of mechanisms, leading to profound shock
  - But, in a nutshell, true etiology is unknown:
    - Injection of amniotic fluid (AF) into some animals causes no problems, while in others it elicits the disease
    - Arachidonic acid metabolites, including leukotrienes are a candidate
    - A heat-stable pressor agent in meconium may be responsible for the severe derangements
      - As evidence for this, amniotic fluid with meconium measured in sufferers of AFE leads to dismal outcome
  - One popular misconception is that amniotic fluid routinely enters most mothers in small quantities – this is false!
  - Can occur at vaginal / c-section delivery, during 1st / 2nd trimester abortion, after abdominal trauma, or during postpartum period
  - A strong association with spontaneous or artificial rupture of membranes
  - No association with oxytocin use
  - Mothers with a history of AFE (who survive!) can have successful further pregnancies without apparent repeat AFE (this is based on 2 case reports)
  - Amniotic fluid is "walled off" from the mother throughout pregnancy
    - During "normal" delivery there can be tears in the endometrium and separation of the placenta, with a resulting communication between amniotic fluid and mother, but there is no pressure gradient into the maternal circulation due to uterine contractions, therefore no AFE
    - However, in the lower uterine segment, endocervical tears may occur without effective contractions – this is the postulated portal of entry
- **Pathogenesis**
  - Amniotic fluid access to maternal circulation is essential to its pathogenesis
  - The disruption of integrity of fetal membranes, open uterine or cervical veins and concomitant pressure gradient facilitate movement of amniotic fluid into the maternal circulation
  - Initial phase of AFE results in **mechanical blockage** of the pulmonary circulation & intense **pulmonary vasoconstriction** due to chemical mediators (PG, leukotrienes, serotonin)
    - Hypoxemia, pulmonary hypertension & cor pulmonale occur and are thought to be transient (less than 30 min duration)
    - May explain early sudden death & neurological sequelae
  - Secondary phase of severe left ventricular dysfunction
    - Myocardial ischemia in the setting of hypoxemia
    - Leftward shift of interventricular septum due to RV dilatation
    - Decreased coronary blood flow & circulating myocardial depressants
    - All result in hypotension & decreased cardiac output
    - Pulmonary edema
      - Alveolar capillary leak & microvascular embolic insult

- Coagulopathy – DIC

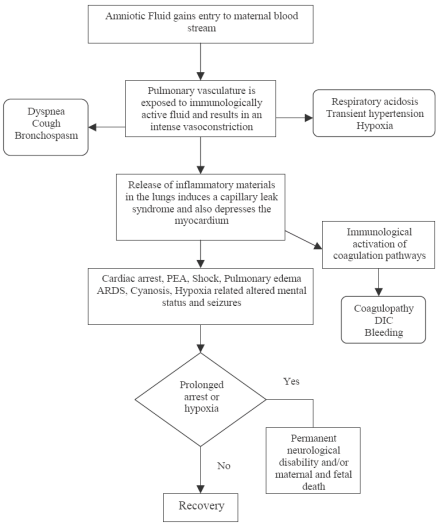

Fig. 1. Postulated mechanism for the pathogenesis of amniotic fluid embolism. ARDS, acute respiratory distress syndrome; PEA, pulseless electrical activity.

- **Clinical presentation**
  - Multiple signs and symptoms may occur with amniotic fluid embolism
    - None of these signs seem to be definitive in making the diagnosis; however, the presence of hypotension seems to be universal
  - Dramatic and abrupt onset of dyspnea, arterial hypoxemia, cyanosis, seizures, loss of consciousness, hypotension & cardiac arrest
  - Pulmonary edema occurs in up to 70% of patients
  - Coagulopathy & hemorrhage are common
  - Fetal distress is often present
  - **Respiratory**
    - Pulmonary hypertension, then normalization, then back to pulmonary hypertension
    - Hypoxia, sometimes so severe that it is refractory to all treatments and neurological damage ensues
    - Pulmonary edema
  - **Cardiovascular**
    - Severe left sided heart failure, the etiology of which is unknown, but theories include:
      - Ischemic injury secondary to hypoxia
      - Ischemia due to the initial bowing of the intraventricular septum into the left ventricle, leading to decreased coronary perfusion
      - Amniotic fluid may contain a direct myocardial depressant – possibly endothelin, causing constriction of coronaries
    - Decreased cardiac output
  - **Hematological**
    - Consumptive coagulopathy (DIC)
      - In a small number of patients maternal hemorrhage may be the first indication of a problem
      - The presence of DIC carries a dismal outcome
    - Once again, etiology unknown, but some theories:
      - Circulating trophoblast
      - Amniotic fluid contains sloughed fetal cells that act as a tissue activating factor, activating the extrinsic pathway in the maternal lungs
    - Leads to microthrombosis and release of endothelin, with the cardiac complications listed above
    - There is an association with AFE and uterine atony, which may contribute to coagulopathy through dilutional massive hemorrhage

Signs and symptoms of amniotic fluid embolism and their reported frequency*

Signs and symptoms	Percentage
Hypotension	100
Fetal distress	100
Pulmonary edema or ARDS	93
Cardiopulmonary arrest	87
Cyanosis	83
Coagulopathy	83
Dyspnea	49
Seizure	48
Atony	23
Bronchospasm	15
Transient hypertension	11
Cough	7
Headache	7
Chest pain	2

- **Diagnosis:**
  - Amniotic fluid embolism is a diagnosis of exclusion in any situation of cardiorespiratory collapse or massive hemorrhage

- Differential diagnosis includes:
  - Medical:
    - Gastric aspiration
    - Thrombotic or venous air embolism
    - Septic shock or anaphylaxis
    - Transfusion reaction
    - Acute MI or peripartum cardiomyopathy
  - Obstetrical: Placental abruption, eclampsia or uterine rupture
  - Anesthetic: Local anesthetic toxicity, high epidural & total spinal

- **Outcome**
  - Anticipate a prolonged ICU stay
  - 50% mortality within 1st hour
  - Total mortality rate ~ 60-80%

REFERENCES

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