Amniotic Embolism in a Lupic Patient - What’s the Role of Complement Activation?

Felipe Favorette Campanharo¹, Stephanno G P Sarmento¹, Eduardo F M Santana¹, Renato T Souza, Fernanda Couto Fernandes, Daniel Born², Sue Y Sun¹, Rosiane Mattar¹, Antonio F Moron¹

1 Obstetrics, UNIFESP - EPM, Brazil
2 Cardiology, UNIFESP - EPM, Brazil
Amniotic Embolism

RARE AND POTENTIALLY FATAL!
In the Developed Countries
One of the Main Causes of Direct Obstetric Mortality
1.9 to 6.1 cases/100,000 pregnancies

- LACK OF DIAGNOSTIC CRITERIA –

- EXCLUSION DIAGNOSIS -
  
  Clinical Findings
  Cardiovascular Collapse, Respiratory failure,
  Coagulopathy and Coma/Seizures.

Actual Suggested Pathophysiology
  Complement Activation
  Primary Factor in the Mechanism of Disease
Case Report

33 Weeks Pregnant, 6G 2P 3Ab, LUPUS
(Previous Hematologic and Renal Activity)
Prednisone 40mg/d and Hydroxychloroquine 400mg/day
Admission due Oligohydramnios and Fetal Growth Restriction.

Preterm labor and Spontaneous Rupture of Membranes
Delivery was indicated by C/S due Intrapartum Fetal Distress
(CTG Category III).

Anesthetic Block
Acute Respiratory Distress with Severe Hypoxemia and Desaturation
(PO2 54 with PaO2/FiO2 200) Hypotension and Increased Lactate.

Emergency C/S Uneventful
Newborn Male, Apgar 8/9 weighting 1920g (small for gestacional age)

Forwarded to the ICU
Ventilatory and Hemodynamic Support
(CPAP and Vasoactive Drugs)
Bilateral Consolidations
Infiltrated "Ground Glass"
Results: 11

1. [Amniotic fluid embolism: an update].
   Legrand M, Rossignol M, Muller F, Payen D.
   PMID: 23422343 [PubMed - indexed for MEDLINE]
   Related citations

2. Current concepts of immunology and diagnosis in amniotic fluid embolism.
   Benson MD.
   Related citations

3. Complement C3a expression and tryptase degranulation as promising histopathological tests for diagnosing fatal amniotic fluid embolism.
   Fineschi V, Riezzo I, Cantatore S, Pomara C, Turillazzi E, Neri M.
   PMID: 19172292 [PubMed - indexed for MEDLINE]
   Related citations

4. A hypothesis regarding complement activation and amniotic fluid embolism.
   Benson MD.
   PMID: 17112682 [PubMed - indexed for MEDLINE]
   Related citations
Amniotic fluid activates complement. A role in amniotic fluid embolism syndrome?

Hammerschmidt DE, Ogburn PL, Williams JE.

Abstract
A 30-year-old woman died with massive pulmonary microvascular leukostasis immediately after cesarean hysterectomy. We postulated that this might have resulted from amniotic fluid embolization and, therefore, tested amniotic fluids as activators of granulocytes and the plasma complement system. Normal human amniotic fluid failed to aggregate granulocytes, provoke a respiratory burst, or attract the cells chemotactically. However, amniotic fluid activated complement when incubated with normal plasma. The ability to activate complement resided in lipid-rich particulate material in the fluid, and activation proceeded mainly (but probably not exclusively) via the alternative complement pathway. Amniotic fluids varied widely in their ability to activate complement, with the most potent samples derived from women with distressed pregnancies. Plasma samples from donors also varied widely in their ability to be activated by amniotic fluid, and many of the most activatable plasma samples derived from gravid women. We propose that amniotic fluid embolization can, like "shock lung" syndrome, have a leukostatic early phase, and that complement and granulocyte activation on embolization of amniotic fluid can contribute to the pulmonary collapse characteristic of that syndrome, especially when a potently activating fluid is combined with a potently activatable plasma.

PMID: 6502001 [PubMed - indexed for MEDLINE]
Amniotic Embolism in a Lupic Patient
What's the Role of Complement Activation?

On Hospital Admission
Complement Level
Total 59
(Reference 70 – 150)

Complement Activation
Fetal Antigens “Leaking” into Maternal Circulation

Diagram:
- Antigen
- Antibody
- C1 complex
- C2a & C4b fragments
- C3 convertase
- Classical pathway
- Alternative pathway
- C3 hydrolysis
- C3b and C3a fragments
- C3b cleaves C5 into C5a and C5b
- Cell swells and bursts
- C5b, C6, C7, C8 and C9 together form the membrane attack complex
A hypothesis regarding complement activation and amniotic fluid embolism.

Benson MD.

Abstract

Amniotic fluid embolism, a rare, sudden and often fatal illness of pregnancy may not be a true embolic event resulting from the physical obstruction of the pulmonary vasculature. The high degree of variability in symptoms, the lack of characteristic findings on radiological exam, the absence of a dose-response effect on symptoms, and the occasional occurrence of coagulopathies are not entirely consistent with a physical block to the circulation as the main mechanism of disease. Alternatively, it might be the result of complement activation initiated by fetal antigen leaking into the maternal circulation. This rare immune response may be initiated by a rare pathological antigen, or by common antigens presented uncommonly—in amount, timing, or frequency of entry into the maternal circulation. Some very early evidence in AFE patients supports this hypothesis but is not conclusive. Complement levels remain well within the normal range during uncomplicated parturition. A prior theory that AFE might be a result of maternal anaphylaxis to fetal antigen has much less evidence to support it. The disseminated intravascular coagulation often seen in this and other serious obstetrical illnesses may be a secondary result of complement activation rather than the direct introduction of pro-coagulants into the maternal circulation although the link between the complement and coagulation pathways, if any, remains poorly defined. Through currently available laboratory testing, both the complement hypothesis and the anaphylaxis mechanism are able to be assessed. Direct measurement of serum complement as well as serum tryptase and urinary histamine are readily obtained tests in community hospitals as well as tertiary care hospitals. If the hypothesis proves true, this investigation may be of profound importance to understanding immune tolerance. Rather, than asking why one pregnant woman in 20,000 develops a violent immune reaction to the fetus, a better question is why do not all pregnant women reject the fetus which is a large collection of foreign antigens?
Complement C3a expression and tryptase degranulation as promising histopathological tests for diagnosing fatal amniotic fluid embolism.

Fineschi V, Riezzo I, Cantatore S, Pomara C, Turillazzi E, Neri M.

Author information

Abstract
To date, the most recent specific diagnostic investigations for amniotic fluid embolism have been unable to conclusively identify any mechanism of disease other than a physical block to the circulation. We selected eight fatal cases in previously healthy women with uneventful singleton term pregnancies who presented to tertiary care centers in Italy for delivery. Pathologic features were assessed immunohistochemically using anti-fibrinogen, anti-tryptase, anti-C(3a), and anti-cytokeratin antibodies. AE1/AE3 cytokeratin stains proved positive, and tryptase-positive material was documented outside pulmonary mast cells. In all studied cases, expression of complement C(3a) was twofold lower than in the control group, suggesting a possible complement activation in AFE, initiated by fetal antigen leaking into the maternal circulation.

PMID: 19172292 [PubMed - indexed for MEDLINE]
Scary Hum???
No Coagulopathy
Doppler Negative DVT
Normal Echo

ICU Discharged Day 3
Clear Lungs!

CT D6
Respiratory Failure in Pregnancy

Differential Diagnoses
Pulmonary Edema X Embolism
Non-Thrombotic Embolic Event

Clinical Suspicious Multidisciplinary Team
Availability of Diagnostic Resources
Supportive Teraphy
Essential for Successful Treatment

The Role of Complement Activation in This Case May Have Been Secondary, Since the Nature of the Underlying Disease (Lupus)
Thank You!

favorette@hotmail.com