Amniotic Fluid Embolism: A Plea for Better Brain Protection

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Amniotic fluid embolism is uncommon (1:8000 to 1:80,000 deliveries) but lethal. It is a leading cause of maternal death in the developed world. Up to 61% of women who sustain it either die or suffer permanent neurological damage. The patient experiences sudden dyspnea, rapidly followed by hypotension, desaturation, cyanosis, cardiac dysrhythmia and cardiorespiratory arrest. This is followed by consumption coagulopathy manifested by persistent bleeding from vein puncture sites or massive vaginal bleeding. We recently encountered a case of amniotic fluid embolism during labor in which bleeding was eventually controlled by the use of recombinant factor VIIa.

Patient Description

A 40 year old gravida 13, para 11, was admitted in the 42nd week of pregnancy for induction of labor due to non-reassuring fetal heart rate monitoring and reduced fetal movements. Her medical and obstetric history was unremarkable and the physical examination was normal, with the fetus in the vertex position and weight estimated at 3500–3700 g. Vaginal examination revealed an uneffaced and undilated cervix.

Induction of labor was initiated with a vaginal tablet of 0.5 mg prostaglandin E_2. A second tablet was inserted after 5 hours due to lack of uterine activity. Thirteen hours later, a third dose of 0.5 mg PGE_2 was administered for the same reason. At this time the cervix was uneffaced and dilated to 2 cm. One hour and 20 minutes later, epidural analgesia was administered to relieve the pain of contractions. Thirty minutes following the epidural injection, at 7 cm dilatation, the membranes were artificially ruptured. Ten minutes later, the cervix was fully dilated and the patient began bearing down. At this point respiratory distress appeared with cyanosis over the upper half of her trunk and head. She was immediately ventilated and intubated without delay. No palpable carotid pulse was detected at this stage and her pupils were widely dilated. Cardiopulmonary resuscitation was initiated with 100% oxygen plus cardiac massage, followed by intravenous adrenaline and atropine administration, and by the conventional Advanced Cardiac Life Support resuscitation protocol. An external cardiac pacemaker failed to restore cardiac contractions and a single chamber internal cardiac pacemaker was inserted via the femoral vein into the right atrium. Five minutes later ventricular fibrillation was noted on the electrocardiogram tracing and sinus rhythm was restored after defibrillation with successive direct current shocks of 200, 300 and finally 360 joules. At this stage, her pupils were noted to

PGE_2 = prostaglandin E_2

Table 1. Blood counts and coagulation profile before and after the occurrence of amniotic fluid embolism

Time (min)	Before	30	60	90	120	150	180	210	240	270
Prothrombin time (9.5–12.7")	10.1	59.1	40.2	36.5	32.0	41.0	26.1	17.0	15.9	13.7
Partial thromboplastin time (25–34")	29.1	NO	NO	NO	74.0	86.0	81.0	72.0	65.0	54.4
Fibrinogen (180–500 mg/dl)	587.0	NO	NO	Slight	57.0	68.0	84.0	79.4	103.0	163.0
D-dimer (< 0.5 µg/ml)		10,000								
White blood cells (4.2–5.4 10^6/mm^3)	8.3	6.2	13.6	27.9	12.6	10.5	7.5	7.8	8.1	7.6
Hemoglobin (12.3–17.5 g/dl)	11.4	12.5	12.2	10.0	11.2	12.4	10.9	8.7	10.5	9.4
Hematocrit (%)	32.8	37.0	36.6	33.0	35.0	36.7	35.8	25.5	31.6	32.3
Platelets (140–400 10^3/mm^3)	250	45	66	89	143	166	136	151	139	144

have become normal in size, but did not respond to light. Immediate transthoracic echocardiography revealed severe left ventricular enlargement and motion abnormality in most cardiac chambers.

Parallel to the cardiopulmonary resuscitation, a 3266 g male infant was successfully delivered by forceps extraction, with Apgar scores of 4 and 9 at 1 and 5 minutes, respectively, and umbilical blood pH of 7.038. After the expulsion of the placenta there was severe vaginal bleeding as well as bleeding from all venous puncture sites. Disseminated intravascular coagulopathy was confirmed on laboratory analysis of the coagulation profile [Table 1]. The patient received i.v. crystalloids, packed red cells, fresh frozen plasma, cryoprecipitate, thrombocytes, incremental boluses of adrenaline 1:100,000 and i.v. sodium bicarbonate as well as i.v. hydrocortisone. Wrist pulse became palpable at 45 minutes after the initial collapse.

Persistence of hemorrhage despite oxytocin and massive blood and blood component replacement dictated the need for abdominal hysterectomy. During the operation, due to persistent oozing from all the cut surfaces in the pelvis she was given two successive doses of recombinant activated factor VII (NovoSeven®), 7.4 mg and 3.7 mg, respectively. The second dose led to prompt cessation of all oozing.

Overall, she received 23 units of packed red cells, 45 units of fresh-frozen plasma, 44 units of cryoprecipitate, 29 units of thrombocytes, 4 L of 0.9% saline and 350 ml sodium bicarbonate 8.4%. She also received mannitol 20% 200 ml and furosemide 250 mg intravenously. By the conclusion of the laparotomy, 5½ hours after the initial collapse, she had passed 2.5 L of urine and became hemodynamically stable. A blood sample from the subclavian vein contained fetal squamous mucin and hair, indicative of amniotic fluid embolization.

The patient did not return to full consciousness but breathed spontaneously. She subsequently underwent tracheostomy and has remained in this condition with significant neurological impairment. An electroencephalogram performed on the fifth day after the cardiopulmonary collapse showed severe generalized slowing, but no epileptic activity.

Comment

The presented case met all the criteria used by Clark et al. [1] in their analysis of the National Registry of Amniotic Fluid Embolism. The acute hypotension in our patient appeared within a few minutes after artificial rupture of the membranes. Her relatively rapid response to resuscitation can be attributed to the early placement of an internal right atrial pacemaker, once external cardiac pacemaking proved ineffective. The availability and administration of rFVIIa doubtlessly contributed to the cessation of bleeding, which was not adequately controlled by the surgical approach combined with massive blood and blood component administration.

Some studies have demonstrated that a reduction in pH from 7.4 to 7.0 nearly abolishes FVIIa activity. In our patient the first dose of rFVIIa was indeed unsuccessful, when she was in severe metabolic acidosis, whereas after correction of metabolic changes the administration of the second dose of rFVIIa was effective. Two previous cases have been published in which rFVIIa was used following the event of an amniotic fluid embolism [2,3], These two cases did not differ significantly from the viewpoint of coagulation and the bleeding scenario.

A theoretical concern may be raised regarding the use of rFVIIa in a hypercoagulable state such as immediate postpregnancy. However, this is offset by the acute nature of the loss of the majority of the coagulation factors within a matter of a few minutes.

Despite early suggestions regarding the role of vigorous contractions, the only single irrefutable predisposing factor to amniotic fluid embolism appears to be pregnancy [1].

The presented patient never regained consciousness. It is possible that the introduction of invasive methodologies – such as cardiopulmonary bypass [4], extracorporeal membrane oxygenation, and antegrade or retrograde selective cerebral perfusion [5] – could further improve the outcome. In addition, the timely administration of rFVIIa following correction of metabolic acidosis could possibly protect the patient from massive bleeding and avoid the need for undesirable over-blood transfusion. Nevertheless, despite all these, the prospect of parturients afflicted by amniotic fluid embolism remains grim.

rFVIIa = recombinant activated factor VII

References

1. Clark SL, Hankins GD, Dudley DA, Dildy GA, Porter TF. Amniotic fluid embolism: analysis of the national registry. *Am J Obstet Gynecol* 1995;172:1158–69.
2. Prosper SC, Goudge CR, Lupo VR. Recombinant factor VIIa to successfully manage disseminated intravascular coagulation from amniotic fluid embolism. *Obstet Gynecol* 2007;109:524–5.
3. Lim Y, Loo CC, Chia V, Fun W. Recombinant factor VIIa after amniotic fluid embolism and disseminated intravascular coagulopathy. *Int J Gynaecol Obstet* 2004;87:178–9.
4. Stanten RD, Iverson LI, Daugharty TM, Lovett SM, Terry C, Blumenstock E. Amniotic fluid embolism causing catastrophic pulmonary vasoconstriction: diagnosis by transesophageal echocardiogram and treatment by cardiopulmonary bypass. *Obstet Gynecol* 2003;102:496–8.
5. Okita Y, Minatoya K, Tagusari O, Ando M, Nagatsuka K, Kitamura S. Prospective comparative study of brain protection in total aortic arch replacement: deep hypothermic circulatory arrest with retrograde cerebral perfusion or selective antegrade cerebral perfusion. *Ann Thorac Surg* 2001;72:72–9.

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Fool me once, shame on you
Fool me twice, shame on me

Chinese proverb