


CASE REPORT **OPEN ACCESS**

Dilemma Diagnosis Between Pulmonary Embolism and Amniotic Fluid Embolism During First Stage of Labor—A Case Report

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ABSTRACT

We report the sudden onset of dyspnea and loss of consciousness and fetal bradycardia in a middle-aged obese nulliparous woman at 39 weeks of gestation during first stage of labor leading to the decision for emergency cesarean section. Still during surgery, the mother underwent cardiac arrest. Transesophageal echocardiography during resuscitation showed right ventricular failure leading to the diagnosis of pulmonary embolism. Return of spontaneous circulation was achieved after emergency administration of thrombolysis with alteplase and cardiopulmonary resuscitation after 40 min. Severe bleeding, coagulopathy and persistent right ventricular failure resulted in persistent hemodynamic instability leading to supracerical hysterectomy and veno-arterial extracorporeal life support. Both mother and baby survived without hypoxic brain injury.

JEL Classification: Obstetrics/Gynecology

1 | Introduction

The risk of venous thromboembolism and pulmonary embolism (PE) significantly increases during pregnancy with the highest risk directly after delivery [1]. Especially in high-income countries, acute PE is a leading cause of direct maternal mortality with 1 death per 100,000 maternities [2]. Severe pregnancy-related PE is a rare but potentially life-threatening event for both mother and fetus [3]. Evidence on differential diagnosis and management of massive PE compared with amniotic fluid embolism (AFE) is scarce due to the nature of emergency and point-of-care setting. We describe the case of a PE during first stage of labor with cardiac arrest after delivery in a patient

with 39 weeks of gestation presumably due to fulminant PE. Second, we reviewed standards of interdisciplinary emergency management.

2 | Case History

A 41-year-old obese (body mass index 36 kg/m²) nulliparous at 39 weeks of gestation was admitted to our hospital (university hospital with high level perinatal care) for planned pharmacological induction of labor with misoprostol. Indication for induction of labor was based on the high-risk constellation of high maternal age, polyhydramnios and obesity. Fetal sonography

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Summary

- Sudden cardiac arrest related to pregnancy is a rare event with difficult differentiation of the cause.
- Interdisciplinary decision-making during emergency situations in pregnant women is of crucial importance.

throughout the pregnancy suggested a fetus with appropriate growth for gestational age. To our knowledge she had no prior thromboembolic events or coagulation disorders. The patient received 50 µg misoprostol orally three to four times per day with regular cardiotocography and vaginal examinations over 3 days according to local guidelines [4]. After rupture of the membranes and during first stage of labor, she developed a sudden onset of dyspnea with imminent loss of consciousness in the inpatient setting.

3 | Treatment

Immediately, routine emergency protocols were initiated. Peripheral oxygenation was not measurable in initial assessment with only a feeble carotid pulse tangible. Parallely performed sonographic check for fetal heart action was negative (Figure 1), which led to the interdisciplinary decision (anesthetist and obstetrician) for emergency cesarean section. Seven minutes later, a male neonate was born weighing 3380g with APGAR scores 1/6/8 after 1, 5, and 10 min respectively. The neonate suffered from severe acidosis (arterial umbilical pH = 6.68, base excess -21.4). Immediate resuscitation measures and consecutive asphyxia treatment were administered on our neonatal intensive care unit. The newborn was discharged after 4 days of asphyxia treatment without any signs of hypoxic brain damage in cranial MRI scan.

Meanwhile maternal blood gas analysis revealed a severe acidosis (Table 1). Shortly after delivery, still during surgery, the mother went under cardiac arrest for approximately 40 min with

initial pulseless cardiac activity and later ventricular fibrillation. Transesophageal echocardiography (TEE) showed severe right ventricular overload with a D-shaped left ventricle (D sign) and thrombotic material in the central pulmonary artery strongly suggesting fulminant PE. We decided on emergency thrombolysis therapy during surgery. After systemic application of 50 mg alteplase return of spontaneous circulation (ROSC) was accomplished. Parallely, uterine atonic hemorrhage persisted under oxytocin and relevant blood loss under these measures obliged us to perform supracerivical hysterectomy. Due to persistent hemodynamic instability non-respondent to high dose catecholamines, our heart team simultaneously inserted catheters for veno-arterial extracorporeal membrane oxygenation (ECMO) via the right femoral vessels including an antegrade limb perfusion cannula. Due to continuous intraoperative bleeding massive transfusion protocol was set in place, consisting of 23 red blood cell concentrates, 24 fresh frozen plasma, 4 platelet concentrates, 10g fibrinogen, 8000 units prothrombin complex concentrates, 1 factor eight concentrate, and 3 mg recombinant activated coagulation factor VIIa. Laboratory measurements suggested disseminated intravascular coagulation (DIC) (Table 1). After 8 h surgery time including extensive intraabdominal packing, the patient was transferred to the surgical intensive care unit. Postoperative computed tomography (CT) scan did not show any residues of PE, but pulmonary edema and acute respiratory distress syndrome. No hypoxic brain damage was detected. Because of pulmonary deterioration, ECMO therapy had to be extended requiring a veno-arterial venous system. The timeline of our emergency management is depicted in Figure 2. As a direct consequence of hemorrhagic shock and reperfusion syndrome with DIC, the patient had to undergo three re-laparotomies with packing attempts and ligatures of the iliac arteries to gain control of the bleeding during the first 3 days after the initial event. Antibiotics were started with piperacillin and tazobactam.

4 | Outcome and Follow-Up

In the following days, the patient developed acute compartment syndrome in the right lower limb, where ECLS was performed,

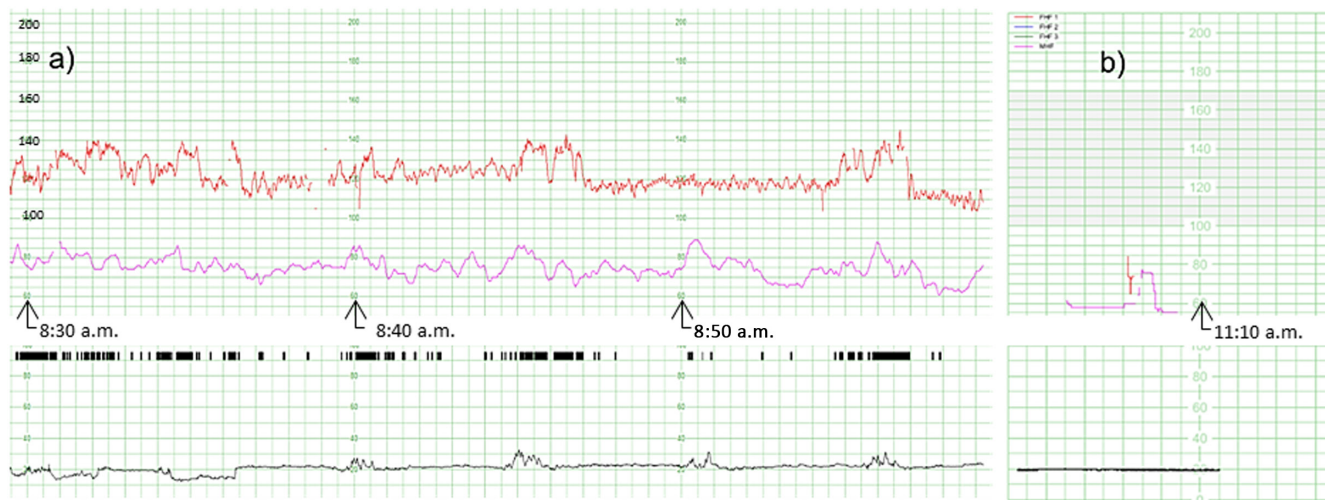
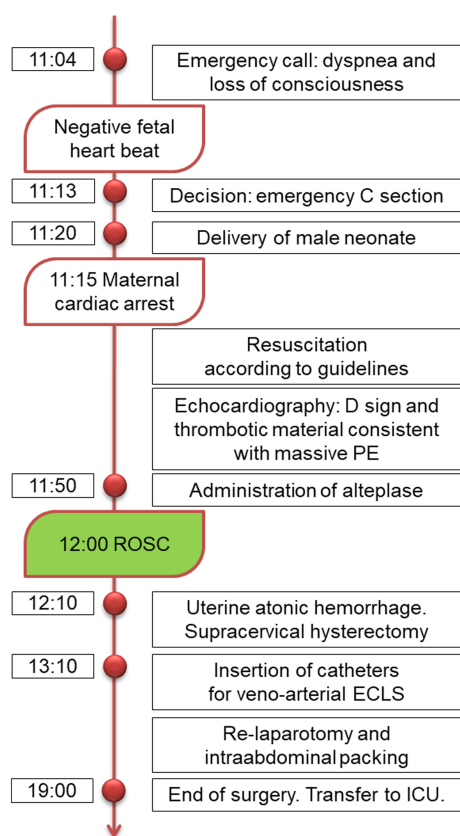


FIGURE 1 | (a) Normal cardiotocography (CTG) 2h before the event; (b) CTG at the time of loss of consciousness with no detectable fetal heart beat. Parallel sonographic check for fetal heart action was negative, too (not shown).

TABLE 1 | Intraoperative blood gas analysis and coagulation parameters after emergency cesarean delivery showing acidosis and DIC.

Parameter	11:30	12:20	12:46	13:13	15:34
pH	6.68	6.79	6.95	7.16	
pCO ₂ [mmHg]	127	69.6	48.2	31.4	
pO ₂ [mmHg]		57	150	162	
Base excess [mmoL/L]		-23.9	-20.7	-16.5	
Sodium [mmoL/L]	134	141	142	141	
Potassium [mmoL/L]	6.80	5.47	4.24	4.27	
Lactate [mg/dL]	134	140.7	143	126.5	
Bicarbonate [mmol/L]		10.3	10.5	10.9	
Quick [%]					11.2%
INR					4.83
aPTT [s]					> 120
AT3 [%]					29.6
Fibrinogen [g/L]					0.64

**FIGURE 2** | Timeline of the case report. ECLS, extracorporeal life support; ICU, intensive care unit; ROSC, return of spontaneous circulation.

finally leading to its amputation and emergency cannulation of the opposite limb. Additionally, hypoxic damage led to renal and liver failure indicating dialysis and plasmapheresis, as well as it led to myocardial infarction type II and new onset atrial

fibrillation (Table 2). Decannulation of tracheostoma was successfully performed 42 days after delivery. After 6 months on intensive and intermediate care units with treatment of multiple wound healing complications, she was transferred to a general ward within the same hospital and is to be released to postoperative rehabilitation clinic around 80 weeks post cardiac arrest. Maintenance anticoagulation was continued with low-molecular-weight-heparin.

5 | Discussion

Our case report describes an acute and fulminant PE with cardiac arrest and successful resuscitation by combination of pharmacological thrombolysis and ECLS. It includes all hallmarks of AFE and shows how appropriate emergency management can save two lives.

5.1 | Causes of Cardiac Arrest

Sudden onset of dyspnea, hypotension and cardiac arrest can have several causes like myocardial infarction, aortic dissection or pericardial tamponade and PE. As current guidelines recommend, AFE should always be considered as a relevant differential diagnosis in pregnant women with cardiac arrest. However diagnosis of AFE remains a diagnosis of exclusion due to the lack of specific diagnostic measures [5, 6]. Both AFE and PE involve consecutive pulmonary hypertension with right heart failure, which should best be confirmed by TEE [7, 8]. Although postoperative CT scan did not reveal any signs of PE in our case, intraoperative TEE was highly suspicious of thrombotic occlusion and hemodynamics slightly improved after systemic administration of thrombolysis suggesting a successful fragmentation of the thrombus. Still, thoracic CT scans showed pulmonary edema and signs of acute respiratory distress syndrome suggesting AFE. Additionally,

TABLE 2 | Laboratory parameters during the first postpartum days with diagnoses of myocardial infarction type II, acute kidney failure, fulminant liver failure, hyperbilirubinemia, acute pancreatitis.

	Day of cardiac arrest 8 h postpartum	First postoperative day	Second postoperative day	Third postoperative day
Creatinine mg/dL	1.16	2.26	2.09	3.54
Lactate dehydrogenase U/L	950	6228	7855	3869
Glutamic oxaloacetic transaminase U/L	497	7538	3824	5664
Bilirubin mg/dL	0.8	3.5	5.5	8.1
Creatine kinase U/L		6633	59,843	
High sensitivity cardiac troponin T pg/mL			2903	
Lipase U/L			2412	
Leukocytes nL ⁻¹	8.98	10.32	12.69	15.68
Hemoglobin g/dL	11.1	15.5	13.4	10.8
Thrombocytes nL ⁻¹	48	43	106	82

our patient suffered from DIC: a hallmark of AFE. On the other hand, cardio-pulmonary arrest due to PE or lysis therapy can also trigger DIC [9, 10]. A large population-based cohort revealed a total rate of AFE of 2.5 per 100,000 deliveries and found increased risks among women of 35 years or older, cesarean or instrumental vaginal delivery, polyhydramnios, uterine rupture, placenta previa, eclampsia, and induction of labor [11, 12], of which our patient fulfilled multiple risk factors. Although induction of labor seems to nearly double the risk of AFE, the absolute excess risk remains extremely low and must be weighed against the benefits of induction of labor in certain high-risk situations. Thromboembolic risk factors like obesity, last stage of pregnancy and age should not be ignored and distinguishing in hindsight between AFE or PE as definitive cause of the event is not possible and highlight the dilemma diagnosis between AFE and PE [13, 14].

5.2 | Resuscitation Management

Resuscitative measures are rarely needed on the labor ward, but are critical in the event of cardiac arrest. Considerations of both the mother's and her infant's potential outcome are extremely challenging for the responding team.

Therapeutic management guidelines for resuscitation of a pregnant woman are scarce. Literature agrees that fast and multidisciplinary decision-making and immediate life support improve survival. Immediate cesarean delivery has shown to not only improve fetal but also maternal outcome as a direct consequence of improved thoracic compliance and the relief of the inferior vena cava [15, 16]. In our case cardiac arrest appeared after emergency cesarean section, which can be explained by the increased preload due to the relief of inferior vena cava. Transporting the patient from the labor room to the operation theater is generally not advised due to the loss of time. In our case nevertheless it had the clear advantage of

a better equipped setting for the difficult intubation and the complicated management of hemorrhage later on [16]. Typical therapeutic options for PE include thrombolysis, interventional and surgical thrombectomy with or without ECLS. A recent systematic review analyzed cases of severe PE of which 23% of the women suffered from cardiac arrest: Thrombolysis and surgical thrombectomy were associated with 94% and 86% survival rates respectively; although thrombolysis was successfully applied in most cases, hemodynamic instability persisted with additional need of ECLS in 11% [17]. Thrombolysis during pregnancy and after delivery bears major risk to hemorrhagic shock. Therefore, thrombolysis should be reserved to life-threatening situations [5] but is not contraindicated in maternal resuscitation under an ongoing surgical procedure [18, 19]. In the presented case our multidisciplinary team of obstetricians, anesthesiologists and heart surgeons primarily decided against surgical thrombectomy due to higher maternal mortality rates and favored thrombolysis knowing the risk of maternal hemorrhage with massive perioperative blood loss. Interventional reperfusion treatment seemed not reasonable due to the loss of time. Therefore, in a life-threatening situation, thrombolytic treatment should not be withheld because of an ongoing surgical procedure as in our case or as described by Fasullo et al. during pregnancy itself [20].

Many authors described cesarean hysterectomy as part of the management of PE because of the high risk of severe bleeding due to the associated coagulopathy [21, 22]. Initial conservation of the uterus carries a high risk of secondary emergency laparotomy for hysterectomy as reported by Karakosta et al. [21]. In contrary, waiving initial hysterectomy was successfully performed by Vuong et al. with a shorter total surgery time [14]. Atonic uterine bleeding made it impossible in our case to preserve the uterus may necessitate emergency hysterectomy due to a potential high blood loss over a short time. We suggest that even without uterine atony the multiple re-laparotomies would not have been avoided by uterine conservation.

5.3 | Prevention

Prediction of cases like ours can save lives, but is difficult, because commonly used tools like the Wells score or Geneva score are not validated in pregnancy. Cohen et al. compared seven international societal guidelines for diagnosing pregnant women with PE [23]. They emphasized the need for defining a clear risk stratification tool for pregnant patients as thresholds of for example D-Dimers concentration in blood differs significantly between pregnant and non-pregnant patients. Van Der Pol et al. suggested in a prospective trial of 510 women a pregnancy-adapted YEARS algorithm using clinical criteria in relation to D-Dimer levels to screen for PE [24]. This algorithm could safely rule out PE avoiding up to 65% of CT pulmonary angiographies, hence minimizing radiation exposure of the mother and fetus. As there was no prior thromboembolic event nor coagulation disorder nor prior symptoms of deep vein thrombosis, prediction in our case was not possible. There is a big knowledge gap on how to predict PE and AFE in pregnant women or have a better risk stratification to avoid future emergencies.

Being in the fortunate situation of having relatively low maternal mortality rates due to a well-equipped health system leaves cases like ours to be unique and tragic for both the family and the involved health care staff. As a consequence, interdisciplinary (midwives, obstetricians, surgeons, anesthesiologists, intensivists, and nurses) emergency drills with mock patients were intensified.

6 | Conclusion

The differential diagnosis of AFE and PE remains a clinical challenge. Our case showed that time (during standard working hours), place (university hospital), and the immediate interdisciplinary management ameliorated the individual mortality and morbidity. Administration of thrombolysis in life-threatening situation should not be delayed. However, major bleeding complications must be anticipated.

Author Contributions

Kristina Killinger: conceptualization, data curation, formal analysis, investigation, methodology, project administration, resources, software, supervision, visualization, writing – original draft. **Fabian Riedel:** conceptualization, data curation, validation, writing – review and editing. **Mascha O. Fiedler:** writing – review and editing. **Thomas Müller:** writing – review and editing. **Markus Wallwiener:** writing – review and editing. **Stephanie Wallwiener:** writing – review and editing. **Michael Elsässer:** supervision, writing – review and editing. **Markus A. Weigand:** writing – review and editing. **Dittmar Böckler:** writing – review and editing. **Philipp Erhart:** writing – review and editing. **Philipp Grieshaber:** writing – review and editing. **Thilo Hackert:** writing – review and editing. **Günter Germann:** writing – review and editing. **Anna Sophie Scholz:** conceptualization, data curation, formal analysis, investigation, methodology, project administration, resources, software, supervision, visualization, writing – original draft.

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Ethics Statement

The authors have nothing to report.

Consent

Written informed consent was obtained from the patient for their anonymized information and material to be published in this article as open access.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The clinical dataset used and/or analyzed during the current study is available from the corresponding author on reasonable request.

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