

Severe maternal respiratory distress due to the amniotic fluid embolism syndrome in a twin pregnancy

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ABSTRACT

A 28-year-old female with a twin pregnancy at 29 6/7 weeks who was having premature uterine contractions developed acute respiratory failure due to sudden pulmonary oedema requiring mechanical ventilation. No evidence for venous thromboembolism, pulmonary infection or myocardial infarction was found. Subsequently a mild coagulopathy and foetal distress developed. Ultrasonography revealed oligohydramnios of one of the foetuses. A Caesarean section was performed and postoperatively mother and babies had an uneventful clinical course. By exclusion of other causes, we diagnosed severe maternal acute respiratory distress due to the amniotic fluid embolism syndrome in a twin pregnancy.

In 70% of cases AFES occurs during labour. The occurrence of AFES in twin pregnancy is extremely rare. Öney described the first case in 1982 at 39 weeks of pregnancy during normal labour.³ In the USA national registry analysis, another twin gestation was reported in 1995, however not described in detail.¹ Recently a third case of AFES in twin pregnancy was described during preterm uterine contractions with ruptured membranes despite tocolytic therapy.⁴ We report the occurrence of AFES in a twin pregnancy at 29 6/7 weeks during preterm uterine contractions with tocolytic therapy before vaginal loss of amniotic fluid.

INTRODUCTION

The occurrence of the amniotic fluid embolism syndrome (AFES) is a rare and often fatal obstetric complication. This condition was first described by Meyer in 1926 as reported by Clark *et al.*¹ but it was not until 1941 before it became recognised as a clinical entity after the publication by Steiner and Lushbaugh.² Classically, AFES is a sudden event characterised by acute respiratory failure with severe maternal hypoxaemia, cardiovascular collapse and coagulopathy.¹ It has a reported incidence varying from 1 in 8000 to 1 in 80,000 pregnancies with a maternal mortality rate of up to 61%. In the USA, this condition is the most common cause of peripartum maternal death and is responsible for roughly 10% of all maternal deaths.¹

CASE REPORT

A 28-year-old healthy female with a twin pregnancy (gravida 2 para 1) at 29 6/7 weeks was admitted to a general hospital elsewhere with premature uterine contractions. Vaginal examination revealed a cervix dilated to 2-3 cm; no amniotic fluid loss was seen. To decrease preterm uterine contractions maximal doses of fenoterol (2 g iv) were administered and indomethacin (100 mg supp.) was added as a tocolyticum. Betamethasone (12 mg iv) was added to accelerate foetal lung maturation. The patient's medical history revealed a previous twin pregnancy, which had ended in a partus immatures at 25 6/7 weeks after two weeks of tocolytic therapy. One of the children died shortly after birth, so this time she was transferred to our university centre because of the possible need of neonatal intensive care unit (NICU) facilities.

Upon arrival the patient was fully orientated, mildly pyretic (temperature of 37.6°C), with a heart rate of 136 beats/min and blood pressure of 100/70 mmHg. Cardiotocography (CTG) revealed no signs of foetal distress and ultrasound did not show any abnormalities and revealed normal quantities of amniotic fluid around both foetuses. Fenoterol was stopped because of the tachycardia and replaced by nifedipine (60 mg-30 mg-60 mg orally) as tocolytic. Antibiotic treatment (amoxicillin/clavulanic acid 1000 mg/100 mg qid, iv) was started to prevent intra-uterine infection, and nadroparin calcium (2850 IU od, sc) was added for venous thromboprophylaxis. Twenty-four hours after the first dose of betamethasone the patient was given a second dose. There were no signs of pre-eclampsia. She had no allergic constitution. After three days of bed rest, the patient became acutely dyspnoeic with a respiratory rate of 30 breaths/min and bilateral rhonchi. The haemodynamic parameters remained stable. Arterial blood gas analysis, without oxygen suppletion, showed a severe hypoxaemia (pH 7.46; PaO₂ 7.2 kPA; 4.0 kPA, PaCO₂, bicarbonate 21.7 mmol/l, BE -0.3 mmol/l, and SaO₂ 90%). The chest X-ray revealed central bilateral pulmonary oedema (*figure 1*). The electrocardiogram showed a sinus tachycardia of 120 beats/min; there were no signs of right-sided heart strain or ischaemia. CTG showed both foetuses in a tachycardia (180 beats/min and 190 beats/min). Treatment was started with oxygen via nasal spectacles, antibiotic treatment was changed to erythromycin (1 g qid, iv) and ceftriaxon (2 g od, iv) to treat a possible pneumonia. Serial duplex scanning of the lower extremities did not reveal thrombosis of the femoral and popliteal veins. The patient had no skin rash. In spite of treatment with oxygen her peripheral oxygen saturation decreased (88%) and she became even more tachypnoeic (50 to 60 breaths/min).



Figure 1
Acute central bilateral pulmonary oedema

The patient was transferred to the intensive care unit (ICU) for treatment of respiratory failure. After intubation and initial alveolar recruitment she was subsequently ventilated with pressure-controlled inverse ratio ventilation (PC-IRV 34/20 cm H₂O, F_IO₂ 0.6), which improved oxygen saturation to 99% within a few hours. A central venous catheter was inserted in the right internal jugular vein. Central venous pressure was 11 mmHg. Since the patient was haemodynamically stable no pulmonary artery catheter was inserted. On the third day after admission to the ICU she developed fever (38.3°C), a leucocytosis (17*10⁹/l) and mild coagulopathy (APTT 52 sec, INR 1.43, and platelet count 175*10⁹/l). CTG then showed foetal distress and abdominal ultrasound revealed an oligohydramnion around the first foetus. Clinically the moment of rupture of the membranes had not been identified. On the suspicion of an intra-uterine infection a Caesarean section was performed at 30 5/7 weeks. She delivered twins (one male, one female) who were taken to the NICU. After that crucial intervention the patient made a quick and uneventful recovery with complete resolution of the pulmonary oedema and was extubated two days later on the fifth day of ICU admission. Extensive laboratory tests and cultures obtained from mother and infants all remained negative (*table 1*). Histology of the placenta showed no signs of chorioamnionitis. By exclusion of other causes, we made the clinical diagnosis of acute respiratory distress due to acute pulmonary oedema based upon the amniotic fluid embolism syndrome.

DISCUSSION

The differential diagnosis for severe acute respiratory failure during pregnancy includes septic shock, aspiration pneumonia, acute myocardial infarction, pulmonary embolism, placental abruption, pre-eclampsia, complication of tocolytic therapy with β-sympathomimetics as well as the amniotic fluid embolism syndrome (AFES). In 1988, a national registry for AFES cases was established in the USA. Analysis of this registry by Clark *et al.*¹ suggests that AFES is clinically, haemodynamically and haematologically undistinguishable from anaphylaxis and septic shock. AFES appears to be initiated after maternal intravascular exposure to foetal tissue. Variations in nature and severity of the clinical syndrome may be dependent on variations in antigenic exposure and in individual response. According to Green *et al.* the diagnosis of AFES is based on its clinical presentation and supportive laboratory studies.⁵ The finding of squamous cells in the maternal pulmonary circulation, once considered pathognomonic, is neither specific nor sensitive for the diagnosis of AFES. Kostamovaara *et al.* showed that squamous cells can also be detected in nonpregnant patients and even in males.⁴

Table 1
Serological tests, cultures and histology obtained from mother and infants

SEROLOGY OF MOTHER	
CMV	Negative
EBV	Negative
HSV IgM	Negative
<i>Rubella</i>	
IgG	Positive
IgM	Negative
<i>Mycoplasma pneumoniae</i>	<1:40
<i>Legionella</i>	Negative
<i>Lues</i>	
VDRL	Negative
TPHA	Negative
<i>Chlamydia</i>	
PnIgG	Negative
PnIgA	Negative
CULTURES FROM MOTHER	
Multiple blood cultures	No micro-organism
Sputum cultures	No micro-organism
Vagina culture	<i>Candida albicans</i> ++
β-haemolytic streptococcus	Negative
HISTOLOGY OF THE PLACENTA	
No signs of chorioamnionitis	
CULTURES OF INFANTS	
Blood cultures	Negative
Skin cultures	Negative

CMV = cytomegalovirus, EBV = Epstein-Barr virus, HSV = herpes simplex virus, Ig = immunoglobulin, VDRL = venereal disease research laboratories, TPHA = treponema pallidum haemagglutination

A clinically or subclinically consumptive coagulopathy of unknown aetiology almost invariably accompanies AFES.⁶ There is no diagnostic test for AFES. The diagnosis is therefore made by exclusion of other causes.⁷ In any individual patient, the haemodynamic, pulmonary or haematological disturbances can dominate the presentation or be entirely absent, which makes the clinical presentation very variable.⁸ One factor that is consistently related to the occurrence of AFES is a tear in the foetal membranes. The occurrence of AFES has been described during first trimester suction curettage, a time when the total volume of amniotic fluid is relatively low. Apparently, AFES can result from simple exposure to even small volumes of foetal tissue. According to the USA national registry, five patients had the onset of the syndrome with intact membranes. These findings suggest that certain conditions may permit exposure of foetal tissue to the maternal vasculature and may increase the risk of AFES. In our patient the diagnosis of AFES was made after

exclusion of other causes. Sepsis or septic shock was not supported by any positive cultures or serological parameters. Pneumonia was not supported by positive cultures and less probable with the rapid resolution of pulmonary oedema and the subsequent absence of infiltrates. Acute myocardial infarction was not supported by elevated enzymes or typical electrocardiographic disturbances. Deep venous thrombosis was made unlikely by the absence of thrombosis by serial duplex scanning of both lower extremities. A normal central venous pressure made pulmonary embolism less probable especially during concomitant high ventilation pressures. Tocolytic therapy with fenoterol was an unlikely cause because the elimination half-life of fenoterol is three hours and the administration of the drug was stopped more than 48 hours before onset of the acute respiratory failure. Anaphylaxis was clinically highly unlikely. Finally, there were no signs of pre-eclampsia or placental abruption. We believe this case represents one of the atypical presentations of AFES in which severe hypoxaemia was the presenting symptom followed by a mild consumptive coagulopathy. Our patient did not develop haemodynamic disturbances. Respiratory distress is found to be the first symptom in 51% of patients, hypotension in 27%, and coagulopathy in 12%.⁶ The acute development of bilateral pulmonary oedema has recently been recognised to follow a biphasic model. If even a small volume of amniotic fluid enters the maternal circulation, the initial haemodynamic response consists of acute pulmonary hypertension and vasospasm complicated by severe hypoxaemia and right-sided heart failure, followed by a second phase of more sustained left ventricular failure.⁶ The first phase might be due to the introduction of a potent vasoconstrictor arising from the amniotic fluid, and the second phase is thought to be due to a direct myocardial depressant also from the amniotic fluid. The responsible substance might be endothelin, which has been found in high concentrations in the amniotic fluid.⁶ In conclusion, AFES should be considered as a differential diagnosis in pregnant patients or immediate postpartum patients with acute profound haemodynamic, pulmonary or haematological disturbances. Physicians should maintain a high index of suspicion. The therapy for AFES is nonspecific and directed towards ventilatory and circulatory support and correction of the coagulopathy. The occurrence of AFES in twin pregnancy is very rare.

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