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Successful Venoarterial Extracorporeal Membrane Oxygenation Treatment in a Pregnant Woman with Amniotic Fluid Embolism

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Abbreviations: PROM: premature rupture of membrane; ER: emergency room; EMC: Eulji Medical Center; AFE: amniotic fluid embolism; EM C-S: emergent cesarean section; C-S: cesarean section; CPR: cardiopulmonary resuscitation; NICU: neonatal intensive care unit; PPH: postpartum hemorrhage; TTE: transthoracic echocardiography; LVF: left ventricular failure; VA-ECMO: venoarterial extracorporeal membrane oxygenation; CS doctor: cardiac surgery doctor; C-hysterectomy: Cesarean hysterectomy; RBC: red blood cell; FFP: fresh frozen plasma; PC: platelet concentrate; SICU: surgical intensive care unit.

Abstract

Amniotic fluid embolism (AFE) is a rare, but catastrophic, obstetric complication with a high mortality rate. Moreover, >50% of maternal deaths occur within 1 h of symptom development. Further, it involves a high perinatal mortality rate, with 50% of affected neonates presenting neurological impairments. AFE is characterized by cardiovascular collapse, respiratory failure, and coagulopathy, followed by encephalopathy, multi-organ failure, and fetal distress. Therefore, its treatment strategy includes cardiopulmonary support, massive transfusion, and early cesarean section. However, venoarterial extracorporeal membrane oxygenation (VA-ECMO) has been used in cases with rapid progression of cardiac dysfunction, which has significantly decreased the maternal mortality rate. Therefore, VA-ECMO has been accepted as a useful treatment method for patients with AFE, including cardiac dysfunction. This article describes a case in which a patient with AFE was successfully treated with VA-ECMO and presents a literature review.

Introduction

Amniotic fluid embolism (AFE) is a rare, but catastrophic, obstetric complication with a high mortality [1]. According to Stafford et al., the incidence of AFE was 1/15,200 to 1/53,800; however, it accounted for 5.4% of all maternal deaths in the US [1]. It is the fifth most common obstetric cause of maternal death. AFE is considered to occur upon disruption of the maternal–placental interface, resulting in the entry of amniotic components into the maternal circulation, which stimulates the maternal immune and coagulation systems [2–4]. This may lead to cardiovascular collapse, respiratory failure, and disseminated intravascular coagulation (DIC), followed by vasovagal syncope [2–5]. Finally, it can progress to encephalopathy, multi-organ failure, and fetal distress [2–5].

Potential entry sites of amniotic fluid (AF) into the endocervical veins, uterine injured sites, and veins of placental implantation sites have been suggested [6]. AF has several components, including fetal squames, meconium, pro-coagulant factors, and pro-inflammatory factors. These components can stimulate the maternal immune and coagulation systems in rare cases, which can result in maternal cardiovascular collapse, respiratory failure, and DIC [4,7].

AFE has a very high maternal mortality rate of >61–86%, with >50% of patients dying within 1 h [5,8]. Additionally, it has a high perinatal mortality rate. However, the introduction of venoarterial extracorporeal membrane oxygenation (VA-ECMO) and medical technological developments has significantly decreased this mortality rate [9]. The maternal death rate was recently reported to be 20–40% [1,8]. Further, the perinatal mortality rate is 20–25%, with 50% of affected neonates presenting neurological impairment [1].

Recently, VA-ECMO has gained attention as an active treatment option for patients with cardiac dysfunction [9–13]. There was controversy regarding the use of VA-ECMO for AFE treatment owing to possible complications, including bleeding due to the use of anticoagulants [9]. However, there have been established guidelines regarding the use of systemic anticoagulants, including IV unfractionated heparin, which are not used in

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cases of DIC, platelet count <50,000 G/L, or bleeding [9], with several cases being subsequently reported [11–13]. Moreover, Adachi et al. reported that VA-ECMO is an effective early treatment for AFE with cardiac arrest. They suggested that early treatment is an important method for recovery without complications since it prevents neurological defects and multi-organ dysfunction. Since AFE is a self-controlled disease, VA-ECMO may prevent complications by providing respiratory and hemodynamic support until the patient's cardiopulmonary function recovers. In our case, VA-ECMO effectively treated the patient given the initial symptoms of respiratory failure. However, since respiratory failure occurred first and the patient was transferred to a private hospital for treatment, the fetus experienced damage from extended exposure to hypoxia and eventually died. Therefore, VA-ECMO can be used as an active treatment not only in cases of cardiac arrest but also in cases of respiratory failure and heart failure. This article describes a case in which a patient with AFE was successfully treated with VA-ECMO and presents a literature review.

Case presentation

A 40-year-old mother at 38+2 weeks of pregnancy visited the emergency room with tracheal intubation because of sudden shortness of breath, cyanosis, and mental changes after premature rupture of membranes (PROM) during labor at a private hospital. Her medical history was unremarkable except for gestational diabetes mellitus. On physical examination, her vital signs were unstable as follows: blood pressure (BP), 108/80 mmHg; pulse rate (PR), 111 beats/min; tachycardia; respiratory rate, 16 breaths/min; and body temperature, 36.5°C (Figure 1). The patient was in an intubation state with SaO2 maintained at 85–90%, her mental status was semi-comatose, and her skin showed general cyanosis. Vaginal examination revealed that cervical dilatation was 5 cm and that the effacement was 80%. Ultrasonography revealed fetal bradycardia, with a fetal heart rate of 60–70 beats/min. Complete blood count performed at the time of the visit revealed the following findings: Hb/Hct/platelets, 12.3/37/35,000; partial thromboplastin time/activated partial thromboplastin time, 120/180 s; fibrinogen, <60 mg/dL; fibrin degradation products, 252.3 μg/dL. The patient developed thrombocytopenia and coagulopathy. Her DIC score was >5 according to the Modified International Society on Thrombosis and Hemostasis scoring system [14,15].

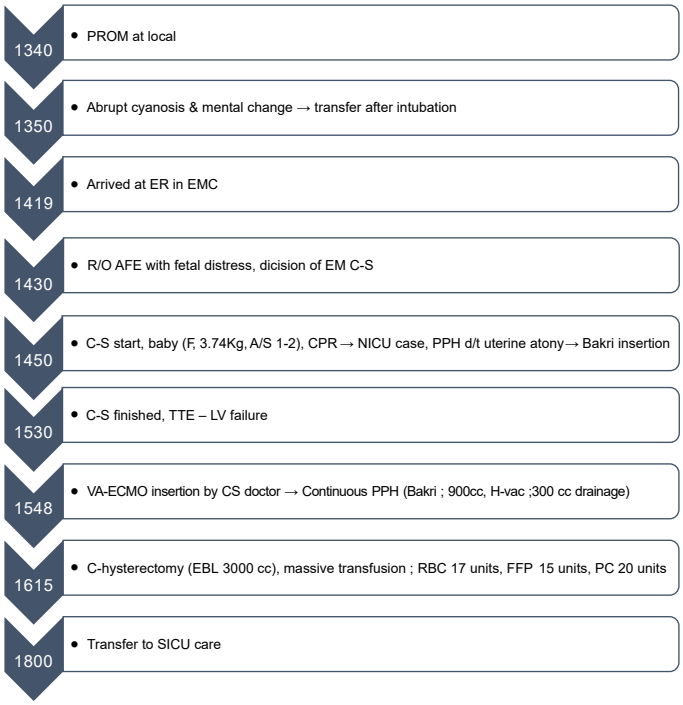

Figure 1. *Time course of clinical observation and management from the time of development of symptoms to transfer to SICU care.*

Arterial blood gas analysis revealed acidosis with a pH of 7.0. Electrocardiography revealed sinus tachycardia (128 beats/minute). The patient was transferred to the operating room with suspected AFE with respiratory failure, DIC, fetal distress, and hypoxic encephalopathy, where she underwent an emergency cesarean section (Figure 1).

After surgery, the baby weighed 3.74 kg and was transferred to the neonatal intensive care unit after intubation, with Apgar scores of 1 and 2 at 1 and 5 min, respectively. After the infant was discharged, her BP continued to decrease to 57/39 mmHg. Since the patient had poor uterine contractions, an intrauterine Bakri balloon was inserted. After cesarean section, transthoracic echocardiography (TTE) revealed left ventricular failure (LVF). Accordingly, VA-ECMO was performed as described by Mirabel et al. [16] and Aissaoui N et al. [10]. The pump speed was set to yield a blood flow rate of 3–5 L/min. Systemic anticoagulants were not used owing to the presence of DIC.

However, her BP slightly decreased; moreover, intrauterine bleeding persisted through the inserted Bakri balloon into the uterus, reaching 800 cc. Therefore, cesarean hysterectomy was performed, which stabilized the patient's BP and PR. Extensive transfusion was promptly performed using 17 units of packed red blood cells, 15 units of fresh frozen plasma, and 20 units of platelet concentrate. Subsequently, the patient was transferred to the surgical intensive care unit.

The newborn died on postoperative day 1 owing to respiratory distress syndrome and cardiac arrest. The mother stabilized postoperatively, and VA-ECMO was discontinued at postoperative day 5. On postoperative day 9, the patient complained of foot drops. Accordingly, she underwent electromyography and nerve conduction studies and was diagnosed with an incomplete bilateral lumbosacral plexus injury. She was monitored for severe axonal injury in the lumbosacral plexus during a follow-up 19 days after surgery owing to minor paraplegia. After the surgery, she received comprehensive medical and integrated treatment on the 24th day. The only strength compared to before was that according to manual muscle strength testing (passive motor function), the right hip joint was grade 3, the knee joint grade 3, the ankle joint grade 1, the left hip joint grade 3 or higher, the knee joint grade 4 or higher, and the hemi-joint grade 3 or higher. Maximal assist standing movements (sitting to standing) were possible, but doctrinal gait (independent walking) was not possible. After wearing a right ankle joint orthosis (right ankle-foot orthosis) for paralysis of the lower body, she rarely did stress-strengthening exercise therapy (gradual strengthening), p-bar championship training (gait training), or electrical stimulation therapy (electrical stimulation). The spectrum of drug treatment for neuropathic pain and follow-up examination at 50 days shows increased contralateral motor unit action potential in the left lower extremity. After approximately 3 months (89 days) of comprehensive rehabilitation treatment, the patient was discharged. Her muscle strength level was grade 3 in the right hip joint, grade 4 in the knee joint, grade 1 in the ankle joint, grade 4

in the left hip joint, grade 4 in the knee joint, and grade 4 in the ankle joint. These findings indicated improved overall bilateral lower extremity paralysis; however, paralysis of the right ankle joint persisted. The patient functionally improved to monoplane gait with right ankle-foot orthosis and was discharged.

Discussion

An AFE is a rare condition that can cause maternal cardiovascular collapse, respiratory failure, and DIC. It progresses to fetal distress, maternal encephalopathy, and multi-organ failure. AFE is considered due to an immunological storm induced by pro-inflammatory factors in the AF and a coagulation storm caused by pro-coagulant factors and physical components in the AF [4,7]. Additionally, after the onset of these symptoms, vasovagal syncope caused by the vagal reflex worsens, leading to cardiac arrest within 1 h of symptom onset [5]. Our patient was hospitalized for respiratory failure, encephalopathy, and coagulopathy, which occurred 10 min after PROM. Additionally, TTE revealed LVF. These findings met the diagnostic criteria for AFE suggested by Clark et al. [3]. These diagnostic criteria were as follows: (1) sudden onset of cardiorespiratory arrest or both hypotension and respiratory compromise, (2) documentation of overt DIC, (3) clinical onset during labor or within 30 min of placental delivery, and (4) no fever during labor. After being diagnosed with AFE, our patient underwent cesarean section, hysterectomy, and cardiopulmonary support with VA-ECMO. She recovered successfully; however, her newborn died 3 days after delivery.

Previously described treatment strategies for AFE include cardiopulmonary support and massive transfusion for DIC [3]. However, since the mortality rate within 1 h of symptom onset is >50%, there is a need for more active and effective treatments. Therefore, although patients experience severe bleeding and DIC, the use of VA-ECMO treatment without systemic anticoagulant has been attempted [9,12]. James et al. analyzed 10 cases of AFE treatment using VA-ECMO [9]. Although AFE is very rare in ECMO indications, a 70% survival rate has been reported regardless of the extreme pre-ECMO severity [9]. VA-ECMO is considered clinically useful despite DIC and active bleeding owing to the rarity of complications during delivery [9]. Notably, massive blood transfusions are required on the first day of ECMO insertion. Additionally, patients with AFW have a lower long-term health-related quality of life than healthy controls of the same age; moreover, they present significant impairment in physical roles, pain, and general health components compared with other survivors rescued by ECMO.

Therefore, an accurate diagnosis of AFE is required. It is difficult to establish a diagnosis of AFE given its nonspecific symptoms and biomarkers; moreover, a thorough search for alternative diagnoses is not uniformly performed [17–21]. Accordingly, AFE diagnosis is based on the exclusion of similar diseases, including septic shock, pulmonary thromboembolism, preeclampsia, or placental abruption. Clark et al. explained the differential points of AFE [3] and proposed its diagnostic criteria.

If patients develop refractory right ventricular failure (RVF) or LVF after the diagnosis of AFE, VA-ECMO should be recommended, despite DIC, when maintaining circulation. Since it is an invasive treatment, it must be supported by sufficiently extensive transfusion. Bleeding is the most common complication associated with VA-ECMO. Accordingly, since patients with AFE have DIC, the introduction of VA-ECMO has been controversial. However, patients with AFE rapidly progress to shortness of breath and heart failure owing to the vasovagal reflex [23,24]. Therefore, if self-circulation and oxygen supply are maintained through VA-ECMO during this period, the progression of this pathophysiological process can be slowed, which can prevent systemic complications such as multi-organ failure due to hypoxia. This increases the likelihood of preventing cardiac arrest and the chance of self-recovery. Since AFE may develop because of immune and coagulation storms, it can recover through self-correction after a certain period. Moreover, it is aggravated by the vasovagal reflex, and drug treatment may be attempted [25–28]. However, if cardiac arrest progresses and ischemic multi-organ failure progresses, irreversible complications may occur. Therefore, the early use of VA-ECMO may provide time to support the patient's self-recovery process by restoring cardiac and pulmonary function.

To date, AFE has been primarily managed through supportive treatment. Several studies have described the use of immunotherapy, including C1-esterase inhibitor and A-OK (atropine, ondansetron, and ketorolac) protocols [25–29]. Additionally, if immune and coagulation storms persist, plasma exchange may be attempted. However, there remain no clinical and experimental studies on these treatments. Additionally, they have minimal effectiveness in cases where respiratory failure and cardiovascular collapse. Therefore, in cases of LVF or refractory RVF, patients should be provided with the opportunity to recover independently through active VA-ECMO treatment. Additionally, concurrent treatment with various previously reported treatments can reduce the time spent on VA-ECMO by promoting patient recovery.

Guennec et al. reported spinal cord infarction as a side effect of VA-ECMO [30]. Specifically, among 1,893 patients who received VA-ECMO, 112 (5.9%) had ECMO-related neurovascular injury, 65 cases (3.4%) had ischemic stroke, 40 (2.1%) had intracranial bleeding, 1 (0.05%) had cerebral thrombophlebitis, and 6 (0.3%) had spinal cord infection (SPI). They indicated that SPI may be associated with insufficient neurovascular circulation since monitoring the neurological status of patients on ECMO is challenging owing to sedation requirements and intensive care unit-acquired weakness after sedation withdrawal, which leads to delayed diagnosis. Although there is no specific treatment for SPI, prompt diagnosis is important to prevent secondary spinal insults of systemic origin. Moreover, daily sedation interruption and neurological examination of the lower limbs should be performed in patients on VA-ECMO.

Our patient showed findings suggestive of spinal cord injury. On postoperative day 5, VA-ECMO was discontinued. On the 9th day, the patient presented with right foot drop and walking difficulties. Therefore, the patient underwent rehabilitation therapy. Subsequently, the patient recovered and was discharged in almost normal condition.

Therefore, VA-ECMO is crucially involved in restoring health by providing patients with self-recovery time. This is an important, lifesaving treatment strategy for patients with LVF or refractory RVF. However, given the possibility of bleeding and neurovascular injury, including SPI, this treatment should be performed based on an accurate diagnosis and indications. Efforts should be made to minimize sedation and achieve the optimal timing of installing the VA-ECMO device to prevent complications such as SPI after implementation.

Herein, we report a case of AFE with LVF that was successfully treated using VA-ECMO.

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Declaration of conflicting interests

No conflicting interests.

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