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Infection caused by amniotic fluid embolism complicated with disseminated intravascular coagulation: a case report

Yi-HuaZhou[1*], Li-Hua Hu[2*], Cha-Hua Huang[2], Hui-hui Bao[2], Xie-Fei Qi[1], Xiao-Shu Cheng[2]

[1]Department of ICU, [2]Department of Cardiovascular Medicine, the Second Affiliated Hospital of Nanchang University, Nanchang of Jiangxi (China)

Summary

Objective: Amniotic fluid embolism (AFE) is a life-threatening obstetric complication characterized by sudden cardiac arrest, acute respiratory distress syndrome (ARDS), disseminated intravascular coagulation (DIC), seizures, and encephalopathy. Due to the difficulty of its diagnosis and management, its maternal and infant mortality becomes very high. Heparin plays an crucial role in DIC. However, there is no specific standard about the type and timing and dosage of heparin. Furthermore the pollution amniotic fluid has a tendency to cause infection and never attracts attention. *Case Report:* Here, the authors report a case of infection caused by AFE complicated with DIC. In this case, the patient was timely diagnosed with AFE when appeared with hypotension, pulmonary edema, and cyanosis during delivery. When the patient bled seriously and platelet and coagulation factors progressively decreased, the authors gave heparin to block the progress of DIC. Her vital signs became stable after she was accepted proper management. However, ultimately the patient died of septic shock. *Conclusion:* Early recognition and prompt initiation of proper management is critical in optimizing outcomes for the patient with AFE and the early small dose of heparin can cut the progression of DIC. Microbial invasion of amniotic fluid, once flowing into the blood circulation, is also likely to cause infection.

Key words: Amniotic fluid embolism; Disseminated intravascular coagulation; Heparin; Infection.

Introduction

Amniotic fluid embolism (AFE), a rare but devastating complication of pregnancy, is a fatal syndrome that takes place during delivery or in the immediate postpartum period. Globally, the reported incidence of AFE is approximately seven to eight per 100,000 births. With a mortality of 11% to 44%, it is among the leading direct causes of maternal death. As known, there is no specific diagnostic test for AFE currently, and it essentially remains a diagnosis of exclusion. In other words, AFE should be strongly considered in every case of acute hypotension, cardiovascular collapse, acute hypoxemia or respiratory distress, and disseminated intravascular coagulation (DIC) [1]. Amniotic fluid activates Factor VII and platelets with consequent DIC. Inflammatory response further activates clotting cascade. Hemorrhage contributes to hemodynamic instability. Diffuse intravascular clotting from DIC contributes to ischemic distal organ dysfunction and multi-organ failure. Early recognition and prompt initiation of proper management is critical in optimizing outcomes for the patient with AFE. At present, the treatment of AFE is supportive and heparin plays an crucial role in cases of persistent bleeding, coagulopathy, or DIC treatment. Anticoagulants in DIC remain a matter of debate. It is worth mentioning that there is a large body of evidence that indicates that microbial invasion of the amniotic cavity is common. The use of molecular microbiologic techniques suggests that the frequency of microbial invasion may be higher than is recognized now [2]. Some patients with the clinical diagnosis of AFE may have infection/systemic inflammation. At present, the polluted amniotic fluid has a tendency to cause infection that never attracts our attention.

Case Report

A 28-year-old healthy woman with a pregnancy at 41 weeks was admitted to the local hospital with premature uterine contractions on April 3, 2015 and her vital signs were normal at the time of hospitalization. She was brought into the delivery room because of amniorrhea at 4 p.m. on that day. After one hour, she suddenly appeared with chest congestion, dyspnea, then unconsciousness, whole body cyanosis, mouth and nose bleeding with a tachycardia of 170 beats/minute, blood pressure of 40/25 mmHg, and oxygen saturation was also undetectable. After emergency capacity, anti-shock, endotracheal intubation, intravenous dexamethasone and other supportive measures, her consciousness turned clear and she gave birth to a baby after minutes. However, the patient soon bled from her vagina, and then her blood pressure was undetectable. Immediately, she was promptly administered blood component transfusion, expansion, boosting blood pressure, and emergency hysterectomy surgery. After that, she was rapidly transferred to the intensive care unit (ICU) of the present hospital for further rescue attempts.

When arriving, the patient presented dysphoria, unconsciousness, severe hemorrhage from the oral cavity, nasal mucosa, incision, drainage tubes, and vagina. Her vital signs were unstable.

[*] *Contributed to this work equally.*

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Her abdomen obviously bulged, with tenderness but no rebound tenderness. Repeatedly routine blood test prompted hemoglobin reduced to 21g/L, platelet progressively declined to 16×109/L, and coagulation function showed that PT and APTT significantly extended more than twice. Fibrinogen was only 0.65 g/L and D-dimmer was 36.2 ug/ml. In the meantime, she produced no urine and her creatinine was progressively rising. The authors continued to give respiratory and circulatory support, anti-allergy, heparin blocking the progress of DIC, blood component transfusion, and continuous renal replacement therapy (CRRT). The patient then gradually became stable. Furthermore, the bleeding stopped and her vital signs returned to normal. On April 16, the patient developed a fever (39.8°C), leukocytosis(14.49×109/L), high neutrophil percentage (91.3%), and procalcitonin (PCT) (>100 ng/ml). Chest CT (Figure 1) showed a pulmonary infection, especially a fungal infection. The bacterial culture of drainage fluid was negative. Consequently, the infection index decreased gradually to normal and hematoma became roughly narrow. Nevertheless, the patient developed fever once again (39°C) on May 1. At the same time, hemogram and PCT significantly increased once again. Multiple bilateral abdominal drainage fluid and blood culture showed drug-resistant pneumonia klebsiella bacteria infection, which was only sensitive to Tigecycline. Ultimately the authors failed to control infection and consequently the patient died of septic shock.

Written informed consent was obtained from the patient' husband for publication of this Case Report and any accompanying images.

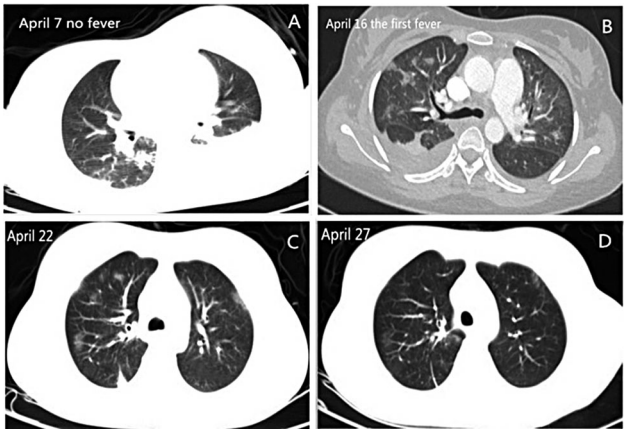

Figure 1. — The change of chest CT after anti-infection treatment The CT indicates pulmonary multiple seepage on admission (A). Chest CT shows the lung infection lesions along the blood vessels and mostly located at the end of the blood vessels (B). After anti-infection treatment, the chest CT gradually became normal (C and D).

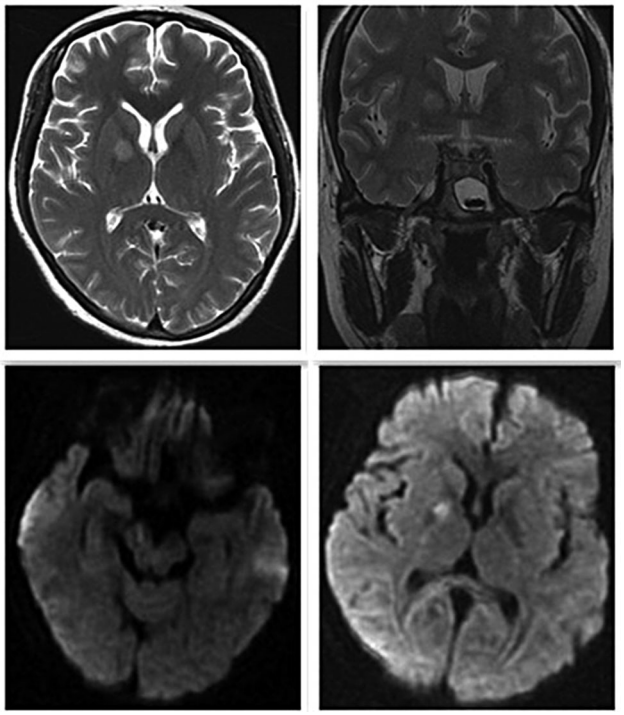

Figure 2. — Head MRI showing long T1 and T2 signals with diffuse punctuates, and high signal intensity on DWI.

Discussion

On one hand, the present case highlights the difficulty of diagnosing AFE. The diagnosis of AFE is clinically important and difficult because there is no specific diagnostic laboratory test to either confirm or refute it other than autopsy [3]. To date, diagnosis of AFE is based on clinical symptoms after other causes/diagnoses have been excluded. It should be considered in every case of sudden maternal cardiovascular collapse and/or maternal death in childbirth with unexplained etiology. Although there are currently no uniform clinical diagnostic criteria for AFE, the United States of America, the United Kingdom, and Japan have similar clinical diagnostic criteria and national registries [4]. In this case, the patient appeared with hypotension, pulmonary edema, and cyanosis during delivery, and above all with massive hemorrhage of more than 1,500 mL with DIC within two hours after delivery, and there were no other medical explanations for the clinical course, meeting the clinical criteria for AFE in Japan. Acute cerebral infarction was implied by MRI (Figure 2). Autopsy finally also confirmed that this patient died of AFE complicated with septic shock.

The treatment of AFE is mainly supportive and involves the delivery of the fetus when indicated, respiratory support (usually in the form of endotracheal intubation and mechanical ventilation), and hemodynamic support with the judicious use of fluids, vasopressors, inotropes, and pulmonary vasodilators. Rapid initiation of treatment, aided by a high index of clinical suspicion, is essential. DIC is a syndrome characterized by the systemic activation of blood coagulation, which generates intravascular thrombin and fibrin, resulting in the thrombosis of small-to medium-sized vessels, and ultimately organ dysfunction and severe bleeding. DIC may result as a complication of infection, solid

cancers, hematological malignancies, obstetric diseases, trauma, aneurysms, and liver diseases, etc. DIC is categorized into bleeding, organ failure, massive bleeding, and non-symptomatic types according to the sum of vectors for hypercoagulation and hyperfibrinolysis [5]. When the vector for hyperfibrinolysis is remarkable and dominant, bleeding is the primary symptom; when the vector for hypercoagulation is remarkable and dominant, organ failure is the main symptom; when both vectors for hypercoagulation and hyperfibrinolysis are remarkable, major bleeding occurs, followed by death, if a sufficient amount of blood is not transfused; when both vectors are weak, there are almost no clinical symptoms, although abnormalities in clinical laboratory tests are observed. The diagnosis and treatment of DIC should be carried out in accordance with the type of DIC. The current guidelines on the treatment of DIC associated with AFE claim to remove the cause, anticoagulation, and component blood transfusion [6]. It is necessary to use large volumes of plasma in order to correct coagulation defects associated with a prolonged APTT or PT (greater than 1.5 times the normal value) or decreased fibrinogen level (less than 1.5 g/dl).

On the other hand, the present case focuses on the conundrum of anticoagulation in DIC. Anticoagulants in DIC remain a matter of debate [7-9]. Experimental investigations have demonstrated that heparin can block the hemostatic activation in DIC. However, there are no RCTs demonstrating that the use of heparin in patients with DIC results in an improvement in clinically relevant outcomes. So the administration of heparin is not recommended in patients with bleeding or massive bleeding type of DIC due to the increased risk of bleeding. Heparin is only recommended in those with the non-symptomatic type of DIC [5]. Moreover, the choice of heparin also remains controversial [9-11]. A small RCT indicates that low molecular weight heparin (LMWH) is preferred to unfractionated heparin (UFH) in DIC [12]. However, in those with a high risk of bleeding and renal failure, UFH is chosen due to its easier reversibility. In the present case, the authors gave UFH at 12,500 U / 24 hours slowly via continuous pumping when the patient bled seriously and platelet and coagulation factors progressively decreased; in the meanwhile, they gave platelet and clotting factors. About a few hours later, the patient's systemic hemorrhage decreased gradually and eventually stopped. Hemoglobin and platelets gradually increased to the normal range; consequently, smooth breathing and blood pressure returned to normal. The reason why heparin was used was because the patient was still bleeding seriously after removing the uterus. In this period, microthrombosis is the major factor of consumption of platelets and clotting factors. It is likely to interrupt the progress of DIC by heparin. From the present case, the use of heparin blocked bleeding, which is different from the current guidelines.

Although the present authors successfully corrected DIC, the patient eventually died of septic shock. In the present case, combined with patient characteristic that the young woman without immune deficiency had no long-term use of hormones, and other risk factors, furthermore, CT did not suggest fungal infection during the early hospitalization. So it is unlikely due to fungal infection. The lung infection lesions were along the blood vessels and mostly located at the end of the blood vessels. The present authors considered microbial invasion in amniotic fluid remained at the end of pulmonary vascularization with infection, leading to lung abscesses, which were mostly gram-positive bacteria infection. Therefore, linezolid was added to resist infection. After the above treatment, the infection index declined gradually to normal. Chest CT was restored to almost normal. Nevertheless, the patient developed fever once again. Multiple abdominal drainage fluid and blood culture showed drug-resistant pneumonia klebsiella bacteria infection. Strengthening drainage was not effective in spite of resisting infection. It is not difficult to discern that co-infection in this case has its particularity. Microbial invasion of the amniotic cavity can be phagocyted once into the blood, but remaining at the end of pulmonary vascularization and hematoma which lacks blood supply, it is more prone to infection. Therefore, it is likely that the lung abscess and abdominal abscess were associated with this.

In conclusion, AFE not only leads to multiple organ dysfunction but also more easily to infection. Furthermore an early small dose of heparin can cut the progression of DIC.

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Corresponding Author:
XIAOSHU CHENG, M.D.
Department of Cardiology
The Second Affiliated Hospital of Nanchang University
No. 1 Minde Road
Nanchang 330006, Jiangxi Province (China)
e-mail: xiaoshumenfan126@163.com.